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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2018

OR

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

For the transition period from _____to_____

Commission file number: 001-38443

UNUM THERAPEUTICS INC.

(Exact name of registrant as specified in its charter)

Delaware	**46-5308248**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**
200 Cambridge Park Drive, Suite 3100 Cambridge, Massachusetts	**02140**
(Address of principal executive offices)	**(Zip Code)**

(617) 945-5576
(Registrant's telephone number, including area code)

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

Title of each class	**Name of exchange on which registered**
Common Stock, $0.001 Par Value	**The Nasdaq Global Select Market**

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

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

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

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

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

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

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

The aggregate market value of Common Stock held by non-affiliates of the registrant computed by reference to the price of the registrant's Common Stock as of June 29, 2018, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $208.4 million (based on the last reported sale price on the Nasdaq Global Select Market as of such date).

As of February 28, 2019, there were 30,090,862 shares of the registrant's Common Stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement for its 2019 Annual Meeting of Stockholders, which the registrant intends to file with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2018, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements, which reflect our current views with respect to, among other things, our operations and financial performance. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our future results of operations and financial position, business strategy and plans, and objectives of management for future operations, are forward-looking statements. These statements involve known and unknown risks, uncertainties, and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “should,” “expects,” “might,” “plans,” “anticipates,” “could,” “intends,” “target,” “projects,” “contemplates,” “believes,” “estimates,” “predicts,” “potential,” “seek,” “would” or “continue,” or the negative of these terms or other similar expressions. The forward-looking statements in this Annual Report on Form 10-K are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K and are subject to a number of risks, uncertainties and assumptions described in the “Risk Factors” section and elsewhere in this Annual Report on Form 10-K. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Some of the key factors that could cause actual results to differ from our expectations include:

- the success, cost, and timing of our product development activities and clinical trials;
- our ability to obtain and maintain regulatory approval for our ACTR087 and ACTR707 product candidates and any other product candidates we may develop, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- the potential for our identified research priorities to advance our ACTR and BOXR platform;
- the ability to license additional intellectual property relating to our product candidates from third-parties and to comply with our existing license agreements and collaboration agreements;
- the ability and willingness of our third-party research institution collaborators to continue research and development activities relating to our product candidates;
- our ability to commercialize our products in light of the intellectual property rights of others;
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates;
- the scalability and commercial viability of our manufacturing methods and processes;
- the commercialization of our product candidates, if approved;
- our plans to research, develop, and commercialize our product candidates;
- the potential benefits of our existing collaboration with Seattle Genetics and our ability to attract other collaborators with development, regulatory, and commercialization expertise;
- future agreements with third parties in connection with the commercialization of our product candidates and any other approved product;

- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates;
- the pricing and reimbursement of our product candidates, if approved;
- regulatory developments in the United States and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements, and needs for additional financing;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act;
- our use of the proceeds from the initial public offering and the concurrent private placement; and
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates.

While we may elect to update these forward-looking statements at some point in the future, whether as a result of any new information, future events, or otherwise, we have no current intention of doing so except to the extent required by applicable law.

PART I

Unless the context otherwise requires, we use the terms "Unum," "company," "we," "us," and "our" to refer to Unum Therapeutics Inc. and, where appropriate, our subsidiary.

ITEM 1. BUSINESS

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of novel immunotherapy products designed to harness the power of a patient's immune system to cure cancer. Our proprietary technologies include a universal, engineered cell therapy, referred to as Antibody-Coupled T cell Receptor (ACTR), that is intended to be used in combination with a wide range of tumor-specific antibodies to target different tumor types. In addition, we have developed a second novel technology, Bolt-On Chimeric Receptor (BOXR), for improving T cell functionality in solid tumor cancer applications by overcoming immunosuppressive tumor microenvironments. BOXR T cells may be directed to attack tumor cells using a variety of targeting strategies and our efforts to date have demonstrated activity using either ACTR or scFv-based CAR receptors. Our vision is to use our ACTR and BOXR product candidates to transform cancer treatment and deliver patient cures in many different hematologic and solid tumor cancers, improving upon current therapies.

We have a broad product pipeline that includes five programs. Four clinical-stage programs are based on the ACTR platform, composed of either ACTR087 or ACTR707 T cells co-administered with approved and investigational antibodies. ACTR087 is our original ACTR construct, comprising the ectodomain of CD16, the costimulatory domain of 4-1BB, and the signaling domain of CD3-zeta. ACTR707 is a modified ACTR construct selected for improved performance across a number of dimensions, including increased proliferation, cytokine secretion, and persistence in a repeat stimulation test. ACTR707 differs from ACTR087 in terms of its costimulatory domain (CD28) and other structural components. Our most advanced programs are comprised of ACTR087 or ACTR707 used in combination with rituximab to treat adult patients with relapsed or refractory CD20+ non-Hodgkin lymphoma (r/r NHL). These combinations are being tested in two ongoing, multi-center, open-label Phase I clinical trials called ATTCK-20-2 and ATTCK-20-03.

We completed patient enrollment and dosing of ACTR707 in combination with rituximab in the first two dose levels of the ATTCK-20-03 trial and presented preliminary data from these dose levels at the Sixtieth annual American Society of Hematology (ASH) meeting in December 2018 (2018 ASH Meeting). We have subsequently completed enrollment of patients in the third dose level of this trial and initiated enrollment at the fourth dose level. In 2019, we expect to define a recommended phase II dose (RP2D) based upon analysis of the cohorts tested during the dose escalation phase of the trial and to initiate a cohort expansion at the preliminary RP2D in the second half of 2019.

In the fourth quarter of 2017, we completed patient enrollment and dosing of ACTR087 in combination with rituximab in the dose escalation phase of the ATTCK-20-2 trial, and in the second quarter of 2018 we initiated the cohort expansion phase of the trial using an optimized dose of ACTR087. We completed enrollment in the cohort expansion phase of the ATTCK-20-2 study in the first quarter of 2019. Preliminary data from the dose escalation phase of the ATTCK-20-2 trial were presented on December 2017 at the Fifty-Ninth annual ASH meeting (2017 ASH Meeting). In both Phase I trials, we believe that we have demonstrated clinical proof of concept, as evidenced by ACTR T cell expansion and persistence, a favorable tolerability profile at defined dose levels, and anti-tumor activity. Based on emerging clinical data from the Phase I ATTCK-20-03 trial, the continuing progress in that trial, and our desire to efficiently manage resources, we have selected ACTR707 used in combination with rituximab to be the lead lymphoma program for advancement to further clinical development. We plan to report data on all enrolled patients in the ATTCK-20-2 trial at the end of 2019.

Our third program, ACTR087 used in combination with SEA-BCMA, is the first program resulting from our strategic collaboration with Seattle Genetics, Inc. (Seattle Genetics). We are currently enrolling and dosing adult

patients with r/r multiple myeloma in a Phase I multi-center trial, ATTCK-17-01. We reported initial data from the first three cohorts of this trial at the 2018 ASH Meeting. We are currently enrolling and dosing patients in the fourth cohort and expect to continue dose escalation during 2019 and to report data from multiple dose cohorts in the second half of 2019.

Our fourth program is ACTR707 used in combination with trastuzumab. We have an active IND to evaluate ACTR707 used in combination with trastuzumab as a potential treatment for advanced HER2+ solid tumor cancers, and in December 2018 we initiated a Phase I multi-center trial called ATTCK-34-01 testing this regimen in patients with HER2+ solid tumor cancers. We plan to enroll patients into this dose escalation trial throughout 2019 and to report initial clinical data from the ongoing dose escalation trial at the end of 2019.

Our fifth program is derived from our BOXR platform and is designated BOXR1030. BOXR1030 is comprised of a GPC3 CAR T cell therapy that includes an undisclosed bolt-on transgene expected to improve T cell metabolism and, preserve functionality in the environment of highly glycolytic tumors. We have initiated formal preclinical development activities, including safety testing and GMP process development, to prepare for future clinical testing and plan to present additional information regarding BOXR1030 in the second half of 2019.

In the longer term, we aim to leverage our ACTR and BOXR platforms to develop a broad range of programs to address many different hematologic and solid tumor cancers.

Immuno-oncology, the use of a patient's immune system to treat cancer, is one of the most actively pursued areas of research in drug discovery and development. Adoptive cell therapies are one immuno-oncology approach for cancer treatment. Adoptive cell therapy starts with the isolation of immune cells from a patient, often followed by genetic modification of these cells outside the patient's body. Modified immune cells are then re-introduced into the patient to treat disease. Chimeric antigen receptor (CAR)-T cells are one type of adoptive cell therapy. While the efficacy of CAR-T cells in hematologic cancers has been impressive, limited clinical data have been reported on their use in solid tumor cancers and the results have been much less encouraging than in the hematologic cancer setting. Severe side effects, such as cytokine release syndrome (CRS) and neurotoxicity, have been observed in some patients. For certain CAR-Ts, on-target, off-tumor effects have led to patient deaths. These toxicities and specific solid tumor challenges create a need to better control the activity of these therapies.

Our ACTR product candidates use patient-derived T cells, which are genetically modified to express the ACTR protein and co-administered with a tumor-specific antibody. ACTR is a chimeric protein which combines components from proteins normally found on both T cells and natural killer cells, two types of human immune cells. The natural killer cell component enables binding to tumor cell-bound antibodies and the T cell component enables potent cytotoxicity, proliferation, and persistence. Tumor-targeting antibodies administered with ACTR T cells bind to the surface of the tumor cell and, in effect, label it for ACTR T cell attack. When an ACTR T cell encounters a tumor cell bound with antibodies, it binds to those antibodies and kills the tumor cell through a process known as antibody-dependent cellular cytotoxicity (ADCC), a function not normally observed with T cells. No special modification of the tumor-specific antibody is required in order for ADCC to take place.

ACTR T cells can be directed to a wide range of different cancer cell antigens through the co-administration of antigen-specific antibodies. Thus, we believe an ACTR T cell can be used in many different cancer types. Preclinical data from *in vivo* testing show that ACTR T cell-mediated tumor killing activity may be adjusted by modulating the dose of the targeting antibodies. This ability to adjust ACTR T cell activity could make it possible to define an optimal dose through clinical testing to maximize tumor-killing activity and minimize toxicity.

