Filed Pursuant to Rule 424(b)(4)
Registration No. 333-230034

Prospectus

7,900,000 shares

Common stock

This is an initial public offering of shares of common stock by Precision BioSciences, Inc. We are selling 7,900,000 shares of our common stock. The initial public offering price is $16.00 per share.

Prior to this offering, there has been no public market for our common stock. Our common stock has been approved for listing on The Nasdaq Global Select Market under the symbol “DTIL.”

We are an “emerging growth company” under the federal securities laws and are subject to reduced public company reporting requirements for this prospectus and future filings.

	Per share	Total
Initial public offering price	$ 16.00	$126,400,000
Underwriting discounts and commissions(1)	$ 1.12	$ 8,848,000
Proceeds to Precision BioSciences, Inc., before expenses	$ 14.88	$117,552,000

(1) See “Underwriting” for a description of compensation payable to the underwriters.

We have granted the underwriters an option for a period of 30 days to purchase up to 1,185,000 additional shares of our common stock.

Investing in our common stock involves a high degree of risk. See “Risk factors” beginning on page 12 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of commons stock to purchasers on or about April 1, 2019.

J.P. Morgan **Goldman Sachs & Co. LLC** **Jefferies** **Barclays**

March 27, 2019.

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Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus or in any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

Through and including April 21, 2019 (the 25th day after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

We have proprietary rights to trademarks, trade names and service marks appearing in this prospectus that are important to our business. Solely for convenience, the trademarks, trade names and service marks may appear in this prospectus without the ® and ™ symbols, but any such references are not intended to indicate, in any way, that we forgo or will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, trade names and service marks. All trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

For investors outside the United States: Neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

Prospectus summary

This summary highlights selected information contained in greater detail elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the risks of investing in our common stock discussed under "Risk factors" and our financial statements and the related notes thereto included at the end of this prospectus, before making an investment decision. As used in this prospectus, unless the context otherwise requires, references to "we," "us," "our," "the Company" and "Precision" refer to Precision BioSciences, Inc. and its subsidiaries on a consolidated basis.

Overview

We are a genome editing company dedicated to improving life through our groundbreaking proprietary genome editing platform, "ARCUS." 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 believe the versatility and breadth of ARCUS support our ability to develop products across the spectrum of biotechnology. We are actively developing product candidates in three innovative and high value areas where we believe our technology has the potential to overcome the limitations of other genome editing technologies: allogeneic CAR T immunotherapy, *in vivo* gene correction, and food. The U.S. Food and Drug Administration, or FDA, recently accepted our investigational new drug, or IND, application for our first gene-edited allogeneic CAR T cell candidate targeting CD19. We are currently screening patients for our planned Phase 1/2a clinical trial in patients with relapsed or refractory, or R/R, B-cell precursor acute lymphoblastic leukemia and R/R non-hodgkin lymphoma and expect to dose our first patient in this trial in April 2019. We believe this trial will be the first clinical investigation of an allogeneic CAR T therapy for non-hodgkin lymphoma. We believe our proprietary, one-step engineering process for producing allogeneic CAR T cells at large scale in a cost-effective manner will enable us to overcome the fundamental challenges of manufacturing that have limited the CAR T field to date.

Our genome editing platform

Genome editing is a biotechnology process that removes, inserts or repairs a portion of DNA at a specific location in a cell's genome. Our proprietary genome editing platform, 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.

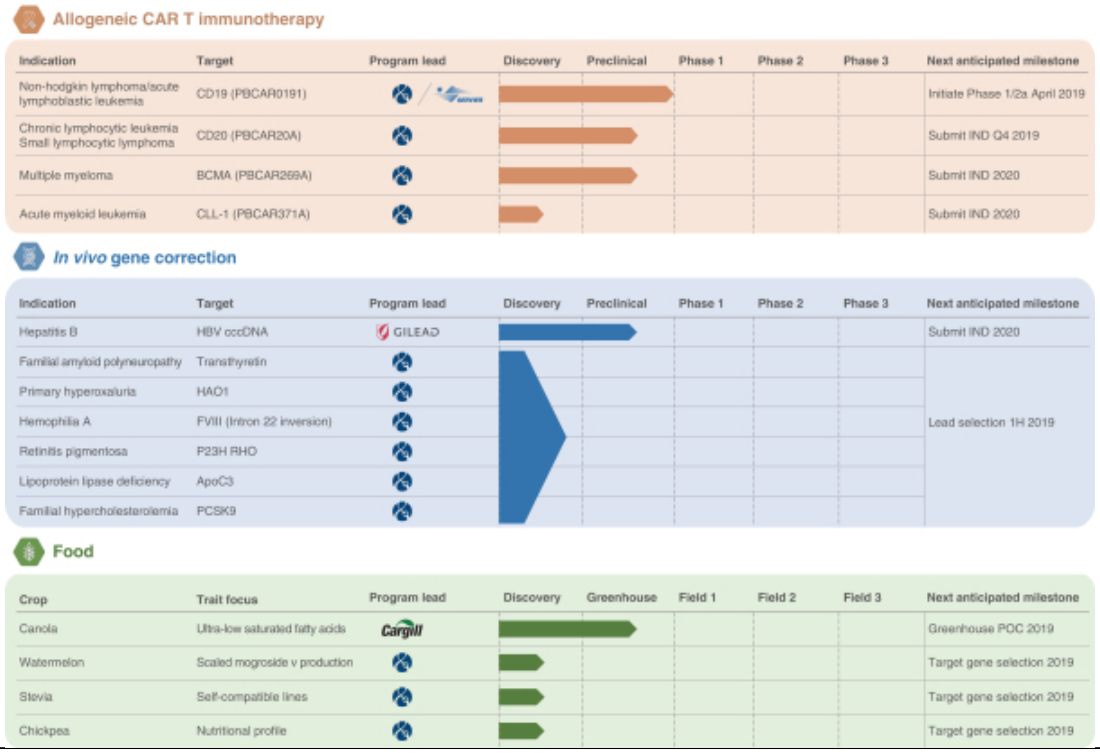
ARCUS is not a CRISPR/Cas9 technology. ARCUS is a collection of protein engineering methods that we developed specifically to re-program the DNA recognition properties of the natural genome editing enzyme, I-CreI. In nature, I-CreI is an endonuclease found in the genome of the algae *Chlamydomonas reinhardtii*, which evolved for the purpose of carrying out a complex gene insertion edit.

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 to bind and cut a different DNA sequence. Using ARCUS, we create customized endonucleases for particular applications. We call these custom endonucleases "ARCUS nucleases."

We believe ARCUS has a number of attributes that are beneficial for genome editing applications, such as:

- **High 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.
- **High Efficiency**. In our preclinical studies conducted to date, ARCUS has shown the ability to achieve a high level of on-target editing while rarely cutting off-target.
- **Easy Delivery**. ARCUS is very small relative to other genome editing endonucleases. As such, we believe it will be compatible with many different delivery mechanisms.
- **Type of cut**. The three prime, or 3', overhangs created when ARCUS cuts DNA have been observed 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. We believe this adds significant versatility to ARCUS and will enable us to efficiently insert or repair DNA as well as delete DNA.
- **Programmability**. ARCUS has been observed in our preclinical studies to recognize its DNA target site through a complex network of interactions that is challenging to re-program for new editing applications involving different DNA sequences. 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.

Our product pipeline



We are leveraging ARCUS to develop product candidates in three high value areas: allogeneic CAR T immunotherapy, *in vivo* gene correction and food. In each area, we have surrounded ARCUS with ancillary technologies and manufacturing capabilities specific to that field. This enables us to advance three independent pipelines with separate and distinct opportunity and risk profiles.

Allogeneic CAR T immunotherapy. We believe that we have developed a transformative allogeneic chimeric antigen receptor, or 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 lessen the product-to-product variability seen in autologous therapies and will allow us to consistently produce a potent product by selecting donors with high quality T cells. We are able to produce allogeneic CAR T cells at 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.

In February 2016, we entered into a development and commercial license agreement, as amended, with Baxalta (now Shire Plc), which we refer to as the Servier Agreement. This agreement was assigned to Les Laboratoires Servier, or Servier, in connection with Servier's acquisition of Shire's oncology business in August 2018. 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 by Baxalta at the inception of the agreement and the remaining five of which may be selected by Servier over the first four years 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. Our most advanced program, PBCAR0191, is an allogeneic CAR T cell therapy targeting the well-validated tumor target CD19 and is being developed for acute lymphoblastic leukemia, or ALL, and non-hodgkin lymphoma, or NHL. CD19 is a protein that is expressed on the surface of B cells. Our IND for PBCAR0191 was accepted by the FDA in November 2018. We are currently screening patients for our planned Phase 1/2a clinical trial in patients with R/R B-cell precursor ALL and R/R NHL and expect to dose our first patient in this trial in April 2019. We expect to report interim data results from this trial in early 2020. The FDA has granted PBCAR0191 orphan drug designation for the treatment of ALL. We are also in preclinical development of CAR T cell therapies targeting the tumor antigens CD20, BCMA and CLL-1. We expect to submit an IND to the FDA for our CD20 product candidate in the fourth quarter of 2019 and for each of our BCMA product candidate and our CLL-1 product candidate in 2020.

We have used the qualities of ARCUS to develop a one-step cell engineering process for allogeneic CAR T cells that is designed to rapidly yield a consistent cell product at a significantly lower cost than autologous CAR T cell therapies. 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 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 are advancing a deep portfolio of diverse programs toward *in vivo* efficacy and toxicity studies. We are generating a

significant large animal dataset that we believe will 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 two 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 September 2018, we announced a collaboration with Gilead Sciences, Inc. to co-develop an ARCUS-based product candidate that is designed to cure chronic Hepatitis B infection. We intend to submit an IND to the FDA in 2020 for this product candidate. We are also in the discovery stage for other *in vivo* indications: familial amyloid polyneuropathy, primary hyperoxaluria, hemophilia A, retinitis pigmentosa, lipoprotein lipase deficiency and familial hypercholesterolemia. We intend to select an indication and target for our next *in vivo* product candidate in the first half of 2019.

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 pre-breeding materials in collaboration with leading food producers. Pre-breeding material is a gene edited crop intermediate that the collaborating partner can integrate into their breeding program and use in producing new crop varieties. We believe we have the most in-depth experience in crop genome editing in the industry. 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-based 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. Prior to commercialization of any of our food product candidates, we must complete greenhouse studies and three phases of field testing.

Our strategy

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.
- Accelerate advancement of our first four allogeneic CAR T immunotherapy product candidates while investing in the research and development of additional allogeneic CAR T programs.
- Advance *in vivo* genetic correction programs into human clinical trials.
- Build a food business focused on developing products designed to improve human health and respond to the impacts of climate change.

- Continue investing in the optimization of ARCUS and enabling technologies.
- Create an environment that is a destination of choice for premier talent within the life sciences industry.
- Expand the breadth of our operations through additional product platforms and strategic relationships.

Sources of capital

To date, we have generated approximately $317 million from third parties through a combination of preferred stock and convertible note financings, an upfront payment under the Servier Agreement and additional funding from other strategic alliances and grants. Across our preferred stock financings, we received investments from venBio, F-Prime, ArrowMark Partners, Franklin Templeton, Cowen Healthcare, Gilead, Brace Pharma, Portfax AgTech, OCV Partners, Adage Capital, RA Capital, Amgen Ventures, Vivo and Ridgeback Capital, among others.

In March 2019, we sold and issued $39.6 million aggregate principal amount of convertible promissory notes, or the 2019 Notes, in a private placement transaction. The 2019 Notes accrue interest at a rate of 6% per annum and will automatically settle into shares of our common stock in connection with the closing of this offering at a settlement price equal to the lesser of (1) 85% of the initial public offering price per share set forth on the cover page of this prospectus or (2) a price per share equal to $800.0 million divided by our fully diluted capitalization as of immediately prior to the closing of this offering.

Risks associated with our business

Our business is subject to a number of risks that you should be aware of before making an investment decision. You should carefully consider all of the information set forth in this prospectus and, in particular, should evaluate the specific factors set forth under “Risk factors” in deciding whether to invest in our common stock. Among these important risks are the following:

- 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 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.
- 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.
- 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 any product candidates in humans.
- 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.
- Adverse public perception of genome editing may negatively impact the developmental progress or commercial success of potential products.

- Our research and development programs may not lead to the successful identification, development or commercialization of any potential products.
- Positive results, if any, obtained from early preclinical studies or clinical trials of our product candidates may not be predictive of results of later studies or trials, and failure to replicate positive results from early studies or clinical trials may inhibit our ability to further develop and commercialize product candidates.
- Clinical trials are difficult to design and implement, expensive, time-consuming and involve an uncertain outcome, and the inability to obtain regulatory approval for product candidates would substantially harm our business.
- 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.
- Delays in completing our planned manufacturing facility or failure to achieve operating efficiencies from it may require us to devote additional resources and management time to manufacturing operations and may delay our product development timelines.
- Our ability to compete may decline if we do not adequately protect our proprietary rights, and our proprietary rights do not necessarily address all potential threats to our competitive advantage.
- 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 prohibit our use of proprietary technology or sale of potential products or put our patents and other proprietary rights at risk.

Implications of being an emerging growth company

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more, (2) the last day of the fiscal year following the fifth anniversary of the date of the completion of this offering, (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 Securities and Exchange Commission, or 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 audited financial statements and only two years of related “Management’s discussion and analysis of financial condition and results of operations” in this prospectus;
- 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 prospectus 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 prospectus and may elect to take advantage of other reduced reporting requirements in future filings. In particular, in this prospectus, we have provided only two years of audited financial statements and corresponding “Management’s discussion and analysis of financial condition and results of operations” disclosure and 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 provision of the JOBS Act 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.

Even after we no longer qualify as an emerging growth company, we may still qualify as a “smaller reporting company,” which would allow us to take advantage of many of the same exemptions from disclosure requirements including reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements.

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 prospectus.

The offering

Common stock offered by us	7,900,000 shares
Common stock to be outstanding immediately after this offering	49,029,024 shares (or 50,214,024 shares if the underwriters exercise their option to purchase additional shares in full).
Option to purchase additional shares	We have granted the underwriters a 30-day option to purchase up to 1,185,000 additional shares of our common stock at the public offering price less the underwriting discounts and commissions.
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $113.3 million (or approximately $130.9 million if the underwriters exercise in full their option to purchase additional shares of common stock), after deducting underwriting discounts and commissions and the estimated offering expenses payable by us. We anticipate that we will use the net proceeds of this offering to advance and expand our clinical and preclinical development programs, fund the build-out of our planned cGMP-compliant manufacturing facility and the remainder for ongoing research and development activities and working capital and other general corporate purposes. For a more complete description of our intended use of the proceeds from this offering, see “Use of proceeds.”
Risk factors	You should carefully read the “Risk factors” beginning on page 12 and the other information included in this prospectus for a discussion of factors you should consider carefully before deciding to invest in our common stock.
Nasdaq Global Select Market symbol	“DTIL”

The number of shares of our common stock to be outstanding after this offering is based on 15,906,645 shares of our common stock outstanding as of December 31, 2018, and excludes:

- 7,763,464 shares of common stock issuable upon exercise of stock options outstanding under our 2006 Stock Incentive Plan, referred to as our 2006 Plan, and our 2015 Stock Incentive Plan, referred to as our 2015 Plan, in each case as of December 31, 2018, at a weighted-average exercise price of $5.00 per share;
- 4,750,000 shares of our common stock reserved for future issuance under our 2019 Incentive Award Plan, referred to as our 2019 Plan, which became effective upon the effectiveness of the registration statement of which this prospectus forms a part, and from which we intend to grant options to purchase shares of our common stock having an aggregate value of $350,000 to one of our directors as more fully described in “Executive and Director Compensation—Director compensation—IPO grants to non-employee directors under the 2019 Plan,” which number does not include any automatic increases in the number of shares of our common stock reserved for future issuance under our 2019 Plan; and

- 525,000 shares of our common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan, referred to as our 2019 ESPP, which became effective upon the effectiveness of the registration statement of which this prospectus forms a part, which number does not include any automatic increases in the number of shares of our common stock reserved for future issuance under our 2019 ESPP.

Unless otherwise indicated, this prospectus reflects and assumes the following:

- a 1 -for- 2.134686 reverse stock split of our common stock effected on March 15, 2019;
- the automatic conversion of all outstanding shares of our convertible preferred stock outstanding into an aggregate of 22,301,190 shares of our common stock upon the closing of this offering;
- the issuance of 2,921,189 shares of common stock upon the automatic settlement of the 2019 Notes, including accrued interest, based on the initial public offering price per share of $16.00, in connection with the closing of this offering;
- no exercise of outstanding options after December 31, 2018;
- the filing of our amended and restated certificate of incorporation, which will occur upon the closing of this offering; and
- no exercise by the underwriters of their option to purchase additional shares of our common stock.

Summary consolidated financial data

The following tables present a summary of our historical financial data for the periods ended on and as of the dates indicated. We have derived the summary consolidated statements of operations data for the years ended December 31, 2017 and 2018 and summary consolidated balance sheet data as of December 31, 2018 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that should be expected for any future period. You should read the following summary consolidated financial data together with the more detailed information contained in "Selected consolidated financial data," "Management's discussion and analysis of financial condition and results of operations" and our consolidated financial statements and the related notes included elsewhere in this prospectus.

	Years ended December 31,	
(in thousands, except share and per share data)	**2017**	**2018**
Consolidated Statements of Operations Data:		
Revenue	$ 6,484	$ 10,883
Operating expenses:		
Research and development	20,324	45,122
General and administrative	8,016	13,673
Impairment of intangible assets	118	—
Total operating expenses	28,458	58,795
Loss from operations	(21,974)	(47,912)
Other income:		
Interest income	872	1,875
Net loss and net loss attributable to common stockholders—basic and diluted	$ (21,102)	$ (46,037)
Net loss per share attributable to common stockholders—basic and diluted	$ (1.33)	$ (2.92)
Weighted-average shares of common stock outstanding—basic and diluted(1)	15,906,793	15,775,541
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)(1)		$ (1.37)
Pro forma weighted-average shares of common stock outstanding—basic and diluted (unaudited)(1)		33,653,835

(1) See Note 10 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma basic and diluted net loss per share of common stock and the weighted-average number of shares used in the computation of the per share amounts.

	As of December 31, 2018		
(in thousands)	**Actual**	**Pro forma(1)**	**Pro forma as adjusted(2)**
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$103,193	$ 142,743	$ 256,037
Working capital(3)	101,600	141,150	254,443
Total assets	138,600	178,150	291,443
Total liabilities	98,640	98,640	98,640
Accumulated deficit	(85,187)	(92,376)	(92,376)
Stockholders' equity	39,960	79,505	192,798

(1) The pro forma consolidated balance sheet data gives effect to the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 22,301,190 shares of common stock, which will occur upon the closing of this offering, the receipt of $39.6 million in cash proceeds from the sale of the 2019 Notes in March 2019 and the automatic settlement of the 2019 Notes, including accrued interest, into 2,921,189 shares of our common stock in connection with the closing of this offering, and an aggregate charge to accumulated deficit of $7.2 million relating to the loss resulting from the change in fair value of the 2019 Notes from the issuance date through their settlement.

(2) Reflects the pro forma adjustments described in footnote (1) and the issuance and sale of 7,900,000 shares of common stock in this offering at the initial public offering price of $16.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

(3) We define working capital as current assets less current liabilities. See our consolidated financial statements included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

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 contained in this prospectus, including our consolidated financial statements and the related notes appearing herein. The occurrence of any of the following risks could materially adversely affect our business, financial condition, results of operations and prospects. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

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 $46.0 million for the year ended December 31, 2018. As of December 31, 2018, we had an accumulated deficit of $85.2 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 private placements of our convertible preferred stock 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;
- 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 a commercial-scale manufacturing facility 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.

No clinical studies have begun on any of our therapeutic product candidates, and 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 breeding 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 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, upon the closing of this offering, we expect 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, together with the net proceeds from this offering, will be sufficient to fund our expected operating expenses and capital expenditure requirements through 2020. 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 operating 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.

Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, 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 not yet commenced human clinical trials for any of our product candidates, nor have we commenced field trials for any of our product candidates from our food platform. We have not yet demonstrated an ability to initiate or 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 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 2018 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 any product candidates in humans.

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, none of which has utilized our technology, and no therapeutic product candidates created with other genome editing technologies have received marketing approval in the United States or Europe. Because our therapeutic research programs are all in research or preclinical stages, we have not yet been able to assess the safety or efficacy of any product candidates in humans. 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, or other existing or future technologies, may lead to the development of 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 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.

Even if we do commence clinical trials of product candidates and continue to identify new product candidates, such product candidates 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.

Interim "top-line" and preliminary 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 preliminary data from preclinical or greenhouse studies or clinical or field trials. 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. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary 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 preliminary 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.

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. 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 when we begin clinical trials

and 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 is 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 addition to the submission of an investigational new drug application, or IND, to the FDA, before initiation of a clinical trial in the United States, certain human clinical trials for cell therapy products and gene therapy had historically been subject to review by the Recombinant DNA Advisory Committee, or the RAC, of the National Institutes of Health, or NIH, Office of Biotechnology Activities, or OBA, pursuant to the NIH Guidelines for Research Involving Recombinant DNA Molecules, or NIH Guidelines. Following an initial review, RAC members would make a recommendation as to whether the protocol raises important scientific, safety, medical, ethical or social issues that warrant in-depth discussion at the RAC's quarterly meetings. Even though the FDA decides whether individual cell therapy or gene therapy protocols may proceed under an IND, the RAC's recommendations were shared with the FDA and the RAC public review process, if undertaken, could delay the initiation of a clinical trial, even if the FDA had reviewed the trial design and details and has not objected to its initiation or has notified the sponsor that the study may begin. Conversely, the FDA can put an IND on clinical hold even if the RAC provided a favorable review or has recommended against an in-depth, public review.

On August 17, 2018, the NIH issued a notice in the Federal Register and issued a public statement proposing changes to the oversight framework for gene therapy trials, including changes to the applicable NIH Guidelines to modify the roles and responsibilities of the RAC with respect to human clinical trials of gene therapy products, and requesting public comment on its proposed modifications. During the public comment period, which closed October 16, 2018, the NIH has announced that it will no longer accept new human gene transfer protocols for review as part of the protocol registration process under the existing NIH Guidelines or convene the RAC to review individual clinical protocols. These trials will remain subject to the FDA's oversight and other clinical trial regulations, and oversight at the local level will continue as otherwise set forth in the NIH Guidelines. Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment 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. Even though we may not be required to submit a protocol for our gene therapy product candidates through the NIH for RAC review, we will still be 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.

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. 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. To date, neither we nor our collaborators have initiated any clinical trials for any product candidates. We do not know whether planned clinical trials will begin on time, 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 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.

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. 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 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, 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 establishing our own capabilities and infrastructure, including a manufacturing facility. We believe that development of our own manufacturing facility will provide us with enhanced control of material supply for both clinical trials and the commercial market, enable the more rapid implementation of process changes and help us achieve better long-term margins. We have no experience in developing a manufacturing facility and may never be successful in developing our own manufacturing facility or capability. 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.

Delays in completing the manufacturing facility we are building or failure to achieve operating efficiencies from it may require us to devote additional resources and management time to manufacturing operations and may delay our product development timelines.

We have leased approximately 17,300 square feet of space for our manufacturing facility at a location approximately seven miles from our headquarters in Durham, North Carolina, at which we intend to establish and equip a manufacturing facility compliant with cGMP. We may face delays in the completion of the manufacturing facility and cannot guarantee that this facility will be available for manufacturing beginning with our BCMA product candidate. In addition, we may not experience the anticipated operating efficiencies as we commence manufacturing operations at the new facility. Any such delays 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.

In order to complete our planned manufacturing facility, we may be forced to devote greater resources and management time than anticipated, particularly in areas relating to operations, quality, regulatory, facilities and information technology. 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 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. The use of our genome editing technology in our product candidates has never undergone testing in humans and has only been tested in a limited manner in animals, and results from animal studies may not be predictive of clinical trial results. Even if any 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.

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 train 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 training in recognizing or managing 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 privacy 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. 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;

- U.S. federal civil and criminal false claims laws and civil monetary penalties laws, including the civil False Claims Act, which can be enforced through civil whistleblower or qui tam actions, prohibits, 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;
- 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.
- 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;
- 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) 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 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; state and non-U.S. laws 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; state and non-U.S., enacted and proposed, laws and regulations regarding the collection, distribution, use, security, and storage of personally identifiable information and other data relating to individuals (including the EU General Data Protection Regulation 2016/679 and the California Consumer Protection Act); and federal and state consumer protection laws are being applied to enforce regulations related to the online collection, use, and dissemination of data, thus complicating compliance efforts.

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 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.

We have received orphan drug designation for PBCAR0191 for the treatment of ALL 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 for some or all of our product candidates, but we may not receive such designation, 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 and review 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. Thus, even if we or our collaborators believe a particular product candidate is eligible for this designation, the FDA may decide not to grant it. Moreover, even if we do receive fast track designation, we or our collaborators may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from the clinical development program.

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 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 establishes an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; increases in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, extends manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, expands eligibility criteria for Medicaid programs, expansion of the entities eligible for discounts under the Public Health program, addresses 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, creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% commencing January 1, 2019) 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 creates a licensure framework for follow-on biologic products.

At this time, we are unsure of the full impact that the Affordable Care Act will have on our business. There have been judicial and political challenges to certain aspects of the Affordable Care Act. For example, since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or

loosen certain requirements mandated by the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. Tax legislation enacted on December 22, 2017 entitled "an Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018, Pub.L. 115–97," or the Tax Cuts and Jobs Act of 2017, includes a provision repealing, effective January 1, 2019, 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 that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share. Further, the Bipartisan Budget Act of 2018, among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." More recently, in July 2018, the CMS published a final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. Congress may consider other legislation to repeal or repeal and replace other elements of 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, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals for spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes 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, including the BBA, will remain in effect through 2027 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 for pharmaceutical products, some of which are included in the Trump administration's budget proposal for fiscal year 2019. 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 the process of 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 will require authorization through additional legislation 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 federal, or the 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 obtain access to physicians or persuade adequate numbers of physicians to prescribe any 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. 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 affect.

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 chimeric antigen receptor 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 will likely 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 find it more difficult to find a suitable 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 and negatively impact the perception of our company in business and financial communities. 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 prospectus 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, 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.

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and expect that we may 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 our proprietary rights do not necessarily address all potential threats to our 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 or effectively protected trade secrets 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. 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. Furthermore, we employ reputable law firms and other professionals to help us comply with the various procedural, documentary, fee payment and other similar provisions we are subject to and, in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. 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 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 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 Bayh-Dole Act. 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 United States Patent and Trademark Office, or 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 all claims are 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, 2018, we had 127 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 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, and Jeff Smith, our Chief Technology 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. We maintain a $1 million "key man" life insurance policy for our benefit on each of the lives of Drs. Jantz and Smith, but not on the lives of any of our other team members. 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 will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices, including establishing and maintaining proper and effective internal control over financial reporting.

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. We will be 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 devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs, make some activities more difficult, time consuming or costly, and increase 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 initial public offering. 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, 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, 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.

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, 2018, we had cash and cash equivalents of $103.2 million. While we are not aware of any downgrades, material losses or other significant deterioration in the fair value of our cash and cash equivalents since December 31, 2018, 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 intend to adopt, prior to the completion of this offering, 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.

The recently passed Tax Cuts and Jobs Act of 2017 could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation, known as the Tax Cuts and Job Act of 2017, or the Tax Act, that significantly revises the Internal Revenue Code of 1986, as amended, or the Code. The Tax Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted taxable income (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions). Notwithstanding the reduction in the corporate income tax rate, the overall impact of the Tax Act is uncertain, and our business and financial condition could be adversely affected. In addition, it is unknown if and to what extent various states will conform to the Tax Act. The impact of the Tax Act on holders of our common stock is likewise uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

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. We recently formed a subsidiary in Australia and 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, 2018, we had U.S. federal and state net operating loss carryforwards of $40.0 million and $39.8 million, respectively. Our federal net operating loss carryforwards of $19.4 million will begin to expire in 2030 while the remaining federal net operating loss carryforwards of $20.6 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 $3.6 million and an amount less than $0.1 million as of December 31, 2018, respectively, available to offset future U.S. federal and state income taxes, which begin to expire in 2027 and 2030, respectively. 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, 2018, 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 this offering, 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 this offering and owning our common stock

An active trading market for our common stock may not develop, and you may not be able to sell your shares at or above the initial public offering price.

Prior to this offering, there has been no public market for shares of our common stock. Although our common stock has been approved for listing on the Nasdaq Global Select Market, an active trading market for our common stock may never develop or be sustained following this offering. The lack of an active trading market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable, reduce the market value of your shares, impair our ability to raise capital and impair our ability to attract, motivate and retain our employees through equity incentive awards. The initial public offering price of our common stock was determined through negotiations between us and the underwriters, and it may not be indicative of the market price of our common stock in an open market after this offering. Consequently, you may not be able to sell your common stock at or above the initial public offering price and may lose a portion or all of your investment.

We expect that our common stock price will fluctuate significantly, which could result in substantial losses for purchasers of shares in this offering.

Our stock price is likely to be volatile. You should invest in our common stock only if you can withstand a significant loss and wide fluctuations in the market value of your investment. The market price for our common stock may be influenced by many factors, including those discussed in this “Risk factors” section and the following:

- 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.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

The initial public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. Based on the initial public offering price of $16.00 per share, you will experience immediate dilution of $12.15 per share, representing the difference between our pro forma as adjusted net tangible book value per share, after giving effect to this offering. As of December 31, 2018, there were 7,763,464 shares subject to outstanding options with a weighted-average exercise price of $5.00 per share. To the extent these outstanding options are ultimately exercised, you will incur further dilution. In addition, purchasers of common stock in this offering will have contributed approximately 56.3% of the aggregate price paid by all purchasers of our stock but will own only approximately 43.7% of our common stock outstanding after this offering. For a further description of the dilution that you will experience immediately after this offering, see “Dilution.”

A significant portion of our total outstanding shares is restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Based on the number of shares of common stock outstanding on December 31, 2018, after this offering and after giving effect to the conversion of all outstanding shares of our convertible preferred stock into 22,301,190 shares of our common stock upon the closing of this offering and the automatic settlement of our convertible promissory notes, or the 2019 Notes, including accrued interest, into 2,921,189 shares of our common stock in connection with the closing of this offering, based on the initial public offering price per share of $16.00, we will have 49,029,024 shares of common stock outstanding, or 50,214,024 if the underwriters exercise their option to purchase additional shares in full. Of these shares, the 7,900,000 shares, or 9,085,000 shares if the underwriters exercise their option to purchase additional shares in full, we are selling in this offering may be resold in the public market immediately, unless purchased by our affiliates. The remaining 41,129,024 shares are currently restricted under securities laws or as a result of lock-up or other agreements, but will be able to be sold after this offering as described in the “Shares eligible for future sale” section of this prospectus.