Building beyond our ACTR programs, we have explored ways that we can broadly improve the fitness and functionality of T cell therapies, enabling them to be more effective, especially in solid tumors. A key hallmark of solid tumors is that they create an environment that actively blocks T cell attack through the presence of certain cell types, protein factors, and molecules that have immunosuppressive activity. In addition, solid tumors often consume the nutrients required for T cell metabolism and may lack some of the cellular signals that enable

T cells to activate properly when they encounter a tumor cell. Our efforts have resulted in the development of a second technology platform called BOXR. BOXR T cells express a chimeric receptor, such as an ACTR or a CAR, that targets a T cell to tumor cells. An additional transgene, encoding a separate protein product, is effectively 'bolted-on' within the same T cell in order to improve its fitness or functionality.

As presented at the Society for Immunotherapy of Cancer Annual Meeting (SITC) in November 2018, we have evaluated dozens of bolt-on candidates using functional assays to simulate adverse conditions that define the solid tumor microenvironment. Through these studies we have identified specific bolt-ons that work with either ACTR T cells or CAR T cells, or both, to significantly improve their functionality. We see the BOXR technology as an important complement to the ACTR technology that further enhances the opportunity to develop innovative cell therapies in solid tumors.

We have a broad product pipeline that includes four clinical stage programs and one pre-clinical program:

- ACTR707 and ACTR087, each used in combination with rituximab, are being tested in adult patients with r/r NHL in ongoing Phase I clinical trials called ATTCK-20-03 and ATTCK-20-2, respectively. We have selected ACTR707 as the lead product for potential further clinical development in r/r NHL.
- We completed patient enrollment and dosing of ACTR707 in combination with rituximab in the first two dose levels of the ATTCK-20-03 trial and presented preliminary data from these dose levels at the 2018 ASH Meeting in December 2018. Expansion and persistence of ACTR T cells was observed in all patients evaluable for response, consistent with what has been observed in the ATTCK-20-2 trial. At the first dose level of this trial, six patients were treated with ACTR707 used in combination with rituximab and six patients were evaluable for response. Of the six evaluable patients, three complete responses were observed. Three of the six evaluable patients experienced disease progression. At the second dose level, three patients were treated with ACTR707 in combination with rituximab, and three patients were evaluable for response. Of these three evaluable patients, one complete response was observed, and two patients experienced disease progression. As of November 1, 2018, three of the four complete responses were ongoing. No serious adverse events commonly associated with T cell activation (i.e., CRS or neurologic events) were observed. There were no dose-limiting toxicities observed. We have subsequently completed enrollment of patients in the third dose level of this trial and initiated enrollment at the fourth dose level. In 2019, we expect to define an RP2D and to initiate a cohort expansion at the RP2D in the second half of 2019.
- Two dose levels were explored in the dose escalation phase of the ATTCK-20-2 trial and data are summarized as of November 1, 2018. Expansion and persistence of ACTR T cells was observed in all patients in both tested dose levels for as long as monitoring continued. At the first dose level of this trial, with a dose of up to 0.5 x 10^6 ACTR T cells/kg (Dose Level One), eight patients were treated with ACTR087 used in combination with rituximab and six patients were evaluable for response. Of the six evaluable patients, two complete responses and one partial response were observed (with duration of responses of 661+ ongoing, 86, and 43 days, respectively). No adverse events commonly associated with T cell activation (CRS or neurologic events) of any grade were observed at the first dose level.

  At the second dose level of this trial, with a dose of 1.5 x 10^6 ACTR T cells/kg (Dose Level Two), nine patients were treated with ACTR087 used in combination with rituximab (a tenth patient was treated at Dose Level One due to patient cell production limitations). Six of these patients were evaluable for response. Of the six patients evaluated for response, one patient demonstrated a complete response ongoing for 311+ days and two patients demonstrated partial responses (6, 45 days). In Dose Level Two, two patients experienced ACTR087-related severe CRS and one patient experienced ACTR087-related neurotoxicity, which was fatal. Of the two events of CRS, one patient subsequently experienced a fatal case of enterococcal sepsis considered related to ACTR087 and one patient subsequently experienced a fatal case of sepsis considered not related

to ACTR087. After review of the observed safety events, we concluded that under this treatment regimen, Dose Level Two exceeds the maximum tolerated dose. In the second quarter of 2018, we began the cohort expansion phase of the trial using an optimized flat dose of ACTR087 that is between Dose Level One and Dose Level Two. We have completed enrollment in the cohort expansion phase of the trial and expect to report updated data from all patients enrolled in the ATTCK-20-2 trial at the end of 2019.

- Our third clinical stage program, ACTR087 used in combination with SEA-BCMA, is the first program resulting from our strategic collaboration with Seattle Genetics. We are currently enrolling and dosing adult patients with r/r multiple myeloma in a Phase I multi-center trial, ATTCK-17-01. Preliminary data from the first three cohorts of this study were presented at the 2018 ASH Meeting. We are enrolling patients at the fourth dose level. We plan to continue enrolling patients in this dose escalation Phase I trial and to report additional data from this study in the second half of 2019.
- Our fourth clinical stage program is ACTR707 used in combination with trastuzumab. We have an active IND to evaluate ACTR707 used in combination with trastuzumab as a potential treatment for advanced HER2+ solid tumor cancers. We have initiated a Phase I multi-center trial called ATTCK-34-01 to test this regimen in patients with HER2+ solid tumor cancers and we plan to report initial clinical data at the end of 2019.
- Our pre-clinical program is BOXR1030. It targets GPC3, an oncofetal antigen expressed in a variety of tumors including certain liver and lung cancers. We have initiated formal pre-clinical development for BOXR1030, putting it on the path for future clinical development and plan to present additional information regarding BOXR1030 in the second half of 2019.

In the longer term, we aim to leverage our ACTR and BOXR platforms to develop a broad range of programs to address many different hematologic and solid tumor cancers.

Our Pipeline

The following table summarizes our product candidate pipeline:

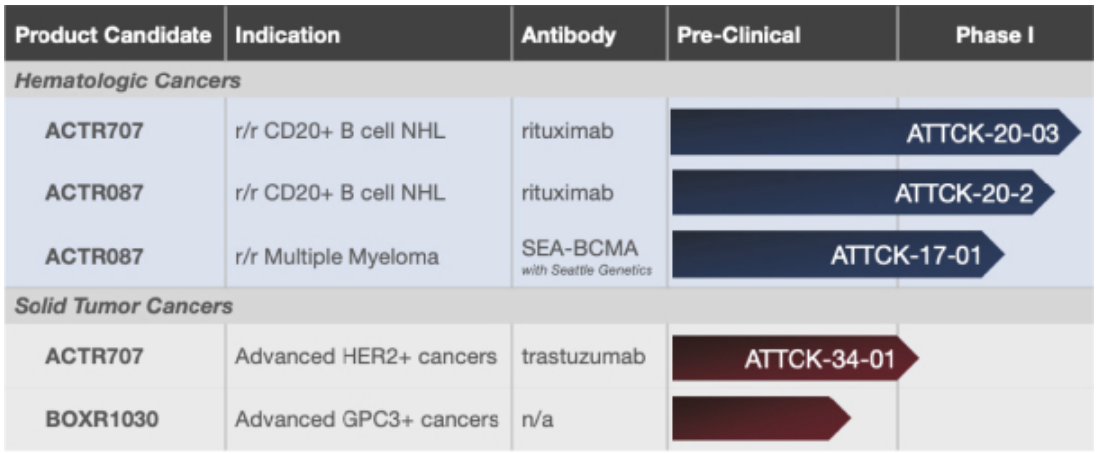


Figure 1. Product Candidate Pipeline

We aim to continue to improve the functionality of the ACTR T cell product candidates in solid tumor cancers through (i) further expansion of the BOXR platform and (ii) introduction of new manufacturing process modifications.

We have obtained and retained worldwide commercial rights to the majority of our programs, including our lymphoma programs, ACTR087 and ACTR707, each used in combination with rituximab, and our first solid tumor programs, ACTR707 used in combination with trastuzumab. Our BOXR platform has been internally developed through our sole efforts and we intend to obtain and retain worldwide commercial rights for this platform. We intend to establish our own commercial organization in the United States where we believe we can address physicians with a direct specialty sales force. Our commercial strategy for markets outside the United States may include the use of strategic partners or the establishment of our own commercial infrastructure. We plan to further evaluate these alternatives as we approach potential approval of our programs.

In June 2015, we announced a global strategic collaboration with Seattle Genetics to identify, research, develop, and commercialize two novel antibody-coupled ACTR therapies incorporating Seattle Genetics' proprietary antibodies. Under the terms of the collaboration, we will conduct preclinical research and clinical development activities through Phase I clinical trials and Seattle Genetics will provide all of the funding for those activities. We plan to work together to co-develop and fund product candidates after Phase I clinical trials unless either company opts-out from further development and commercial activities. Seattle Genetics has the option to opt-out from further development and commercialization activities for each of the two product candidates under the collaboration during two specified periods subsequent to Phase I clinical development. We and Seattle Genetics have an option to opt-out from further development and commercialization activities for each of the two product candidates under the collaboration during a specified period subsequent to Phase II clinical development. If neither party elects to opt-out of further development and commercialization activities, we will co-commercialize any successfully developed product candidates and share equally any profits and losses on any co-developed product candidates in the United States. Seattle Genetics retains exclusive commercial rights outside of the United States. The first product candidate under our collaboration is ACTR087 used in combination with Seattle Genetics' SEA-BCMA antibody for r/r multiple myeloma.

Clinical development and commercialization of ACTR and BOXR products are supported by our efforts to optimize manufacturing from the initial collection of a patient's white blood cells through the re-infusion of a formulated engineered T cell product (i.e., from "vein-to-vein"). To this end, we have developed a largely automated T cell manufacturing process with quality, scalability, cost, and consistency in mind. We plan to continuously enhance this process using a toolkit of individually optimized process components in order to be able to rapidly customize manufacturing to our specific needs, relying as much as possible upon non-proprietary equipment and processes. We are currently addressing clinical manufacturing needs for both viral vector and engineered T cells with contract manufacturing organizations (CMOs) to increase flexibility and mitigate risks. In the future, we plan to establish our own good manufacturing practices (GMP) manufacturing facility to increase our control of product quality, scheduling, and process knowledge. As our programs advance through clinical trials, we expect to secure commercial manufacturing capacity using one or more CMOs or by establishing our own commercial manufacturing GMP facility.