Substantially all of our shares of common stock will be available for sale in the public market beginning 180 days after the date of this prospectus following the expiration of lock-up agreements between our stockholders and the underwriters. JP Morgan Securities LLC, Goldman Sachs & Co. LLC and Jefferies LLC may release these stockholders from their lock-up agreements with the underwriters at any time and without notice, except for officers and directors, for whom notice of such waiver would be provided two business days before the effective date thereof, which would allow for earlier sales of shares in the public market.

In addition, as of December 31, 2018, up to 9,304,492 shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, or the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Moreover, after this offering, holders of an aggregate of 35,753,545 shares of our common stock will have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also plan to

register all 13,215,287 shares of common stock that we may issue under our equity compensation plans or that are issuable upon exercise of outstanding options. Once we register these shares, they can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates and the lock-up agreements described in “Underwriting.” If substantial portions of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

After this offering, our executive officers, directors and significant stockholders will have the ability to directly or indirectly influence all matters submitted to stockholders for approval.

Based on their beneficial ownership as of December 31, 2018, our executive officers, directors, current 5% or greater stockholders and affiliated entities will beneficially own approximately 25.0% of the outstanding shares of our common stock after this offering, assuming no exercise of the underwriters’ option to purchase additional shares and assuming that group does not participate in this offering. As a result, these stockholders, acting together, will have significant influence over all matters that require approval by our stockholders, including the election of directors and approval of significant corporate transactions. Corporate action might be taken even if other stockholders, including those who purchase shares in this offering, oppose them. This concentration of ownership might also have the effect of delaying or preventing a change of control of our company that other stockholders may view as beneficial.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, and we could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. We expect that we will use the net proceeds from this offering to advance and expand our clinical and preclinical development programs and for working capital and other general corporate purposes, which may include the costs of establishing a manufacturing facility, as set forth under “Use of proceeds.” However, our use of these proceeds may differ substantially from our current plans. The failure by our management to apply these funds effectively could harm our business and financial condition. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value. These investments may not yield a favorable return to our investors.

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. 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 do not publish research or reports about us and our business, or if they 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 will be influenced by the research and reports that industry or securities analysts publish about us and our business. We do not currently have, and may never obtain, research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, the trading price for our stock would be negatively impacted. In the event we obtain securities or industry analyst coverage, 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 that will become effective upon the closing of this offering 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, which will become effective upon the closing of this offering, 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 the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more, (2) the last day of the fiscal year following the fifth anniversary of the date of the completion of this offering, (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 audited financial statements and only two years of related "Management's discussion and analysis of financial condition and results of operations" disclosure in this prospectus;

- 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 prospectus 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 prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and corresponding "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. 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. 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.

Special note regarding forward-looking statements

This prospectus contains forward-looking statements. All statements other than statements of present and historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, prospective products, planned preclinical or greenhouse studies and clinical or field trials, regulatory approvals, research and development costs, and timing and likelihood of success, as well as plans and objectives of management for future operations, may be forward-looking statements. Without limiting the foregoing, the words “anticipate,” “believe,” “could,” “expect,” “should,” “plan,” “intend,” “estimate,” “target,” “may,” “will,” “would,” “potential,” the negative thereof and similar words and expressions are intended to identify forward-looking statements.

Forward-looking statements are based on our management’s beliefs and assumptions and on information currently available to us. Such 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 under “Risk factors” and “Management’s discussion and analysis of financial condition and results of operations” and elsewhere in this prospectus. These risks and uncertainties include factors relating to:

- the initiation, cost, timing, progress and results of research and development activities, preclinical or greenhouse studies and clinical or field trials;
- our or our collaborators’ ability to identify, develop and commercialize product candidates;
- our or our collaborators’ ability to advance product candidates into, and successfully complete, clinical or field trials;
- the potential for off-target editing or other adverse events, undesirable side effects or unexpected characteristics associated with any of our product candidates;
- our or our collaborators’ ability to obtain and maintain regulatory approval of future product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate;
- the success of our existing collaboration agreements;
- our ability to enter into new collaboration arrangements;
- our ability to achieve our anticipated operating efficiencies as we commence manufacturing operations at our new facility;
- our ability to obtain funding for our operations;
- public perception about genome editing technology and its applications;
- our ability to obtain and maintain intellectual property protection for our technology and any of our product candidates;
- our or our collaborators’ ability to successfully commercialize any of our product candidates;
- the rate and degree of market acceptance of any of our product candidates;
- regulatory developments in the United States and international jurisdictions;
- competition in the genome editing, biopharmaceutical, biotechnology and agricultural biotechnology fields;
- potential manufacturing problems associated with any of our product candidates;

- potential liability lawsuits and penalties related to our technology, our product candidates and our current and future relationships with third parties;
- our ability to attract and retain key scientific and management personnel;
- our ability to effectively manage the growth of our operations;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately under those arrangements;
- our use of proceeds from this offering;
- our financial performance; and
- expected fluctuations of our stock price.

All forward-looking statements speak only as of the date of this prospectus, and 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.

Industry and other data

We obtained the industry, statistical and market data in this prospectus from our own internal estimates and research as well as from industry and general publications and research, surveys and studies conducted by third parties. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires. All of the market data used in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. While we believe that each of these studies and publications is reliable, the industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of important factors, including those described in “Risk factors.” These and other factors could cause results to differ materially from those expressed in the estimates made by third parties and by us.

Use of proceeds

We estimate that the net proceeds to us from the issuance and sale of shares of our common stock in this offering will be approximately $113.3 million, based on the initial public offering price of $16.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters' option to purchase additional shares from us is exercised in full, we estimate that our net proceeds will be approximately $130.9 million.

The principal purposes of this offering are to obtain additional capital to support our operations, to create a public market for our common stock and to facilitate our future access to the public equity markets. We anticipate that we will use the net proceeds from this offering as follows:

- approximately $7.0 to $9.0 million to initiate and complete a Phase 1/2a clinical trial for our CD19 CAR T cell product candidate;
- approximately $50.0 to $52.0 million to advance and expand the development of our other CAR T cell product candidates and allogeneic CAR T immunotherapy platform, including to submit an IND for each of our CD20, BCMA and CLL-1 CAR T cell product candidates;
- approximately $18.0 to $20.0 million to advance and expand the preclinical development of our *in vivo* gene correction platform, including early discovery efforts, chemistry, manufacturing and controls, or CMC, and IND-enabling studies;
- approximately $12.0 to $14.0 million to fund the build-out of our planned cGMP-compliant manufacturing facility; and
- the remainder to fund new and ongoing research and development activities, to fund the portion of expenses we are responsible for with respect to the development of our food platform and for working capital and other general corporate purposes.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. We may also use a portion of the net proceeds to in-license, acquire or invest in additional businesses, technologies, products or assets, although currently we have no specific agreements, commitments or understandings in this regard. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. Predicting the cost necessary to develop our technology and product candidates can be difficult, and we anticipate that we will need additional funds to complete our development programs. The amounts and timing of our actual expenditures and the extent of our preclinical studies and clinical trials and other development efforts may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from preclinical studies and any clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Based on our current operating plan and planned use of the net proceeds from this offering and our existing cash and cash equivalents, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements through 2020. We have based this estimate on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect. We may satisfy our future cash needs through the sale of equity securities, debt financings, working capital lines of credit, corporate collaborations or license agreements, grant funding, interest income earned on invested cash balances or a combination of one or more of these sources.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

Dividend policy

We have never declared or paid any cash dividends on our capital stock. 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. 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.

Capitalization

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2018:

- on an actual basis;
- on a pro forma basis to reflect:
  - the automatic conversion of all outstanding shares of our convertible preferred stock into 22,301,190 shares of common stock upon the closing of this offering;
  - the receipt of $39.6 million in cash proceeds from the sale of the 2019 Notes in March 2019;
  - the settlement of the 2019 Notes, including accrued interest, into 2,921,189 shares of our common stock and an aggregate charge to accumulated deficit of $7.2 million relating to the loss resulting from the change in fair value of the 2019 Notes from the issuance date through their settlement, based on the initial public offering price per share of $16.00, in connection with the closing of this offering; and
  - the filing and effectiveness of our amended and restated certificate of incorporation, which will occur upon the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of 7,900,000 shares of our common stock in this offering based on the initial public offering price of $16.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma and pro forma as adjusted information below assumes we elect the fair value option to account for the 2019 Notes. Additionally, we have assumed for purposes of the pro forma and pro forma as adjusted information that the fair value of the 2019 Notes upon conversion is equal to $46.7 million, reflecting the 15% conversion discount provided to holders of the 2019 Notes, based on the initial public offering price per share of $16.00. The loss resulting from the change between the $39.6 million aggregate principal amount of the 2019 Notes upon issuance and the assumed $46.7 million fair value of the 2019 Notes upon conversion, including accrued interest, is reflected as an increase in accumulated deficit in the pro forma and pro forma as adjusted amounts. You should read this information in conjunction with our consolidated financial statements and the related notes included elsewhere in this prospectus and the “Management’s discussion and analysis of financial condition and results of operations” section and other financial information contained in this prospectus.

	As of December 31, 2018		
	Actual	Pro forma	Pro forma as adjusted
(in thousands, except share and per share amounts)			
Cash and cash equivalents	$ 103,193	$ 142,743	$ 256,037
Convertible preferred stock, $0.0001 par value per share: 47,606,100 shares authorized, 22,301,190 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	$ 5	$ —	$ —
Common stock, $0.000005 par value per share: 130,000,000 shares authorized, 16,717,117 shares issued and 15,906,645 shares outstanding, actual; 200,000,000 shares authorized, pro forma and pro forma as adjusted; 41,939,496 shares issued and 41,129,024 shares outstanding, pro forma; 49,839,496 shares issued and 49,029,024 shares outstanding, pro forma as adjusted	0	0	0
Preferred stock, $0.0001 par value per share: no shares authorized, issued and outstanding, actual; 10,000,000 shares authorized, pro forma and pro forma as adjusted; no shares issued and outstanding, pro forma and pro forma as adjusted	—	—	—
Additional paid-in capital	126,094	172,833	286,126
Accumulated deficit	(85,187)	(92,376)	(92,376)
Treasury stock	(952)	(952)	(952)
Total stockholders' equity	39,960	79,505	192,798
Total capitalization	$ 39,960	$ 79,505	$ 192,798

The number of shares of our common stock on a pro forma and pro forma as adjusted basis set forth in the table above is based on 15,906,645 shares of our common stock outstanding as of December 31, 2018 and does not include:

- 7,763,464 shares of common stock issuable upon exercise of stock options outstanding under our 2006 Plan and our 2015 Plan as of December 31, 2018, at a weighted-average exercise price of $5.00 per share;
- 4,750,000 shares of our common stock reserved for future issuance under our 2019 Incentive Award Plan, referred to as our 2019 Plan, which became effective upon the effectiveness of the registration statement of which this prospectus forms a part, and from which we intend to grant options to purchase shares of our common stock having an aggregate value of $350,000 to one of our directors as more fully described in "Executive and Director Compensation—Director compensation—IPO grants to non-employee directors under the 2019 Plan," which number does not include any automatic increases in the number of shares of our common stock reserved for future issuance under our 2019 plan; and
- 525,000 shares of our common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan, referred to as our 2019 ESPP, which became effective upon the effectiveness of the registration statement of which this prospectus forms a part, which number does not include any automatic increases in the number of shares of our common stock reserved for future issuance under our 2019 ESPP.

Dilution

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

As of December 31, 2018, we had a historical net tangible book value of $36.0 million, or $2.27 per share of common stock, based on 15,906,645 shares of common stock outstanding as of such date. Our historical net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding as of December 31, 2018. We define net tangible book value as total assets less total liabilities, intangible assets and deferred offering costs. We define total tangible assets as total assets less intangible assets and deferred offering costs.

Our pro forma net tangible book value as of December 31, 2018 was $75.5 million, or $1.84 per share. Pro forma net tangible book value represents the amount of our total tangible assets less total liabilities, after giving effect to the automatic conversion of all shares of our convertible preferred stock outstanding as of December 31, 2018 into an aggregate of 22,301,190 shares of our common stock in connection with this offering, the receipt of $39.6 million in cash proceeds from the sale of the 2019 Notes in March 2019, the automatic settlement of the 2019 Notes, including accrued interest, into 2,921,189 shares of our common stock and an aggregate charge to accumulated deficit of $7.2 million relating to the loss resulting from the change in fair value of the 2019 Notes from their issuance date through their settlement in connection with the closing of this offering, based on the initial public offering price per share of $16.00. Pro forma net tangible book value per share represents our pro forma net tangible book value divided by the total number of shares outstanding as of December 31, 2018, after giving effect to the pro forma adjustment described above.

After giving further effect to the receipt of the net proceeds from our issuance and sale of 7,900,000 shares of common stock in this offering at the initial public offering price of $16.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2018 would have been $188.8 million, or $3.85 per share. This amount represents an immediate increase in pro forma net tangible book value of $2.01 per share to our existing stockholders and an immediate dilution of $12.15 per share to new investors participating in this offering. We determine dilution by subtracting the pro forma as adjusted net tangible book value per share after this offering from the amount of cash that a new investor paid for a share of common stock. The following table illustrates this dilution:

Initial public offering price per share		$16.00
Historical net tangible book value per share as of December 31, 2018	$ 2.27	
Pro forma decrease per share attributable to the issuance of the 2019 Notes, the conversion of our convertible preferred stock and settlement of the 2019 Notes	(0.43)	
Pro forma net tangible book value per share as of December 31, 2018	1.84	
Increase in the pro forma net tangible book value per share attributable to this offering	2.01	
Pro forma as adjusted net tangible book value per share after this offering		3.85
Dilution per share to new investors participating in this offering		$12.15

If the underwriters exercise their option to purchase additional shares of our common stock in full, the pro forma as adjusted net tangible book value per share after this offering would be $4.11 per share, and the dilution per share to new investors would be $11.89 per share, in each case based on the initial public offering price of $16.00 per share, after deducting underwriting discounts and commissions and the estimated offering expenses payable by us.

The following table summarizes, as of December 31, 2018, on the pro forma as adjusted basis described above, the total number of shares of common stock purchased from us on an as converted to common stock basis, the total consideration paid or to be paid and the average price per share paid or to be paid by existing stockholders and by new investors in this offering based on the initial public offering price of $16.00 per share, before deducting the underwriting discounts and commissions and estimated offering expenses payable by us. As the table shows, new investors purchasing common stock in this offering will pay an average price per share substantially higher than our existing stockholders paid.

	Shares purchased		Total consideration		Average price per share
	Number	Percent	Amount	Percent	
Existing stockholders	41,129,024	83.9%	$163,033,474	56.3%	$ 3.96
New investors	7,900,000	16.1	126,400,000	43.7	16.00
Total	49,029,024	100.0%	$289,433,474	100.0%	

If the underwriters exercise their option to purchase additional shares of our common stock in full, the percentage of shares of common stock held by existing stockholders will decrease to approximately 81.9% of the total number of shares of our common stock outstanding after this offering, and the number of shares held by new investors will increase to 9,085,000, or approximately 18.1% of the total number of shares of our common stock outstanding after this offering.

The foregoing tables and calculations (other than the historical net tangible book value calculation) are based on the number of shares of our common stock outstanding as of December 31, 2018, after giving effect to the automatic conversion of all outstanding shares of our convertible preferred stock into common stock and the automatic settlement of the 2019 Notes into shares of our common stock in connection with this offering, and exclude:

- 7,763,464 shares of common stock issuable upon exercise of stock options outstanding under our 2006 Plan and our 2015 Plan as of December 31, 2018, at a weighted-average exercise price of $5.00 per share;
- 4,750,000 shares of our common stock reserved for future issuance under our 2019 Incentive Award Plan, referred to as our 2019 Plan, which became effective upon the effectiveness of the registration statement of which this prospectus forms a part, and from which we intend to grant options to purchase shares of our common stock having an aggregate value of $350,000 to one of our directors as more fully described in “Executive and Director Compensation—Director compensation—IPO grants to non-employee directors under the 2019 Plan,” which number does not include any automatic increases in the number of shares of our common stock reserved for future issuance under our 2019 plan; and
- 525,000 shares of our common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan, referred to as our 2019 ESPP, which became effective upon the effectiveness of the registration statement of which this prospectus forms a part, which number does not include any automatic increases in the number of shares of our common stock reserved for future issuance under our 2019 ESPP.

To the extent that these outstanding stock options are exercised, new stock options are issued or we issue additional shares of common stock in the future, there will be further dilution to new investors. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

Selected consolidated financial data

You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes included elsewhere in this prospectus and "Management's discussion and analysis of financial condition and results of operations." We have derived the consolidated statement of operations data for the years ended December 31, 2017 and 2018 and the consolidated balance sheet data as of December 31, 2017 and 2018 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that should be expected in any future period.

	Years ended December 31,	
(in thousands, except share and per share data)	**2017**	**2018**
Consolidated Statements of Operations Data:		
Revenue	$ 6,484	$ 10,883
Operating expenses:		
Research and development	20,324	45,122
General and administrative	8,016	13,673
Impairment of intangible assets	118	—
Total operating expenses	28,458	58,795
Loss from operations	(21,974)	(47,912)
Other income:		
Interest income	872	1,875
Net loss and net loss attributable to common stockholders—basic and diluted	$ (21,102)	$ (46,037)
Net loss per share attributable to common stockholders—basic and diluted	$ (1.33)	$ (2.92)
Weighted-average shares of common stock outstanding—basic and diluted(1)	15,906,793	15,775,541
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited) (1)		$ (1.37)
Pro forma weighted-average shares of common stock outstanding—basic and diluted (unaudited) (1)		33,653,835

(1) See Note 10 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical basic and diluted net loss per share of common stock and the weighted-average number of shares used in the computation of the per share amounts.

	As of December 31,	
(in thousands)	**2017**	**2018**
Consolidated Balance Sheet Data:		
Cash and cash equivalents	$ 62,802	$ 103,193
Working capital(1)	55,129	101,600
Total assets	72,682	138,600
Total liabilities	99,051	98,640
Accumulated deficit	(39,111)	(85,187)
Stockholders' (deficit) equity	(26,369)	39,960

(1) We define working capital as current assets less current liabilities. See our consolidated financial statements included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

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 prospectus. 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 prospectus captioned "Risk factors" and elsewhere in this prospectus, our actual results may differ materially from those anticipated in these forward-looking statements.

Overview

We are a genome editing company dedicated to improving life through our groundbreaking proprietary genome editing platform, "ARCUS." 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 believe the versatility and breadth of ARCUS support our ability to develop products across the spectrum of biotechnology. We are actively developing product candidates in three innovative and high value areas where we believe our technology has the potential to overcome the limitations of other genome editing technologies: allogeneic CAR T immunotherapy, *in vivo* gene correction, and food. The U.S. Food and Drug Administration, or FDA, recently accepted our investigational new drug, or IND, application for our first gene-edited allogeneic CAR T cell candidate targeting CD19. We are currently screening patients for our planned Phase 1/2a clinical trial in patients with relapsed or refractory, or R/R, B-cell precursor acute lymphoblastic leukemia and R/R non-hodgkin lymphoma and expect to dose our first patient in this trial in April 2019. We believe this trial will be the first clinical investigation of an allogeneic CAR T therapy for non-hodgkin lymphoma. We believe our proprietary, one-step engineering process for producing allogeneic CAR T cells at large scale in a cost-effective manner will enable us to overcome the fundamental challenges of manufacturing that have limited the CAR T field to date.

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 the sale of our convertible preferred stock and upfront payments from licensing arrangements. To date, we have generated approximately $317 million from third parties through a combination of preferred stock and convertible note financings, an upfront payment under the Servier Agreement and additional funding from other strategic alliances and grants. In March 2019, we sold and issued $39.6 million aggregate principal amount of convertible promissory notes, or the 2019 Notes, in a private placement transaction.

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 $21.1 million and $46.0 million for the years ended December 31, 2017 and 2018, respectively. As of December 31, 2018, we had an accumulated deficit of $85.2 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, following the closing of this offering, we expect 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 or private equity or 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 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.

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

Servier

In February 2016, we entered into the Servier Agreement, pursuant to which we have agreed to develop allogeneic chimeric antigen receptor T cell therapies for up to six unique antigen targets. One target was selected at the agreement’s inception, and Servier is entitled to select the remaining five targets over the first four years of the agreement. 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 supply 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.

We recognized $5.8 million in revenues under the Servier Agreement during each of the years ended December 31, 2017 and 2018. The amount recorded as deferred revenue was $94.4 million and $88.6 million as of December 31, 2017 and 2018, respectively. No development or sales-based milestones were received for the fiscal years ended December 31, 2017 and 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 stock-based compensation expense, for personnel engaged in research and development functions;
- expenses incurred under agreements with third parties, including 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 future clinical trials, including the costs of CMOs that will manufacture our clinical trial material for use in our preclinical studies 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 costs are specifically identifiable to a product candidate. 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:

	Years ended December 31,		
	2017	2018	Increase
(in thousands)			
Direct research and development expenses by product candidate:			
CD19 external development costs	$ 3,844	$13,654	$ 9,810
Platform development, early-stage research and unallocated expenses:			
Employee-related costs	9,878	14,784	4,906
Laboratory supplies and services	2,183	4,061	1,878
Outsourced research and development	1,455	7,055	5,600
Laboratory equipment and maintenance	324	519	195
Facility-related costs	832	1,431	599
Depreciation and amortization	1,205	1,759	554
Other research and development costs	603	1,859	1,256
Total research and development expenses	$20,324	$45,122	$ 24,798

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 initiate a Phase 1/2a clinical trial for our CD19 product candidate and continue to discover and develop additional product candidates.

We cannot determine with certainty the duration and costs of future clinical trials of our CD19 product candidate 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 product candidate 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 product candidate, 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 stock-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. Following this offering, 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.

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, 2018, we had federal and state net operating loss carryforwards of $40.0 million and $39.8 million, respectively, which may be available to offset future taxable income. The U.S. federal net operating loss carryforwards of $19.4 million will begin to expire in 2030 while the remaining federal net operating loss carryforwards of $20.6 million carry forward indefinitely. The state net operating loss carryforwards begin to expire in 2025, As of December 31, 2018, we also had federal research and development tax credit carryforwards of $3.6 million, which begin to expire in 2027. As of December 31, 2018, we also have federal contribution carryforwards of less than $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 Tax Cuts and Jobs Act was signed into United States law. The Tax Cuts and Jobs Act 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 Tax Cuts and Jobs Act.

Results of operations

Comparison of years ended December 31, 2017 and 2018

The following table summarizes our results of operations for the years ended December 31, 2017 and 2018, together with the changes in those items in dollars:

	Years ended December 31,		
	2017	2018	Change
(in thousands)			
Revenue	$ 6,484	$ 10,883	$ 4,399
Operating expenses:			
Research and development	20,324	45,122	24,798
General and administrative	8,016	13,673	5,657
Impairment of intangible assets	118	—	(118)
Total operating expenses	28,458	58,795	30,337
Loss from operations	(21,974)	(47,912)	(25,938)
Other income:			
Interest income	872	1,875	1,003
Net loss	$ (21,102)	$ (46,037)	$ (24,935)

Revenue

Revenue for the year ended December 31, 2017 was $6.5 million, compared to $10.9 million for the year ended December 31, 2018. The increase of $4.4 million in revenue during the year ended December 31, 2018 was generally the result of increases in research funding of $3.7 million from Gilead and of $1.0 million from another joint development collaboration partner, which was partially offset by a $0.3 million decrease in license fees from a biopharmaceutical manufacturer and a $0.1 million decrease in license fees from a collaboration partner.

Research and development expenses

	Years ended December 31,		
	2017	2018	Increase
(in thousands)			
Direct research and development expenses by product candidate:			
CD19 external development costs	$ 3,844	$13,654	$ 9,810
Platform development, early-stage research and unallocated expenses:			
Employee-related costs	9,878	14,784	4,906
Laboratory supplies and services	2,183	4,061	1,878
Outsourced research and development	1,455	7,055	5,600
Laboratory equipment and maintenance	324	519	195
Facility-related costs	832	1,431	599
Depreciation and amortization	1,205	1,759	554
Other research and development costs	603	1,859	1,256
Total research and development expenses	$20,324	$45,122	$ 24,798

Research and development expenses for the year ended December 31, 2017 were $20.3 million, compared to $45.1 million for the year ended December 31, 2018. The increase of $24.8 million was primarily due to increases of $9.8 million in direct research and development expenses related to our CD19 program and $15.0 million in platform development and early-stage research expenses. Our CD19 program incurred expenditure increases of $7.3 million to CMOs for clinical trial material, $0.7 million to CROs for clinical trial costs, $0.8 million in lab services, $0.4 million in scientific service providers, and $0.6 million in other costs. Platform development and early-stage research expenses increased primarily due to a $5.6 million increase in outsourced research and development spending on our development programs, excluding our CD19 program, and $4.9 million of additional employee-related cost associated with increased headcount to support our technology platform development and manufacturing capabilities.

General and administrative expenses

General and administrative expenses were $8.0 million for the year ended December 31, 2017, compared to $13.7 million for the year ended December 31, 2018. The increase of $5.7 million was primarily due to an increase of $3.0 million in employee-related costs as we increased our general and administrative headcount. General and administrative expenses also increased due to costs required to meet our growing infrastructure needs. Contributing to the increase were $0.5 million in facility related costs, including equipment, $1.1 million in consulting fees, $0.5 million in information technology costs, and $0.3 million in depreciation and amortization.

Interest income

Interest income was $0.9 million for the year ended December 31, 2017 compared to $1.9 million for the year ended December 31, 2018. The increase of $1.0 million of interest income generated on our cash and cash equivalent balances for the year ended December 31, 2018 compared to the year ended December 31, 2017 was the result of higher interest rates and having higher cash balances invested in 2018 compared to 2017.

Segment results

The following tables summarize segment revenues and segment operating loss for the years ended December 31, 2017 and 2018 (see Note 14 to our audited consolidated financial statements included elsewhere in this prospectus for additional information regarding our segments):

	Years ended December 31,	
	2017	**2018**
(in thousands)		
Revenue:		
Therapeutics	$ 6,064	$ 9,523
Food	420	1,360
Total segment revenue	6,484	10,883
Segment operational cash expenditures:		
Therapeutics	$ 11,062	$ 35,045
Food	1,699	9,125
Total segment operational cash expenditures	12,761	44,170
Allocation of centralized research and development operational cash expenditures:		
Therapeutics	$ 6,948	$ 11,605
Food	1,164	2,901
Total allocation of centralized research and development operational cash expenditures	8,112	14,506
Segment operating income (loss):		
Therapeutics	$ (11,946)	$ (37,127)
Food	(2,443)	(10,666)
Total segment operating loss	(14,389)	(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 from 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) plus an allocation of centralized research and development expenditures for early stage research, nuclease development and the purchase of general laboratory supplies. These expenditures are allocated to the segments based on headcount. The reportable segment and centralized research and development operational cash expenditures include cash disbursements for compensation, lab 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, 2017 was $6.1 million, compared to $9.5 million for the year ended December 31, 2018. The increase of $3.4 million was attributable to a $3.7 million increase in research funding received from Gilead, which was partially offset by a $0.3 million decrease in license fees from a biopharmaceutical manufacturer.

Segment operational cash expenditures for the year ended December 31, 2017 were $11.1 million, compared to $35.0 million for the year ended December 31, 2018. The increase of $23.9 million was primarily due to an

increase in payments made to service providers for research and development, contract manufacturing, clinical trial research, lab supplies and services, and an increase in employee headcount and related costs. Segment operating loss increased $25.2 million from $11.9 million for the year ended December 31, 2017 to $37.1 million for the year ended December 31, 2018 primarily due to the factors discussed above.

Food segment

Revenue for the year ended December 31, 2017 was $0.4 million, compared to $1.4 million for the year ended December 31, 2018. The increase of $0.9 million was primarily attributable to an increase in research funding of $1.0 million from another joint development collaboration partner.

Segment operational cash expenditures for the year ended December 31, 2017 were $1.7 million, compared to $9.1 million for the year ended December 31, 2018. The increase of $7.4 million was primarily due to an increase in leasehold improvements, equipment and lab supply expenditures and employee headcount and related costs. Segment operating loss increased $8.3 million from $2.4 million for the year ended December 31, 2017 to $10.7 million for the year ended December 31, 2018 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 CMOs and building out internal capacity to have product manufactured to support 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. To date, we have financed our operations primarily with proceeds from the sale of our convertible preferred stock and upfront payments from licensing arrangements. To date, we have generated approximately $317 million from third parties through a combination of preferred stock and convertible note financings, an upfront payment under the Servier Agreement and additional funding from other strategic alliances and grants.

Cash flows

Our cash and cash equivalents totaled $103.2 million as of December 31, 2018. We had no indebtedness as of December 31, 2018.

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

	Years ended December 31,	
	2017	**2018**
(in thousands)		
Net cash used in operating activities	$ (24,169)	$ (51,723)
Net cash used in investing activities	(5,515)	(15,663)
Net cash (used in) provided by financing activities	(937)	107,777
Increase (decrease) in cash and cash equivalents	$ (30,621)	$ 40,391

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 stock-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 planned initial public offering.

Cash flows for the year ended December 31, 2017

Operating activities

Net cash used in operating activities for the year ended December 31, 2017 was $24.2 million, primarily consisting of our net loss of $21.1 million as we incurred expenses associated with research activities on our CD19 program and research activities on other applications for our technology and incurred general and administrative expenses. In addition, we had a loss of $0.1 million on the disposal of assets and non-cash charges of $2.0 million for depreciation and stock-based compensation expense and the impairment of intangible assets. Net cash used in operating activities was also impacted by $5.1 million in changes in operating assets and liabilities, including $6.2 million in deferred revenue and $0.6 million in prepaid expenses and other current assets, partially offset by changes of $0.9 million in accounts payable, $0.7 million in accrued expenses and other current liabilities and $0.1 million in other assets.

Investing activities

Net cash used in investing activities for the year ended December 31, 2017 was $5.5 million, which was attributable to purchases of property, equipment and software of $5.6 million, partially offset by $0.1 million from the proceeds from the disposal of equipment.

Financing activities

Net cash used in financing activities for the year ended December 31, 2017 was $0.9 million, consisting of repurchases of common stock of $1.0 million, partially offset by less than $0.1 million in proceeds from stock option exercises.

Funding requirements

Our operating expenses have increased substantially in 2017 and 2018 and are expected to increase substantially in 2019 and in the future in connection with our ongoing activities, particularly as we advance our preclinical activities including pre-IND enabling studies, scale-up of manufacturing processes and engagement with CMOs and initiation of human clinical trials. In addition, following the closing of this offering, we expect to incur additional costs associated with operating as a public company.

Specifically, our costs and expenses will increase as we:

- pursue the clinical development of our CD19 program;
- pursue the preclinical and clinical development of our other CAR T cell product candidates and allogeneic CAR T immunotherapy platform, our gene correction platform and our other product candidates;
- further scale up our internal manufacturing processes and capabilities and contract with CMOs to support our preclinical studies and clinical trials of our product candidates and make other capital expenditures to support our operations;
- in-license or acquire the rights to other products, product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;
- hire additional personnel in research, manufacturing and regulatory and clinical development as well as management personnel; and
- expand our operational, financial and management systems and increase personnel, including personnel to support our operations as a public company.

We believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements through 2020. 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 and initial clinical trials for our CD19 program;
- 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 program 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, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making 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 and commitments

The following is a summary of our contractual obligations and commitments as of December 31, 2018:

		Payments due by period			
	Total	Less than 1 year	1—3 years	3-5 years	More than 5 years
(in thousands)					
Operating lease obligation(1)	$14,530	$ 1,999	$4,384	$4,663	$ 3,484

(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, 5 Laboratory Drive, Research Triangle Park, North Carolina expiring in April 2026 and 20 TW Alexander Drive, Research Triangle Park, North Carolina expiring in August 2026 (see Note 9 to our consolidated financial statements included elsewhere in this prospectus for additional information on these lease agreements).

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. 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 prospectus, 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.

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 (see Note 13 to our consolidated financial statements included elsewhere in this prospectus). 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.

Revenue is recognized when all of the following conditions are met: (1) persuasive evidence of an arrangement exists, (2) delivery has occurred or services have been rendered, (3) fees are fixed or determinable, and (4) collection of fees is reasonably assured.

We analyze our collaboration arrangements to assess whether they are within the scope of Accounting Standards Codification 808, 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 requires that we determine whether 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 within the scope of Accounting Standards Codification 605-25, Revenue Recognition—Multiple-Element Arrangements, or ASC 605. To date, we have no arrangements that are within the scope of ASC 808.

When evaluating multiple element arrangements under ASC 605, we determine whether the arrangement should be divided into separate units of accounting and how the arrangement consideration should be measured and allocated among the separate units of accounting. An element qualifies as a separate unit of accounting when the delivered element has standalone value to the customer. Any delivered elements that do not qualify as separate units of accounting are combined with other undelivered elements within the arrangement as a single unit of accounting. If the arrangement constitutes a single combined unit of accounting, we determine the revenue recognition method for the combined unit of accounting and recognize the revenue over the period from inception through the date the last deliverable within the single unit of accounting is delivered. Our arrangements do not include a general right of return relative to delivered elements.

Amounts received prior to satisfying all revenue recognition criteria are recorded as deferred revenue in our accompanying consolidated balance sheets. Our deferred revenue includes nonrefundable upfront license fees. The deferred revenue is recognized into revenue on a proportional or straight-line basis over the estimated period of our substantive performance obligations or the period the rights granted are in effect. Analyzing the arrangement to identify deliverables requires the use of judgment and each deliverable may be an obligation to deliver services, a right or license to use an asset or another performance obligation.

In arrangements that include license rights and other noncontingent deliverables, these deliverables do not have standalone value because the noncontingent deliverables are dependent on the license rights, are not sold separately and cannot be resold. In addition, when noncontingent deliverables are sold with upfront license rights, the license rights do not represent the culmination of a separate earnings process. As such, we account for the license and the noncontingent deliverables as a single combined unit of accounting. In such instances, the license revenue in the form of nonrefundable upfront payments is deferred and recognized over the applicable relationship period, which historically has been the estimated period of our substantive performance obligations or the period the rights granted are in effect.

We will recognize clinical and development, regulatory, and sales milestone payments as revenue when earned if they are substantive and we have no ongoing performance obligations related to the milestone payment. A milestone payment is considered substantive if it (1) is commensurate with either our performance to achieve the milestone or the enhanced value of the delivered item as a result of a specific outcome from our performance to achieve the milestone, (2) relates solely to past performance, and (3) is reasonable relative to all of the deliverables and payment terms, including other potential milestone consideration, within the arrangement.

Royalties earned on product sales, if any, are recognized based on contractual terms of the agreement when reported sales are reliably measurable and collectibility is reasonably assured, provided that there are no performance obligations then remaining. To date, none of our product candidates have been approved and, therefore, we have not earned any royalty revenue from product sales.

In the event an agreement was to be terminated and we have no further performance obligations at that time, we would recognize as revenue any portion of the non-refundable upfront payment and other payments that had not previously been recorded as revenue and were classified as deferred revenue at the date of such termination.

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.

Stock-based compensation

We measure stock options and other stock-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.

For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed. At the end of each financial reporting period prior to the completion of the service, the fair value of these awards is re-measured using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

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.

Determination of fair value of common stock

As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors as of the date of each option grant, with input from management, taking into consideration our most recently available third-party valuations of common stock at the time of the grants, as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. Third-party valuations, or valuation reports, were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*.

Our common stock valuation reports were prepared using a market approach, utilizing either the guideline M&A or guideline public company methodologies. Under the guideline M&A methodology, a set of mergers and acquisitions within the biotechnology and pharmaceutical industries for similar stage companies were reviewed and an applicable equity value was selected to apply to the company. Under the guideline public company methodology, the market capitalizations of similar public companies were analyzed and an applicable capitalization for the company was selected on the basis of qualitative and quantitative factors.

For each valuation report, an option pricing allocation method, or OPM, was selected to allocate the total equity value across the various securities outstanding at the time of the valuation. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. These third-party valuations resulted in a valuation of our common stock of $2.01, $13.20 and $13.80 per share as of December 31, 2017, November 30, 2018 and January 31, 2019, respectively.

In addition to considering the results of the valuation reports, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development programs, including the status and results of preclinical studies for our product candidates;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the biopharmaceutical industry and trends within that industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our convertible preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

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

Once a public trading market for our common stock has been established in connection with the closing of this offering, it will no longer be necessary for our board of directors to estimate the fair value of our common stock in connection with our accounting for granted stock options and other such awards we may grant, as the fair value of our common stock will be determined based on the quoted market price of our common stock.

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 prospectus.

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.

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 $103.2 million, or 74.5% of our total assets, at December 31, 2018. Interest income earned on these assets was $1.9 million for the year ended December 31, 2018. Our interest income is sensitive to changes in the general level of interest rates, primarily U.S. interest rates. At December 31, 2018, 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, historical fluctuations in interest income have not been significant for us and we do not expect significant fluctuations in the future. We had no debt outstanding as of December 31, 2018.

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; and as a result of this election, our financial statements may not be comparable to companies that comply with public company effective dates. 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 generally is when we have more than $700 million in market value of our stock held by non-affiliates and we have been a public company for at least 12 months and have filed one annual report on Form 10-K.

Business

Overview

We are a genome editing company dedicated to improving life through our groundbreaking proprietary genome editing platform, “ARCUS.” 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 believe the versatility and breadth of ARCUS support our ability to develop products across the spectrum of biotechnology. We are actively developing product candidates in three innovative and high value areas where we believe our technology has the potential to overcome the limitations of other genome editing technologies: allogeneic CAR T immunotherapy, *in vivo* gene correction, and food. The U.S. Food and Drug Administration, or FDA, recently accepted our investigational new drug, or IND, application for our first gene-edited allogeneic CAR T cell candidate targeting CD19. We are currently screening patients for our planned Phase 1/2a clinical trial in patients with relapsed or refractory, or R/R, B-cell precursor acute lymphoblastic leukemia and R/R non-hodgkin lymphoma and expect to dose our first patient in this trial in April 2019. We believe this trial will be the first clinical investigation of an allogeneic CAR T therapy for non-hodgkin lymphoma. We believe our proprietary, one-step engineering process for producing allogeneic CAR T cells at large scale in a cost-effective manner will enable us to overcome the fundamental challenges of manufacturing that have limited the CAR T field to date.

Our Pipeline

Allogeneic CAR T immunotherapy

We believe that we have developed a transformative allogeneic chimeric antigen receptor, or 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.

We have used the qualities of ARCUS to develop a one-step cell engineering process for allogeneic CAR T cells that is designed to rapidly yield a consistent cell product at a significantly lower cost than autologous CAR T cell therapies. 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 amended, with Baxalta (now Shire Plc), which we refer to as the Servier Agreement. This agreement was assigned to Les Laboratoires Servier, or Servier, in connection with Servier’s acquisition of Shire’s oncology business in August 2018. 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 by Baxalta at the inception of the

agreement and the remaining five of which may be selected by Servier over the first four years 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 targeting the well-validated tumor target CD19 and is being developed for acute lymphoblastic leukemia, or ALL, and non-hodgkin lymphoma, or NHL. CD19 is a protein that is expressed on the surface of B cells. Our IND for PBCAR0191 was accepted by the FDA in November 2018. We are currently screening patients for our planned Phase 1/2a clinical trial in patients with R/R B-cell precursor ALL and R/R NHL and expect to dose our first patient in this trial in April 2019. We expect to report interim data results from this trial in early 2020. The FDA has granted PBCAR0191 orphan drug designation for the treatment of ALL. We are also in preclinical development of CAR T cell therapies targeting the tumor antigens CD20, BCMA, and CLL-1. We expect to submit an IND to the FDA for our CD20 product candidate in the fourth quarter of 2019 and for each of our BCMA product candidate and our CLL-1 product candidate in 2020.

***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 are advancing a deep portfolio of diverse programs toward *in vivo* efficacy and toxicity studies. We are generating a significant large animal dataset that we believe will 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 two 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 September 2018, we announced a collaboration with Gilead Sciences, Inc. to co-develop an ARCUS-based product candidate that is designed to cure chronic Hepatitis B infection. We intend to submit an IND to the FDA in 2020 for this product candidate. We are also in the discovery stage for other *in vivo* indications: familial amyloid polyneuropathy, primary hyperoxaluria, hemophilia A, retinitis pigmentosa, lipoprotein lipase deficiency and familial hypercholesterolemia. We intend to select an indication and target for our next *in vivo* product candidate in the first half of 2019.

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 pre-breeding materials in collaboration with leading food producers. Pre-breeding material is a gene edited crop intermediate that the collaborating partner can integrate into their breeding program and use in producing new crop varieties. We believe we have the most in-depth experience in crop genome editing in the industry. 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-based 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. Prior to commercialization of any of our food product candidates, we must complete greenhouse studies and three 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. Over half of our team of Precisioneers have advanced degrees, including 48 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 and commercial capabilities that provide control and oversight of our product candidates from discovery through commercialization.
- **Accelerate advancement of our first four allogeneic CAR T immunotherapy product candidates while investing in the research and development of additional allogeneic CAR T programs.** We believe that we have developed the first allogeneic CAR T cell manufacturing platform capable of producing drug product at scale today. We have selected four validated CAR T cell targets that we believe offer the greatest chance of clinical success for our initial product candidates, which we intend to rapidly advance into clinical development. In November 2018, the FDA accepted the IND for our lead CAR T cell product candidate targeting CD19. We are currently screening patients for our planned Phase 1/2a clinical trial in patients with R/R B-cell precursor ALL and R/R NHL and expect to dose our first patient in this trial in April 2019.
- **Advance *in vivo* genetic correction programs into human clinical trials.** In our preclinical studies, we observed the high-efficiency and tolerability of *in vivo* genome editing in a non-human primate, 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 intend to build 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 large animal studies, we intend to advance a subset of these programs to human clinical trials.

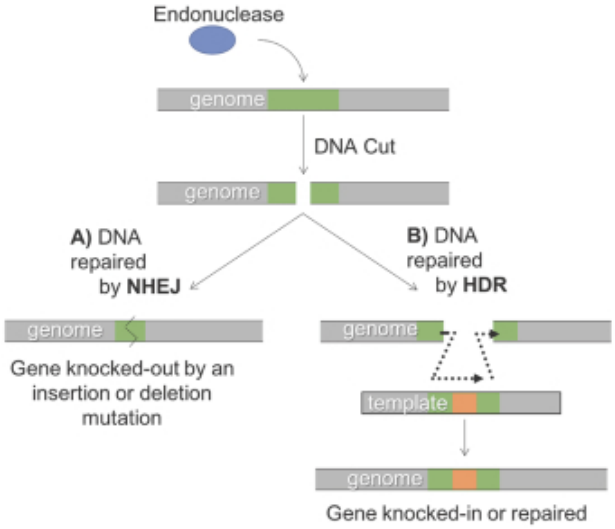
- **Build a food business focused on developing products designed to improve human health and respond to the impacts of climate change.** We believe that rapidly changing consumer preferences and food insecurity resulting from population growth and climate change will drive significant demand for genome-edited 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 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.

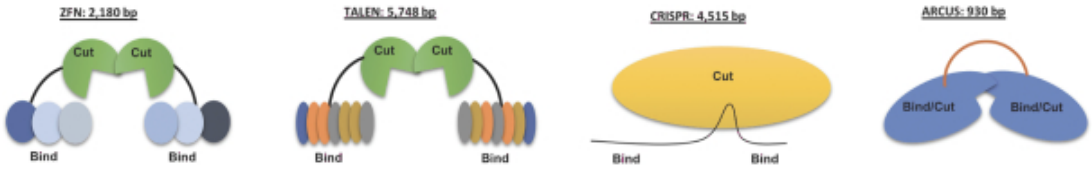
Our approach to genome editing

We are pioneers in the field of genome editing and have extensive experience with a breadth of genome editing technologies. Our Precision 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

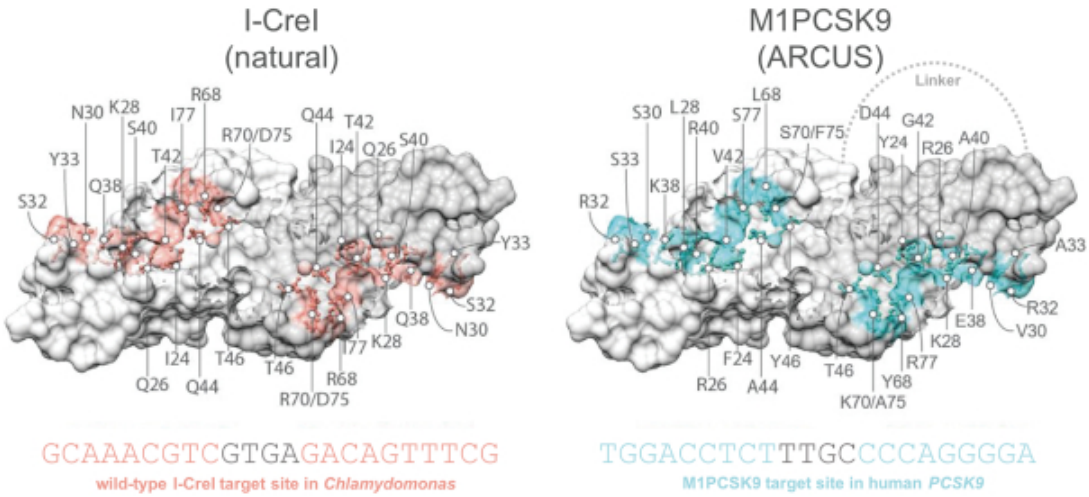
ARCUS is a collection of protein engineering methods that we developed specifically to re-program the DNA recognition properties of I-CreI. In nature, the I-CreI endonuclease recognizes and cuts a DNA sequence in the genome of algae. To apply I-CreI to genome editing in other cells or organisms, we must 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, 2018, we have obtained U.S. patents with

claims directed to three ARCUS nucleases as compositions of matter, and currently claim over 250 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.



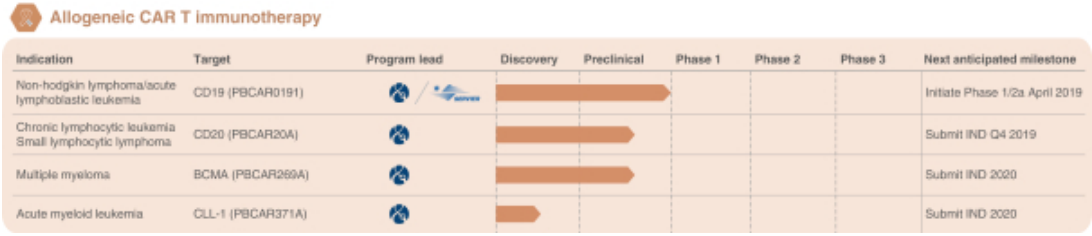
Since creating an ARCUS nuclease requires such extensive reengineering of I-CreI, it is, generally, an iterative process that involves multiple cycles of design and testing. We can typically produce a first-generation ARCUS nuclease in seven weeks. First-generation nucleases are suitable for research 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 allogeneic CAR T cell immunotherapies. A key to the success of this platform is a 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 manufacture CAR T cell product candidates rapidly, at large scale and with greater consistency than currently marketed CAR T cell therapies. 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

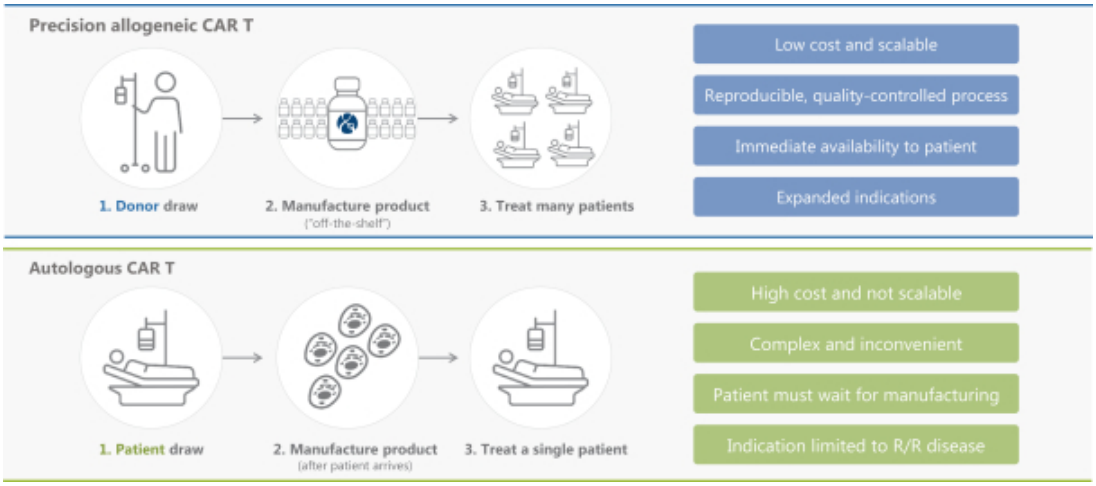
CAR T cell therapy is a form of cancer immunotherapy that uses a patient’s immune system to kill cancer cells. T cells are a component of the immune system that can distinguish pathogen-infected or tumor cells from healthy cells and kill them. Recognition of pathogen-infected cells or tumor cells occurs 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 cells 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 that 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 of low T cell numbers and poor 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 CAR T cells can take several weeks, there is a significant delay in treating what can often be very aggressive tumors. 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 CAR T cell manufacturing process is complex and expensive. In the case of an autologous therapy, the process 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, which we expect will 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 graft versus host disease, or 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 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. These subsets are distinguished by the unique combination of proteins they express on their cell surface, which is described as their “phenotype.”

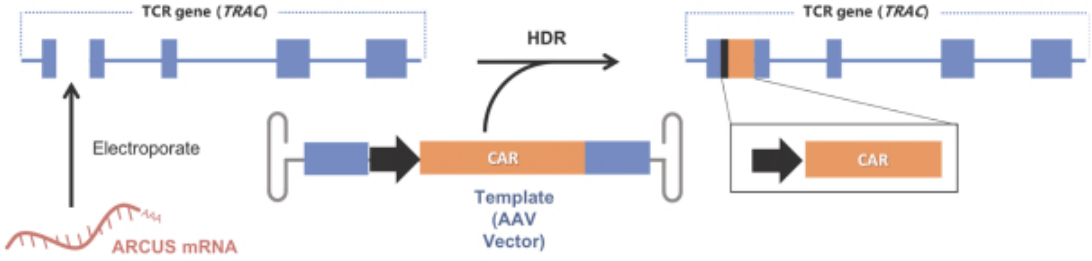
Understanding what phenotypes of T cells are best for a CAR T cell therapy is important, as is the ability to maintain the stability of those phenotypes throughout the manufacturing process. Depending on growth conditions, phenotypes of T cells may change over the course of a manufacturing run, and the final product may not be the desired mix of T cell subtypes.

- **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. If an allogeneic CAR T cell therapy cannot be manufactured at large scale, it has few advantages over an autologous therapy. While generating allogeneic CAR T cells at lab scale (a few million cells) is 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

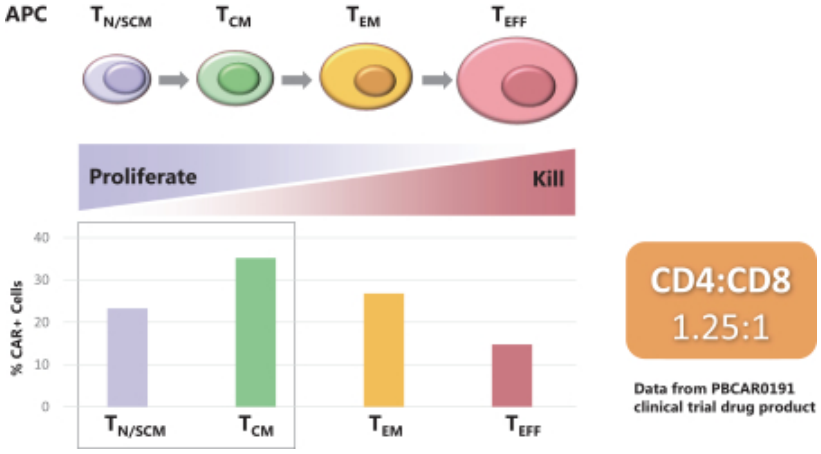
We have used the qualities of ARCUS to create a one-step cell engineering process for allogeneic CAR T cells that we believe yields a well-defined cell product in a cost-effective manner. To produce an allogeneic CAR T cell, it is necessary to make two edits to the DNA of T cells from a healthy donor. 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. Precision 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.

One-step engineered allogeneic CAR T cells

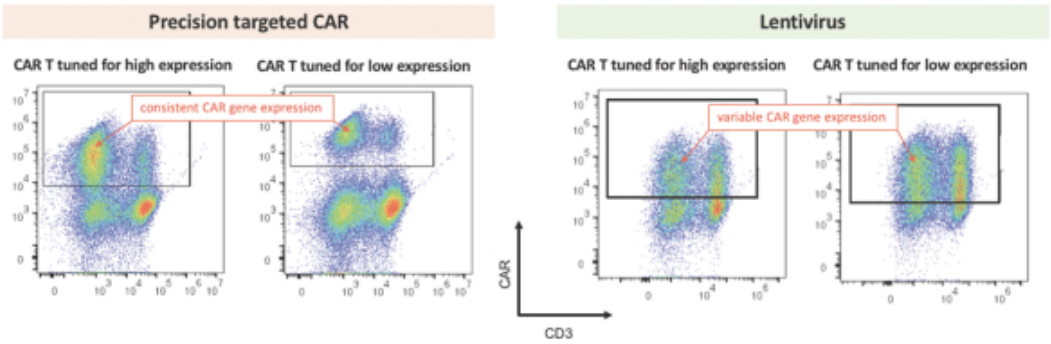


We believe that our one-step engineering approach, and the differentiated attributes of the ARCUS nucleases used to implement it, will overcome many of the critical challenges associated with allogeneic CAR T cell production as follows:

- **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 proliferation 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 the selected phenotype throughout the CAR T manufacturing process. Importantly, our one-step genome editing approach helps minimize 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 phenotype data from PBCAR0191 CAR T cells that were produced as anticipated drug product for our planned Phase 1/2a clinical trial in patients with R/R B-cell precursor ALL and R/R NHL. The drug product comprises mostly naïve ($T_{N/SCM}$) and central memory (T_{CM}) T cells in a CD4:CD8 ratio of 1.25:1.



- **Consistency.** By targeting the 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. 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. 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, and our best manufacturing runs have yielded over one hundred doses of drug product at a dose of 1.0 x 10^6 CAR T cells/kg, which is one of the expected dose levels in our planned Phase 1/2a clinical trial in patients with R/R B-cell precursor ALL and R/R NHL. The table below summarizes results from our last three full-scale manufacturing campaigns, each of which occurred in the last six months and produced a GMP batch of PBCAR0191 to support this planned trial.

Batch name	Product	Total CAR T cell yield	# vials frozen (60M CAR T cells/vial)
CTM1	PBCAR0191 (GMP)	15.0e9	130
CTM2	PBCAR0191 (GMP)	9.6e9	114
CTM3	PBCAR0191 (GMP)	8.3e9	100

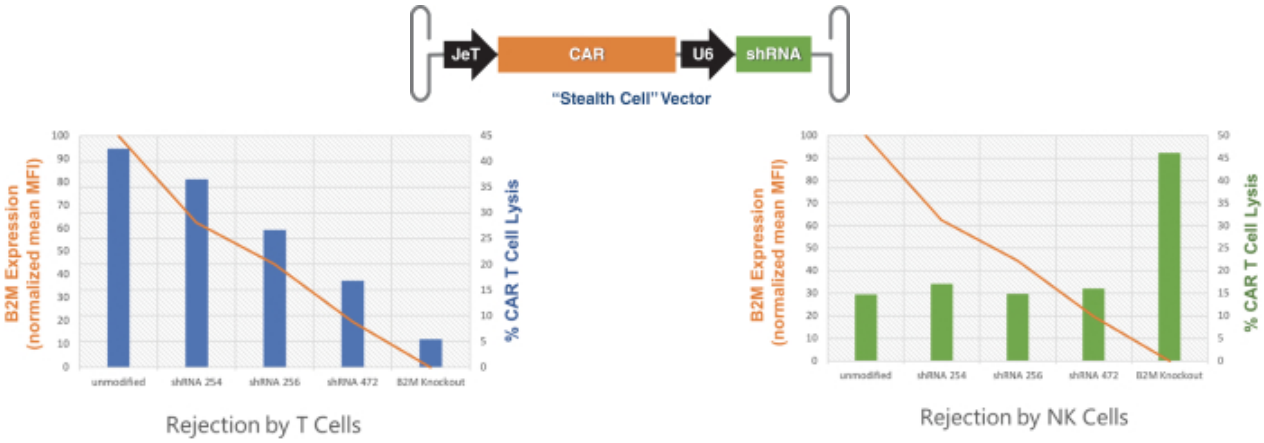
In order to maximize the potential of our CAR T cell platform, we have developed extensive in-house capabilities to support the entire process, from discovery to manufacturing, including:

- A fully human antibody platform for the production of novel CAR binding domains.

- A proprietary collection of costimulatory signaling domains that, if incorporated into a CAR, induce the cell to multiply in response to exposure to cancer cells.
- A high-throughput method for screening new CARs to evaluate their cancer killing activity and target specificity.
- ARCUS for knocking genes out or in to optimize the genetics of our CAR T cells.
- An in-house adeno-associated virus, or AAV, platform for the production of CAR-encoding AAV vectors.
- An in-house mRNA platform for the production of ARCUS-encoding mRNA.
- An in-house animal facility with real-time tumor imaging capabilities.
- Proprietary cytometry panels, potency assays and other bioanalytics for product quality control and release.
- Proprietary manufacturing process for large-scale production of GMP CAR T cells.
- In-house GMP manufacturing facility expected to be completed in the second half of 2019.

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 lympho-depleting drugs such as cyclophosphamide or fludarabine, which significantly 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 receiving our CAR T treatments. Nonetheless, to help mitigate this risk, we intend to evaluate multiple lymphodepletion regimens in our planned Phase 1/2a clinical trial of PBCAR0191 in patients with R/R B-cell precursor ALL and R/R NHL. Standard cyclophosphamide/fludarabine preconditioning is optimized for autologous CAR T but higher concentrations of the drugs have been delivered safely to patients. Therefore, in the event that we observe PBCAR0191 CAR T cell rejection following standard lymphodepletion, we plan to switch to a more intense cyclophosphamide/fludarabine preconditioning protocol. If this approach is still not sufficient to enhance CAR T cell persistence, we plan to incorporate an additional piece of our technology that we call "stealth cell" into the 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. 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. 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. We are currently developing stealth cell versions of our anti-CD19, anti-CD20 and anti-BCMA CAR T vectors.



Our allogeneic CAR T immunotherapy pipeline

We plan to leverage our CAR T cell platform to develop product candidates against validated CAR T cell targets in the near term. By focusing on vetted 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. In parallel to advancing product candidates for validated CAR T cell targets, we are performing early-stage research on more challenging solid tumor targets for which the quality and efficiency of the genome editing is expected to be critical for success. Therefore, we expect that we will gradually shift from a focus on validated liquid tumor targets to more challenging solid tumor targets.

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

- **PBCAR0191**. We are developing PBCAR0191 as an allogeneic anti-CD19 CAR T cell product candidate for the treatment of R/R B-Cell precursor ALL and R/R NHL. 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 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 and up to five additional unique antigen targets selected by Servier.

  Our accepted IND for PBCAR0191 included data from three preclinical studies in mice aimed at establishing therapeutic efficacy. The first of these studies was an *in vitro* potency assessment. In this study, the potency of PBCAR0191 CAR T cells was evaluated by measuring cell proliferation, cytotoxic killing, and production of effector cytokines in response to co-culture with CD19+ or CD19- target cells in mice. PBCAR0191 CAR T cells generated from three different donors were observed to proliferate in response to stimulation by CD19+ target cells including Raji (human Burkitt lymphoma), NALM/6 (human acute lymphoblastic leukemia) and K19 (K562 myelogenous leukemia cells transfected to express human CD19) at a wide range of doses (effector to target ratios ranging from 10:1 to 1:10). These observations show that, in this study, PBCAR0191 cells became activated by and killed CD19+ cells at a wide range of cell doses. In this study, we observed that PBCAR0191 cells did not proliferate in response to cells that lack CD19 (co-culture with gene-edited CD19 negative NALM/6 tumor targets or CD19 negative cell lines of myelogenous leukemia or histiocytic lymphoma). Further, we observed T cell receptor knockout control T cells generated from the same donors did not proliferate in response to CD19+ target cells.

  We further evaluated PBCAR0191 in a pair of *in vivo* studies in mice. As shown below, PBCAR0191 was observed to prolong survival in mouse models of leukemia and lymphoma at multiple doses. The pharmacokinetics of PBCAR0191 were evaluated by counting CAR T cells in the blood, marrow, or spleen during the lymphoma study. PBCAR0191 was observed to be well-tolerated in these studies and no adverse events were observed.