Intellectual property is an important component of our assets. We are working to establish strong patent protection and trade secrets to position us as a leader in the practice of the ACTR and BOXR technology. In December 2018, the United States Patent and Trademark Office issued US patent 10,144,770, entitled "Chimeric Receptors and Uses Thereof in Immune Therapy." The '770 patent covers design and use of the ACTR technology. Unum has exclusive, worldwide rights to the '770 patent under the terms of its license agreement with the National University of Singapore and St. Jude Children's Research Hospital. In addition to the '770 patent covering ACTR in the United States, previously granted patents protect the technology in Europe, Japan, and other important territories. Additional filed patent applications cover both the ACTR platform as well as specific product candidates. We are simultaneously seeking patent protection for the BOXR technology platform and have completed filings for several patent applications covering different aspects of the technology. In our efforts to both patent Unum inventions and license additional technologies, we have focused on trying to ensure our ability to operate freely within the complex patent landscape of cell therapy.

We believe that the quality of our people has a strong and positive impact on our ability to develop and capitalize on our ACTR platform. We have assembled a team of highly skilled and experienced employees, directors, scientific advisors, and consultants with broad capabilities in oncology drug discovery and development. In addition, our scientific founder and an inventor of our key patents relating to ACTR087, Dario Campana, M.D., Ph.D., is considered a world leader in cancer cell therapy. Dr. Campana continues to support our efforts as Chair of our Scientific Advisory Board.

Since our inception in March 2014, we have raised $77.3 million from sales of our preferred stock to our venture capital investors, major mutual funds, healthcare-dedicated funds, and others. In addition, through December 31, 2018, we had received $25.0 million in an upfront payment and $14.2 million in research and development funding from Seattle Genetics as part of the strategic collaboration. Collectively, these stakeholders share our commitment to bringing our product candidates to market and our vision of revolutionizing medicine through developing a broadly applicable cell-based platform.

On April 3, 2018, we completed our initial public offering (IPO) of our common stock and issued and sold 5,770,000 shares of our common stock at a public offering price of $12.00 per share, resulting in net proceeds of approximately $61.5 million, after deducting underwriting discounts and commissions and other offering costs. In addition, we completed a concurrent private placement of $5.0 million of shares of common stock at the public offering price of $12.00 per share, or 416,666 shares, with Seattle Genetics (the Concurrent Private Placement). On April 25, 2018, we issued and sold an additional 215,000 shares of our common stock at the IPO price of $12.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock, resulting in additional net proceeds of $2.4 million to us, after deducting underwriting discounts and commissions.

Our Strategy

Our goal is to transform cancer treatment through the application of our ACTR and BOXR platforms in a wide range of hematologic and solid tumor cancers. Key elements of our strategy include the following objectives:

- ***Expedite clinical development, regulatory approval, and commercialization of our lead lymphoma programs used in combination with rituximab.*** We plan to leverage data from the ongoing Phase I clinical trials, ATTCK-20-03 and ATTCK-20-2, to advance clinical development of our lead program, ACTR707 used in combination with rituximab for the treatment of adult patients with r/r NHL. If we believe the Phase I data are compelling, we plan to discuss with the FDA the potential to move to a registration trial in adult patients with r/r NHL upon completion of the current Phase I clinical trial of the selected lead product candidate, ACTR707.
- ***Leverage our universal ACTR platform to broaden our product portfolio rapidly and cost effectively.*** ACTR is an investigational engineered cell therapy that we believe can be used in combination with a wide range of tumor-targeting antibodies to pursue different antigens and cancer indications. ACTR does not need to be modified for use with different antibodies, and antibodies do not need to be modified for use with ACTR. This allows us to leverage our investment in ACTR and the investment by third parties in existing antibodies across different ACTR–antibody combinations, tumor types, and indications. The universality of the ACTR platform has enabled us to initiate clinical prosecution of four programs as of the end of 2018.
- ***Expand our pipeline with increased focus on solid tumor product candidates***. With a particular aim at creating an ACTR that addresses the specific challenges associated with attacking solid tumor cancers, we have developed a modified ACTR construct called ACTR707. We plan to use ACTR707 to rapidly progress ACTR product candidates targeting solid tumor cancers into clinical development, starting with ACTR707 used in combination with trastuzumab for HER2+ cancers. With the development of the BOXR platform, we believe we have the potential to enable a broad

range of tumor-targeting T cells, including both ACTR and CAR T cells, for solid tumor applications. We plan to expand a pipeline of solid tumor programs based upon both the ACTR and BOXR platforms.

- ***Establish manufacturing capacity and leverage our process development capabilities to create a competitive advantage in T cell manufacturing.*** We designed a process using a closed automated system to support our clinical development plans and have devoted significant resources to optimizing process development. We currently engage CMOs to use our process for production of GMP material. In the future, we intend to establish our own GMP manufacturing facility.
- ***Establish commercialization and marketing capabilities to support current and future product candidates.*** We plan to establish a U.S.-focused specialty sales and marketing organization in advance of receipt of regulatory approval of our first product candidate. We intend to leverage the infrastructure developed for our first approved product to facilitate commercialization of any additional product candidates for which we gain approval. In addition, we will build upon physician familiarity and experience with the first approved ACTR and BOXR products to accelerate adoption of subsequent products.

Background

Immune System and T cells

Our immune system has evolved to respond to injury and attacks to the body. It provides continuous surveillance and defense against attacks both by foreign pathogens and by mutated cells that lead to cancer. Cells and proteins produced by the immune system are found in all the tissues of the body and in the blood.

The immune system triggers two different types of response. The *innate response* is an unspecific, unspecialized response, composed of immune components capable of reacting against a broad range of stimuli. Innate immune components, including proteins (e.g., complement factors) and cells (e.g., natural killer cells, macrophages), are ever present, always ready for immediate activation. In contrast, the *adaptive response* allows for a slower but tailored response to specific insult. It evolves following an initial assault and strengthens with each subsequent infection or mutational event, thereby allowing for long-term protection. As a result of this increased specificity, adaptive responses can be more potent: they selectively target the pathogen or mutated cell while sparing normal, healthy tissues.

Adaptive responses include a humoral component, comprised of antibodies, and a cellular component, comprised of T cells. Antibodies are secreted proteins capable of binding to specific toxins or foreign substances generated during infection or mutation, referred to as antigens. Once bound to an antigen, an antibody can work *directly* to block the biological function of the antigen or *indirectly* by recruiting components of the innate immune system like natural killer cells to drive attack. T cells recognize infected or mutated cells when their TCR recognizes and binds to a foreign or mutated peptide presented through a set of proteins on the surface of the targeted cell called the major histocompatibility complex (MHC). The binding of a TCR to an infected or mutated cell, such as a tumor cell, can trigger T cell activation, resulting in direct killing of the cell through release of toxins, as well as the stimulation of cytokines and other molecules that recruit and activate additional immune cells.

Immunotherapies in Oncology

Historically, cancer treatment has relied upon a combination of surgery, radiation, and chemotherapy. More recently, targeted therapies that modulate specific signaling pathways in cancer cells have been the focus of many drug discovery efforts. Unfortunately, targeted pathways are often also functional in normal cells, leading to significant toxicities. More selective small molecules are better tolerated by patients and can have dramatic initial effects. In many cases, however, these benefits are short lived as persisting cancer cells acquire drug resistance. Most metastatic cancers remain incurable despite the enormous investment in novel therapies.

Immunotherapy seeks to harness a patient's immune system to fight cancer. The high specificity of the adaptive immune system translates into a reduced risk of toxicity by distinguishing between normal tissue cells and cancer cells. The ability to adaptively respond enables the immune system to overcome some of the mechanisms by which cancer cells acquire drug resistance, translating into more durable responses. There are several current approaches that use the immune system to treat cancer.

Immune checkpoint inhibitors are therapeutic antibodies that activate a patient's own T cells by blocking inhibitory signals released by the tumor to suppress the immune system's natural T cell activity. Antibodies targeting the antigens CTLA4, PD-1, and PD-L1 have yielded significant responses in patients with a range of indications including melanoma, non-small cell lung cancer, and renal cancer.

Additionally, monoclonal antibodies can be used to exert cancer cell cytotoxicity through specialized mechanisms, including ADCC, which is the primary mechanism of action of many cancer therapeutic antibodies. ADCC occurs when the tail region of an antibody, referred to as the Fc domain, binds to Fc receptors on the surface of certain immune cells, especially natural killer cells. A naturally occurring variant of CD16, one type of Fc receptor expressed on natural killer cells and macrophages, has been shown to bind more tightly to the Fc domain and patients expressing this variant demonstrate better responses to ADCC-inducing therapeutic antibodies. These results have inspired efforts to enhance ADCC activity in engineered monoclonal antibodies to improve efficacy across a broader patient population.

Finally, therapies have been developed based upon adoptive cell transfer, the process of isolating immune cells, modifying them outside the patient's body, and then introducing them into a patient to treat disease. The current wave of adoptive cell therapy efforts is largely focused on the use of T cells engineered to express either TCRs or CARs. In order to be effective as a therapy, an engineered T cell must (i) selectively target tumor cells, (ii) activate cytotoxic tumor cell killing, and (iii) simultaneously activate pathways to ensure the T cell's proliferation and survival. The matrix below shows the mechanisms of action for many current TCRs and CARs, and for ACTR:

Activity	Tumor Targeting	Cytotoxic Killing Trigger	Proliferation and Survival
TCR	TCR-alpha/beta on T cell bind peptide+MHC on tumor	CD3zeta	None
CAR	scFv (antibody fragment) of CAR-T cell binds tumor antigen	CD3zeta	Costimulatory domain (for example, 4-1BB or CD28)
ACTR	CD16 domain of ACTR T cell binds to co-administered antibody, antibody binds tumor antigen	CD3zeta	Costimulatory domain (for example, 4-1BB or CD28)

T cell Receptors (TCRs) are naturally occurring protein complexes expressed on the surface of T cells. They are the primary mechanism by which T cells normally distinguish "foreign" cells from "self" and trigger immune attack. In most T cells, a TCR contains a pair of proteins, TCR-alpha and TCR-beta, which directly recognize processed peptides of the MHC presented on the surface of cells and exert cytotoxicity when engaged. In some cases, these TCRs can be used "as is" with no further modifications. In other cases, activity can be improved by engineering the TCR to recognize the tumor peptide with higher affinity. TCR-based cellular therapies have shown promising clinical activity in treating certain cancers.