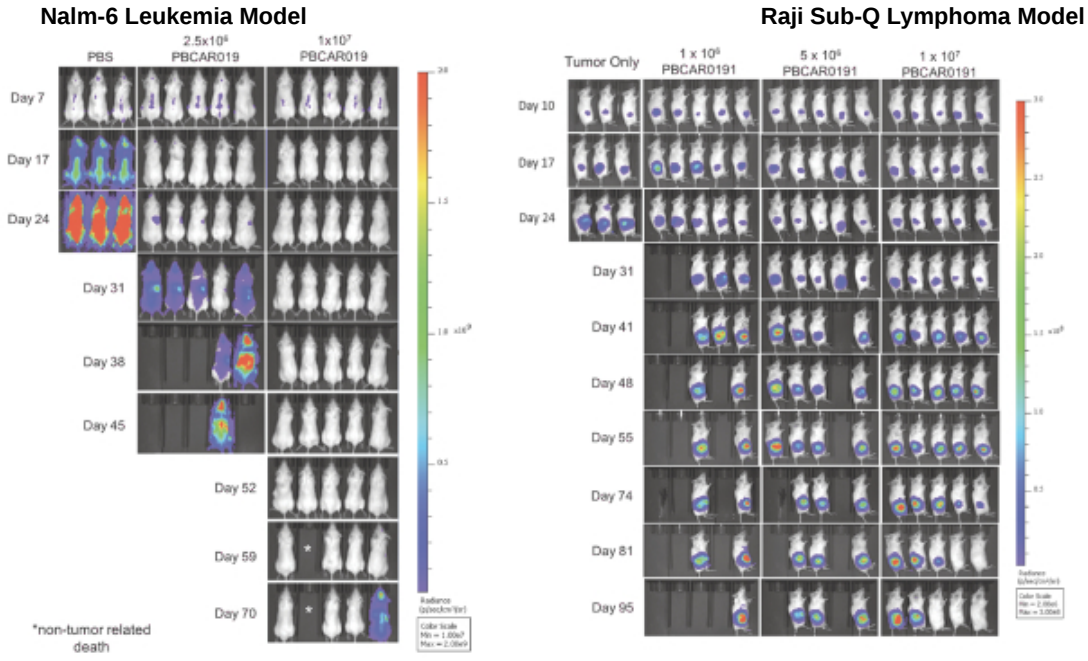
  We have also assessed the safety of PBCAR0191 in four preclinical studies in mice. First, the potential of PBCAR0191 to elicit GvHD was assessed in an *in vitro* study in which we observed that gene-edited PBCAR0191 cells, unlike natural T cells, showed only a minimal amount of proliferation when co-cultured with dendritic cells from an unrelated donor, suggesting that PBCAR0191 cells do not appear capable of killing CD19- cells from a different person and will not be expected to elicit GvHD as a result.

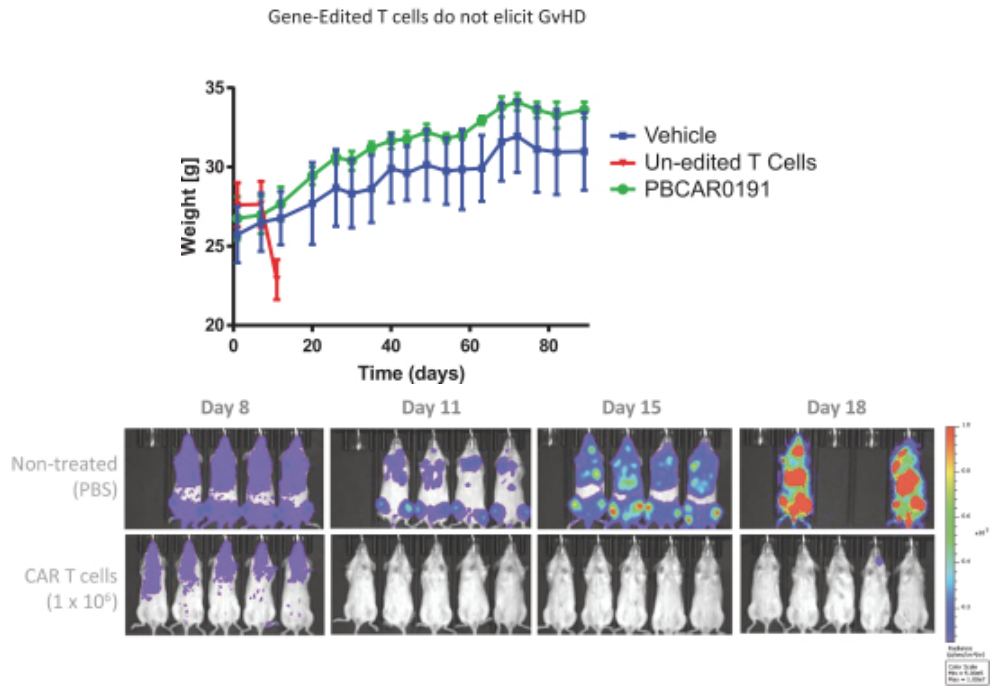
  The potential for GvHD was further assessed *in vivo* in a mouse xenograft model. As shown below, $3x10^7$ PBCAR0191 cells (or $3x10^7$ natural peripheral blood mononuclear cells) were infused into an immunodeficient mouse. Mice were monitored for weight loss and survival. In this study, we observed that PBCAR0191-treated mice gained weight at the same rate as the control group and were healthy for the duration of the study, whereas the peripheral blood mononuclear cell-injected animals lost weight and would not have survived the study.

  The third safety study was a karyotype analysis in mice. No clonal chromosomal abnormalities were observed in 100 metaphase spreads from three different donors, showing that PBCAR0191 cells did not have a high frequency of chromosome abnormalities that may cause tumorigenesis in this study.

  Finally, the potential for tumorigenicity was evaluated using an interleukin, or IL-2 independent growth assay. IL-2 independent growth is a standard test for T cell tumorigenesis. PBCAR0191 cells produced from three different donors continued to proliferate when IL-2 was added to the culture media with a decline in proliferative capacity observed in excess of ten days. In contrast, PBCAR0191 cells cultured in the absence of exogenous IL-2 did not exhibit continued proliferation, and by 14 days of culture in the absence of IL-2 viable

PBCAR0191 cells could no longer be detected in the sample. Thus, PBCAR0191 cells were not observed to be tumorigenic in this study. Taken together, we believe that these studies support the further development of PBCAR0191.



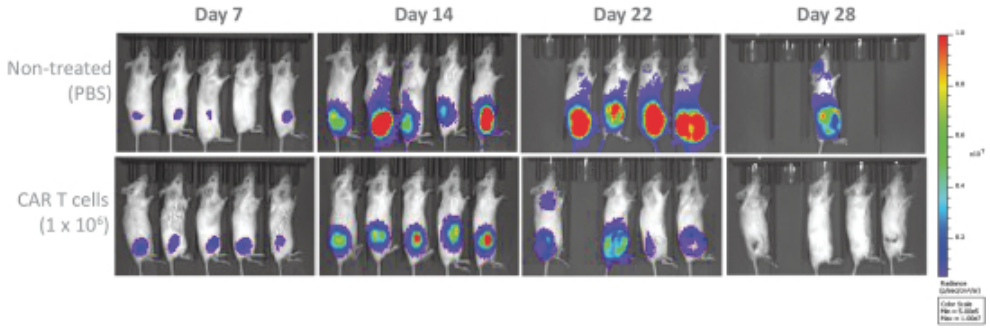


We are currently screening patients for our planned Phase 1/2a clinical trial in patients with R/R B-cell precursor ALL and R/R NHL and expect to dose our first patient in this trial in April 2019. The primary objective of this trial is to evaluate the safety and tolerability of PBCAR0191, as well as to determine the maximum tolerated dose. Secondary objectives will include evaluating the anti-tumor activity of PBCAR0191. We will also evaluate the expansion, trafficking and persistence of PBCAR0191 in this trial. We expect to enroll a total of 9-18 patients in the Phase 1 portion of this trial in both the ALL and the NHL cohorts and we will investigate up to three dose levels: 3.0 x 10^5 cells/kg, 1.0 x 10^5 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 will be conducted at four clinical sites across the United States. We expect to report interim data results from this trial in early 2020.

- **PBCAR20A.** We are developing PBCAR20A as an allogeneic anti-CD20 CAR T cell product candidate for the treatment of 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 an established target for cancer treatment and several CD20-targeted therapies, such as the monoclonal antibody Rituxan, have long histories of clinical success. Because CD19 and CD20 are expressed on similar cell types, PBCAR20A will also be evaluated as an option for leukemia/lymphoma patients who relapse with CD19-negative disease following autologous anti-CD19 CAR T failure. Success in this patient population would potentially enable a combination product comprising both PBCAR0191 and PBCAR20A. We have selected a development candidate for our anti-CD20 CAR T cell product and IND-enabling efficacy and toxicology studies are underway.

  We have conducted a preclinical study in PBCAR20A in mice to measure 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 9:1). 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 x 10^6 and 5 x 10^6 cells per mouse), which we believe supports further development. PBCAR20A was observed to be well-tolerated in this study.

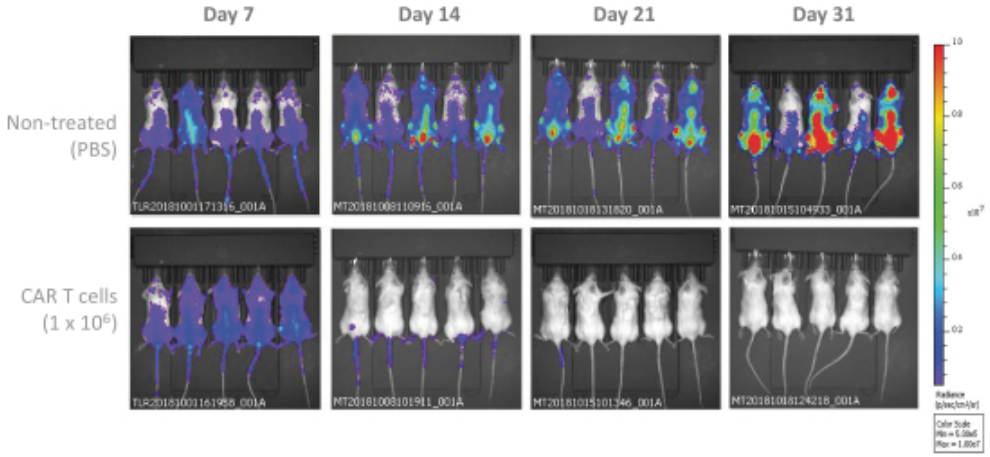


  We anticipate submitting an IND to the FDA for PBCAR20A in the fourth quarter of 2019 and commencing a Phase 1 open-label, multi-center, dose escalation clinical trial in patients with R/R CLL.

- **PBCAR269A.** We are developing PBCAR269A as an allogeneic anti-BCMA CAR T cell product candidate for the treatment of 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. We have selected a development candidate for our anti-BCMA product.

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 (human multiple myeloma) 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.

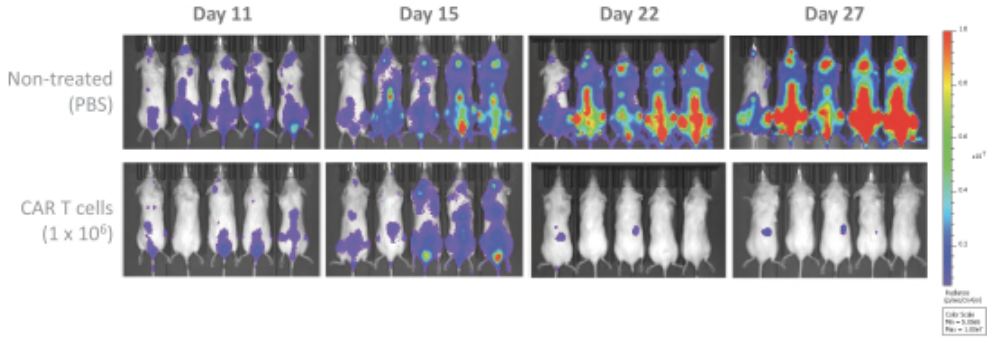
We also evaluated the potency of PBCAR269A *in vivo*. As shown below, PBCAR269A was observed to prolong survival in a mouse model of multiple myeloma, which we believe supports further development. PBCAR269A was observed to be well-tolerated in this study.



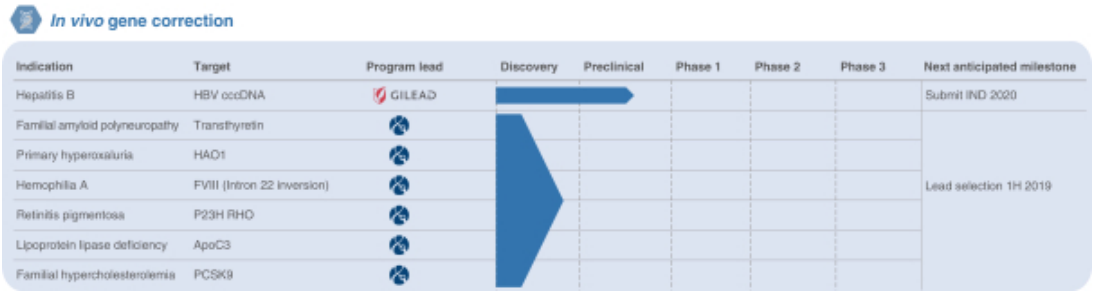
We anticipate submitting an IND to the FDA for PBCAR269A in 2020 and commencing a Phase 1 open-label, multi-center, dose-escalation clinical trial in patients with R/R multiple myeloma.

- **PBCAR371A.** We are developing PBCAR371A as an allogeneic anti-CLL-1 CAR T cell product candidate for the treatment of acute myeloid leukemia, or AML. CLL-1 is a protein that is expressed on myeloid cells, including many AML cancer cells. We believe AML represents a significant unmet need.

We are currently evaluating multiple anti-CLL-1 therapeutic candidates for *in vitro* and *in vivo* potency in mice to identify a candidate for preclinical development. As shown below, multiple candidates have already been identified that efficiently kill the AML cell line HL-60 *in vitro* and in mice and have been observed to be well tolerated. We anticipate submitting an IND to the FDA for PBCAR371A in 2020 and commencing a Phase 1 open-label, multi-center, dose-escalation clinical trial in patients with R/R AML.



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.

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.

A second platform gene therapy approach, RNA interference, or RNAi, has been shown to be an effective treatment strategy for many gain-of-function genetic disorders. These therapies usually take the form of a small-interfering RNA, or siRNA, which is a short piece of synthetic RNA that can "silence" or partially inactivate a deleterious gene if it is delivered to a cell in sufficient quantities. Therapeutic siRNA is most frequently used to silence genes with gain-of-function mutations that are expressed in the liver. This is because the siRNA molecules can be delivered efficiently to liver cells following IV infusion using a variety of different delivery approaches. Like AAV-based gene therapy, the primary limitation of RNAi approaches is that they lack permanence. siRNA drugs have a limited lifetime and, therefore, must be administered repeatedly for the life of the patient in order to be effective. While longer half-life siRNA drugs are showing persistence for up to six months, we believe there is a need for therapeutic options that untether the patient from regular drug treatments by addressing the underlying cause of the disease.

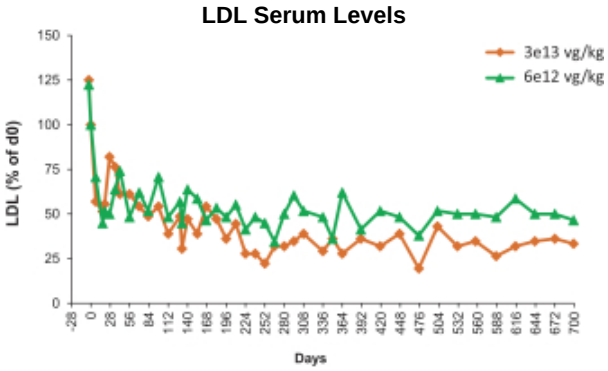
Our approach to* in vivo *gene correction

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 enumerated 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 delivery technologies suitable for the delivery of genome editing endonucleases 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 eye and liver, 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 a good deal of 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.



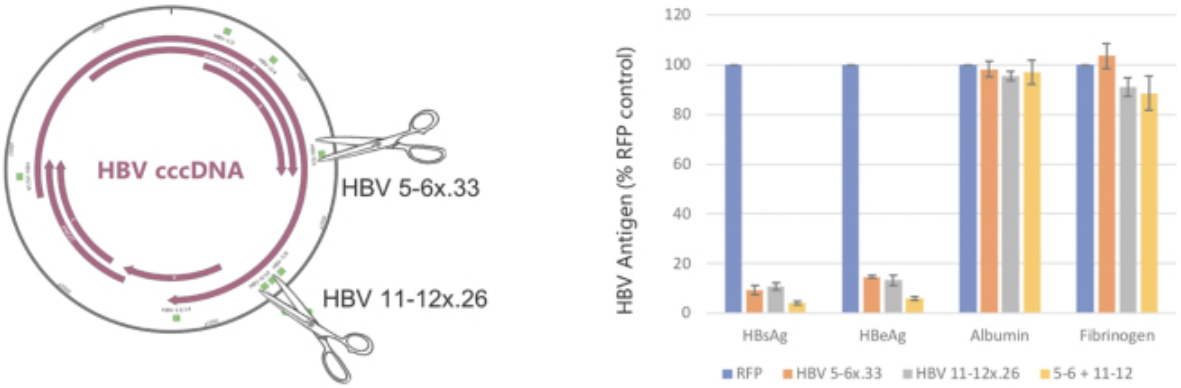
We believe that establishing collaborations with other groups that have domain expertise and access to the most relevant animal models will be important to advancing our *in vivo* gene correction platform, and we have

entered into a number of collaborations and licensing agreements with third parties to help us advance our *in vivo* editing portfolio. In particular, in September 2018 we announced a sponsored research agreement with the Orphan Disease Center at the University of Pennsylvania. This organization, led by Dr. Jim Wilson, is dedicated to curing rare genetic diseases and has access to unique expertise and resources, including AAV vector production and non-human primate models. Several of our liver-directed projects are being conducted in collaboration with Dr. Wilson under this agreement.

Hepatitis B program

In September 2018, we announced a partnership 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 virus DNA, either integrated or cccDNA, from infected liver cells. We intend to submit an IND to the FDA in 2020 for this product candidate.

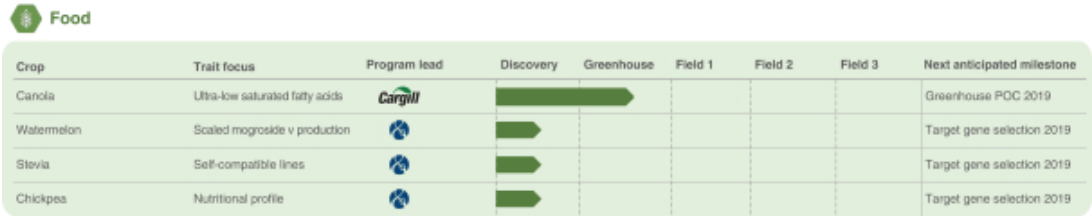
In preclinical studies, we developed a pair of ARCUS nucleases called “HBV 5-6x.33” and “HBV 11-12x.26” that recognized and cut conserved DNA sequences in the Hepatitis B genome. We observed that these nucleases, if administered to HBV-infected primary human hepatocytes, selectively eliminated virus DNA from the cells. As shown below, this resulted in a loss of the virus-produced antigens HBsAg and HBeAg from the culture without affecting the expression of normal hepatocyte genes.



We believe that our proprietary ARCUS genome editing platform, strong collaborations and a disciplined approach to preclinical development that emphasizes large animal studies will help position us to unlock the enormous potential of therapeutic *in vivo* editing.

We are also in the discovery stage for other *in vivo* indications: familial amyloid polyneuropathy, primary hyperoxaluria, hemophilia A, retinitis pigmentosa, lipoprotein lipase deficiency and familial hypercholesterolemia. We intend to select an indication and target for our next *in vivo* product candidate in the first half of 2019.

Our food platform



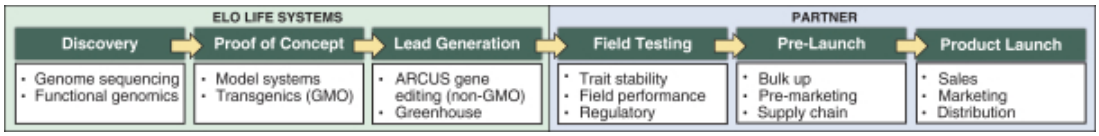
Technology-centric solutions to meet changing demands in food and agriculture

The total global food and agriculture market, estimated to be at $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. Elo 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, the 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. We expect to commence Field 1 trials in 2019.

Low-calorie sweeteners from stevia and monk fruit

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. 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.

Over the past decade, stevia has emerged as a preferred low-calorie sugar substitute. However, stevia is subject to a number of disadvantages, including undesirable aftertaste, complex biology, unsustainable production practices and supply chain issues. Self-incompatibility, or a genetic condition that prevents self-fertilization and promotes outcrossing for flowering plants, has been identified as one of the main impediments to improving stevia as a crop. We are working to produce self-compatible stevia lines suitable for breeding and domestication. We believe that changing this property of stevia will enable new breeding strategies that will allow Elo and its partners to rapidly domesticate and improve the crop.

We believe that the best low calorie sweetener comes from monk fruit. The monk fruit compound mogroside V is approximately 300 times sweeter than cane sugar and has been identified as an excellent alternative to cane sugar and stevia. Monk fruit is a low biomass species that grows exclusively in southeast Asia and is frequently harvested and processed using questionable labor practices. This makes mogroside V expensive, difficult to obtain and controversial. However, monk fruit is closely related to watermelon and the genes encoding all components of the mogroside V pathway are present, though inactive, in watermelon. We are currently collaborating with a large beverage company to re-activate the latent mogroside V pathway in watermelon to produce this high value metabolite in a crop that is readily cultivated across North America and Europe.

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 November 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 improved protein and nutritional profiles in legumes 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.

Citrus varieties resistant to Citrus Greening Disease

Citrus greening is one of the most serious citrus plant diseases in the world. Rising global temperatures have shortened the life cycle of the insect pests that carry the citrus greening pathogen and enabled rapid spread of the disease to most citrus producing areas of the world. Infected trees produce fruits that are unsuitable for sale as produce, and once a tree is infected, there is no cure. In the state of Florida alone, the economic impacts of citrus greening since the disease was first detected in 2005 were estimated at a loss of more than $8 billion.

At Elo, we are leveraging recent insights into citrus-pathogen interactions to generate novel citrus varieties with resistance to citrus greening. Our citrus greening program is designed to utilize ARCUS nucleases to disrupt plant-pathogen interactions to, we believe, generate non-GMO, citrus greening resistant trees. Citrus greening is one of many examples of how the food industry was caught off-guard by the impact of global warming.

Manufacturing

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. 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.

We are building strong internal scientific process development and manufacturing capabilities, including investing in building a cGMP-compliant manufacturing facility to support our therapeutic product development platforms. We believe that having internal manufacturing capacity and expertise will be a competitive advantage that enables enhanced control over process development timelines, costs and intellectual property.

We are in the process of building a cGMP-compliant manufacturing facility. We have leased approximately 17,300 feet of space for our manufacturing facility at a location approximately seven miles from our headquarters in Durham, North Carolina. We expect to 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. We expect that our manufacturing facility will leverage single use, disposable, closed system operations aligned to our technology platforms to ensure both flexibility and cost effectiveness. The initial scope will be for preclinical through Phase 1/2a manufacturing. We expect the facility to be operational in the second half of 2019.

License and collaboration agreements

Servier

In February 2016, we entered into the Servier Agreement with Baxalta (now Shire). This agreement was assigned to Servier in connection with Servier's acquisition of Shire's oncology business in August 2018. 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 by Baxalta at the inception of the agreement and the remaining five of which may be selected by Servier over the first four years 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 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 "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 Cellectis S.A., CRISPR Therapeutics, AG, Editas Medicine, Inc., Intellia Therapeutics, Inc. and Sangamo 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 development and commercialization will face substantial competition from those focusing on immunotherapy solutions. Several companies, including Novartis Pharmaceuticals Corp. and Gilead Sciences, Inc., 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 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, where patent protection is available. 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 “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, 2018, we have an exclusive license from Duke University under 12 issued U.S. patents and two pending U.S. patent applications. In addition, as of December 31, 2018, we own 16 issued U.S. patents, 12 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 two 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 each of the United States, 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, two issued patents in each of Europe and Japan, and one issued Australian patent. 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 one issued patent in the United States, and two issued patents in each of Europe and Australia. This family also includes two pending patent applications in the United States and one pending patent application in 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.

Immunotherapy patent families

We own nine 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, 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 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, if issued, will have a standard expiration date of October 5, 2036, subject to potential extensions.

The third family includes a pending provisional patent application in the United States. That provisional 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 12, 2039, subject to potential extensions.

The fourth family includes a pending PCT international patent application. That PCT patent application includes 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 a pending PCT international patent application. That PCT patent application includes 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 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. That PCT patent application includes 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 have a standard expiration date of May 8, 2038, subject to potential extensions.

The eighth family includes a pending PCT international patent application. That PCT patent application includes 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 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.

Hepatitis B virus gene therapy patent families

We own two patent families that are directed to gene therapy for Hepatitis B Virus.

The first family includes a pending PCT international patent application. That PCT patent application includes 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 U.S. provisional patent application. That provisional patent application includes 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 12, 2039, subject to potential extensions.

Hemophilia A gene therapy patent families

We own two patent families that are directed to gene therapy for Hemophilia A.

The first family includes 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 recognition sites in a mutant Factor VIII gene, (2) nucleic acids and vectors encoding such engineered meganucleases, (3) pharmaceutical compositions comprising such nucleic acids or meganucleases, and (4) methods for treating Hemophilia A using such meganucleases, nucleic acids and/or pharmaceutical

compositions. 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. That PCT patent application includes claims directed to (1) engineered meganucleases that recognize and cleave non-methylated recognition sites in a mutant Factor VIII gene, (2) nucleic acids and vectors encoding such engineered meganucleases, (3) pharmaceutical compositions comprising such nucleic acids or meganucleases, and (4) methods for treating Hemophilia A using such meganucleases, nucleic acids and/or pharmaceutical compositions. Patents in this family, if issued, will likely have a standard expiration date of November 1, 2038, subject to potential extensions.

Other patent families

We own a pending PCT international patent application directed to engineered meganucleases and methods of treatment targeting the PCSK9 gene, which is associated with familial hypercholesterolemia. Patents in this family, if issued, will have a standard expiration date of April 20, 2038, subject to potential extensions.

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

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

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

We own a pending United States provisional patent application directed to the genetic modification of the hydroxyacid oxidase 1 gene for the treatment of primary hyperoxaluria. Patents in this family, if issued, will likely have a standard expiration date of December 21, 2039, subject to potential extensions.

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

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

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

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 two registered trademarks, specifically ARC nuclease and ARCUS, in the United States. In addition, there are two pending applications in the United States for the marks Elo Life Systems and Precision Breeding Technologies. Finally, our international portfolio contains seven registered trademarks around the world for ARC nuclease and ARCUS.

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 had historically been subject to review by the Recombinant DNA Advisory Committee, or the RAC, of the NIH Office of Biotechnology Activities, or the OBA, pursuant to the NIH Guideline. On August 17, 2018, the NIH issued a notice in the Federal Register and issued a public statement proposing changes to the oversight framework for gene therapy trials, including changes to the applicable NIH Guidelines to modify the roles and responsibilities of the RAC with respect to human clinical trials of gene therapy products, and requesting public comment on its proposed modifications. During the public comment period, which closes October 16, 2018, the NIH has announced that it will no longer accept new human gene transfer protocols for review as a part of the protocol registration process or convene the RAC to review individual clinical protocols. These trials will remain subject to the FDA's oversight and other clinical trial regulations, and oversight at the local level will continue as set forth in the 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.

Fast Track designation, priority review and breakthrough therapy 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.

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. 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. federal civil and criminal false claims laws and civil monetary penalties laws, including the civil False Claims Act, which can be enforced through civil whistleblower or qui tam actions, prohibits, 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.

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) 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 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. Third-party payors may limit coverage to specific products on an approved list, or also known as a formulary, which might not include all of the FDA-approved products for a particular indication. 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 agree to offer 50% point-of-sale discounts, which through subsequent legislative amendments, will be increased to 70%, starting in 2019, 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.

Some of the provisions of the Affordable Care Act have yet to be implemented, and there have been legal and political challenges to certain aspects of the Affordable Care Act. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, 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 that is commonly referred to as the “individual mandate.” Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share. Further, the Bipartisan Budget Act of 2018, among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole.” More recently, in July 2018, CMS published a final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment.

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, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals for spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation’s automatic reduction to several government programs. This includes 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, including the BBA, will remain in effect through 2027 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 for pharmaceutical products, some of which are included in the Trump administration’s budget proposal for fiscal year 2019. 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 the process of 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 will require authorization through additional legislation 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.

Facilities

We currently occupy approximately 49,000 square feet of office and laboratory space at our corporate headquarters in Durham, North Carolina under a lease that expires in 2024. This lease provides us the option to lease an additional 20,000 square feet of office space. We also occupy approximately 15,500 square feet of laboratory and office space in Research Triangle Park, North Carolina under a lease that expires in 2026, and we occupy approximately 17,300 square feet of laboratory and office space in Research Triangle Park, North Carolina under a lease that expires in 2026. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Employees

As of December 31, 2018, we had 127 full-time Precisioneers, over half of whom have advanced degrees, including 49 with Ph.D. degrees. Of these full-time employees, 94 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.

Legal proceedings

We are not currently party to any material legal proceedings.

Management

Executive officers and directors

The following table sets forth the name, age and position of each of our executive officers and directors as of the date of this prospectus.

Name	Age	Position
Executive officers		
Matthew Kane	42	President, Chief Executive Officer and Director
Derek Jantz, Ph.D.	43	Chief Scientific Officer and Director
Abid Ansari	41	Chief Financial Officer
Fayaz Khazi, Ph.D.	46	Chief Executive Officer, Elo Life Systems
David Thomson, Ph.D.	58	Chief Development Officer
Non-employee directors		
Robert Adelman, M.D.(1)	56	Director
Raymond Schinazi, Ph.D.(2)(3)	68	Director
Shalini Sharp(1)(2)	44	Director
Tony Yao, M.D., Ph.D.(1)(2)(3)	47	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 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. 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.

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 Key Gene USA. 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 Development Officer since June 2017. Prior to joining us, he served as Senior Vice President Research and Nonclinical Development for Shire plc 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

Robert Adelman, M.D., has served on our board of directors since April 2015. Since 2011, Dr. Adelman has been Managing Partner of venBio Partners LLC, a venture capital firm Dr. Adelman founded in 2011. Dr. Adelman currently serves on the board of directors of Metacrine, Inc., ALX Oncology and TP Therapeutics, Inc. Prior to founding venBio, Dr. Adelman had a seven-year tenure as a Private Equity Partner at OrbiMed Advisors LLC. Dr. Adelman has also previously co-founded a number of biotechnology companies and practiced surgery in New York and New Jersey. Dr. Adelman received a B.A. in biochemistry from the University of California at Berkeley and a M.D. from Yale University, and he completed his residency at Cornell University Medical Center.

We believe that Dr. Adelman's medical background and experience in the venture capital industry, particularly with biotechnology and pharmaceutical companies, qualify him to serve as a member of our board of directors.

Raymond Schinazi, Ph.D., D.Sc., has served on our board of directors since March 2019. Since 1992, Dr. Schinazi has been the Frances Winship Walters Professor of Pediatrics and Director of the Laboratory of Biochemical Pharmacology at Emory University. From November 2014 to February 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. 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 Array BioPharma Inc. and Sutro Biopharma, Inc. and previously served on the board of directors of Agenus, Inc. from May 2012 to June 2018. 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, 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 B.Sc. 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.

Board composition and election of directors

The primary responsibility of our board of directors is to provide oversight, strategic guidance, counseling and direction to our management. Our board of directors meets on a regular basis and additionally as required. Our board of directors currently consists of six directors. The members of our board of directors were elected in compliance with the provisions of our amended and restated certificate of incorporation in effect at such time and an amended and restated voting agreement, which we refer to as our voting agreement, among us and certain of our stockholders. Our voting agreement will terminate upon the closing of this offering and none of our stockholders will have any special rights regarding the election or designation of members of our board of directors following the closing of this offering. See "Certain relationships and related party transactions—Voting agreement" for a discussion of our voting agreement.

Director independence

Our board of directors has determined that, of our six directors, Robert Adelman, M.D., 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. There are no family relationships among any of our directors or executive officers.

Classified board of directors

In accordance with our amended and restated certificate of incorporation that will go into effect upon the closing of this offering, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Upon the effectiveness of the registration statement of which this prospectus forms a part, our directors will be divided among the three classes as follows:

- the Class I directors will be Raymond Schinazi, Ph.D. and Matthew Kane, and their terms will expire at our first annual meeting of stockholders following this offering;
- the Class II directors will be Tony Yao, M.D., Ph.D. and Derek Jantz, and their terms will expire at our second annual meeting of stockholders following this offering; and
- the Class III directors will be Robert Adelman, M.D. and Shalini Sharp, and their terms will expire at the third annual meeting of stockholders following this offering.

Our amended and restated certificate of incorporation and amended and restated bylaws that will go into effect upon the closing of this offering will provide that the authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control of our company. Our directors may be removed only for cause by the affirmative vote of the holders of at least two-thirds of our outstanding voting stock entitled to vote in the election of directors.

Role of the board in risk oversight

One of the key functions of our board of directors is informed oversight of our risk management process. Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through our board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure and our audit committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management are undertaken. Our audit committee also monitors compliance with legal and regulatory requirements. Our nominating and corporate governance committee monitors the effectiveness of our corporate governance practices, including whether they are successful in preventing illegal or improper liability-creating conduct. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, our entire board of directors is regularly informed through committee reports about such risks.

Board committees

Our board of directors has established three standing committees—audit, compensation, and nominating and corporate governance—each of which operates under a charter that has been approved by our board of directors. Upon our listing on The Nasdaq Global Select Market, each committee's charter will be available under the Corporate Governance section of our website at www.precisionbiosciences.com. 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 prospectus.

Audit committee

Our audit committee's responsibilities include:

- appointing, approving the compensation of and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- coordinating our board of directors' oversight of our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- establishing procedures for the receipt, retention and treatment of complaints we receive regarding financial controls, accounting or auditing matters and other matters;
- discussing our risk management policies;
- meeting independently with our internal auditing staff, if any, independent registered public accounting firm and management;
- reviewing on a periodic basis our investment policy;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by SEC rules.

The members of our audit committee are Shalini Sharp, Tony Yao, M.D., Ph.D. and Robert Adelman, M.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 Shalini Sharp, Tony Yao, M.D., Ph.D. and Robert Adelman, M.D. each meet the independence requirements of Rule 10A-3 under the Exchange Act and the applicable Nasdaq rules. Our board of directors has determined that 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.

Compensation committee

Our compensation committee's responsibilities include:

- reviewing and approving, or recommending for approval by the board of directors, the compensation of our CEO and our other executive officers;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation;
- reviewing and discussing annually with management our "Compensation discussion and analysis," to the extent required; and
- preparing the annual compensation committee report required by SEC rules, to the extent required.

The members of our compensation committee are Raymond Schinazi, Ph.D., Shalini Sharp and Tony Yao, M.D., Ph.D. Raymond Schinazi serves as the chairperson of the committee. Our board of directors has determined that Raymond Schinazi, Ph.D., Shalini Sharp and Tony Yao, M.D., Ph.D. are each independent under the applicable Nasdaq rules, including the Nasdaq rules specific to membership on our compensation committee, and is a “non-employee director” as defined in Rule 16b-3 promulgated under the Exchange Act.

Nominating and corporate governance committee

Our nominating and corporate governance committee’s responsibilities include:

- identifying individuals qualified to become board members;
- recommending to our board of directors the persons to be nominated for election as directors and to each board committee;
- developing and recommending to our board of directors corporate governance guidelines, and reviewing and recommending to our board of directors proposed changes to our corporate governance guidelines from time to time; and
- overseeing a periodic evaluation of our board of directors.

The members of our nominating and corporate governance committee are Matthew Kane, Raymond Schinazi, Ph.D. and Tony Yao, M.D., Ph.D. Matthew Kane serves as the chairperson of the committee. Our board of directors has determined that Raymond Schinazi, Ph.D., and Tony Yao, M.D., Ph.D. are each independent under the applicable Nasdaq rules. We are permitted to phase in our compliance with the independent nominating and corporate governance committee requirements set forth by the Nasdaq listing standards as follows: (1) one independent member at the time of listing, (2) a majority of independent members within 90 days of listing and (3) all independent members within one year of listing. Within one year of our listing on The Nasdaq Global Select Market, we expect that Mr. Kane will have resigned from our nominating and corporate governance committee and that any new directors added to the nominating and corporate governance committee will be independent under Nasdaq listing rules.

Compensation committee interlocks and insider participation

No member of our compensation committee is or has been our current or former officer or employee. None of our executive officers served as a director or a member of a compensation committee (or other committee serving an equivalent function) of any other entity, one of whose executive officers served as a director or member of our compensation committee during the fiscal year ended December 31, 2018.

Code of ethics and code of conduct

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. Upon our listing on The Nasdaq Global Select Market, our code of business conduct and ethics will be 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 prospectus.

Executive compensation

This section discusses the material components of our 2018 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;
- Abid Ansari, Chief Financial Officer; and
- David Thomson, Chief Development Officer.

This discussion may contain forward-looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt following the completion of this offering may differ materially from the currently planned programs summarized in this discussion.

Summary compensation table

The following table sets forth information concerning the compensation of our named executive officers for the years ended December 31, 2017 and 2018:

Name and principal position	Year	Salary ($)	Bonus ($)(1)	Option awards ($)(2)	All other compensation($)	Total ($)
Matthew Kane	2018	350,000	157,500	1,068,616	11,016(3)	1,587,131
President and Chief Executive Officer	2017	350,000	124,900	18,041	8,863	501,804
Abid Ansari	2018	250,000	87,500	1,068,616	10,048(5)	1,416,164
Chief Financial Officer(4)						
David Thomson	2018	355,000	124,250	1,367,919	11,000(6)	1,858,169
Chief Development Officer	2017	176,346	176,000	173,178	16,962	542,486

(1) The amounts reported represent bonuses based upon our board’s assessment of the achievement of company and individual performance objectives for 2018, which were paid in January 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 7 to our consolidated financial statements included in this prospectus.

(3) The amount reported includes 401(k) matching contributions by us of $11,000 and tax gross-ups of $16 in connection with nondiscriminatory wellness reimbursements for 2018.

(4) Mr. Ansari was not one of our named executive officers in 2017, and accordingly, compensation information for 2017 is not included in the table above.

(5) The amount reported includes 401(k) matching contributions by us of $10,000 and tax gross-ups of $48 in connection with nondiscriminatory wellness reimbursements.

(6) The amount reported in 2018 represents 401(k) matching contributions by us of $11,000.

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 2017, 2018 and 2019 of our named executive officers:

Name and principal position	2017 Base salary ($)	2018 Base salary ($)	2019 Base salary ($) (1)
Matthew Kane President and Chief Executive Officer	350,000	350,000	523,000
Abid Ansari Chief Financial Officer	235,000	250,000	316,000
David Thomson Chief Development Officer	350,000	355,000	370,000

(1) These amounts reflect base salaries effective upon the effectiveness of the registration statement of which this prospectus forms a part. See "—Employment agreements."

Bonuses

In addition to base salaries, our named executive officers were eligible to receive a cash bonus based on company and individual performance for 2018. Pursuant to the employment arrangements entered into with our named executive officers, during 2018 Mr. Kane was eligible to receive an annual bonus of up to 30% of his base salary; Mr. Ansari was eligible to receive an annual bonus in the discretion of our board; and Dr. Thomson was eligible to receive an annual bonus of up to 35% of his base salary. In January 2019, we paid performance bonuses of $157,500 to Mr. Kane, $87,500 to Mr. Ansari and $124,250 to Dr. Thomson with respect to 2018. Upon the effectiveness of the registration statement of which this prospectus forms a part, Mr. Kane, Mr. Ansari and Dr. Thomson will be eligible to receive an annual bonus of up to 50%, 35% and 35% of their respective base salaries. See "—Employment agreements."

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.

We granted the following stock options to our named executive officers during 2018 under our 2015 Plan, which is described below:

Named executive officers	Stock options granted
Matthew Kane	140,535
Abid Ansari	140,535
David Thomson	187,381

In connection with this offering, we adopted our 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 effective date of our 2019 Plan, we will not make any further grants under our 2015 Plan. However, our 2015 Plan will continue to govern the terms and conditions of the outstanding awards granted under it. For additional information about our 2019 Plan, see "—Incentive plans" below.

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. We have historically matched participants' elective salary deferral contributions to the 401(k) Plan up to 50% of the first 4% of the employee's salary deferred. Matching contributions made by us vest 25% each year and are fully vested after four years. 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 Ansari and Dr. Thomson, 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 2018 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, 2018.

	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
	10,247	13,175(1)	1.18	3/23/2027
	—	140,535(2)	11.98	9/27/2028
Abid Ansari	79,051	61,484(3)	1.20	8/10/2026
	6,148	7,905(1)	1.18	3/23/2027
	—	140,535(2)	11.98	9/27/2028
David Thomson	87,834	146,392(1)	1.18	6/29/2027
	63,709	123,672(2)	11.98	9/27/2028

(1) Award vested as to 25% of the underlying shares on March 24, 2018 with respect to Mr. Kane, March 24, 2018 with respect to Mr. Ansari and May 31, 2018 with respect to Dr. Thomson and will vest in equal installments at the end of each three-month period over the following 36 months, subject to the named executive officer's continued employment with us.
(2) Award vests as to 25% of the underlying shares on September 28, 2019 and in equal installments at the end of each three-month period over the following 36 months for Messrs. Kane and Ansari and vested as to 34% of the underlying shares on October 12, 2018, and will vest in equal installments at the end of each three-month period from September 28, 2019 through September 28, 2021 for Dr. Thomson, in each case subject to the named executive officer's continued employment with us.
(3) Award vested as to 25% of the underlying shares on August 11, 2017 and will vest in equal installments at the end of each three-month period over the following 36 months, subject to the named executive officer's continued employment with us.

Employment agreements

In February 2019, we entered into new 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 for each named executive officer, which is subject to our discretionary review and adjustment in accordance with our policies, procedures and practices as they may exist from time to time provided that no named executive officer's base salary may be decreased unless the decrease is an across-the-board decrease in the base salaries of all senior management employees of our company. See "Summary compensation table—Annual base salaries" above for the base salaries in effect for 2018 and 2019. Each of our named executive officers is also eligible to receive an annual bonus in the discretion of our board. Effective as of the closing of this offering, the employment agreements with each executive officer provide for new terms for base salary and bonus potential. Mr. Kane's annual base salary will be $523,000; Mr. Ansari's annual base salary will be $316,000; and Mr. Thomson's annual base salary will be $370,000. Mr. Kane will be eligible to receive an annual bonus of up to 50% of his base salary, Mr. Ansari will be eligible to receive an annual bonus of up to 35% of his base salary, and Dr. Thomson will be eligible to receive an annual bonus of up to 35% of his base salary. The named executive officers are eligible to participate in all 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 employment agreement further provides for the reimbursement of reasonable and necessary business expenses actually incurred by the named executive officer in performing services for us.

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, or upon shorter notice by us for cause. 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 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, inventions, non-competition and non-solicitation agreement, he will be entitled to receive (1) payment of an amount equal to 12 months of the named executive officer's base salary in the case of Mr. Kane or nine months in the case of Mr. Ansari and Dr. Thomson, paid in substantially similar installments on same payroll applicable to him immediately prior to his separation from service, subject to certain exceptions, 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 the applicable severance period or, if sooner, until comparable coverage is available in connection with subsequent employment. Upon termination of the employment of any of the named executive officers by us for cause or due to death or disability, or termination of employment by a named executive officer other than for good reason, the named executive officer will not be entitled to any additional compensation beyond any earned but unpaid salary or other accrued obligations.

Notwithstanding 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 or 12 months after the occurrence of a change in control, as defined in the employment

agreements, then, subject to his timely executing a release of claims and continuing to comply with obligations under his proprietary information, inventions, non-competition and non-solicitation agreement, then such named executive officer shall be entitled to (1) in the case of Mr. Kane, an amount equal to 18 months of his then current monthly base salary plus 1.5 times his target bonus for the year during which separation occurs, payable in a lump sum, and in the case of Mr. Ansari and Dr. Thomson, 12 months of monthly base salary plus one times their target bonus for the year, payable in a lump sum, (2) reimbursement of the additional costs the executive incurs for continued coverage under our group health insurance under COBRA until, in the case of Mr. Kane, the 18-month anniversary of the executive's separation date, and in the case of Mr. Ansari and Dr. Thomson, the 12-month anniversary of the executive's separation date, or earlier if the executive becomes eligible to receive substantially similar coverage from another source or is no longer eligible to receive COBRA, 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, Mr. Ansari and Dr. Thomson, each named executive officer has agreed to refrain from competing with us or soliciting our employees, in each case, while employed and following the termination of his employment for any reason for a period of one year and has acknowledged our ownership rights in any intellectual property and assigned any such ownership rights to us.

Incentive plans

The following summarizes the material terms of the long-term incentive compensation plan in which our named executive officers will be eligible to participate following the consummation of this offering and our 2015 Plan and 2006 Plan under which we have previously made periodic grants of equity and equity-based awards to our named executive officers and other key employees.

2019 Incentive award plan

In connection with this offering, we adopted and our stockholders approved our 2019 Plan, which became effective upon the effectiveness of the registration statement of which this prospectus forms a part, under which we may grant cash and equity-based incentive awards to eligible service providers in order to attract, retain and motivate the persons who make important contributions to our company. The material terms of our 2019 Plan are summarized below.

Eligibility and administration

Our employees, consultants and directors, and employees and consultants of our subsidiaries, will be eligible to receive awards under our 2019 Plan. Our 2019 Plan will be administered by our board of directors, which may delegate its duties and responsibilities to one or more committees of our directors and/or officers (referred to collectively as the plan administrator below), subject to the limitations imposed under our 2019 Plan, Section 16 of the Exchange Act, stock exchange rules and other applicable laws. The plan administrator will have the authority to take all actions and make all determinations under our 2019 Plan, to interpret our 2019 Plan and award agreements and to adopt, amend and repeal rules for the administration of our 2019 Plan as it deems advisable. The plan administrator will also have the authority to determine which eligible service providers receive awards, grant awards and set the terms and conditions of all awards under our 2019 Plan, including any vesting and vesting acceleration provisions, subject to the conditions and limitations in our 2019 Plan.

Shares available for awards

An aggregate of 4,750,000 shares of our common stock will initially be available for issuance under our 2019 Plan. The number of shares initially available for issuance will be increased by an annual increase on January 1

of each calendar year beginning in 2020 and ending in and including 2029, equal to the least of (1) 4% of the shares outstanding on the final day of the immediately preceding calendar year and (2) a smaller number of shares determined by our board of directors. No more than 5,000,000 shares of common stock may be issued under our 2019 Plan upon the exercise of incentive stock options, or ISOs. Shares issued under our 2019 Plan may be authorized but unissued shares, shares purchased on the open market or treasury shares.

If an award under our 2019 Plan, our 2015 Plan or our 2006 Plan expires, lapses or is terminated, exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited, any unused shares subject to the award will, as applicable, become or again be available for new grants under our 2019 Plan. Awards granted under our 2019 Plan in substitution for any options or other stock or stock-based awards granted by an entity before the entity's merger or consolidation with us or our acquisition of the entity's property or stock will not reduce the shares available for grant under our 2019 Plan, but will count against the maximum number of shares that may be issued upon the exercise of ISOs, as applicable.

In addition, the maximum aggregate grant date fair value as determined in accordance with ASC 718 (or any successor thereto), of awards granted to any non-employee director for services as a director pursuant to our 2019 Plan during any fiscal year may not exceed $750,000. The plan administrator may, however, make exceptions to such limit on director compensation in extraordinary circumstances, subject to the limitations in our 2019 Plan.

Awards

Our 2019 Plan provides for the grant of stock options, including ISOs, and nonqualified stock options, or NSOs, stock appreciation rights, or SARs, restricted stock, dividend equivalents, restricted stock units, or RSUs, and other stock or cash based awards. Certain awards under our 2019 Plan may constitute or provide for payment of "nonqualified deferred compensation" under Section 409A of the Code. All awards under our 2019 Plan will be set forth in award agreements, which will detail the terms and conditions of awards, including any applicable vesting and payment terms and post-termination exercise limitations. A brief description of each award type follows.

- Stock Options and SARs. Stock options provide for the purchase of shares of our common stock in the future at an exercise price set on the grant date. ISOs, by contrast to NSOs, may provide tax deferral beyond exercise and favorable capital gains tax treatment to their holders if certain holding periods and other requirements of the Code are satisfied. SARs entitle their holder, upon exercise, to receive from us an amount equal to the appreciation of the shares subject to the award between the grant date and the exercise date. The plan administrator will determine the number of shares covered by each option and SAR, the exercise price of each option and SAR and the conditions and limitations applicable to the exercise of each option and SAR. The exercise price of a stock option or SAR will not be less than 100% of the fair market value of the underlying share on the grant date (or 110% in the case of ISOs granted to certain significant stockholders), except with respect to certain substitute awards granted in connection with a corporate transaction. The term of a stock option or SAR may not be longer than ten years (or five years in the case of ISOs granted to certain significant stockholders).
- Restricted Stock and RSUs. Restricted stock is an award of nontransferable shares of our common stock that remain forfeitable unless and until specified conditions are met and which may be subject to a purchase price. RSUs are contractual promises to deliver shares of our common stock in the future, which may also remain forfeitable unless and until specified conditions are met and may be accompanied by the right to receive the equivalent value of dividends paid on shares of our common stock prior to the delivery of the underlying shares. The plan administrator may provide that the delivery of the shares underlying RSUs will be deferred on a mandatory basis or at the election of the participant. The terms and conditions applicable to

restricted stock and RSUs will be determined by the plan administrator, subject to the conditions and limitations contained in our 2019 Plan.

- Other Stock or Cash Based Awards. Other stock or cash based awards are awards of cash, fully vested shares of our common stock and other awards valued wholly or partially by referring to, or otherwise based on, shares of our common stock or other property. Other stock or cash based awards may be granted to participants and may also be available as a payment form in the settlement of other awards, as standalone payments and as payment in lieu of compensation to which a participant is otherwise entitled. The plan administrator will determine the terms and conditions of other stock or cash based awards, which may include any purchase price, performance goal, transfer restrictions and vesting conditions.

Performance criteria

The plan administrator may select performance criteria for an award to establish performance goals for a performance period. Performance criteria under our 2019 Plan may include, but are not limited to, the following: net earnings or losses (either before or after one or more of interest, taxes, depreciation, amortization, and non-cash equity-based compensation expense); gross or net sales or revenue or sales or revenue growth; net income (either before or after taxes) or adjusted net income; profits (including but not limited to gross profits, net profits, profit growth, net operation profit or economic profit), profit return ratios or operating margin; budget or operating earnings (either before or after taxes or before or after allocation of corporate overhead and bonus); cash flow (including operating cash flow and free cash flow or cash flow return on capital); return on assets; return on capital or invested capital; cost of capital; return on stockholders' equity; total stockholder return; return on sales; costs, reductions in costs and cost control measures; expenses; working capital; earnings or loss per share; adjusted earnings or loss per share; price per share or dividends per share (or appreciation in or maintenance of such price or dividends); regulatory achievements or compliance; implementation, completion or attainment of objectives relating to research, development, regulatory, commercial, or strategic milestones or developments; market share; economic value or economic value added models; division, group or corporate financial goals; customer satisfaction/growth; customer service; employee satisfaction; recruitment and maintenance of personnel; human resources management; supervision of litigation and other legal matters; strategic partnerships and transactions; financial ratios (including those measuring liquidity, activity, profitability or leverage); debt levels or reductions; sales-related goals; financing and other capital raising transactions; cash on hand; acquisition activity; investment sourcing activity; and marketing initiatives, any of which may be measured in absolute terms or as compared to any incremental increase or decrease. Such performance goals also may be based solely by reference to the company's performance or the performance of a subsidiary, division, business segment or business unit of the company or a subsidiary, or based upon performance relative to performance of other companies or upon comparisons of any of the indicators of performance relative to performance of other companies. When determining performance goals, the plan administrator may provide for exclusion of the impact of an event or occurrence which the plan administrator determines should appropriately be excluded, including, without limitation, non-recurring charges or events, acquisitions or divestitures, changes in the corporate or capital structure, events unrelated to the business or outside of the control of management, foreign exchange considerations, and legal, regulatory, tax or accounting changes.

Certain transactions

In connection with certain corporate transactions and events affecting our common stock, including a change in control, or change in any applicable laws or accounting principles, the plan administrator has broad discretion to take action under our 2019 Plan to prevent the dilution or enlargement of intended benefits, facilitate the transaction or event or give effect to the change in applicable laws or accounting principles. This includes

canceling awards for cash or property, accelerating the vesting of awards, providing for the assumption or substitution of awards by a successor entity, adjusting the number and type of shares subject to outstanding awards and/or with respect to which awards may be granted under our 2019 Plan and replacing or terminating awards under our 2019 Plan. In addition, in the event of certain non-reciprocal transactions with our stockholders, the plan administrator will make equitable adjustments to our 2019 Plan and outstanding awards as it deems appropriate to reflect the transaction.

Plan amendment and termination

Our board of directors may amend or terminate our 2019 Plan at any time; however, no amendment, other than an amendment that increases the number of shares available under our 2019 Plan, may materially and adversely affect an award outstanding under our 2019 Plan without the consent of the affected participant, and stockholder approval will be obtained for any amendment to the extent necessary to comply with applicable laws. Further, the plan administrator cannot, without the approval of our stockholders, amend any outstanding stock option or SAR to reduce its price per share. Our 2019 Plan will remain in effect until the tenth anniversary of its effective date, unless earlier terminated by our board of directors. No awards may be granted under our 2019 Plan after its termination.

Foreign participants, claw-back provisions, transferability and participant payments

The plan administrator may modify awards granted to participants who are foreign nationals or employed outside the United States or establish subplans or procedures to address differences in laws, rules, regulations or customs of such foreign jurisdictions. All awards will be subject to any company claw-back policy as set forth in such claw-back policy or the applicable award agreement. Except as the plan administrator may determine or provide in an award agreement, awards under our 2019 Plan are generally non-transferrable, except by will or the laws of descent and distribution, or, subject to the plan administrator's consent, pursuant to a domestic relations order, and are generally exercisable only by the participant. With regard to tax withholding obligations arising in connection with awards under our 2019 Plan, and exercise price obligations arising in connection with the exercise of stock options under our 2019 Plan, the plan administrator may, in its discretion, accept cash, wire transfer or check, shares of our common stock that meet specified conditions, a promissory note, a "market sell order," such other consideration as the plan administrator deems suitable or any combination of the foregoing.

2015 Stock incentive plan

Our board of directors and stockholders have approved our 2015 Plan, under which we may grant stock options, restricted stock, RSUs and other stock-based awards to employees, officers, directors, consultants, advisors, advisory board members and other service providers. A total of 8,211,980 shares of our common stock have been authorized for issuance under our 2015 Plan. As of the date of this prospectus, awards of 6,543,084 stock options are outstanding under our 2015 Plan.

Following the effectiveness of our 2019 Plan, we will not make any further grants under our 2015 Plan. However, our 2015 Plan will continue to govern the terms and conditions of the outstanding awards granted under it. Shares of our common stock subject to awards granted under our 2015 Plan that are forfeited, lapse unexercised or are settled in cash and which following the effective date of our 2019 Plan are not issued under our 2015 Plan will be available for issuance under our 2019 Plan.

Administration

Our 2015 Plan is administered by our board of directors, which may delegate its duties and responsibilities to one or more committees of our directors (referred to collectively as our board of directors below) to the extent

permitted by applicable law. Our board of directors has the authority to grant awards under our 2015 Plan and to adopt, amend, and repeal such administrative rules, guidelines, and practices relating to our 2015 Plan as it shall deem advisable. Our board of directors may correct any defect, supply any omission, or reconcile any inconsistency in our 2015 Plan or any award thereunder in the manner and to the extent it deems expedient to carry our 2015 Plan into effect.

Types of awards

Our 2015 Plan provides for the grant of stock options, including NSOs and ISOs, restricted stock, RSUs and other stock-based awards to employees, officers, directors, consultants, advisors, advisory board members or other service providers, except that stock options intended to qualify as ISOs under the Code may only be granted to employees.

Certain adjustments

In the event of certain changes in capitalization, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, the number and class of securities available under our 2015 Plan and the number and class of securities and exercise price per share of each outstanding option will be equitably adjusted by us (or substituted awards may be made, if applicable) in the manner determined by our board of directors.

Change in control

Unless otherwise specifically provided in an award agreement, our board of directors may take any one or more of the following actions as to all (or any portion of) outstanding options on such terms as our board of directors determines in connection with a change in control, as defined in our 2015 Plan: (1) provide for the assumption or substitution of the award; (2) upon written notice to a participant, provide for the termination of all unexercised options unless exercised within a specific period; (3) provide that outstanding options will become exercisable prior to or upon such change in control; (4) in the event of a change in control in which holders of our common stock will receive cash payment for shares surrendered, make or provide for a cash payment to participants based on the excess, if any of (a) the change in control consideration times the number of shares subject to outstanding options less (b) the aggregate exercise price of the outstanding options, in exchange for termination of such options; (5) provide that, in connection with our liquidation or dissolution, awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise price thereof); or (c) any combination of the foregoing.

Plan amendment and termination

Our board of directors may amend, suspend or terminate our 2015 Plan at any time; provided, however, that if at any time the approval of our stockholders is required as to any modification or amendment under Section 422 of the Code or any successor provision with respect to ISOs, our board may not effect such modification or amendment without such approval. Unless otherwise specified in the amendment, any amendment to our 2015 Plan will apply to, and be binding on the holders of, all awards outstanding under our 2015 Plan at the time the amendment is adopted, provided our board determines that such amendment does not materially and adversely affect the rights of participants under our 2015 Plan. Our 2015 Plan will remain in effect until the tenth anniversary of its effective date, unless earlier terminated by our board of directors. No awards may be granted under our 2015 Plan after its termination.

Transferability of awards

Except as our board may otherwise expressly determine or provide in an award, awards under our 2015 Plan may not be sold, assigned, transferred, pledged or otherwise encumbered by the person to whom they are granted, either voluntarily or by operation of law, except by will or the laws of descent and distribution or, other than in the case of an ISO, pursuant to a qualified domestic relations order, and, during the life of the participant, shall be exercisable only by the participant.

2006 Stock incentive plan

Our board of directors previously adopted and our stockholders approved our 2006 Plan in May 2006. Our 2006 Plan expired in accordance with its terms in May 2016 and no further stock awards may be granted under our 2006 Plan. Any awards granted under our 2006 Plan remain subject to the terms of our 2006 Plan and applicable award agreements, until such outstanding awards that are stock options are exercised, or until they terminate or expire by their terms.

Administration

Our 2006 Plan is administered by our board of directors, which may delegate its duties and responsibilities to one or more committees of our directors (referred to collectively as our board of directors below) to the extent permitted by applicable law. Prior to the expiration of our 2006 plan, our board of directors had the authority to grant awards under our 2006 Plan, and our board of directors has the authority to adopt, amend, and repeal such administrative rules, guidelines, and practices relating to our 2006 Plan as it shall deem advisable. Our board of directors may correct any defect, supply any omission, or reconcile any inconsistency in our 2006 Plan or any award thereunder in the manner and to the extent it deems expedient to carry our 2006 Plan into effect.

Types of awards

Our 2006 Plan provided for the grant of stock options, including NSOs and ISOs, restricted stock, RSUs and other stock-based awards to employees, officers, directors, consultants and advisors, except that stock options intended to qualify as ISOs under the Code were only permitted to be granted to employees. As of the date of this prospectus, 1,397,203 awards of stock options are outstanding under our 2006 Plan.

Certain adjustments

In the event of certain changes in capitalization, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, the number and class of securities available under our 2006 Plan and the number and class of securities and exercise price per share of each outstanding option will be equitably adjusted by us (or substituted awards may be made, if applicable) in the manner determined by our board of directors.

Reorganization

Our board of directors may take any one or more of the following actions as to all (or any portion of) outstanding awards on such terms as our board of directors determines in connection with a reorganization, as defined in our 2006 Plan: (1) provide for the assumption or substitution of the award, (2) upon written notice to a participant, provide for the termination of all unexercised options unless exercised within a specific period, (3) provide that outstanding options will become exercisable prior to or upon such reorganization, (4) in the event of a reorganization in which holders of our common stock will receive cash payment for shares

surrendered, make or provide for a cash payment to participants equal to (a) the reorganization consideration times the number of shares subject to outstanding options minus (b) the aggregate exercise price of the outstanding options, in exchange for termination of such options, (5) provide that, in connection with our liquidation or dissolution, awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise price thereof) and (6) any combination of the foregoing.

Transferability of awards

Except as our board may otherwise have expressly determined or provided in an award, awards under our 2006 Plan may not be sold, assigned, transferred, pledged or otherwise encumbered by the person to whom they are granted, either voluntarily or by operation of law, except by will or the laws of descent and distribution or, other than in the case of an ISO, pursuant to a qualified domestic relations order, and, during the life of the participant, shall be exercisable only by the participant.