Several challenges have been encountered with TCR-based approaches. Some tumor cells acquire mutations that change the MHC molecule or reduce the level of MHC expressed on their surface. This prevents or limits recognition by TCRs and thus makes tumor cells resistant to T cell attack. In addition, engineering TCRs to

improve their affinity can also change their specificity and cause them to direct T cell attack towards normal tissues. This change in specificity has in some cases led directly to patient deaths. Lastly, there are many naturally occurring variants of MHC in the human population. A TCR recognizes only certain MHC variants, meaning that a given TCR construct can only potentially work with a fraction of patients.

Chimeric Antigen Receptors (CARs) are synthetic proteins, assembled by linking together individual protein domains from different genes (in this context, a *chimera* is a molecule with sequences derived from two or more different starting molecules). All CARs contain an extracellular recognition domain responsible for recognizing and binding an antigen specifically presented on a target cell (hence the name, "chimeric *antigen* receptor"). Most often, this recognition domain is a small single chain variable fragment (scFv) isolated from a larger, full-length antibody. The scFv is tethered to the surface of the T cell by a "hinge" or "spacer" domain. This domain provides positional flexibility, allowing the scFv to orient properly to engage the antigen. Passing through the plasma membrane of the cell, a transmembrane domain effectively connects the extracellular domains involved in target cell recognition to the intracellular domains that cause the T cell to respond.

In the earliest CAR examples (known as first generation CARs), a single intracellular signaling domain was used, isolated from the CD3-zeta chain of the T cell receptor complex. CARs built with this domain were shown to be capable of driving the killing of target cells in laboratory experiments but results in patients were generally unimpressive. With few exceptions, first generation CAR-T cells failed to persist in patients long enough to exert significant anti-tumor activity and provide therapeutic benefit.

Second generation CARs include additional signaling domains from certain proteins (known as co-stimulatory molecules) in order to improve activation of the CAR-T cells. These signaling domains turn on additional pathways in the T cell that promote cytokine secretion, survival, and proliferation, all of which strengthen the anti-tumor response. Second generation CARs have yielded more positive results in clinical testing. Promising results have been observed in therapy-resistant patient populations with ALL and B cell NHL, leading to recent approvals in both indications.

Notwithstanding the observed effectiveness and favorable response rates, severe side effects have also been observed with these therapies, in some cases leading to patient deaths. Toxicities include CRS, neurotoxicity, and on-target, off-tumor effects. These have spurred the desire to develop better-controlled therapies. Additionally, the vast majority of programs with demonstrated responses have been limited to hematologic cancers, such as ALL, NHL, and multiple myeloma. The cellular environment in which solid tumor cancers exist (known as the tumor microenvironment) is inimical to T cells due to several factors including: (1) immunosuppressive cells (e.g., regulatory T cells (Tregs), myeloid derived suppressor cells (MDSCs)), (2) immunosuppressive enzymes and signaling molecules (e.g., IDO1, TGF-beta), (3) limited nutrients (e.g., oxygen, glucose), and (4) toxic metabolites (e.g., reactive oxygen species, lactic acid). Together, these factors can limit the ability of CAR-T cells both to penetrate into the solid tumor and to function properly once there. While the number of clinical trials focused on solid tumor cancers is growing, limited clinical data have been reported and results to date have been less encouraging.

CARs target tumor cells using an scFv prepared from a tumor-specific antibody. Given that tumors express indication-specific tumor antigens, creating a CAR-T therapy for a new cancer indication typically requires the construction of a new CAR made from a newly engineered scFv. scFvs typically show reduced affinity and a higher likelihood of misfolding than antibodies. scFv misfolding drives receptor aggregation which triggers signaling and activation of the CAR-T cell in the absence of a tumor cell. This signaling in the absence of a tumor antigen, known as tonic signaling, promotes premature T cell differentiation and exhaustion, reducing CAR-T anti-tumor activity.

The graphic below illustrates the structure of a CAR, including the engineered scFv, and the interaction between the scFv and the applicable antigen on the tumor cell:

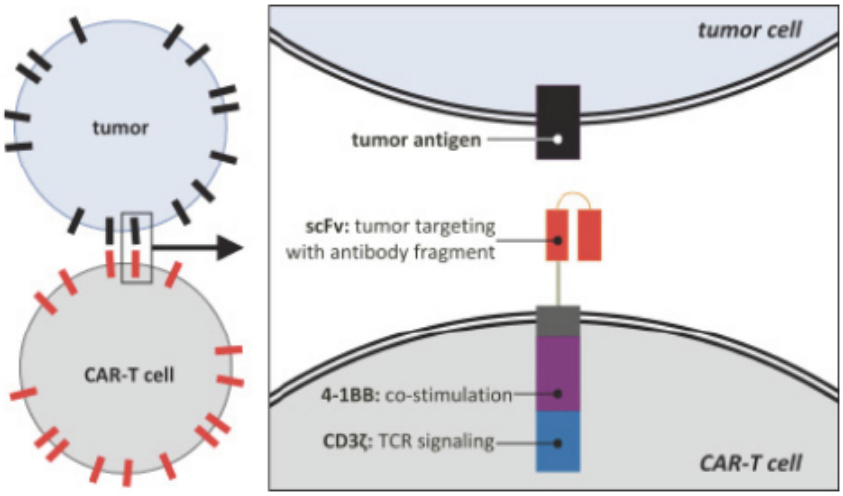


Figure 2. Structure of a CAR, including the engineered scFv

Our Solutions

Antibody-Coupled T cell Receptor (ACTR) is a different kind of chimeric receptor, initially invented in the laboratories of our scientific founder, Dr. Dario Campana, at St. Jude's Children's Research Hospital and the National University of Singapore, and later expanded and improved by our scientists. ACTR is a single construct that we believe can be used in combination with a wide variety of separately administered tumor-targeting antibodies to pursue different antigens and tumor types. Antibodies have been developed to target many different cancers. Our approach leverages existing antibodies to mobilize a cytotoxic cellular response to attack antibody-labeled cancer cells.

ACTR's design differs from CAR in its extracellular domain. In lieu of the scFv found in a CAR, the extracellular domain of ACTR consists of the Fc-binding domain of CD16. As previously noted, CD16 is normally expressed on natural killer cells and macrophages, where it recognizes the Fc domain of cell-bound antibodies. Without an scFv attached to its surface, the ACTR T cell is unable to recognize tumor cells directly. However, when a tumor-targeting antibody is provided, the ACTR T cell is able to recognize tumor cells through antibodies bound to the surface of the tumor cells. Once it is bound to an antibody on the tumor cell, an ACTR T cell exerts ADCC, a function not normally observed with T cells, to kill the tumor cell. No special engineering of either the therapeutic antibody or of the ACTR receptor is required in order for a functional interaction to take place.

Once an ACTR T cell engages a tumor cell bound with the therapeutic antibody, it works in several different ways to drive an anti-tumor response:

- The ACTR T cell injects protein toxins (known as granzymes and perforins) which quickly kill the tumor cell.
- After attacking and killing one tumor cell, it serially disengages and moves on to attack others.
- It secretes cytokines that recruit other immune cells such as natural killer cells and macrophages with a broader range of activities.

- It undergoes cell division to produce daughter cells with the same Fc extracellular domain to perpetuate the response.

The graphic below illustrates the structure of an ACTR T cell, showing how the Fc receptor recognizes and binds to the tumor-bound antibody.

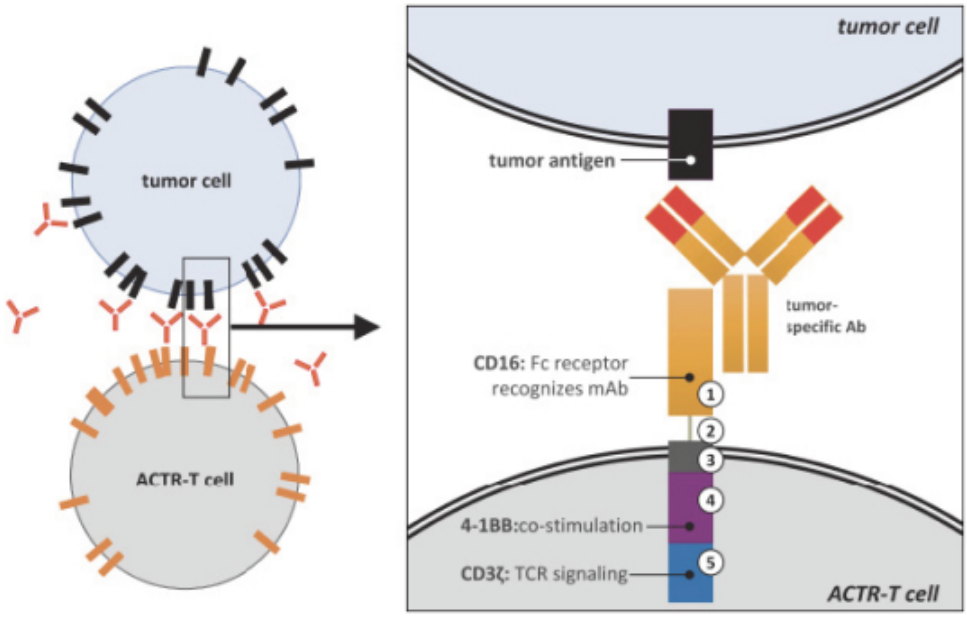


Figure 3. Structure of an ACTR T cell

The five domains of the ACTR T cell, shown in the above graphic, function to facilitate the T cell attack of the tumor cell in the following ways:

1. An *extracellular* domain (e.g., CD16) serves as an Fc receptor, binding to a tumor-bound therapeutic antibody through its constant Fc domain.
2. A *hinge* domain (e.g., CD8) provides flexibility to allow the extracellular domain to effectively orient and engage antibody bound to a target cell.
3. A *transmembrane* domain (e.g., CD8) anchors ACTR within the proper location in the cell and functionally couples antigen engagement by the extracellular domain with signaling activities in the intracellular domain.
4. A *co-stimulatory* domain (e.g., 4-1BB or CD28) provides added cytokine and survival signals essential for prolonged anti-tumor activity.
5. A TCR *signaling* domain (e.g., CD3zeta) initiates a signaling cascade to trigger cytotoxic attack.