2019 Employee stock purchase plan

In connection with this offering, we adopted and our stockholders approved our 2019 ESPP which became effective upon the effectiveness of the registration statement of which this prospectus forms a part. The material terms of our 2019 ESPP are summarized below.

Shares available for awards; administration

A total of 525,000 shares of our common stock will initially be reserved for issuance under our 2019 ESPP. In addition, the number of shares available for issuance under our 2019 ESPP will be annually increased on January 1 of each calendar year beginning in 2020 and ending in and including 2029, by an amount equal to the least of (1) 1% of the shares outstanding on the final day of the immediately preceding calendar year and (2) such smaller number of shares as is determined by our board of directors, provided that no more than 5,250,000 shares of our common stock may be issued under our 2019 ESPP. The foregoing numbers are subject to adjustment in certain events, as described below. Our board of directors or a committee of our board of directors will have authority to interpret the terms of our 2019 ESPP and determine eligibility of participants. We expect that the compensation committee will be the initial administrator of our 2019 ESPP.

Eligibility

Our employees are eligible to participate in our 2019 ESPP if they are customarily employed by us or a participating subsidiary for more than twenty hours per week and more than five months in any calendar year. However, an employee may not be granted rights to purchase stock under our 2019 ESPP if the employee, immediately after the grant, would own (directly or through attribution) stock possessing 5% or more of the total combined voting power or value of all classes of our stock.

Grant of rights

Our 2019 ESPP is intended to qualify under Section 423 of the Code and stock will be offered under our 2019 ESPP during offering periods. The length of the offering periods under our 2019 ESPP will be determined by the plan administrator and may be up to twenty-seven months long. Employee payroll deductions will be used to purchase shares on each purchase date during an offering period. The purchase dates for each offering period will be the final trading day in the offering period. Offering periods under our 2019 ESPP will commence when determined by the plan administrator. The plan administrator may, in its discretion, modify the terms of future offering periods.

Our 2019 ESPP permits participants to purchase common stock through payroll deductions of up to 25% of their eligible compensation, which includes a participant's gross base compensation for services to us, including overtime payments and excluding sales commissions, incentive compensation, bonuses, expense reimbursements, fringe benefits and other special payments. The plan administrator will establish a maximum number of shares that may be purchased by a participant during any offering period, which, in the absence of a contrary designation, will be 25,000 shares. In addition, no employee will be permitted to accrue the right to purchase stock under our 2019 ESPP at a rate in excess of $25,000 worth of shares during any calendar year during which such a purchase right is outstanding (based on the fair market value per share of our common stock as of the first day of the offering period).

On the first trading day of each offering period, each participant will automatically be granted an option to purchase shares of our common stock. The option will expire at the end of the applicable offering period, and will be exercised at that time to the extent of the payroll deductions accumulated during the offering period. 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. Participants may voluntarily end their participation in our 2019 ESPP at any time at least one week prior to the end of the applicable offering period, and will be paid their accrued payroll deductions that have not yet been used to purchase shares of common stock. Participation ends automatically upon a participant's termination of employment.

A participant may not transfer rights granted under our 2019 ESPP other than by will or the laws of descent and distribution.

Certain transactions

In the event of certain non-reciprocal transactions or events affecting our common stock known as "equity restructurings," the plan administrator will make equitable adjustments to our 2019 ESPP and outstanding rights. In the event of certain unusual or non-recurring events or transactions, including a change in control, the plan administrator may provide for (1) either the replacement of outstanding rights with other rights or property or termination of outstanding rights in exchange for cash, (2) the assumption or substitution of outstanding rights by the successor or survivor corporation or parent or subsidiary thereof, if any, (3) the adjustment in the number and type of shares of stock subject to outstanding rights, (4) the use of participants' accumulated payroll deductions to purchase stock on a new purchase date prior to the next scheduled purchase date and termination of any rights under ongoing offering periods or (5) the termination of all outstanding rights.

Plan amendment

The plan administrator may amend, suspend or terminate our 2019 ESPP at any time. However, stockholder approval will be obtained for any amendment that increases the aggregate number or changes the type of shares that may be sold pursuant to rights under our 2019 ESPP, changes the corporations or classes of corporations whose employees are eligible to participate in our 2019 ESPP or changes our 2019 ESPP in any manner that would cause our 2019 ESPP to no longer be an employee stock purchase plan within the meaning of Section 423(b) of the Code.

Director compensation

2018 director compensation

Except as described below, we only provide compensation to our non-employee directors who are not designated by holders of our preferred stock. In 2018, our only such director was Ms. Sharp. In connection with

her appointment in December 2018, our board of directors determined that Ms. Sharp would receive annual cash compensation in an amount equal to $35,000 until such time as our board of directors adopted a non-employee director compensation policy and that she would receive an award of stock options to purchase up to 147,562 shares of our common stock pursuant to the 2015 Plan in connection with her appointment. Ms. Sharp's award vests as to 34% of the underlying shares on the first anniversary of the date of grant and in equal installments at the end of each three-month period over the following 24 months.

The following table provides information related to the 2018 compensation of Ms. Sharp, who was the only director who received compensation from us during 2018.

Name	Fees earned or paid in cash	Option awards(1)	Total
Shalini Sharp	$ 8,750	$1,212,086	$1,220,836

(1) Amount reflects the grant date Black-Scholes value of option awards granted during 2018, computed in accordance with ASC Topic 718 as further described in Note 7 to our audited consolidated financial statements included elsewhere in this prospectus. As of December 31, 2018, 147,562 shares of our common stock were subject to this award. Award vests as to 34% of the underlying shares on December 5, 2019 and in equal installments at the end of each three-month period over the following 24 months.

IPO grants to non-employee directors under the 2019 Plan

Effective upon the pricing of this offering, we will grant to Dr. Schinazi an option under the 2019 Plan to purchase a number of shares of our common stock having an aggregate value on the grant date of $350,000 (as determined using the Black-Scholes option pricing model and using as inputs into such model the initial public offering price per share of our common stock and such other assumptions used to calculate the value of the option awards as described in Note 7 to our consolidated financial statements included elsewhere in this prospectus), at an exercise price per share equal to the initial public offering price per share of our common stock sold in this offering. The option will vest as to 34% of the underlying shares on the first anniversary of the grant date and as to 8.25% of the underlying shares at the end of each three month period thereafter, subject to Mr. Schinazi's continued service through each applicable vesting date.

Non-employee director compensation policy

Effective upon the effectiveness of the registration statement of which this prospectus forms a part, in connection with this offering, we adopted and our stockholders approved a compensation program for our non-employee directors under which each non-employee director will 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 that occurs after our initial public offering, 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 will be 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 and no fee will be payable in respect of any period prior to the effective date of the registration statement of which this prospectus is a part.

Stock options granted to our non-employee directors under the program will have an exercise price equal to the fair market value of our common stock on the date of grant and will expire not later than ten years after the date of grant. The stock options granted upon a director's initial election or appointment will vest in thirty-six substantially equal monthly installments following the date of grant. The stock options granted annually to directors will 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 will vest in full upon the occurrence of a change in control.

Certain relationships and related party transactions

The following includes a summary of transactions since January 1, 2016, to which we have been a party in which the amount involved exceeded or will exceed $120,000, and in which any of our directors or executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under "Executive compensation." We also describe below certain other transactions with our directors, executive officers and stockholders.

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, 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. Mr. Auspitz does not hold voting or dispositive power over the shares held by F-Prime Capital Partners Healthcare Fund IV LP. See "Principal stockholders" below for more information.

(3) Robert Adelman, M.D., a member of our board of directors, is a partner at venBio Global Strategic Fund, L.P. See "Principal stockholders" below 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 "Principal stockholders" below 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 "Principal stockholders" below for more information.

Convertible note financing

In March 2019, we sold and issued $39.6 million aggregate principal amount of convertible promissory notes, 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. See "Principal stockholders" below for more information.

Immediately prior to the completion of this offering, the 2019 Notes will be converted into a number of shares of common stock determined at a settlement price equal to the lesser of (i) 85% of the price per share of the

shares offered hereby or (ii) a price per share equal to $800.0 million divided by our fully diluted capitalization as of immediately prior to the closing of this offering.

Investors' rights agreement

We are party to an amended and restated investors' rights agreement, 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 each of our directors (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 will survive this offering. See "Description of capital stock—Registration rights" for additional information. This right of first offer does not apply to this offering and will terminate by its terms in connection with the closing of this offering.

Voting agreement

We are a party to an amended and restated voting agreement with certain of our stockholders, pursuant to which each of our directors was elected to serve as members on our board of directors and, as of the date of this prospectus, continue to so serve. Our voting agreement will terminate by its terms in connection with the closing of this offering, and members previously elected to our board of directors pursuant to this voting agreement will continue to serve as directors until they resign, are removed or their successors are duly elected by the holders of our common stock. The composition of our board of directors after this offering is described in more detail under "Management—Board composition and election of directors."

Right of first refusal and co-sale agreement

We are party to an amended and restated right of first refusal and co-sale agreement with each holder of our convertible preferred stock 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 (or, in some cases, entities affiliated therewith), pursuant to which we have a right of first refusal in respect of certain sales of securities by Drs. Jantz and Smith and Mr. Kane. To the extent we do not exercise such right in full, the holders of our convertible preferred stock are granted certain rights of first refusal and co-sale in respect of such sale. The right of first refusal and co-sale agreement will terminate by its terms in connection with the closing of this offering.

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. See "Description of capital stock—Limitations on liability and indemnification matters."

Employment agreements

We have entered into employment agreements with our certain of our executive officers, including our named executive officers. For more information regarding the agreements with our named executive officers, see "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 "Executive compensation."

Other transactions

In April 2017, in connection with a repurchase program approved by our board of directors, we repurchased 600,662 shares of common stock from J. Christopher Rhodes, a beneficial owner of more than 5% of our common stock, for aggregate proceeds of $0.7 million.

Chelsea Lynam, Mr. Kane's wife, serves as our Manager, Facilities Planning & Design. Ms. Lynam received 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 that were granted in 2018. Ms. Lynam also participates in other employee benefit plans and arrangements that are made generally available to other employees.

Policies and procedures for related person transactions

Our board of directors has adopted a written related person transaction policy, to be effective upon the closing of this offering, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, where the amount involved exceeds $120,000 in any fiscal year and a related person had, has or will have a direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest as well as indebtedness, guarantees of indebtedness and our employment of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the effectiveness of this policy.

Principal stockholders

The following table sets forth information with respect to the beneficial ownership of our common stock as of December 31, 2018 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 percentage ownership information under the column entitled “Before offering” is based on 38,207,835 shares of common stock outstanding as of December 31, 2018, assuming conversion of all outstanding shares of our convertible preferred stock into 22,301,190 shares of common stock upon the closing of this offering. The percentage ownership information under the column entitled “After offering” is based on (1) the sale of 7,900,000 shares of common stock in this offering and (2) the automatic settlement of the 2019 Notes, including accrued interest, into an aggregate of 2,921,189 shares of our common stock, based on the initial public offering price of $16.00 per share, in connection with the closing of this offering. The following table does not reflect any potential purchases in this offering, which purchases, if any, will increase the percentage of shares owned by certain of our directors and executive officers after this offering.

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. 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 December 31, 2018 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	
		Before offering	After offering
5% or Greater Stockholders			
venBio Global Strategic Fund, L.P.(1)	4,215,141	11.0%	8.6%
Jeff Smith, Ph.D.(2)	4,178,128	10.8%	8.5%
F-Prime Capital Partners Healthcare Fund IV LP(3)	3,688,248	9.7%	7.5%
Named Executive Officers and Directors			
Matthew Kane(4)	2,150,625	5.6%	4.4%
Abid Ansari (5)	93,982	*	*
David Thomson, Ph.D.(6)	166,183	*	*
Robert Adelman, M.D.(1)	4,215,141	11.0%	8.6%
Derek Jantz, Ph.D.(7)	4,178,128	10.8%	8.5%

Name of beneficial owner	Number of shares beneficially owned	Percentage of shares beneficially owned: Before offering	Percentage of shares beneficially owned: After offering
Raymond F. Schinazi, Ph.D.(8)	56,102	*	*
Shalini Sharp	—	—	—
Tony Yao, M.D., Ph.D.(9)	935,031	2.4%	2.7%
All executive officers and directors as a group (9 persons)(10)	11,866,923	30.7%	25.0%

* Less than 1%.

(1) Consists of 4,215,141 shares of common stock issuable upon conversion of 8,000,000 shares of Series A convertible preferred stock and 998,004 shares of Series B preferred stock. VenBio Global Strategic GP, L.P., or venBio GP, is the sole general partner of venBio Global Strategic Fund, L.P., or venBio, and venBio Global Strategic GP, Ltd., or venBio GP Ltd., is the sole general partner of venBio GP. Robert Adelman, one of our directors, and Corey Goodman are directors of venBio GP Ltd. and share voting and dispositive control over the shares held by venBio. The mailing address of venBio Global Strategic Fund, L.P. is c/o venBio Partners, LLC, 1700 Owens Street, Suite 595, San Francisco, CA 94158.

(2) Consists of (a) 3,845,170 shares of common stock and (b) 332,958 shares of common stock underlying options exercisable within 60 days of December 31, 2018.

(3) Consists of 3,688,248 shares of common stock issuable upon conversion of 7,000,000 shares of Series A convertible preferred stock and 873,253 shares of Series B preferred stock. The general partner of F-Prime Capital Partners Healthcare Fund IV LP is F-Prime Capital Partners Healthcare Advisors Fund IV LP. F-Prime Capital Partners Healthcare Advisors Fund IV LP is solely managed by Impresa Management LLC, the managing member of its general partner and investment manager. Impresa Management LLC is owned, directly or indirectly, by various shareholders and employees of FMR LLC. Each of the entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The mailing address of F-Prime Capital Partners Healthcare Fund IV LP is 245 Summer Street, Boston, MA 02210.

(4) Consists of (a) 1,802,427 shares of common stock held directly by Mr. Kane, (b) 8,067 shares of common stock held by Chelsea Lynam, Mr. Kane's wife, (c) 332,958 shares of common stock underlying options held by Mr. Kane exercisable within 60 days of December 31, 2018 and (d) 7,173 shares of common stock underlying options held by Ms. Lynam exercisable within 60 days of December 31, 2018.

(5) Consists of 93,982 shares of common stock underlying options exercisable within 60 days of December 31, 2018.

(6) Consists of 166,183 shares of common stock underlying options exercisable within 60 days of December 31, 2018.

(7) Consists of (a) 3,845,170 shares of common stock and (b) 332,958 shares of common stock underlying options exercisable within 60 days of December 31, 2018.

(8) Consists of 56,102 shares of common stock issuable upon conversion of 119,761 shares of Series B convertible preferred 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. In addition, the percentage of shares beneficially owned by Dr. Schinazi after the offering includes 36,946 shares of common stock issuable upon conversion of a convertible promissory note held by RFS. The principal business address of RFS is 1860 Montreal Road, Tucker, GA 30084.

(9) Consists of (a) 4,450 shares of common stock issuable upon conversion of 9,500 shares of Series B convertible preferred stock held directly by Dr. Yao, (b) 93,690 shares of common stock issuable upon conversion of 200,000 shares of Series B convertible preferred stock held by ArrowMark Fundamental Opportunity Fund, L.P., (c) 114,570 shares of common stock issuable upon conversion of 244,572 shares of Series B convertible preferred stock held by ArrowMark Life Science Fund, (d) 4,684 shares of common stock issuable upon conversion of 10,000 shares of Series B convertible preferred stock held by CF Ascent LLC, (e) 70,010 shares of common stock issuable upon conversion of 149,451 shares of Series B convertible preferred stock held by Iron Horse Investments, LLC, or Iron Horse, (f) 18,700 shares of common stock issuable upon conversion of 39,920 shares of Series B convertible preferred stock held by Lookfar Investments, LLC, (g) 292,670 shares of common stock issuable upon conversion of 624,759 shares of Series B convertible preferred stock held by Meridian Growth Fund, or Meridian Growth, (h) 261,797 shares of common stock issuable upon conversion of 558,855 shares of Series B convertible preferred stock held by Meridian Small Cap Growth Fund, or Meridian Small Cap, (i) 70,010 shares of common stock issuable upon conversion of 149,451 shares of Series B convertible preferred stock held by THB Iron Rose, LLC, or THB Iron Rose, and (j) 4,450 shares of common stock issuable upon conversion of 9,500 shares of Series B convertible preferred stock held by THB Iron Rose, LLC Life Science Portfolio, or THB Iron Rose Life Science, which are referred to collectively as the ArrowMark Funds. ArrowMark Colorado Holdings LLC, or ArrowMark Colorado, is investment advisor to ArrowMark Funds. 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 Life Science Fund and THB Iron Rose Life Science. Dr. Yao may be considered the beneficial owner of the shares held by ArrowMark Life Science Fund and THB Iron Rose Life Science and disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein. In addition, the percentage of shares beneficially owned by Dr. Yao after the offering includes 369,459 shares of common stock issuable upon conversion of convertible promissory notes held by certain of the ArrowMark Funds. The principal business address of the ArrowMark Funds is 100 Fillmore Street, Suite 325, Denver, Colorado 80206.

(10) Consists of (a) 5,655,664 shares of common stock, (b) 1,004,985 shares of common stock underlying options exercisable within 60 days of December 31, 2018, and (c) 5,206,273 shares of common stock issuable upon conversion of 8,000,000 shares of Series A convertible preferred stock and 3,113,773 of Series B convertible preferred stock. In addition, the percentage of shares beneficially owned after the offering includes 406,405 shares of common stock issuable upon conversion of convertible promissory notes held by RFS and certain ArrowMark Funds.

Description of capital stock

Capital structure

The following description of our capital stock and certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws that will go into effect upon the closing of this offering. Copies of these documents will be filed with the SEC as exhibits to our registration statement, of which this prospectus forms a part. The descriptions of our common stock and preferred stock reflect changes to our capital structure that will occur upon the closing of this offering.

General

Upon the completion of this offering, our authorized capital stock will consist of 200,000,000 shares of common stock, par value $0.000005 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share, all of which will be undesignated.

Common stock

As of December 31, 2018, assuming the conversion of all outstanding shares of our convertible preferred stock into 22,301,190 shares of our common stock upon the closing of this offering, we had outstanding 38,207,835 shares of common stock held of record by 119 stockholders. Additionally, in connection with the closing of this offering, the 2019 Notes, including accrued interest, will automatically settle into 2,921,189 shares of our common stock, based on the initial public offering price per share of $16.00.

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of our common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are, and the shares offered by us in this offering will be, when issued and paid for, validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred stock

As of December 31, 2018, there were 22,301,190 shares of our convertible preferred stock outstanding. Upon the closing of this offering, all outstanding shares of our convertible preferred stock will convert into 22,301,190 shares of our common stock.

Under the terms of our amended and restated certificate of incorporation that will go into effect upon the closing of this offering, our board of directors will be authorized to direct us to issue shares of preferred stock

in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third-party to acquire, or could discourage a third-party from seeking to acquire, a majority of our outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Options

As of December 31, 2018, options to purchase 6,366,261 shares of our common stock were outstanding under our 2015 Plan, of which 2,021,741 options were vested as of that date, and options to purchase 1,397,203 shares of our common stock were outstanding under our 2006 Plan, all of which options were vested as of that date.

Registration rights

Our investors' rights agreement grants the parties thereto certain registration rights in respect of the "registrable securities" held by them, which securities include (1) the shares of our common stock issued upon the conversion of shares of our convertible preferred stock, (2) the shares of our common stock issued to certain of our founders, (3) the shares of our common stock issued upon the settlement of the 2019 Notes, and (4) any shares of our common stock issued as a dividend or other distribution with respect to the shares described in the foregoing clauses (1), (2) and (3).

Demand registration rights

Upon the closing of this offering, certain holders of our registrable securities are entitled to demand registration rights. Under the terms of our investors' rights agreement, we will be required, upon the request of holders of at least 60% of our outstanding registrable securities issued or issuable upon conversion of our convertible preferred stock, to file a registration statement with an anticipated offering amount of at least $15.0 million and use our best efforts to effect the registration of these shares for public resale. We are required to effect up to three registrations pursuant to this provision of our investors' rights agreement. A demand for registration may not be made until six months after the effective date of the registration statement for which this prospectus forms a part.

Short form registration rights

Upon the closing of this offering, the holders of our registrable securities are also entitled to short form registration rights. Pursuant to our investors' rights agreement, if we are eligible to file a registration statement on Form S-3, upon the request of holders of at least 25% of our outstanding registrable securities to sell registrable securities with an anticipated aggregate offering amount of at least $1.0 million net of certain expenses related to the offering, we will be required to use our best efforts to effect a registration of such shares. We are required to effect up to two registrations in any 12-month period and no more than one registration in any four-month period pursuant to this provision of our investors' rights agreement.

Piggyback registration rights

The holders of our registrable securities are also entitled to piggyback registration rights. If we register any of our securities either for our own account or for the account of other security holders, the holders of our outstanding registrable securities are entitled to include their shares in the registration (other than a demand registration, a registration in connection with an initial public offering that becomes effective on or before June 30, 2019, or a registration pursuant to a registration statement on Form S-4 or S-8). Subject to certain exceptions contained in our investors' rights agreement, we and the underwriters may limit the number of shares included in an underwritten offering if the underwriters determine that marketing factors require a limitation of the number of shares to be underwritten.

Expenses and indemnification

Ordinarily, other than underwriting discounts and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a single counsel for the selling security holders and blue sky fees and expenses. Our investors' rights agreement also includes customary indemnification and procedural terms.

Termination of registration rights

The registration rights will expire on the earlier of (1) the date that is five years after the closing of this offering or (2) with respect to each stockholder following the closing of this offering, at such time as such stockholder holds 1% or less of our outstanding common stock and can sell all of its registrable securities without volume limitations pursuant to Rule 144 of the Securities Act during any three-month period.

Anti-takeover provisions

Some provisions of Delaware law and our amended and restated certificate of incorporation and our amended and restated bylaws that will go into effect upon the closing of this offering could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interests or in our best interests, including transactions that provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated preferred stock

The ability of our board of directors, without action by our stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to effect a change in control of our company. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder meetings

Our amended and restated bylaws will provide that a special meeting of stockholders may be called only by the chairman of our board of directors, our chief executive officer or president (in the absence of a chief executive officer), or by a resolution adopted by a majority of our board of directors.

Requirements for advance notification of stockholder nominations and proposals

Our amended and restated bylaws will establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of our board of directors or a committee of our board of directors.

Elimination of stockholder action by written consent

Our amended and restated certificate of incorporation will eliminate the right of stockholders to act by written consent without a meeting.

Staggered board

Our board of directors will be divided into three classes. The directors in each class will serve for a three-year term, with one class being elected each year by our stockholders. For more information on our classified board, see “Management—Board composition and election of directors.” This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of directors

Our amended and restated certificate of incorporation will provide that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of the holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote in the election of directors.

Stockholders not entitled to cumulative voting

Our amended and restated certificate of incorporation will not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors will be able to elect all of the directors standing for election, if they choose, other than any directors that holders of our convertible preferred stock may be entitled to elect.

Choice of forum

Our amended and restated certificate of incorporation will provide 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 of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws, (4) any action to interpret, apply, enforce or determine the validity of our certificate of

incorporation or 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 provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Our amended and restated certificate of incorporation will also provide that any person or entity holding, purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our amended and restated certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

Amendment of charter provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock and the provision prohibiting cumulative voting, would require approval by holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote thereon.

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the General Corporation Law of the State of Delaware, which prohibits persons deemed to be “interested stockholders” from engaging in a “business combination” with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an “interested stockholder” is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation’s voting stock. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by our board of directors.

Limitations on liability and indemnification matters

Our amended and restated certificate of incorporation, which will go into effect upon the closing of this offering, will limit our directors’ liability to the fullest extent permitted under Delaware law, which prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

- any breach of the director’s duty of loyalty to us or our stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or unlawful stock repurchases or redemptions; or
- any transaction from which the director derived an improper personal benefit.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. This limitation of liability does not apply to liabilities arising under the federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our amended and restated bylaws, which will go into effect upon the closing of this offering, will provide that we will indemnify our directors and officers to the fullest extent permitted under Delaware law and that we shall have the power to indemnify our employees and agents to the fullest extent permitted by law. Our amended and restated bylaws will also permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in this capacity, regardless of whether we would have the power to indemnify such person against such expense, liability or loss under the General Corporation Law of the State of Delaware.

We have also entered into separate indemnification agreements with our directors and executive officers, in addition to indemnification provided for in our amended and restated bylaws. These agreements, among other things, provide for indemnification of our directors and executive officers for expenses, judgments, fines and settlement amounts incurred by such persons in any action or proceeding arising out of this person's services as a director or executive officer or at our request. We believe that these provisions in our amended and restated certificate of incorporation and amended and restated bylaws and indemnification agreements are necessary to attract and retain qualified persons as directors and executive officers.

The above description of the limitation of liability and indemnification provisions of our amended and restated certificate of incorporation, our amended and restated bylaws and our indemnification agreements is not complete and is qualified in its entirety by reference to these documents, each of which will be filed as an exhibit to this registration statement to which this prospectus forms a part.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. A stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

Listing

Our common stock has been approved for listing on The Nasdaq Global Select Market under the symbol "DTIL."

Transfer agent and registrar

The transfer agent and registrar for our common stock will be American Stock Transfer & Trust Company, LLC.

Shares eligible for future sale

Immediately prior to this offering, there was no public market for our common stock, and no predictions can be made about the effect, if any, that market sales of our common stock or the availability of such shares for sale will have on the market price prevailing from time to time. Nevertheless, future sales of our common stock in the public market, or the perception that such sales may occur, could adversely affect the market price of our common stock and could impair our ability to raise capital through future sales of our securities. See “Risk factors—Risks related to this offering and owning our common stock—A significant portion of our total outstanding shares is restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.” Furthermore, although our common stock has been approved for listing on the Nasdaq Global Select Market, we cannot assure you that there will be an active public trading market for our common stock.

Upon the closing of this offering, based on the number of shares of our common stock outstanding as of December 31, 2018 and after giving effect to the automatic conversion of all outstanding shares of our convertible preferred stock into 22,301,190 shares of our common stock upon the closing of this offering and the automatic settlement of the 2019 Notes, including accrued interest, into 2,921,189 shares of our common stock in connection with the closing of this offering, based on the initial public offering price per share of $16.00, and assuming no exercise of options after December 31, 2018, we will have an aggregate of 49,029,024 shares of our common stock outstanding (or 50,214,024 shares of our common stock if the underwriters exercise in full their option to purchase additional shares). Of these shares of our common stock, all of the 7,900,000 shares sold in this offering (or 9,085,000 shares if the underwriters exercise in full their option to purchase additional shares) will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our “affiliates,” as that term is defined in Rule 144 under the Securities Act, whose sales would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

The remaining 41,129,024 shares of our common stock, including shares of our common stock issued upon the automatic settlement of the 2019 Notes in connection with the closing of this offering, based on the initial public offering price per share of $16.00, will be “restricted securities,” as that term is defined in Rule 144 under the Securities Act. These restricted securities are eligible for public sale only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act, which are summarized below. We expect that substantially all of these shares will be subject to the 180-day lock-up period under the lock-up agreements described below. Upon expiration of the lock-up period, we estimate that all of these restricted securities will be available for sale in the public market, subject in some cases to applicable volume limitations under Rule 144.

Lock-up agreements

We and each of our directors and executive officers and holders of substantially all of our outstanding capital stock, who will collectively own substantially all of our shares of common stock upon the closing of this offering (after giving effect to the automatic conversion of all outstanding shares of our convertible preferred stock into shares of our common stock upon the closing of this offering and the automatic settlement of the 2019 Notes in connection with the closing of this offering, based on the initial public offering price per share of $16.00, have agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for or repayable with common stock, for 180 days after the date of this prospectus without first obtaining the written consent of J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC and Jefferies LLC.

Upon the expiration of the lock-up period, substantially all of the shares subject to such lock-up restrictions will become eligible for sale, subject to the limitations discussed above. For a further description of these lock-up agreements, see “Underwriting.”

Rule 144

Affiliate resales of restricted securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned shares of our common stock for at least six months would be entitled to sell in “broker’s transactions” or certain “riskless principal transactions” or to market makers, a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 490,000 shares of our common stock immediately after this offering; or
- the average weekly trading volume in shares of our common stock on the Nasdaq Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of $50,000, the seller must file a notice on Form 144 with the SEC and Nasdaq concurrently with either the placing of a sale order with the broker or the execution directly with a market maker.

Non-affiliate resales of restricted securities

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the three months preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

Rule 701

In general, under Rule 701, any of an issuer’s employees, directors, officers, consultants or advisors who purchases shares from the issuer in connection with a compensatory stock or option plan or other written agreement before the effective date of a registration statement under the Securities Act is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

The SEC has indicated that Rule 701 will apply to typical options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act.

Equity plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all shares of our common stock subject to outstanding options and shares of our common stock issued or issuable under our incentive plans. We expect to file the registration statement covering shares offered pursuant to our incentive plans shortly after the date of this prospectus, permitting the resale of such shares by non-affiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market, subject to compliance with the resale provisions of Rule 144.

Registration rights

Upon the closing of this offering, the holders of 35,753,545 shares of our common stock (including shares of our common stock issuable upon the conversion of all outstanding shares of our convertible preferred stock upon the closing of this offering and the automatic settlement of the 2019 Notes, including accrued interest, into 2,921,189 shares of our common stock in connection with the closing of this offering, based on the initial public offering price per share of $16.00, or their transferees will be entitled to various rights with respect to the registration of these shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, except for shares purchased by affiliates. See “Description of capital stock—Registration rights” for additional information. Shares covered by a registration statement will be eligible for sale in the public market upon the expiration or release from the terms of any applicable lock-up agreement.

Material U.S. federal income tax consequences to Non-U.S. Holders

The following discussion is a summary of the material U.S. federal income tax consequences to Non-U.S. Holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or the IRS, in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder of our common stock. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder's particular circumstances, including the impact of the Medicare contribution tax on net investment income or the alternative minimum tax. In addition, it does not address consequences relevant to Non-U.S. Holders subject to special rules, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- brokers, dealers or traders in securities;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- tax-qualified retirement plans;
- "qualified foreign pension funds" as defined in Section 897(l)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds;
- persons who own, or are deemed to own, more than 5% of our capital stock (except to the extent specifically set forth below); and
- persons subject to special tax accounting rules as a result of any item of gross income with respect to the stock being taken into account in an applicable financial statement.

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships (or other entities treated as a partnership for U.S. federal income tax purposes) holding our common stock and the partners in such partnerships or other entities should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a “Non-U.S. Holder” is any beneficial owner of our common stock that is neither a “U.S. person” nor an entity treated as a partnership for U.S. federal income tax purposes.

A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation, or an entity treated as a corporation, created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more “United States persons” (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section entitled “Dividend policy,” we do not anticipate declaring or paying dividends to holders of our common stock in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and will first be applied against and reduce a Non-U.S. Holder’s adjusted tax basis in our common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under “—Sale or other taxable dispositions of common stock.”

Subject to the discussion below on effectively connected income, dividends paid to a Non-U.S. Holder of our common stock will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder timely furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for the lower treaty rate). A Non-U.S. Holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must timely furnish to the applicable withholding agent a valid IRS Form W-8ECI (or applicable successor form), certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Sales or other taxable dispositions of common stock

A Non-U.S. Holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

- the gain is effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such gain is attributable);
- the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes a U.S. real property interest, or USRPI, by reason of our status as a U.S. real property holding corporation, or USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

Gain described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty), which may be offset by U.S. source capital losses of the Non-U.S. Holder (even though the individual is not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a Non-U.S. Holder of our common stock will not be subject to U.S. federal income tax if our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, and such Non-U.S. Holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder's holding period.

Non-U.S. Holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

Information reporting and backup withholding

Payments of dividends on our common stock will not be subject to backup withholding, provided the applicable withholding agent does not have actual knowledge or reason to know the holder is a United States person and the holder either certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any dividends on our common stock paid to the Non-U.S. Holder, regardless of whether any tax was actually withheld.

In addition, proceeds of the sale or other taxable disposition of our common stock within the United States, or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting, if the applicable withholding agent receives the certification described above and does not have actual knowledge or reason to know that such holder is a United States person, or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional withholding tax on payments made to foreign accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or FATCA) on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends on our common stock, and subject to the recently released proposed Treasury

Regulations described below, will apply to payments of gross proceeds from the sale or other disposition of such stock on or after January 1, 2019. The Treasury Department recently released proposed Treasury Regulations which, if finalized in their present form, would eliminate the federal withholding tax of 30% applicable to the gross proceeds of a sale or other disposition of our common stock. In its preamble to such proposed Treasury Regulations, the Treasury Department stated that taxpayers may generally rely on the proposed Treasury Regulations until final Treasury Regulations are issued.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

Underwriting

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC, Jefferies LLC and Barclays Capital Inc. are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	2,765,000
Goldman Sachs & Co. LLC	2,607,000
Jefferies LLC	1,580,000
Barclays Capital Inc.	948,000
Total	7,900,000

The underwriters are committed to purchase all the shares of common stock offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common stock directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $0.67 per share. Any such dealers may resell shares to certain other brokers or dealers at a discount of up to $0.22 per share from the initial public offering price. After the initial offering of the shares to the public, if all of the shares of common stock are not sold at the initial public offering price, the underwriters may change the offering price and the other selling terms. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to 1,185,000 additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is $1.12 per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without option to purchase additional shares exercise	With full option to purchase additional shares exercise
Per Share	$ 1.12	$ 1.12
Total	$ 8,848,000	$ 10,175,200

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $4.3 million. We have agreed to reimburse the underwriters for expenses relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc. in an amount up to $35,000.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that, subject to certain exceptions, we will not (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or file with, the SEC a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (2) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC and Jefferies LLC for a period of 180 days after the date of this prospectus.

Our directors and executive officers, and substantially all of our securityholders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 180 days after the date of this prospectus, may not, without the prior written consent of J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC and Jefferies LLC (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

Our common stock has been approved for listing on The Nasdaq Global Select Market under the symbol “DTIL.”

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters

of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be “covered” shorts, which are short positions in an amount not greater than the underwriters’ option to purchase additional shares referred to above, or may be “naked” shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Prior to this offering, there has been no public market for our common stock. The initial public offering price was determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters considered a number of factors including:

- the information set forth in this prospectus and otherwise available to the representatives;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our common stock, or that shares of our common stock will trade in the public market at or above the initial public offering price.

Other relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment

management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to us and to persons and entities with relationships with us, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of ours (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with us, including long or short positions in our debt or equity securities or loans. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Selling restrictions

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Notice to prospective investors in the European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive, (each, a “Relevant Member State”), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, no offer of shares may be made to the public in that Relevant Member State other than:

(1) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(2) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the underwriters; or

(3) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require the Company or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive and each person who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and the Company that it is a “qualified investor” within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive.

In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an “offer of shares to the public” in relation to any shares in any Relevant Member State means the communication in any form and by means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression “Prospectus Directive” means Directive 2003/71/EC (as amended, including by Directive 2010/73/EU), and includes any relevant implementing measure in the Relevant Member State.

Notice to prospective investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Directive) (1) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the “Order”) and/or (2) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”) or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the Financial Services and Markets Act 2000.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Notice to prospective investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts, or NI 33-105, the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to prospective investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or the SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company or the shares has been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or the CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to prospective investors in the Dubai International Financial Centre ("DIFC")

This document relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority, or the DFSA. This document is intended for distribution only to persons of a type specified in the Markets Rules 2012 of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for this document. The securities to which this document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this document you should consult an authorized financial advisor.

In relation to its use in the DIFC, this document is strictly private and confidential and is being distributed to a limited number of investors and must not be provided to any person other than the original recipient, and may not be reproduced or used for any other purpose. The interests in the securities may not be offered or sold directly or indirectly to the public in the DIFC.

Notice to prospective investors in the United Arab Emirates

The shares have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Notice to prospective investors in Australia

This prospectus:

- does not constitute a product disclosure document or a prospectus under Chapter 6D.2 of the Corporations Act 2001 (Cth), or the Corporations Act;

- has not been, and will not be, lodged with the Australian Securities and Investments Commission, or ASIC, as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document under Chapter 6D.2 of the Corporations Act;
- does not constitute or involve a recommendation to acquire, an offer or invitation for issue or sale, an offer or invitation to arrange the issue or sale, or an issue or sale, of interests to a "retail client" (as defined in section 761G of the Corporations Act and applicable regulations) in Australia; and
- may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, or Exempt Investors, available under section 708 of the Corporations Act.

The shares may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the shares may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any shares may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the shares, you represent and warrant to us that you are an Exempt Investor.

As any offer of shares under this document will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the shares you undertake to us that you will not, for a period of 12 months from the date of issue of the shares, offer, transfer, assign or otherwise alienate those securities to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

Notice to prospective investors in Japan

The shares have not been and will not be registered pursuant to Article 4, Paragraph 1 of the Financial Instruments and Exchange Act. Accordingly, none of the shares nor any interest therein may be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any "resident" of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan in effect at the relevant time.

Notice to prospective investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (1) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance or (2) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to prospective investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (1) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (2) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA, or (3) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

(a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(b) where no consideration is or will be given for the transfer;

(c) where the transfer is by operation of law;

(d) as specified in Section 276(7) of the SFA; or

(e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Solely for the purposes of its obligations pursuant to Section 309B of the SFA, we have determined, and hereby notify all relevant persons (as defined in the CMP Regulations 2018), that the shares are ''prescribed capital markets products'' (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Notice to prospective investors in Bermuda

Shares may be offered or sold in Bermuda only in compliance with the provisions of the Investment Business Act of 2003 of Bermuda which regulates the sale of securities in Bermuda. Additionally, non-Bermudian persons (including companies) may not carry on or engage in any trade or business in Bermuda unless such persons are permitted to do so under applicable Bermuda legislation.

Notice to prospective investors in Saudi Arabia

This document may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Offers of Securities Regulations as issued by the board of the Saudi Arabian Capital Market Authority,

or the CMA, pursuant to resolution number 2-11-2004 dated 4 October 2004 as amended by resolution number 1-28-2008, as amended, or the CMA Regulations. The CMA does not make any representation as to the accuracy or completeness of this document and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this document. Prospective purchasers of the securities offered hereby should conduct their own due diligence on the accuracy of the information relating to the securities. If you do not understand the contents of this document, you should consult an authorised financial adviser.

Notice to prospective investors in the British Virgin Islands

The shares are not being, and may not be offered to the public or to any person in the British Virgin Islands for purchase or subscription by or on behalf of the Company. The Company may be offered to companies incorporated under the BVI Business Companies Act, 2004 (British Virgin Islands), but only where the offer will be made to, and received by, the relevant BVI Company entirely outside of the British Virgin Islands. This prospectus has not been, and will not be, registered with the Financial Services Commission of the British Virgin Islands. No registered prospectus has been or will be prepared in respect of the shares for the purposes of the Securities and Investment Business Act, 2010 or the Public Issuers Code of the British Virgin Islands.

Notice to prospective investors in China

This prospectus does not constitute a public offer of shares, whether by sale or subscription, in the People's Republic of China, or the PRC. The shares are not being offered or sold directly or indirectly in the PRC to or for the benefit of, legal or natural persons of the PRC.

Further, no legal or natural persons of the PRC may directly or indirectly purchase any of the shares or any beneficial interest therein without obtaining all prior PRC's governmental approvals that are required, whether statutorily or otherwise. Persons who come into possession of this document are required by the issuer and its representatives to observe these restrictions.

Notice to prospective investors in Korea

The shares have not been and will not be registered under the Financial Investments Services and Capital Markets Act of Korea and the decrees and regulations thereunder, or the FSCMA, and the shares have been and will be offered in Korea as a private placement under the FSCMA. None of the shares may be offered, sold or delivered directly or indirectly, or offered or sold to any person for re-offering or resale, directly or indirectly, in Korea or to any resident of Korea except pursuant to the applicable laws and regulations of Korea, including the FSCMA and the Foreign Exchange Transaction Law of Korea and the decrees and regulations thereunder, or the FETL. Furthermore, the purchaser of the shares shall comply with all applicable regulatory requirements (including but not limited to requirements under the FETL) in connection with the purchase of the shares. By the purchase of the shares, the relevant holder thereof will be deemed to represent and warrant that if it is in Korea or is a resident of Korea, it purchased the shares pursuant to the applicable laws and regulations of Korea.

Notice to prospective investors in Malaysia

No prospectus or other offering material or document in connection with the offer and sale of the shares has been or will be registered with the Securities Commission of Malaysia, or the Commission, for the Commission's approval pursuant to the Capital Markets and Services Act 2007. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an

invitation for subscription or purchase, whether directly or indirectly, to persons in Malaysia other than (1) a closed end fund approved by the Commission, (2) a holder of a Capital Markets Services Licence, (3) a person who acquires the shares, as principal, if the offer is on terms that the shares may only be acquired at a consideration of not less than RM250,000 (or its equivalent in foreign currencies) for each transaction, (4) an individual whose total net personal assets or total net joint assets with his or her spouse exceeds RM3 million (or its equivalent in foreign currencies), excluding the value of the primary residence of the individual, (5) an individual who has a gross annual income exceeding RM300,000 (or its equivalent in foreign currencies) per annum in the preceding 12 months, (6) an individual who, jointly with his or her spouse, has a gross annual income of RM400,000 (or its equivalent in foreign currencies), per annum in the preceding 12 months, (7) a corporation with total net assets exceeding RM10 million (or its equivalent in a foreign currencies) based on the last audited accounts, (8) a partnership with total net assets exceeding RM10 million (or its equivalent in foreign currencies), (9) a bank licensee or insurance licensee as defined in the Labuan Financial Services and Securities Act 2010, (10) an Islamic bank licensee or takaful licensee as defined in the Labuan Financial Services and Securities Act 2010, and (11) any other person as may be specified by the Commission; provided that, in the each of the preceding categories (1) to (11), the distribution of the shares is made by a holder of a Capital Markets Services Licence who carries on the business of dealing in securities. The distribution in Malaysia of this prospectus is subject to Malaysian laws. This prospectus does not constitute and may not be used for the purpose of public offering or an issue, offer for subscription or purchase, invitation to subscribe for or purchase any securities requiring the registration of a prospectus with the Commission under the Capital Markets and Services Act 2007.

Notice to prospective investors in Taiwan

The shares have not been and will not be registered with the Financial Supervisory Commission of Taiwan pursuant to relevant securities laws and regulations and may not be sold, issued or offered within Taiwan through a public offering or in circumstances which constitutes an offer within the meaning of the Securities and Exchange Act of Taiwan that requires a registration or approval of the Financial Supervisory Commission of Taiwan. No person or entity in Taiwan has been authorised to offer, sell, give advice regarding or otherwise intermediate the offering and sale of the shares in Taiwan.

Notice to prospective investors in South Africa

Due to restrictions under the securities laws of South Africa, the shares are not offered, and the offer shall not be transferred, sold, renounced or delivered, in South Africa or to a person with an address in South Africa, unless one or other of the following exemptions applies:

(1) the offer, transfer, sale, renunciation or delivery is to:

(a) persons whose ordinary business is to deal in securities, as principal or agent;

(b) the South African Public Investment Corporation;

(c) persons or entities regulated by the Reserve Bank of South Africa;

(d) authorised financial service providers under South African law;

(e) financial institutions recognised as such under South African law;

(f) a wholly-owned subsidiary of any person or entity contemplated in (c), (d) or (e), acting as agent in the capacity of an authorised portfolio manager for a pension fund or collective investment scheme (in each case duly registered as such under South African law); or

(g) any combination of the person in (a) to (f); or

(2) the total contemplated acquisition cost of the securities, for any single addressee acting as principal is equal to or greater than ZAR1,000,000.

No “offer to the public” (as such term is defined in the South African Companies Act, No. 71 of 2008 (as amended or re-enacted), or the South African Companies Act, in South Africa is being made in connection with the issue of the shares. Accordingly, this document does not, nor is it intended to, constitute a “registered prospectus” (as that term is defined in the South African Companies Act) prepared and registered under the South African Companies Act and has not been approved by, and/or filed with, the South African Companies and Intellectual Property Commission or any other regulatory authority in South Africa. Any issue or offering of the shares in South Africa constitutes an offer of the shares in South Africa for subscription or sale in South Africa only to persons who fall within the exemption from “offers to the public” set out in section 96(1)(a) of the South African Companies Act. Accordingly, this document must not be acted on or relied on by persons in South Africa who do not fall within section 96(1)(a) of the South African Companies Act (such persons being referred to as “SA Relevant Persons”). Any investment or investment activity to which this document relates is available in South Africa only to SA Relevant Persons and will be engaged in South Africa only with SA relevant persons.

Legal matters

The validity of the shares of common stock offered hereby and certain other legal matters will be passed upon for us by Smith, Anderson, Blount, Dorsett, Mitchell & Jernigan, LLP, Raleigh, North Carolina, and certain other legal matters in connection with this offering will be passed upon for us by Latham & Watkins LLP. Certain legal matters in connection with this offering will be passed upon for the underwriters by Cooley LLP, New York, New York.

Experts

The financial statements included in this prospectus have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report appearing herein. Such financial statements are included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

Where you can find more information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information about us and the common stock offered hereby, we refer you to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. Upon completion of this offering, we will be required to file periodic reports, proxy statements, and other information with the SEC pursuant to the Exchange Act. You can read our SEC filings, including the registration statement, at the SEC's website at www.sec.gov. We also maintain a website at www.precisionbiosciences.com. The information contained in, or accessible through, our website does not constitute a part of this prospectus.

Precision BioSciences, Inc.
Index to consolidated financial statements

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. (the “Company”) as of December 31, 2018 and 2017, 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, 2018, 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, 2018 and 2017, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2018, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

/s/ Deloitte & Touche LLP

Raleigh, North Carolina
February 21, 2019 (March 18, 2019 as to Note 15)

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

Precision BioSciences, Inc.
Consolidated balance sheets

(In thousands, except share and per share amounts)	December 31, 2017	December 31, 2018	Pro forma December 31, 2018 (unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 62,802	$103,193	$ 103,193
Accounts receivable	—	523	523
Prepaid expenses	1,437	8,913	8,913
Other current assets	92	3,046	3,046
Total current assets	64,331	115,675	115,675
Property, equipment, and software—net	8,137	21,147	21,147
Intangible assets—net	90	1,466	1,466
Other assets	124	312	312
Total assets	$ 72,682	$138,600	$ 138,600
Liabilities and Stockholders' Equity (Deficit)			
Current liabilities:			
Accounts payable	$ 1,806	$ 2,218	$ 2,218
Accrued expenses and other current liabilities	1,573	3,421	3,421
Deferred revenue	5,824	8,436	8,436
Total current liabilities	9,203	14,075	14,075
Deferred revenue—noncurrent	88,596	82,807	82,807
Deferred rent—noncurrent	1,252	1,758	1,758
Total liabilities	99,051	98,640	98,640
Commitments and contingencies (Note 9)			
Stockholders' equity (deficit):			
Series A convertible preferred stock; $0.0001 par value—25,650,000 shares authorized as of December 31, 2017 and 2018; 25,650,000 shares issued and outstanding as of December 31, 2017 and 2018; no shares issued and outstanding as of December 31, 2018, pro forma (unaudited)	3	3	—
Series B convertible preferred stock; $0.0001 par value—no shares authorized, issued and outstanding as of December 31, 2017; 21,956,100 shares authorized and 21,956,095 shares issued and outstanding as of December 31, 2018; no shares issued or outstanding as of December 31, 2018, pro forma (unaudited)	—	2	—
Common stock; $0.000005 par value—100,000,000 shares authorized, 16,496,801 shares issued and 15,686,329 shares outstanding as of December 31, 2017; 130,000,000 shares authorized, 16,717,117 shares issued and 15,906,645 shares outstanding as of December 31, 2018; 39,018,307 issued and 38,207,835 outstanding, pro forma (unaudited)	—	—	—
Additional paid-in capital	13,691	126,094	126,099
Accumulated deficit	(39,111)	(85,187)	(85,187)
Treasury stock (at cost, 810,472 shares of common stock at December 31, 2017 and 2018)	(952)	(952)	(952)
Total stockholders' equity (deficit)	(26,369)	39,960	39,960
Total liabilities and stockholders' equity (deficit)	$ 72,682	$138,600	$ 138,600

See notes to consolidated financial statements

Precision BioSciences, Inc.
Consolidated statements of operations

(In thousands, except share and per share amounts)	Years ended December 31, 2017	2018
Revenue	$ 6,484	$ 10,883
Operating expenses:		
Research and development	20,324	45,122
General and administrative	8,016	13,673
Impairment of intangible assets	118	—
Total operating expenses	28,458	58,795
Loss from operations	(21,974)	(47,912)
Other income:		
Interest income	872	1,875
Net loss and net loss attributable to common stockholders	$ (21,102)	$ (46,037)
Net loss per share attributable to common stockholders-basic and diluted	$ (1.33)	$ (2.92)
Weighted-average shares of common stock outstanding-basic and diluted	15,906,793	15,775,541
Pro forma net loss per share attributable to common stockholders-basic and diluted (unaudited)		$ (1.37)
Pro forma weighted-average shares of common stock outstanding-basic and diluted (unaudited)		33,653,835

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 capital	Accumulated deficit	Treasury stock	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance—January 1, 2017	25,650,000	$ 3	—	$ —	16,458,096	$ —	$ 13,257	$ (18,009)	$ —	$ (4,749)
Repurchase of common stock	—	—	—	—	—	—	—	—	(952)	(952)
Stock option exercises	—	—	—	—	38,705	—	15	—	—	15
Share-based compensation expense	—	—	—	—	—	—	419	—	—	419
Net loss	—	—	—	—	—	—	—	(21,102)	—	(21,102)
Balance—December 31, 2017	25,650,000	$ 3	—	$ —	16,496,801	$ —	$ 13,691	$ (39,111)	$ (952)	$ (26,369)
Issuance of Series B convertible preferred stock, net of offering 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

See notes to consolidated financial statements

Precision BioSciences, Inc.
Consolidated statements of cash flows

(In thousands)	Years ended December 31, 2017	2018
Cash flows from operating activities:		
Net loss	$ (21,102)	$ (46,037)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,435	2,354
Share-based compensation	419	2,453
Loss on disposal of assets	56	14
Impairment of intangible assets	118	—
Changes in operating assets and liabilities:		
Prepaid expenses	(550)	(7,476)
Other current assets	—	(260)
Accounts receivable	—	(523)
Other assets	63	(188)
Accounts payable	864	(673)
Accrued expenses and other current liabilities	707	1,790
Deferred revenue	(6,179)	(3,177)
Net cash used in operating activities	(24,169)	(51,723)
Cash flows from investing activities:		
Acquisition of license rights	—	(1,400)
Purchases of property, equipment, and software	(5,565)	(14,278)
Proceeds from disposal of equipment	50	15
Net cash used in investing activities	(5,515)	(15,663)
Cash flows from financing activities:		
Issuance of Series B convertible preferred stock, net of offering costs	—	109,742
Deferred offering costs	—	(2,136)
Proceeds from stock option exercises	15	171
Repurchases of common stock	(952)	—
Net cash (used in) provided by financing activities	(937)	107,777
Net (decrease) increase in cash and cash equivalents	(30,621)	40,391
Cash and cash equivalents—beginning of period	93,423	62,802
Cash and cash equivalents—end of period	$ 62,802	103,193
Supplemental disclosures of noncash financing and investing activities:		
Deferred offering costs included in accrued expenses and other current liabilities	$ —	$ 406
Property, equipment and software additions included in accounts payable and accrued expenses and other current liabilities	$ 218	$ 1,340

See notes to consolidated financial statements

Precision BioSciences, Inc.
Notes to consolidated financial statements

Note 1: Description of business and summary of significant accounting policies

Description of business and basis of presentation

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. The accompanying consolidated financial statements include the accounts of the Company and ELO Life Systems, Inc. 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 and its collaborators’ 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.

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 multiple element arrangements, 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. To date, 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, 2018, the Company incurred a net loss of $46.0 million and, as of December 31, 2018, has an accumulated deficit of $85.2 million. The Company has financed operations to date primarily through the issuance of preferred stock (see Note 6) and with proceeds from its development and commercial license agreement with Les Laboratoires Servier (“Servier”)

Precision BioSciences, Inc.
Notes to consolidated financial statements

(see Note 13). 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 for at least a year from the issuance date of these consolidated financial statements. 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.

Unaudited pro forma consolidated balance sheet

The unaudited pro forma consolidated balance sheet statement presents the Company's capitalization as of December 31, 2018 giving effect to adjustments arising upon the completion of the proposed initial public offering. The adjustments relate to the automatic conversion of all outstanding shares of convertible preferred stock into shares of common stock as if the proposed initial public offering occurred on December 31, 2018.

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, 2017 and 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 89% and 6% of revenue during 2017 and 53% and 34% of revenue during 2018, as well as 97% and 2% of deferred revenue as of December 31, 2018.

Deferred offering costs

The Company capitalizes incremental legal, professional accounting and other third-party fees that are directly associated with the Company's planned initial public offering ("IPO") as other current assets until the IPO is consummated. After consummation of the IPO, these costs will be recorded in stockholders' equity (deficit) as a reduction of additional paid-in capital generated as a result of the offering. If the IPO is not completed, any costs deferred will be expensed immediately.

Precision BioSciences, Inc.
Notes to consolidated financial statements

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 undiscounted 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

The Company's 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 (i) licenses, or options to obtain licenses, to the Company's technology, (ii) research and development activities to be performed on behalf of the collaborative partner, and (iii) in certain cases, services in connection with the manufacturing of preclinical and clinical material. Payments to the Company under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and development efforts; clinical and development, regulatory, and sales milestone payments; and royalties on future product sales.

Precision BioSciences, Inc.
Notes to consolidated financial statements

Revenue is recognized when all of the following conditions are met: (i) persuasive evidence of an arrangement exists, (ii) delivery has occurred or services have been rendered, (iii) fees are fixed or determinable and (iv) collection of fees is reasonably assured.

The Company analyzes its collaboration arrangements to assess whether they are within the scope of Accounting Standards Codification *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 requires the Company to determine whether 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 within the scope of Accounting Standards Codification *605-25, Revenue Recognition—Multiple-Element Arrangements* ("ASC 605"). To date, the Company has no arrangements that are within the scope of ASC 808.

When evaluating multiple element arrangements under ASC 605, the Company determines whether the arrangement should be divided into separate units of accounting and how the arrangement consideration should be measured and allocated among the separate units of accounting. An element qualifies as a separate unit of accounting when the delivered element has stand-alone value to the customer. Any delivered elements that do not qualify as separate units of accounting are combined with other undelivered elements within the arrangement as a single unit of accounting. The Company determines the revenue recognition method for the combined unit of accounting and recognizes the revenue over the period from inception through the date the last deliverable within the single unit of accounting is delivered. The Company's arrangements do not include a general right of return relative to delivered elements.

Cash received prior to satisfying all revenue recognition criteria are recorded as deferred revenue in the accompanying consolidated balance sheets. The Company's deferred revenue primarily includes nonrefundable up-front license fees and advance payments for research and development funding. The deferred revenue is recognized into revenue on a proportional or straight-line basis over the estimated period of the Company's substantive performance obligations or the period the rights granted are in effect. Analyzing the arrangement to identify deliverables requires the use of judgment and each deliverable may be an obligation to deliver services, a right or a license to use an asset or some other performance obligation.

In arrangements that include license rights and other noncontingent deliverables, these deliverables do not have stand-alone value because the noncontingent deliverables are dependent on the license rights, are not sold separately and cannot be resold. In addition, when noncontingent deliverables are sold with up-front license rights, the sale of license rights do not represent the culmination of a separate earnings process. As such, the Company accounts for the license and the noncontingent deliverables as a single unit of accounting. In such instances, the license revenue in the form of nonrefundable up-front payments is deferred and recognized over the applicable relationship period, which historically has been the estimated period of the Company's substantive performance obligations or the period the rights granted are in effect.

The Company will recognize clinical and development, regulatory, and sales milestone payments as revenue when earned if they are substantive and the Company has no ongoing performance obligations related to the milestone payment. A milestone payment is considered substantive if it (i) is commensurate with either the Company's performance to achieve the milestone or the enhanced value of the delivered item as a result of a specific outcome from the Company's performance to achieve the milestone; (ii) relates solely to past performance; and (iii) is reasonable relative to all of the deliverables and payment terms, including other potential milestone consideration, within the arrangement.

Precision BioSciences, Inc.
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Royalties earned on product sales, if any, are recognized based on contractual terms of the agreement when reported sales are reliably measurable and collectibility is reasonably assured, provided that there are no performance obligations then remaining. To date, none of the Company's product candidates have been approved or commercialized, and therefore, the Company has not earned any royalty revenue from product sales.

In the event that an agreement was to be terminated and the Company had no further performance obligations at that time, the Company would recognize as revenue at the date of such termination any portion of the non-refundable upfront payment and other payments that had not previously been recorded as revenue and were classified as deferred revenue at the date of such termination.

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. Accrued amounts are disclosed in Note 5.

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.

Precision BioSciences, Inc.
Notes to consolidated financial statements

Common stock valuation

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, the Company has considered the estimated fair value of the common stock as of the measurement date. The estimated fair value of the common stock has been 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, 2017 and 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, 2017 and 2018 since all potential shares of common stock instruments are anti-dilutive as a result of the net loss.

The Company's convertible preferred stock contractually entitles the holders of such shares to participate in dividends but does not contractually require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss, such losses are not allocated to such participating securities. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive shares of common stock are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss attributable to common stockholders for the years ended December 31, 2017 and 2018.

Share-based compensation

Employees—The Company determines the fair value of stock options issued to employees as of the grant date. Share-based compensation expense equal to the grant-date fair value of the stock options is recognized over the requisite service period, which is equal to the vesting period.

Nonemployees—For nonemployees, the Company determines the fair value of stock options as of the measurement date, which is the earlier of the performance commitment date or the date on which the

Precision BioSciences, Inc.
Notes to consolidated financial statements

nonemployees' performance is complete. Share-based compensation expense equal to the measurement date fair value of the stock options is recognized over the period services are received.

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.

Recent accounting pronouncements

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; and as a result of this election, its financial statements may not be comparable to companies that comply with public company effective dates. 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) the last day of the fiscal year in which it has total annual gross revenues of $1.07 billion or more, (ii) the last day of the fiscal year following the fifth anniversary of the completion of its IPO, (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 ("FASB") issued Accounting Standards Update ("ASU"), No. 2014-09, Revenue (Topic 606): Revenue from Contracts with Customers ("ASU 2014-09"), which will replace existing revenue recognition standards and significantly expand the disclosure requirements for revenue arrangements. The new standard and the subsequent amendments, which are codified in ASC 606, will be

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effective for the Company beginning on January 1, 2019. The guidance permits two methods of adoption: retrospectively to each prior reporting period presented (the full retrospective method), or retrospectively with the cumulative effect of initially applying the guidance recognized at the date of initial application (the modified retrospective method). The Company currently anticipates adopting the new standard effective January 1, 2019 under the modified retrospective method. The Company has engaged outside advisors and is in the process of evaluating the impact of the adoption of ASC 606 on its consolidated financial statements. The Company will continue to assess the potential impact that ASC 606 may have on its financial position and results of operations as it relates to the Company's February 2016 development and commercial license agreement with Servier and the September 2018 collaboration and license agreement with Gilead Sciences, Inc. ("Gilead") (see Note 13 to the consolidated financial statements). The Company has performed an assessment of revenue recognition under the agreements with Servier, for the up-front payment, certain early-stage nonsubstantive development milestones, less fees to exercise the codevelopment and copromotion option, and with Gilead, for research funding. The Company believes revenue recognition under both agreements may not be materially different under ASC 606 as compared to ASC 605. Further, the Company's assessment of revenue for development milestones that are considered substantive under this agreement is that they be recognized over time when the amount of the milestone can be reasonably estimated without a significant reversal under ASC 606. Any prior assessments made by the Company regarding the impact of ASU 2014-09 are subject to change pending the outcome of the Company's final assessment at the conclusion of the first quarter of 2019.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, 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. In July 2018, the FASB issued amendments in ASU 2018-11, which provide a transition election to not restate comparative periods for the effects of applying the new standard. This transition election permits entities to change the date of initial application to the beginning of the year of adoption and to recognize the effects of applying the new standard as a cumulative-effect adjustment to the opening balance of retained earnings. The Company currently anticipates adopting the new standard effective January 1, 2019 under the modified retrospective method. ASU 2016-02 is effective for the Company for annual periods beginning after December 15, 2019 and early adoption is permitted. The Company is evaluating the impact of adoption of this standard on the consolidated financial statements.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation—Stock Compensation: Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"), which amends ASC 718, *Compensation—Stock Compensation*. The amendments simplify several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, forfeitures, and classification in the consolidated statements of cash flows. ASU No. 2016-09 was adopted by the Company on January 1, 2018 and the adoption did not have a material impact on the consolidated financial statements. The Company elected to account for the impact of pre-vesting forfeitures as they occur rather than applying an estimated forfeiture rate and to adopt this standard using the modified retrospective adoption method.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation-Stock Compensation*, or ASU 2017-09. The new guidance is an update to ASC 718 and simplifies the modification accounting for share-based payment awards. ASU 2017-09 is effective for annual periods beginning after December 15, 2017. The Company adopted this standard as of January 1, 2018. The adoption of this guidance had no impact on the consolidated financial statements.