Preclinical studies have demonstrated robust anti-tumor activity of ACTR-expressing T cells when combined with several different tumor-specific antibodies, including rituximab (an anti-CD20 antibody marketed as Rituxan), trastuzumab (an anti-HER2 antibody marked as Herceptin), and hu14.18K322A (an anti-GD2 antibody).

Our initial efforts were directed at testing our original ACTR construct, ACTR087, with different antibodies to identify combinations for clinical testing in new indications. In addition, we systematically explored modifications to the ACTR design. With a particular aim at creating an ACTR optimized for solid tumor cancers, we evaluated 100+ constructs through a series of high throughput screening assays. From these efforts, we identified a modified ACTR construct called ACTR707 which is now in clinical testing. Based on preclinical data, we expect ACTR707 may function particularly well in solid tumor cancers, given its propensity to proliferate, secrete cytokines and persist following a repeated exposure to target tumor cells. We aim to continue to improve the functionality of the ACTR T cell in solid tumor cancers through (i) additional genetic modifications to exploit new supporting biology in the tumor microenvironment and (ii) introducing new manufacturing process modifications.

Key Differentiating Characteristics of ACTR

We believe ACTR offers distinct advantages over alternative immunotherapies:

- **A Universal Approach.** ACTR is a single design that we believe can be used in combination with a wide variety of tumor-targeting antibodies to pursue different antigens and cancer indications. ACTR leverages CD16, a receptor normally found on natural killer cells, to recognize a wide range of tumor cell-bound antibodies and drive cytotoxic attack. Unlike CAR-T, in which a new synthetic receptor has to be created, manufactured, and tested for each new antigen, ACTR relies upon the same CD16 binding irrespective of tumor antigen or co-administered antibody. As a result, our ACTR construct needs to be engineered, manufactured, and preclinically validated only once, and the clinical de-risking of ACTR can be leveraged across many ACTR-antibody combinations. This enables us to rapidly and efficiently expand our product candidate pipeline.
- **Therapy with Potential for Superior Activity.** Preclinical testing of ACTR in combination with a wide range of tumor-targeting antibodies has demonstrated tumor killing potential. Initial data from our ongoing Phase I clinical trials evaluating ACTR087 or ACTR707 used in combination with rituximab in adult patients with r/r NHL suggest that ACTR can achieve tumor reduction. Several factors may contribute to potency:
    - ACTR shows minimal signaling in the absence of tumor antigen (i.e., tonic signaling) in preclinical testing. CAR-T tonic signaling drives accelerated T cell differentiation and ultimately exhaustion, compromising anti-tumor activity.
    - ACTR is composed of fragments of naturally occurring human proteins and, as such, has a reduced likelihood of generating an immune response directed at the ACTR T cell, potentially translating into better persistence. CAR-T, especially those with mouse-derived scFvs, are synthetic constructs that can and have triggered immune responses which can cause rapid clearance of CAR-T cells from patients.
    - The use of a complete, co-administered antibody with ACTR, instead of an antibody fragment in the scFv format used in CAR-T, typically maintains better functional activity, including improved folding, affinity for the antigen, and improved strength of the antibody–antigen target complex through bivalency.
    - Therapeutic activity of the co-administered antibody used to direct the ACTR T cell can supplement the ACTR T cell-mediated cytotoxicity (e.g., signal blockade, Fc effector functions). Antibodies are not part of the treatment for CAR-T therapy.
    - The CD16 domain of ACTR has evolved to efficiently engage a wide range of tumor cell-bound antibodies to drive cytotoxic attack. The scFv domains of CARs are synthetic constructs and must be empirically engineered to optimize function.
- **Increased Control and Tunability.** In preclinical experiments, ACTR activity scales with the amount of the co-administered antibody. As such, we believe ACTR activity can be tuned up or down by modulating antibody dosing. This ability to adjust ACTR T cell activity could make it possible to define an optimal dose through clinical testing to maximize tumor-killing activity and minimize toxicity.

- We believe that optimized dosing of our ACTR product could reduce class toxicities associated with other T cell therapies, including CRS and neurologic events. These toxicities may correlate with the speed of tumor cell killing by T cells. Once CAR-T cells have been administered to a patient, they are effectively armed to attack all cells expressing the CAR-specific antigen and proliferate indefinitely. This means that there is currently no straightforward way to control the intensity of the immune response they trigger. In contrast, preclinical studies suggest that by dosing less antibody, the degree of ACTR T cell activity may be controlled, and capped. Once appropriate dosing is determined through clinical testing, it may be possible to avoid the life-threatening toxicities seen with CAR-Ts.
- The ability to modulate ACTR T cell activity by withdrawing antibody may provide a simple means for minimizing longer term toxicity that is not feasible with CAR-T therapies. For example, several lineage antigens targeted by CAR-T for hematologic indications (e.g., CD19, CD33, CD123) are expressed on normal tissues that serve important functions. Eliminating these normal tissues through an on-target, off-tumor effect may be tolerated in the short-term but they may create long-term toxicity risk to patients. For instance, CD19 CAR-mediated B cell aplasia may increase infection risk. CARs specific for CD123 have the potential to target hematopoietic progenitor cells and risk bone marrow failure.

- **Breadth of Targeting Allows Many Accessible Antibody Combinations.** We believe that the ACTR mechanism of action allows for a number of antigen/indication opportunities that may be difficult or impossible to pursue with alternative T cell therapies.
  - Antibodies have been generated, manufactured as GMP material, and clinically tested against dozens of tumor antigens. Some have demonstrated therapeutic benefit and we believe ACTR may enhance this benefit. Many others have demonstrated tumor specificity but have failed to provide therapeutic benefit, most likely because of the inability to translate tumor cell binding into tumor cell killing, referred to as effector function. We believe many of these non-efficacious antibodies may demonstrate therapeutic benefit when armed with ACTR T cells. Because these antibodies do not need to be modified for use with ACTR, we can leverage all prior investment in their development, including by using the same GMP supply of antibody and leveraging available safety data.
  - Several therapeutically relevant antigens (e.g., CD38, CD7) are expressed on activated T cells, making it challenging or impossible to manufacture T cells that are targeted to these antigens. CARs specific for such antigens undergo cell suicide and fratricide. In contrast, ACTR T cells are made in the absence of targeting antibodies, meaning that they can be manufactured for these antigens without these complications. Once combined with targeting antibodies after manufacturing, ACTR T cells have shown cancer cell killing without apparent suicide or fratricide.
  - Preclinical studies indicate that ACTR T cells can be targeted to multiple antigens using a combination of multiple tumor-specific antibodies. Such combinations may be useful to limit or reduce the development of tumor resistance to therapy, and increase the sensitivity by simultaneously targeting two different parts of a single target antigen.
- **ACTR's Potential for Solid Tumor Cancers.**
  - Many solid tumor antigens (e.g., HER2) are expressed at low levels on certain normal tissues. The ability to discriminate between tumor and normal tissues is critical to ensure the safety of a targeted T cell therapy.
    - CARs have limited ability to distinguish between cancer cells displaying high amounts of an antigen and certain normal tissues that present low levels of the same antigen. As a result, toxicities, including patient deaths, have occurred when CAR-T cells attack normal tissues.
    - We believe ACTR is able to discriminate its killing activity based on the amount of antigen expressed on a target cell. This is likely a result of the fact that recognition of the tumor cell is based upon many weak interactions between ACTR's extracellular domain and the targeting antibodies bound to the tumor cell, which work cooperatively to drive tight but specific binding. A normal cell with low antigen levels will have few bound antibodies and is not expected to activate

the ACTR T cell. As shown in the figure below, in a comparison of ACTR707 used in combination with trastuzumab and a HER2 CAR, ACTR exhibited lower levels of cytotoxicity in non-tumor cell lines.

- In addition, preclinical studies suggest that ACTR T cell activity can be adjusted by modulating antibody dosing. This ability to adjust ACTR T cell activity could make it possible to define an optimal dose through clinical testing to maximize tumor-killing activity and minimize toxicity. CAR-T cells currently have no similar means of adjusting their relative activity.

- Tumor cells have evolved to evade immune system attack, and the tumor microenvironment surrounding solid tumor cancers is hostile to T cell function. To be effective in treating solid tumor cancers, it is important that therapeutic T cells sustain activity under adverse conditions.
  - CAR-T cells often exhibit tonic signaling as a result of receptor misfolding and aggregation, leading to chronic low-level activation. CAR-T cells thus tend towards premature differentiation and exhaustion, compromising their anti-tumor activity.
  - ACTR T cells exhibit very little tonic signaling in preclinical studies, due to the well-folded nature of the CD16 extracellular domain. As such, ACTR T cells may retain a 'younger' phenotype than CAR-T and be enriched with cell types known to drive potent anti-tumor responses.

We have tested ACTR's on-target, off-tumor effect *in vitro*. The figure below shows the results of an *in vitro* study in which ACTR707 used in combination with trastuzumab and a HER2-targeting CAR were exposed to HER2+ tumor cells and non-tumor cells expressing low levels of HER2, and the relative amounts of cytotoxicity observed with each treatment. While cytotoxicity against tumor cells was comparable for CAR and ACTR, CAR treatment resulted in much higher levels of cytotoxicity against non-tumor cells than ACTR treatment.

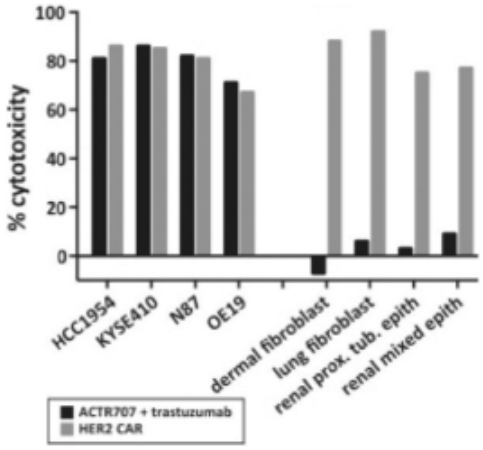


Figure 4. Cytotoxicity results of an in vitro study

Our ACTR Product Candidates

We are leveraging our universal ACTR platform to rapidly and efficiently develop ACTR-based therapies for a wide range of hematologic and solid tumor cancer indications. ACTR does not need to be modified for use with different antibodies, and antibodies do not need to be modified for use with ACTR. As a result, we believe we can leverage our investment in ACTR, as well as the investment made by third parties in available antibodies, across different ACTR-antibody combinations, tumor types, and indications.

Our objective is to use the same ACTR construct in a wide range of ACTR-based therapies for both hematologic and solid tumor cancers. We aim to continue to improve the functionality of the ACTR T cell in solid tumor cancers through (i) additional genetic modifications to exploit new supporting biology in the tumor microenvironment, and (ii) introducing new manufacturing process modifications.

We currently have four clinical stage ACTR programs. Our two most advanced product candidates, ACTR087 and ACTR707, each used in combination with rituximab, are being tested in adult patients with r/r NHL in ongoing Phase I clinical trials called ATTCK-20-2 and ATTCK-20-03, respectively. ACTR707 is a modified ACTR construct designed to generate a more potent and sustained immune response to overcome immunosuppressive tumor microenvironments most commonly found in solid tumor cancers. Our third clinical stage program, ACTR087 used in combination with SEA-BCMA, leverages our ACTR platform to target BCMA, an antigen with high and selective expression on the surface of malignant plasma cells in multiple myeloma. Our fourth clinical stage program, ACTR707 used in combination with trastuzumab, is focused on patients with HER2+ solid tumor cancers. The ATTCK-34-01 Phase I trial with this combination was activated in December 2018.

Any anti-tumor activity, or efficacy, we observe in each of these Phase I clinical trials will be reported in our regulatory submissions to the FDA and any other health authorities as required during development, and we will use these data to inform the emerging benefit/risk profile of each combination and to determine whether to move forward into a registration trial. We believe the data from these Phase I clinical trials will be supportive, if positive, but the primary purpose of our Phase I clinical trial is to evaluate safety. We do not expect the data from these trials to be registration-enabling clinical trial data sets sufficient for marketing authorization. We would only expect to receive marketing authorization for a combination if the combination demonstrated safety and efficacy in at least one subsequent registration trial.

ACTR T Cells Used in Combination with Rituximab for B Cell Non-Hodgkin Lymphoma

Our two most advanced product candidates, ACTR087 and ACTR707, each used in combination with rituximab, are being tested in adult patients with r/r NHL in ongoing Phase I clinical trials called ATTCK-20-2 and ATTCK-20-03, respectively.

ACTR087, our original ACTR construct, uses a 4-1BB co-stimulatory domain. ACTR707, which uses a CD28 co-stimulatory domain, represents an important construct not only for adult patients with CD20+ B cell r/r NHL, when used in combination with rituximab, but also for patients with other cancer types when used in combination with other antibodies. We believe important structural modifications to the ACTR707 construct, including changes to the hinge, transmembrane, and co-stimulatory domain, will translate into meaningful clinical differences when used in combination with antibody therapeutics. ACTR707 was identified through a comprehensive high-throughput screening effort aimed at identifying constructs with properties that would function particularly well in a solid tumor setting, including increased proliferation, cytokine secretion, and persistence in a repeat stimulation test. In particular, we believe that the modifications in ACTR707 will allow the ACTR T cells to behave more favorably in immunosuppressive tumor microenvironments commonly found in solid tumor cancers. Based on emerging clinical data from the Phase I ATTCK-20-03 trial, the continuing progress in that trial, and our desire to efficiently manage resources, we have selected ACTR707 used in combination with rituximab to be the lead lymphoma program for advancement to further clinical development. As a result of this decision, we have concluded enrollment in the ATTCK-20-2 study in the first quarter of 2019.

Rituximab is a chimeric monoclonal antibody that is FDA-approved in the United States (and elsewhere) to treat the blood cancers NHL and chronic lymphocytic leukemia that also affect the body's B cells. Rituximab binds to CD20, a molecule found on the surface of all B cells and is not known to be expressed on any other tissue. While targeting CD20 has the potential to deplete B cells, experience has shown that humans can live without B cells for a prolonged period of time and that the level of B cells recovers upon cessation of therapy. We believe CD20 is an attractive immunotherapeutic target for the treatment of B cell malignancies.

B Cell Non-Hodgkin Lymphoma

NHL is the most common cancer of the lymphatic system, with over 70,000 cases diagnosed each year in the United States, and approximately 85% of NHL cases are of B cell origin. Though B cell NHLs represent a heterogeneous set of lymphomas, many cell surface antigens are shared among them, including CD20.

Most subtypes of B cell NHL may be categorized as either indolent or aggressive. Indolent lymphomas are characterized by a prolonged median survival but are generally considered incurable. Aggressive lymphomas, in contrast, are characterized by more rapid growth but are potentially cured through either initial therapy or hematopoietic stem cell transplantation (HSCT). First-line therapy for patients diagnosed with B cell NHL usually consists of a combination of rituximab and multi-agent chemotherapy, which results in long term remissions or cures of approximately 50-60% of newly diagnosed patients. However, if initial therapy fails (i.e., remission is not achieved or the patient's lymphoma returns), sequential therapeutic interventions typically provide increasingly short-lived remissions. Second-line therapy usually includes other multi-agent chemotherapy regimens, often including platinum chemotherapeutics, with or without rituximab, and in some cases, HSCT. However, HSCT is only curative in a minority of cases and most patients advance to a drug resistant disease with limited treatment options.

CD20 is expressed on cancers of the lymphatic system of B cell lineage, such as CD20 positive (CD20+) B cell ALL in adults. In each of these B cell malignancies, available therapies for newly diagnosed patients include single or multi-agent chemotherapy with or without rituximab, which results in long term remission or cure in variable proportions of patients. However, absent an initial remission, or at the time of progression or relapse of the patient's underlying disease, curative treatment options remain extremely limited.

Clinical Development Plan: ATTCK-20-03 Phase I Trial

We are currently evaluating the safety, tolerability, and anti-lymphoma activity of ACTR707 used in combination with rituximab in adult patients with CD20+ B cell r/r NHL in a Phase I, multi-center, open-label clinical trial called ATTCK-20-03. The primary endpoints of this trial are DLTs, maximum tolerated dose, and incidence and severity of adverse events. Secondary endpoints are efficacy (as measured by ORR, DOR, PFS, OS), ACTR T cell persistence, level of inflammatory markers and cytokines, and rituximab pharmacokinetics (as measured by plasma concentration of rituximab and anti-drug antibody titers). An adaptive design is being used to identify a dose of ACTR707 when administered in combination with rituximab to be used in future trials. In the United States, an IND was submitted in April 2017, and the protocol was recommended by local Institutional Biosafety Committees (IBCs) for NIH waivers of RAC review, which NIH granted.

As of November 1, 2018, six patients were enrolled and dosed with ACTR707 in ATTCK-20-03 at the first dose level. Enrollment to this dose level is complete. Of the six patients dosed with ACTR707, four patients were evaluable for DLT (two patients had disease progression during the 28-day DLT evaluation period and were not evaluable for DLTs) and there were no DLTs reported. All six patients were evaluable for response; three patients experienced complete response (with a duration of 207+, 180+, and 85 days as of November 1, 2018) and three patients experienced disease progression. Treatment-emergent adverse events that occurred in >1 patient and were severe (³ Grade 3) were neutropenia, febrile neutropenia, and thrombocytopenia. The only reported ACTR707-related SAE, Grade 3 febrile neutropenia, has resolved. No severe CRS or neurological events were reported.

As of November 1, 2018, three patients were enrolled and dosed with ACTR707 in ATTCK-20-03 at the second dose level. Enrollment to this dose level is complete. Of the three patients dosed with ACTR707, all were evaluable for DLT and there were no DLTs reported. All three patients were evaluable for response; one patient experienced complete response with a duration of 71+ days as of November 1, 2018 and 2 experienced disease progression. Treatment-emergent adverse events that occurred in >1 patient and were severe (³ Grade 3) were neutropenia, thrombocytopenia and anemia. There were two ACTR707-related SAEs, one each of Grade 3 febrile

neutropenia and Grade 3 pancytopenia, both of which resolved. No severe CRS or neurological events were reported. Enrollment in Dose Level 3 is complete. We expect to continue enrolling patients in this trial into 2019.

The primary objective of the ATTCK-20-03 clinical trial is safety, although anti-lymphoma activity will also be assessed. The ATTCK-20-03 is designed to investigate 'flat' dose levels of ACTR707, meaning that the doses do not vary by patient weight. Dose escalation will be followed by an expansion cohort of the combination at the recommended Phase II dose of ACTR707. The decision to escalate dose and the number of patients in each dose level are defined by statistical testing drawing from the cumulative safety observations across all previous dose levels. This design, in comparison to the more traditional "3+3" design, is anticipated to provide greater flexibility in identifying the dose of ACTR707 used in combination with rituximab to be used in future studies. In 2018, we implemented a change in the analytical method used to calculate ACTR+ T cell dose from isotype control gate (ICG) to population gating (PG) across all actively enrolling clinical trials. PG method takes into consideration variability in starting material and more consistently represents ACTR+ T cells. This change to the analytic method affects the calculation of ACTR+ T cells and ACTR+ T cell dose targets in the ACTR707 drug product. The three initial ATTCK 20-03 dose levels in this study by ICG are 40 x 10^6, 60 x 10^6 and 80 x 10^6 ACTR+T cells, and 25 x 10^6, 40 x 10^6 and 55 x 10^6 by PG, respectively.