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Note 2: Other current assets

Other current assets consisted of the following as of December 31 (in thousands):

	2017	2018
Deferred offering costs	$ —	$ 2,542
Deferred rent asset	70	—
Noncustomer receivables	22	504
Total other current assets	$ 92	$ 3,046

Note 3: Property, equipment and software

Property, equipment and software consisted of the following as of December 31 (in thousands):

	2017	2018
Construction in progress	$ 12	$ 8,600
Leasehold improvements	4,541	5,733
Software	86	278
Laboratory equipment	5,370	10,057
Office equipment	570	839
Furniture and fixtures	751	1,124
Total property, equipment and software	11,330	26,631
Less accumulated depreciation and amortization	3,193	5,484
Property, equipment and software—net	$ 8,137	$21,147

As of December 31, 2018, construction in progress includes $0.6 million related to the construction of additional office and laboratory space at 302 East Pettigrew Street, Durham, North Carolina, $5.4 million related to the construction of additional office and laboratory space at 5 Laboratory Drive, Research Triangle Park, North Carolina, and $2.5 million related to the construction of a cleanroom at 20 TW Alexander Drive, Research Triangle Park, North Carolina.

Depreciation expense, including amortization of leasehold improvements and software, was $1.4 million and $2.3 million for the years ended December 31, 2017 and 2018, respectively. Please refer to Note 9, “Commitments and contingencies,” for further information.

Note 4: Intangible assets

Intangible assets, net, consisted of the following as of December 31 (in thousands):

	2017	2018
License cost	$ 431	$1,831
Less: accumulated amortization	(223)	(247)
Less: impairments	(118)	(118)
Intangible assets, net	$ 90	$1,466

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Amortization expense of the intangible assets was $0.1 million for the years ended December 31, 2017 and 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 216 months.

Note 5: Accrued expenses and other current liabilities

Accrued expenses and other current liabilities consisted of the following as of December 31 (in thousands):

	2017	2018
Accrued compensation	$ 983	$ 965
Accrued research and development expenses	500	1,569
Accrued property, equipment and software	—	219
Accrued deferred offering costs	—	193
Deferred rent	—	198
Accrued legal fees	23	107
Other	67	170
Total accrued expenses and other current liabilities	$1,573	$3,421

Note 6: Stockholders' equity (deficit)

Capital structure

In April 2015, the Company amended and restated its certificate of incorporation and authorized 125,650,000 shares, of which 100,000,000 shares were designated as $0.000005 par value common stock and 25,650,000 shares were designated as $0.0001 par value Series A preferred stock.

In May 2018, the Company amended and restated its certificate of incorporation and authorized 177,606,100 shares, of which 130,000,000 shares were designated as $0.000005 par value common stock, 25,650,000 shares were designated as $0.0001 par value Series A preferred stock, and 21,956,100 shares were designated as $0.0001 par value Series B preferred stock.

Preferred stock

In 2015, the Company issued 25,650,000 shares of Series A preferred stock for gross proceeds of $25.7 million and incurred stock issuance costs of $0.3 million. The Series A preferred stock shares were sold for $1.00 per share (the "Series A Original Issue Price").

From May 2018 to July 2018, the Company issued 21,956,095 shares of its Series B preferred stock and received $110.0 million in gross proceeds, less $0.3 million in aggregate offering costs. The Series B preferred stock shares were sold for $5.01 per share (the "Series B Original Issue Price", together with the Series A Original Issue Price, the "Original Issue Price").

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The rights and privileges of the Series A and Series B preferred stockholders include the following:

Conversion—Each share of Series A and Series B preferred stock may be converted at any time, at the option of the holder, into shares of common stock. Each share of the Series A and Series B preferred stock will be automatically converted into shares of common stock, at the applicable conversion rate then in effect, upon the closing of the proposed initial public offering.

The conversion rate of the Series A and Series B preferred stock is determined by dividing the Original Issue Price by the conversion price for each series of stock. Each share of Series A and Series B preferred stock is convertible on a one-for-2.134686 basis into common stock.

Voting rights—Preferred stock and common stock vote together as one class on an as-converted basis. Holders are entitled to vote on all matters and shall have the number of votes equal to the number of shares of common stock into which the shares of preferred stock held by such holder are then convertible. The Company cannot perform any of the following actions without a vote of approval from at least 60% of outstanding preferred stockholders: execute a liquidation event, amend the Company's certificate of incorporation in a manner detrimental to Series A and Series B preferred stockholders, create or amend any securities to be senior to the Series A and Series B preferred stockholders, issue or increase the amount of the Company's common stock, or change the size of the board of directors. The Company's board of directors is currently comprised of five directors: two directors designated by the common stockholders, two directors designated by the preferred stock stockholders and one independent director. The Company's current shareholder agreements require the board of directors to have seven members. The remaining two directors, neither of whom may have any affiliation with any class of stockholder, will be designated by the four common and preferred directors.

Dividends—No classes of stock are entitled to receive dividends unless preferred stockholders first receive dividends on outstanding shares in an amount at least equal to the amount of dividends payable to the other classes of stock. The preferred shares do not accrue dividends.

Liquidation—Upon liquidation, dissolution, or winding-up of the Company, Series A and Series B preferred stockholders do not receive a liquidation preference in priority to holders of common stock. Assets available for distribution will be allocated ratably among the preferred, on a fully converted basis, and the common stockholders based on their pro rata holdings.

Redemption—The Series A and Series B preferred stock can only be redeemed at the option of the holder for cash or other assets upon the occurrence of specific events following a "Deemed Liquidation Event" (as defined in the Company's amended and restated certificate of incorporation) involving the sale, transfer, lease or other disposition of all or substantially all of the Company's assets.

A Deemed Liquidation Event that would give rise to a preferred stockholder's right of redemption cannot be triggered without approval of the Company's board of directors, because under applicable legal and contractual requirements, the Company's board of directors is required to approve (i) any closing of the sale, transfer, lease or other disposition, of all or substantially all of the Company's assets, (ii) any consummation of the merger or consolidation of the Company with or into another entity and (iii) the Company's participation in any closing of the transfer (whether by merger, consolidation, or otherwise), in which the Company is a constituent party to a person or group of affiliated persons, of the Company's securities, in which, after such closing, such person or group of affiliated persons would hold a majority of the outstanding voting stock of the Company (or the surviving or acquiring entity).

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The holders of the Series A and Series B preferred stock do not have the ability to control whether the Company will redeem the preferred stock or cause the preferred stock to become redeemable (including through a Deemed Liquidation Event) through representation on the Company's board of directors, voting rights or other rights, and there is no event not solely within the Company's control that contractually could cause the holders of the Series A and Series B preferred stock to obtain such control.

Common stock

In March 2017, the Company's board of directors authorized the repurchase of up to 4,258,663 shares of its common stock at a price of $1.18 per share in a solicited offer to non-employees. The Company accounts for its common stock repurchases as treasury stock under the cost method. In April 2017, the Company repurchased 810,472 shares of common stock at a cost of $1.0 million pursuant to this repurchase program.

Voting, dividend and liquidation rights of the holders of the common stock are subject to and qualified by the rights, powers and preferences of the holders of the preferred stock.

The rights and privileges of the holders of common stock include the following:

Voting—Each holder of outstanding shares of common stock shall be entitled to one vote in respect of each share. The number of authorized shares of common stock may be increased or decreased by the affirmative vote of a majority of the outstanding shares of common stock and preferred stock voting together as a single class.

Dividends—Subject to preferred stockholders' right to receive at least an equal amount of dividends payable to the other classes of stock in the event of a dividend, the holders of common stock shall be entitled to receive dividends out of funds legally available at such times and in such amounts as the Company's board of directors may determine in its sole discretion.

Liquidation—Upon liquidation, dissolution, or winding-up of the Company, the common stockholders are entitled to receive assets available for distribution ratably with the preferred stockholders, on a fully converted basis, based on their pro rata holdings.

Redemption—The common stock is not redeemable at the option of the holder.

Note 7: Stock options

Under the terms of its stock option plans, the Company's board of directors may grant stock options to employees, directors and service providers. The Company issued 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; there are no remaining shares available to be granted under the 2006 plan. There were 1,558,558 and 1,397,203 stock options outstanding under the 2006 Plan as of December 31, 2017 and 2018, respectively.

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 of common stock reserved for issuance to 8,211,980. There were 1,363,315 and 1,576,010 shares of common stock available for future grants under the 2015 plan as of December 31, 2017 and 2018, respectively, and 3,857,467 and 6,366,261 stock options outstanding as of December 31, 2017 and 2018, respectively. The Company's board of directors determines the terms of stock options granted under the 2015 plan, including option exercise prices and vesting.

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The Company recorded $0.4 million and an amount less than $0.1 million in employee and nonemployee share-based compensation expense, respectively, during the year ended December 31, 2017 and $2.4 million and an amount less than $0.1 million in employee and nonemployee share-based compensation expense, respectively, during the year ended December 31, 2018.

Share-based compensation expense related to stock options is included in the following line items in the consolidated statements of operations for the year ended December 31 (in thousands):

	2017	2018
Research and development	$286	$1,817
General and administrative	133	636
	$419	$2,453

Determining the appropriate fair value model and the related assumptions requires judgment. The fair value of each option grant is estimated using a Black-Scholes option-pricing model on the date of grant as follows:

	2017		2018	
	Nonemployees	Employees	Nonemployees	Employees
Estimated dividend yield	0.00%	0.00%	0.00%	0.00%
Weighted-average expected stock price volatility	70.28%	73.35%	68.00%	68.44%
Weighted-average risk-free interest rate	1.75%	1.99%	3.03%	2.95%
Expected life of options (in years)	4.60	6.10	6.09	6.01
Weighted-average fair value per option	$ 0.67	$ 0.77	$ 7.60	$ 7.37

The expected volatility rates are estimated based on the actual volatility of comparable public companies over the expected term. The expected life 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 continues to calculate expected life based on the midpoint between the vesting date and the contractual term which is in accordance with the simplified method. The expected term for share-based compensation granted to nonemployees is the contractual life. The risk-free rate is based on the United States Treasury yield curve during the expected life of the option.

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The following table summarizes activity in the Company's stock option plans during the years ended December 31, 2017 and 2018:

	Outstanding option shares		Weighted-average exercise price
Balance as of January 1, 2017	4,052,313	$	0.35
Granted	1,764,150		1.18
Exercised	(38,705)		0.41
Forfeited/canceled	(361,733)		0.35
Balance as of December 31, 2017	5,416,025		0.62
Granted	3,160,097		11.66
Exercised	(220,308)		0.78
Forfeited/canceled	(430,987)		2.77
Expired	(161,355)		0.01
Balance as of December 31, 2018	7,763,464	$	5.00

The intrinsic value of options exercised was $27,720 and $2,735,441 during 2017 and 2018, respectively.

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, 2017 and 2018.

		Number of options	Weighted-average remaining contractual life (in years)		Weighted-average exercise price
2017	Expected to be exercisable	5,277,613	6.96	$	0.61
2017	Currently exercisable	2,607,517	5.06		0.23
2018	Expected to be exercisable	7,763,464	7.50	$	5.00
2018	Currently exercisable	3,418,993	5.37		0.76

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The following table summarizes certain information about stock options outstanding under the stock option plans as of December 31:

	2017		
Exercise price	Number of options outstanding	Weighted-average remaining life	Number of options exercisable
$0.01 — $.02	259,647	2.38	259,647
$0.04	1,298,911	3.38	1,298,911
$0.41	1,617,613	7.65	888,501
$1.20	2,239,854	9.19	160,433
	5,416,025		2,607,492

	2018		
Exercise price	Number of options outstanding	Weighted-average remaining life	Number of options exercisable
$0.01 — $.03	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	748,873
$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		3,418,944

There was $1.5 million and $21.6 million of total unrecognized compensation cost related to unvested stock options as of December 31, 2017, and 2018, respectively, which is expected to be recognized over a weighted-average period of 3.03 and 3.50 years, respectively.

Note 8: 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, 2017 and 2018.

The Retirement Plan includes a discretionary matching employer contribution equal to 100% of participants’ deferral contributions up to a certain percentage amount to be determined by the Company on an annual basis. The Company made contributions of $0.2 million and $0.4 million to the Retirement Plan during the years ended December 31, 2017 and 2018, respectively.

Note 9: 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

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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. All the leases provide tenant improvement allowances and rent abatements as incentives for the Company to either enter into the initial lease agreement or expand within an existing premises already under lease. The Company leases 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. The Company leases laboratory and office space at 5 Laboratory Drive, Research Triangle Park, North Carolina. The property is leased through April 2026 with the option to extend. The Company leases laboratory space at 20 TW Alexander Drive, Research Triangle Park, North Carolina. The property is leased through August 2026 with the option to extend.

The following is a schedule of future minimum lease payments for all leases as of December 31, 2018 (in thousands):

	Operating leases
2019	$ 1,999
2020	2,157
2021	2,227
2022	2,299
2023	2,364
2024 and beyond	3,484

Future minimum lease payments due under certain operating lease arrangements contain fixed rent increases over the term of the lease. Rent expense on these operating leases is recognized over the term of the lease on a straight-line basis. The excess of rent expense over lease payments made has been reported in deferred rent and deferred rent-noncurrent in the consolidated balance sheets. Rent expense was $0.8 million and $1.5 million during the years ended December 31, 2017 and 2018, respectively, and apportioned between the "Research and development" and "General and administrative" lines items in the consolidated statements of operations.

Supply agreements

The Company enters into contracts in the ordinary course of business with CMOs for the manufacturing of clinical trial materials. 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.

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Note 10: Net loss per share and unaudited pro forma net loss per share

Net loss per share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share amounts):

	Years ended December 31,	
	2017	2018
Numerator:		
Net loss attributable to common stockholders	$ (21,102)	$ (46,037)
Denominator:		
Weighted-average shares of common stock outstanding—basic and diluted	15,906,793	15,775,541
Net loss per share attributable to common stockholders—basic and diluted	$ (1.33)	$ (2.92)

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,	
	2017	2018
Series A preferred stock (as converted to common stock)	12,015,818	12,015,814
Series B preferred stock (as converted to common stock)	—	10,285,376
Outstanding stock options converted to common stock	2,759,732	4,796,377
Total	14,775,550	27,097,567

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Unaudited pro forma net loss per share

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2018 has been prepared to give effect to adjustments arising upon the completion of the proposed IPO. The unaudited pro forma net loss attributable to common stockholders, as well as basic and diluted weighted-average shares of common stock outstanding, used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders gives effect to the automatic conversion of all outstanding shares of convertible preferred stock as of January 1, 2018 into shares of common stock as if the proposed initial public offering had occurred on that date or the issuance date of the convertible preferred stock for issuances after January 1, 2018. Unaudited pro forma basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share amounts):

	Year ended December 31, 2018
Numerator:	
Net loss attributable to common stockholders	$ (46,037)
Denominator:	
Weighted-average shares of common stock outstanding—basic and diluted	15,775,541
Pro forma adjustment to reflect automatic conversion of convertible preferred stock to common stock upon the completion of the proposed initial public offering	17,878,294
Pro forma weighted average shares of common stock outstanding—basic and diluted	33,653,835
Pro forma net loss per share attributable to common stockholders—basic and diluted	$ (1.37)

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Note 11: Income taxes

The Company recorded no income tax expense due to the operating losses incurred for the years ended December 31, 2017 and 2018.

Significant components of the Company's deferred tax assets and deferred tax liabilities are as follows as of December 31 (in thousands):

	2017	2018
Noncurrent deferred tax assets:		
Net operating loss carryforwards	$ 4,498	$ 9,185
Contribution carryforwards	10	29
Deferred rent	272	449
Deferred revenue	4,429	9,454
Other assets	102	573
Tax credits	1,697	3,632
Less valuation allowance	(10,464)	(22,736)
Total deferred tax assets, noncurrent	544	586
Noncurrent deferred tax liability:		
Property and equipment	544	586
Total deferred tax liabilities, noncurrent	544	586
Net deferred tax assets	$ —	$ —

As of December 31, 2017 and 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, 2018 of $12.3 million is comprised of an increase in the valuation allowance recorded against the deferred tax assets, primarily deferred revenue, for the year.

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The reasons for the difference between actual income tax benefit for the years ended December 31, 2017 and 2018 and the amount computed by applying the statutory federal income tax rate to losses before income tax benefit are as follows (dollars in thousands):

	2017		2018	
	Amount	% of pretax earnings	Amount	% of pretax earnings
Income tax expense (benefit) at statutory rate	$ (7,174)	34.0%	$ (9,668)	21.0%
State income taxes, net of federal tax benefit	(417)	2.0%	(909)	2.0%
Non-deductible expenses	208	(1.0%)	270	(0.6%)
Credits	(1,039)	4.9%	(1,934)	4.2%
Change in federal tax rate	4,955	(23.5%)	—	—
Change in state tax rate	2	—	—	—
Current blended state tax rate versus deferred rate	—	—	1	0.0%
Other	(110)	0.5%	(32)	0.1%
Change in valuation allowance	3,575	(16.9%)	12,272	(26.7%)
Income tax (benefit) expense	$ —	0.0%	$ —	0.0%

At December 31, 2017, the Company had federal and state net operating loss (“NOL”) carryforwards of $20.1 million and $19.4 million, respectively. As of December 31, 2018, the Company had federal and state NOL carryforwards of $40.0 million and $39.8 million, respectively. The federal NOL carryforwards of $19.4 million will begin to expire in 2030 while the remaining federal NOL carryforwards of $20.6 million carry forward indefinitely. The state NOL carryforwards begin to expire in 2025. At December 31, 2017, the Company had federal and state research and development (“R&D”) tax credits of $1.7 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 R&D tax 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, 2017 and 2018, the Company had federal contribution carryforward amounts of less than $0.1 million and $0.1 million, respectively, which begin to expire in 2020.

The Company incorporated a subsidiary in Australia in 2018. However, the subsidiary has had no activity since inception. As such, the there are no undistributed earnings as of December 31, 2018.

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

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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, 2017 and 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, 2017 and 2018, the Company had no such accruals.

On December 22, 2017, the Tax Cuts and Jobs Act was enacted into law, which reduced the federal corporate income tax rate to 21% for tax years beginning after December 31, 2017. As a result of the newly enacted tax rate, the Company adjusted its deferred tax assets as of December 31, 2017 by applying the new 21% rate, which resulted in a decrease to the deferred tax assets and a corresponding decrease to the valuation allowance of approximately $5 million for the year ended December 31, 2017.

The SEC staff issued Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act ("SAB 118"), which allows the Company to record provisional amounts during a measurement period which is similar to the measurement period used when accounting for business combinations. The measurement period has ended and the Company's accounting related to the 2017 Tax Cuts and Jobs Act is complete. The Company did not make any measurement-period adjustments related to the provision items recorded as of December 31, 2017.

Note 12: 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 data, 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.

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As of December 31, 2017 and 2018, the Company held cash equivalents which is 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, 2017	Fair value	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 251	$ 251	$ —	$ —
Repurchase agreements	58,345	—	58,345	—
	$ 58,596	$ 251	$58,345	$ —

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 13: 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 Baxalta (now Shire), which was assigned to Servier in connection with its acquisition of Shire's oncology business in August 2018. This agreement establishes a collaboration between the Company and Servier to develop allogeneic chimeric antigen receptor T cell therapies for up to six unique antigen targets selected by Servier. Servier selected one target at the agreement's inception, and Servier is entitled to select the remaining five targets over the first four years of the agreement. 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

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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 has determined that the targets are not separable because they are all based on the ARCUS proprietary genome editing platform and has assumed that Servier will nominate all six targets over the term of the agreement. The Company has concluded that the agreement with Servier contains the following deliverables: (i) a development license; (ii) performance of early-stage R&D services, which includes the early stage pre-IND development milestones that are deemed non-substantive and not subject to milestone method accounting, and (iii) JSC participation. The Company assessed whether any of these deliverables should be considered separate units of accounting and concluded that each of these deliverables has no standalone value other than performing early-stage R&D services on the Company's intellectual property and that the Company does not have a practice of selling its intellectual property or providing early-stage R&D services on a standalone basis to other parties. Also, none of these deliverables have any right of return. As a result, the Company concluded that these deliverables are considered a single unit of accounting.

The Company determined the consideration under the agreement consists of the $105.0 million up-front payment and milestone payments that may be earned for the early-stage pre-IND development milestones for the second through sixth antigen targets, if any, selected by Servier, less payment by the Company to exercise the 50/50 co-development and co-promotion option. The Company intends to opt in and participate on all selected targets with respect to the 50/50 co-development and co-promotion option. The Company can estimate its future cost based on the terms of the agreement. Thus, the option fees payable by the Company are considered an element that reduces the total arrangement consideration. The Company will not allocate consideration to the single unit of accounting to the extent of the total estimated future cost of the 50/50 codevelopment and co-promotion option fees it intends to pay. The total arrangement consideration through Phase 1 clinical trials for the single unit of accounting is recognized as revenue over the estimated performance period of 9.5 years, which includes the period of time Servier has to select the remaining 5 targets for development and the estimated time for the Company to complete early-stage R&D activities on all selected targets.

The Company has evaluated all of the milestones in connection with the agreement to determine if they are substantive and assess whether, for each milestone, (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company's performance to achieve the milestone, (ii) the consideration relates solely to past performance, and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the agreement. As noted, the early-stage pre-IND development milestones are deemed to be non-substantive and part of the single unit of accounting identified at the agreement's inception.

Because of the substantive uncertainty at the outset of the agreement that the Company will successfully achieve the development and sales milestones or that Servier will exercise its commercial option, the Company has determined that these are contingent deliverables. The manufacture of clinical trial material for use in Phase 2 clinical trials is also considered a contingent deliverable as the need for these materials will only occur

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if Servier exercises its commercial option. These future contingent deliverables do not contain any discounts that require allocation to the total arrangement consideration. As such, the milestones related to the contingent deliverables should not be allocated to the arrangement's consideration at the outset but rather be accounted for pursuant to ASC 605-28, Milestone Method. The contingent deliverables that are considered substantive are (i) the commercial option exercise fees, (ii) the manufacture of Phase 2 clinical trial material, (iii) development milestones based on specified regulatory and sales events, and (iv) sales-based milestones based on the achievement of specified sales amounts. The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

The Company recognized $5.8 million in revenues during 2017 and 2018 under the agreement with Servier. The amount recorded as deferred revenue was $94.4 and $88.6 million as of December 31, 2017 and 2018, respectively. No development or sales-based milestone payments were received for the years ended December 31, 2017 and 2018.

Sponsored research, collaboration and license agreement with the University of Pennsylvania

On January 1, 2018, the Company entered into a sponsored research, collaboration and license agreement with the University of Pennsylvania ("Penn") to collaborate on the preclinical development of six indications for gene editing products involving the delivery of an ARCUS nuclease. Unless the Company elects to terminate its funding obligations, the Company will provide semi-annual research funding payments of up to $5.0 million, with no minimum funding requirement, for up to a three-year term to fund the cost of the research program 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.

In addition to the research funding payments, if the Company elects to use certain Penn technology, including technology arising out of the collaboration, and achieves certain development and sales milestones, then the Company will be required to make certain 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. In addition to the development and sales milestone payments, low single-digit royalty percentages are also payable on net sales of certain products.

The Company may terminate the agreement by providing written notice at least 60 days prior to the due date of the next semi-annual research funding payment without making termination payments to Penn other than for non-cancelable costs and reasonable wind down costs. If such notice is provided during the research term, the agreement will terminate at the end of the current semi-annual funding period. Following completion or expiration of the three-year research term, the agreement remains in effect for the lifetime of certain patents, and the Company may terminate the agreement upon providing at least 90 days prior written notice.

Penn provided the Company a non-exclusive, worldwide, royalty-bearing license for certain patent rights and know-how to be used on the six indications in a defined field of use involving the delivery and use of an ARCUS nuclease in exchange for an upfront payment of $0.3 million. Once the Company has paid the first $15.0 million in research funding noted above, the license grant for such patent rights and know-how in the field of use will

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be expanded to remove the limitation on indications and the Company may, upon payment of a $1.0 million option fee, obtain a license for certain additional patent rights.

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 termination 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 Precision to manufacture specifically identified products for Gilead to use in clinical trials at price based on the Company’s costs. The Company and Gilead will form 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 agreement with Gilead contains the following deliverables: (i) a development license; (ii) performance of early-stage R&D services, including technology transfer services, and (iii) JSC and JRDC participation. The Company assessed whether any of these deliverables should be considered separate units of accounting and concluded that each of these deliverables has no standalone value other than performing early-stage R&D services and that the Company does not have a practice of selling its intellectual property or providing early-stage R&D services on a standalone basis to other parties. None of these deliverables have any right of return. As a result, the Company concluded that these deliverables are considered a single unit of accounting. The Company will recognize revenue for each semi-annual research funding payment received on a straight-line basis over the six-month period the Company performs early-stage R&D services, as Gilead has the right to terminate the agreement at the conclusion of any six-month period. This method of revenue recognition most closely matches the pattern in which revenue is earned, the Company is paid, and obligations are fulfilled by the Company under the agreement.

The Company has evaluated all of the development and commercial milestones in connection with the agreement to determine if they are substantive and assess whether, for each milestone, (i) the consideration is commensurate with either the Company’s performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company’s performance to achieve the milestone, (ii) the consideration relates solely to past performance, and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the agreement. Because of the substantive uncertainty at the outset of the agreement that the Company will successfully achieve the development and commercial milestones, the Company has determined that these are contingent deliverables. These future contingent deliverables do not contain any discounts that require allocation to the total

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arrangement consideration. As such, the consideration related to the contingent deliverables should not be allocated to the arrangement's consideration at the outset but rather be accounted for pursuant to ASC 605-28, Milestone Method.

The Company recognized $3.7 million in revenues during 2018 under the agreement with Gilead. The amount recorded as deferred revenue was $2.3 million as of December 31, 2018. No development or commercial milestone payments were received for the year ended December 31, 2018.

Note 14: Segment reporting

The Company has developed a genome editing platform and performs 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) plus an allocation of centralized research and development expenditures for early stage research, nuclease development and the purchase of general laboratory supplies. These expenditures are allocated to the segments based on headcount. The reportable segment and centralized research and development operational cash expenditures include cash disbursements for compensation, lab 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 and losses on 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.

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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,	
	2017	2018
Revenue:		
Therapeutics	$ 6,064	$ 9,523
Food	420	1,360
Total segment revenue	6,484	10,883
Segment operational cash expenditures:		
Therapeutics	$ 11,062	$ 35,045
Food	1,699	9,125
Total segment operational cash expenditures	12,761	44,170
Allocation of centralized research and development operational cash expenditures:		
Therapeutics	$ 6,948	$ 11,605
Food	1,164	2,901
Total allocation of centralized research and development operational cash expenditures	8,112	14,506
Segment operating loss:		
Therapeutics	$ (11,946)	$ (37,127)
Food	(2,443)	(10,666)
Total segment operating loss	(14,389)	(47,793)
Adjustments to reconcile segment operating loss to consolidated loss from operations:		
Corporate general and administrative cash expenditures	$ (9,117)	$ (15,892)
Interest income received	(872)	(1,875)
Impairment of intangible assets	(118)	—
Depreciation and amortization	(1,435)	(2,354)
Share-based compensation	(419)	(2,453)
Loss on disposal of assets	(56)	(14)
Adjustments to reconcile cash expenditures to GAAP expenses	4,432	22,469
Total consolidated loss from operations	$ (21,974)	$ (47,912)

Note 15: Subsequent events

In August 2018, the Company entered into a letter of intent with a contractor to begin work on the design and construction of a cGMP facility for the manufacturing of the Company's clinical trial material and future commercial product. The cleanroom will be constructed at the 20 TW Alexander Drive, Research Triangle Park, North Carolina site. The letter of intent allowed the contractor to begin work on the earlier design and engineering phases of the project until the parties could execute an agreement. On February 1, 2019, the

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Company completed a binding agreement with the contractor. The cost of the cleanroom is $5.0 million and the estimated completion date is June 2019. The Company may terminate the agreement upon ten days written notice. Construction-in-progress as of December 31, 2018 includes $2.5 million related to the cleanroom.

In March 2019, we sold and issued $39.6 million aggregate principal amount of convertible promissory notes (the “2019 Notes”) in a private placement transaction. The 2019 Notes accrue interest at a rate of 6% per annum and mature on March 1, 2021, if not previously converted to common stock or preferred stock or repaid in cash prior to the maturity date.

The 2019 Notes will be automatically settled into shares of the Company’s common stock in connection with the closing of an IPO by the Company with gross proceeds of at least $50.0 million at a settlement price equal to the lesser of (i) 85% of the IPO price per share or (ii) a price per share equal to $800.0 million divided by the Company’s fully diluted capitalization as of immediately prior to the closing of such offering. If the gross proceeds of the IPO are less than $50.0 million, the holder of each note may elect to convert the then-outstanding principal and accrued interest into shares of the Company’s common stock equal to 85% of the IPO price per share. If the Company completes a preferred stock financing round with gross proceeds of at least $50.0 million, excluding the conversion of the 2019 Notes, the 2019 Notes will be automatically converted into preferred stock at a settlement price equal to 85% of the lowest per share cash purchase price of preferred stock sold in the financing round.

If the Company sells all or substantially all of its assets, completes a merger or consolidation or transfers a majority of outstanding voting stock that results in a change of control or otherwise liquidates or dissolves (each, a “liquidation event”), the holder will receive 200% of the then-outstanding principal amount. If neither an IPO, nor a qualified preferred stock financing, nor a liquidation event occurs prior to the maturity date, at any time on or after the maturity date, each holder of a 2019 Notes may elect to convert such holder’s 2019 Note into shares of newly authorized Series B-1 Preferred Stock of the Company at a settlement price per share that would be determined based on the then-outstanding principal and accrued interest divided by $6.40 per share, subject to certain recapitalization adjustments.

On March 15, 2019, the Company filed an amendment to the Company’s amended and restated certificate of incorporation to effect a reverse split of shares of the Company’s common stock on a 1-for-2.134686 basis (the “Reverse Stock Split”). In connection with the Reverse Stock Split, the conversion ratio for the Company’s Series A and Series B convertible preferred stock was proportionately adjusted such that the common stock issuable upon conversion of such preferred stock was decreased in proportion to the Reverse Stock Split. Accordingly, all share and per share amounts for all periods presented in these financial statements have been retroactively adjusted, to reflect this reverse stock split and adjustment of the preferred stock conversion ratios.

The Company has evaluated subsequent events through March 18, 2019, the date these consolidated financial statements were issued and has determined that there were no events which have occurred that would require adjustment to or disclosure in these consolidated financial statements other than those disclosed above.

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7,900,000 shares

Common stock

Prospectus

J.P. Morgan **Goldman Sachs & Co. LLC** **Jefferies** **Barclays**

March 27, 2019