We expect to continue enrolling patients in this trial into 2019 and to initiate a cohort expansion in the second half of 2019.

Clinical Development Plan: ATTCK-20-2 Phase I Trial

We are currently evaluating the safety, tolerability, and anti-lymphoma activity of ACTR087 used in combination with rituximab in adult patients with CD20+ B cell r/r NHL in an ongoing Phase I, multi-center, open-label clinical trial called ATTCK-20-2. The purpose of this trial is to evaluate safety, and the primary endpoints of this trial are dose-limiting toxicities (DLTs), maximum tolerated dose, recommended Phase II dose, and safety as manifested by adverse events. Secondary endpoints are overall response rate (ORR), duration of response (DOR), progression free survival (PFS), and overall survival (OS).

A standard "3+3" dose escalation design will define the optimal dose of ACTR087 when used in combination with rituximab. In a "3+3" dose escalation design, at least three patients are treated within each pre-specified dose level of ACTR087 with the FDA-approved dose level of rituximab. Each dose level is expanded to at least six patients if a single DLT is observed within the first three treated patients of that dose level. Prior to further clinical investigation beyond the dose-finding levels of ACTR087 used in combination with rituximab, the protocol requires that we assess at least six patients treated at the maximum tolerated dose of ACTR087, defined in the protocol primarily by DLTs. The maximum tolerated dose is the dose at which a DLT is observed in no more than one of these patients. Once the optimal dose has been determined, an expansion phase at this dose is planned.

During the dose escalation phase, twenty-three patients have been enrolled, and 17 patients have been treated with ACTR087. Of those patients not treated with ACTR087, four discontinued the trial early due to progression of their NHL, receiving no trial treatment, and two discontinued the trial due to serious adverse events (SAEs) that occurred prior to ACTR087 dosing. Dose Level One and Dose Level Two enrollment has been completed. Based on DLT events observed in Dose Level Two, we are not planning any further dose escalation with ACTR087 in this regimen, although the trial is ongoing and patient follow-up on study continues. We have enrolled a cohort of patients at the preliminary recommended Phase II dose of ACTR087 identified from the dose escalation phase of the trial, referred to as the cohort expansion phase of the study.

Eight patients were dosed with ACTR087 at Dose Level One, receiving a target dose of up to 0.5 x 10^6 ACTR T cells/kg (one patient was enrolled in Dose Level Two but treated with a dose consistent with Dose Level One), following lymphodepleting chemotherapy comprised of fludarabine and cyclophosphamide. Six patients were evaluable for DLT-assessment in Dose Level One with 1 DLT of Grade 4 thrombocytopenia persisting more than 14 days observed, without associated bleeding complications. This patient's platelet count

recovered, and subsequent modifications to the assessment of hematologic toxicities were instituted, with no additional hematologic DLT observed in Dose Level One. Of the six patients who were evaluated for response (2 patients came off study early due to rapid disease progression), two demonstrated a complete response, and a third patient demonstrated a partial response following ACTR087 and rituximab treatment, according to standard lymphoma response criteria (known as the Lugano criteria). The remaining three response-evaluable patients had progressive disease. As of November 1, 2018, our most recent data cutoff date for response assessment, one of the patients reaching complete response had an ongoing complete response extending 661+ days.

All patients who received ACTR087 experienced at least one treatment-emergent adverse event. Treatment-emergent adverse events that were severe (³ Grade 3) and in > 1 patient were neutropenia, leukopenia, lymphopenia, and thrombocytopenia.

No severe (³ Grade 3) ACTR087-related SAEs or ACTR087-related deaths have been observed in Dose Level One patients. Other ACTR087-related SAEs include one event of Grade 2 dyspnea and one event of Grade 2 odynophagia.

Nine patients were dosed with ACTR087 in Dose Level Two at a target dose of up to 1.5 x 10^6 ACTR T cells/kg. In Dose Level Two, two patients experienced ACTR087-related severe CRS and one patient experienced ACTR087-related neurotoxicity, which was fatal. Of the two events of CRS, one patient subsequently experienced a fatal case of enterococcal sepsis considered related to ACTR087 and one patient subsequently experienced a fatal case of sepsis considered not related to ACTR087. There were three protocol-defined DLTs in Dose Level Two, including one of the events of severe CRS, the neurotoxicity event, and a hematologic DLT of prolonged (lasting greater than 28 days) Grade 4 thrombocytopenia. Based on this review of the observed safety events, we concluded that Dose Level Two exceeds the maximum tolerated dose under the standard rituximab dosing regimen and do not intend to further escalate the cell dose in this regimen.

Of the six patients treated at Dose Level Two who were evaluable for response, one patient demonstrated an ongoing complete response (response duration 311+ days) and two patients demonstrated a partial response (response duration 12 and 45 days) following ACTR087 used in combination with rituximab treatment according to the Lugano criteria.

Other ACTR087-related SAEs in Dose Level Two include one event each of Grade 1 CRS and Grade 2 CRS. All patients who received ACTR087 experienced at least one treatment-emergent adverse event. Treatment-emergent adverse events that were severe (³ Grade 3) and not otherwise reported as serious events seen in > 1 patient were neutropenia, thrombocytopenia, anemia, leukopenia, and bacteremia.

The severe ACTR087-related SAEs we observed in Dose Level Two resulted in the FDA placing this trial on clinical hold in December 2017 pending submission of certain information relating to the ATTCK-20-2 clinical trial. The clinical hold was removed in February 2018, following review of this information by the FDA. Several protocol and dosing changes were made in early 2018, which we expect to reduce the incidence of severe adverse events and better manage those events that do occur.

Available safety and response data for Dose Level One and Dose Level Two of ATTCK-20-2 were reported at the 59th American Society of Hematology meeting in Atlanta, Georgia in December 2017. These data have informed the ongoing development of ACTR087 used in combination with rituximab in CD20+ B cell NHL, including defining the preliminary recommended Phase II dose (RP2D) for the cohort expansion phase of this clinical trial. In the second quarter of 2018, we began enrollment in the cohort expansion phase of the trial and completed enrollment in this trial in the first quarter of 2019. We plan to report data on all enrolled patients in the ATTCK-20-2 trial at the end of 2019.

ACTR087 Used in Combination with SEA-BCMA for Multiple Myeloma

Our third clinical program is ACTR087 used in combination with SEA-BCMA, which we are currently testing in adult patients with r/r multiple myeloma. SEA-BCMA is a novel humanized antibody that targets the antigen BCMA, developed by Seattle Genetics using their sugar-engineered antibody (SEA) technology. BCMA is expressed on normal plasma cells, some mature B cells, and at comparatively elevated levels on malignant multiple myeloma cells, but is absent from other normal tissues. We believe BCMA presents an attractive immunotherapeutic target for our platform.

Multiple Myeloma

Multiple myeloma, a cancer arising from normal plasma cells, which are of B cell lineage, is diagnosed in approximately 30,000 patients in the United States every year, making it the second most common hematologic malignancy. First-line treatment increasingly involves a three-drug regimen that includes a proteasome inhibitor such as bortezomib or carfilzomib, an immunomodulatory drug such as lenalidomide, and a corticosteroid such as dexamethasone, though if a patient is fit enough they may proceed to autologous HSCT in their first complete remission. First-line therapy typically leads to complete remission, but invariably the disease relapses or progresses, even following HSCT, necessitating subsequent therapy. Several therapeutic options exist for patients with progressive or relapsed multiple myeloma, including recently approved new classes of agents such as monoclonal antibodies. Retreatment with drugs used in first-line therapy, or other drugs within their class, is also feasible, but in most cases subsequent remissions are of shorter duration or cumulative toxicities preclude continuation of existing therapies.

We are developing ACTR087 used in combination with SEA-BCMA, a novel proprietary first-in-human monoclonal antibody that targets the antigen BCMA, which is widely expressed in multiple myeloma. The ACTR087 used in combination with SEA-BCMA product candidate represents the first clinical program arising from our strategic collaboration with Seattle Genetics, as well as our first clinical program incorporating a novel antibody. SEA-BCMA is engineered to enhance its binding to ACTR087, providing additional rationale for this novel-novel combination.

Clinical Development Plan: ATTCK-17-01 Phase I Trial

We are currently testing the safety, tolerability, and anti-myeloma activity of ACTR087 used in combination with SEA-BCMA in adult patients with r/r multiple myeloma in a Phase I, multi-center, open-label clinical trial called ATTCK-17-01. The primary endpoints of this trial are recommended Phase II dose, DLTs, and incidence and severity of adverse events. Secondary endpoints are efficacy (as measured by ORR, DOR, PFS, OS), ACTR T cell persistence, level of inflammatory markers and cytokines, pre-treatment BCMA expression on multiple myeloma cells, and SEA-BCMA pharmacokinetics (as measured by plasma concentration of SEA-BCMA and anti-drug antibody titers). The trial is designed as a dose escalation trial, increasing levels of both ACTR087 and SEA-BCMA. A safe and effective dose of SEA-BCMA has not been previously defined in humans. ATTCK-17-01 is designed to identify both a dose of ACTR087 and SEA-BCMA in combination for use in subsequent clinical trials. Similar to ATTCK-20-03, an adaptive dose escalation study design is being used. Two ACTR087 and up to six SEA-BCMA dose levels may be studied in this trial. We submitted an IND in July 2017. The protocol was recommended by local IBCs for NIH waivers of RAC review, which NIH granted. We are currently enrolling and dosing patients in this trial and expect to report data from multiple dose cohorts in the second half of 2019.

As of November 1, 2018, two patients were enrolled in ATTCK-17-01 into two single-patient cohorts studying ACTR087 (30 x 10^6 ACTR T cells by PG) in combination with SEA-BCMA (0.01mg/kg) (Cohort 1) and ACTR087 (30 x 10^6 ACTR T cells by PG) in combination with SEA-BCMA (0.03mg/kg) (Cohort 2). Five patients were enrolled into Cohort 3 studying ACTR087 (30 x 10^6 ACTR T cells by PG) in combination with SEA-BCMA (0.3 mg/kg). There were no DLTs reported across cohorts. At the first dose levels tested, serum and urinary M protein levels increased during SEA-BCMA single-agent dosing and stabilized or decreased

transiently following ACTR087 administration. Of five patients with responses evaluable post treatment with ACTR087, three patients experienced disease progression and two patients (both in Cohort 3) are ongoing on treatment across cohorts as of November 1, 2018. Treatment-emergent adverse events that occurred in >1 patient and were severe (³ Grade 3) were anemia, neutropenia, lymphocyte count decreased, and WBC count decreased. The only reported ACTR087-related SAE, Grade 1 CRS, resolved without requiring therapeutic intervention with steroids or tocilizumab. No severe CRS or neurological events were reported.

Data from ATTCK-17-01 will inform the ongoing development of ACTR087 used in combination with SEA-BCMA for treatment of multiple myeloma. In ATTCK-17-01, we are testing ACTR087 used in combination with SEA-BCMA in patients that have relapsed, progressed, or are no longer responding to treatment after at least three or more lines of therapy for their multiple myeloma, or are double refractory to a proteasome inhibitor and an immunomodulatory agent, regardless of the number of prior therapies. Patients must have received adequate available therapies, including HSCT for those who are eligible to receive HSCT. We also anticipate that in the future we may study patients with other BCMA-expressing malignancies with ACTR087 used in combination with SEA-BCMA. Initiation of new clinical trials with ACTR087 used in combination with SEA-BCMA will depend upon the tolerability and anti-myeloma activity observed in ATTCK-17-01.

ACTR707 Used in Combination with Trastuzumab for HER2+ Cancers

The ATTCK-34-01 clinical trial has been initiated at clinical sites to evaluate ACTR707 used in combination with trastuzumab for the treatment of patients with cancers that overexpress HER2. Trastuzumab is a humanized monoclonal antibody that targets the HER2 cell surface receptor, and is currently approved to treat HER2+ breast cancers and HER2+ gastric cancers alone and in combination with chemotherapy. While HER2 is overexpressed in a subset of breast and gastric cancers, it is found at very low levels on certain tissues within the body. In preclinical studies, we have shown antigen-specific killing of HER2-overexpressing cell lines with ACTR707 used in combination with trastuzumab, without observing cytotoxic effects in normal cells expressing low amounts of HER2. ACTR707 used in combination with trastuzumab also induces remissions in relevant mouse models of HER2+ cancers.

HER2+ Cancers

Amplification of the ERBB2 gene leads to the overexpression of HER2, a major driver of cell proliferation for a subset of patients with breast and gastric cancers. As many as 37,500 women in the United States, or approximately 15% of all women diagnosed annually with breast cancer, overexpress the HER2 antigen. At least 4,000 patients with gastric cancer in the United States are HER2 positive as well. The development of HER2-directed therapies, including monoclonal antibodies such as trastuzumab and pertuzumab, have substantially improved outcomes for women with HER2+ breast cancer and demonstrated clinical benefit for women in the neo-adjuvant and adjuvant setting (preceding or following definitive local therapy). Women with advanced or metastatic breast cancer may constitute as many as 8,000 patients per year in the United States, and while HER2-directed therapies, such as trastuzumab and pertuzumab, trastuzumab-DM1, and HER2-directed small molecule inhibitors such as lapatinib are available, no curative options exist. Likewise, while trastuzumab has improved outcomes for the subset of patients with HER2+ advanced or metastatic gastric/gastroesophageal junction cancers, relapse or progression is almost inevitable.

Clinical Development Plan: ATTCK-34-01 Phase I trial

An IND to study ACTR707 used in combination with trastuzumab in HER2+ cancers was filed and subsequently cleared by FDA on August 10, 2018. The protocol was reviewed by local oversight bodies an Institutional Biosafety Committee (IBC) and an Institutional Review Board (IRB). Additionally, the NIH granted a waiver and the clinical protocol completed NIH registration. We have initiated a Phase I, multi-center, open-label clinical trial called ATTCK-34-01 to assess the safety, tolerability, and anti-tumor activity of ACTR707 in combination with trastuzumab in patients with HER2+ advanced malignancies. The primary objectives of the

study are to characterize the safety and tolerability of ACTR T cell product in combination with trastuzumab in subjects with HER2-positive advanced malignancies and to determine the recommended Phase II dose of ACTR T cell product in combination with trastuzumab in subjects with HER2+ advanced malignancies. The primary endpoints of this trial are DLTs, maximum tolerated dose and the incidence of adverse events and clinically significant laboratory abnormalities. Secondary endpoints are anti-tumor activity (as measured by ORR, DOR, PFS, OS), ACTR T cell persistence, level of inflammatory markers and cytokines. The trial is designed as a dose escalation trial, increasing levels of both ACTR707 and trastuzumab, which will help identify both doses of ACTR707 and trastuzumab to be used in in combination for subsequent clinical trials. Subsequent clinical development of this product candidate will depend upon the safety and efficacy data observed in the Phase I clinical trial. We plan to report initial clinical data from the ongoing dose escalation trial at the end of 2019.

Additional Product Candidates

We are exploring the potential of our universal ACTR platform in combination with a wide range of tumor-targeting antibodies to pursue hematologic and solid tumor cancers with significant unmet medical needs. We are working on a number of product candidates in early clinical or late-stage preclinical development. We plan to leverage the investment we have already made in ACTR, and the clinical validation and de-risking of ACTR that we are looking to achieve through the current clinical trials, to rapidly expand our pipeline of ACTR-based therapies using both commercially available and de-risked antibodies, as well as antibodies in clinical and preclinical development.

BOXR Platform

As we continue to increase our efforts in solid tumor applications, we have developed a new approach which enhances our core ACTR technology while simultaneously diversifying our pipeline.

Preclinical and clinical studies have demonstrated a number of ways that cancer cells and stromal cells within a solid tumor actively can actively suppress T cell function. This immunosuppression may be partially responsible for the limited efficacy reported to date with engineered T cell therapies in solid tumor indications. With this in mind, we have developed a new technology, called BOXR that specifically addresses some of the most validated mechanisms of T cell suppression in the tumor microenvironment (TME). A BOXR candidate is made up of two components as shown in figure 5 below. The first component is a targeting chimeric receptor that drives tumor cell recognition and attack. We have tested the BOXR approach using both universal targeting by ACTR, as well as antigen-specific targeting by scFv-based CARs. The second BOXR component is an independent transgene, distinct from the chimeric receptor targeting moiety, that re-programs T cell biology to improve T cell functionality in the TME. We refer to this component as the “bolt-on” moiety.

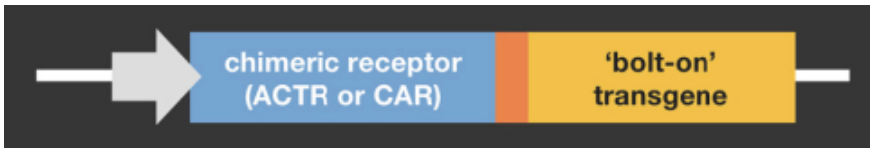


Figure 5. BOXR Construct

Our initial BOXR efforts have been aimed at addressing three key mechanisms of tumor-mediated immunosuppression: exhaustion via chronic T cell signaling, cellular immunosuppression, and metabolic competition. The strategy adopted to identify lead BOXR candidates may be viewed as a traditional drug discovery screening approach, as summarized in the flow chart below (Figure 6).

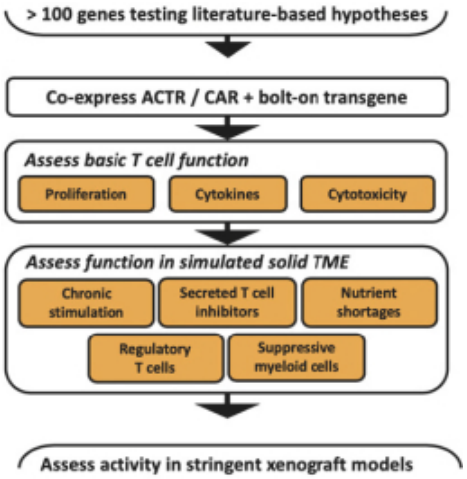


Figure 6 Identify lead BOXR candidates approach

Each "bolt-on" transgene included in the screen is chosen with a specific hypothesis in mind and selected with an expectation that its expression might favorably impact T cell function in the TME. Following an initial quality control step to establish whether the targeting chimeric receptor (either ACTR or a CAR) and the bolt-on transgene can be simultaneously expressed at sufficient levels. All BOXR candidates with good expression are then assessed using a battery of assays to measure T cell function, including antigen-driven T cell proliferation, cytokine secretion, and tumor cell killing. To identify bolt-on transgenes that improve solid tumor functionality, a tertiary screen includes a number of additional assays that recapitulate distinct features of solid TMEs. Finally, highly functional leads are tested using stringent xenograft models where standard engineered T cells have failed to demonstrate activity.

Results from our initial BOXR screen focused on improving metabolism under nutrient-depleted conditions are summarized below. Competition for nutrients in the TME is a well-recognized obstacle to successful eradication of tumor cells in several solid tumor indications. Specifically, certain liver and lung tumors are known to deplete their local environment of required nutrients such as glucose, compromising T cell functionality and correlating with poor patient outcomes. To engineer T cells to attack these tumors, we have used an scFv-based CAR to target GPC3, an oncofetal antigen known to be expressed on many different liver and lung cancer tumor cells. As shown in the first experiment in Figure 7, glucose levels across a range of xenograft models are significantly depleted relative to circulating blood. Without a co-expressed bolt-on transgene, traditional CAR-T cells lose the ability to proliferate under such low glucose conditions (second experiment, Figure 7). While traditional CAR-T cells are functional in non-depleting xenografts such as HepG2 (third experiment, Figure 7), they completely lose the ability to control tumor growth in more stringent models (fourth experiment, Figure 7). In contrast, co-expression of an undisclosed bolt-on transgene together with the GPC3 CAR preserves functionality and enables complete tumor regressions across several more stringent xenografts (fourth experiment, Figure 7). This particular combination of GPC3 CAR and bolt-on transgene has been designated BOXR1030 and is the first BOXR product candidate to advance into formal preclinical testing. We plan to present additional information regarding BOXR1030 in the second half of 2019.

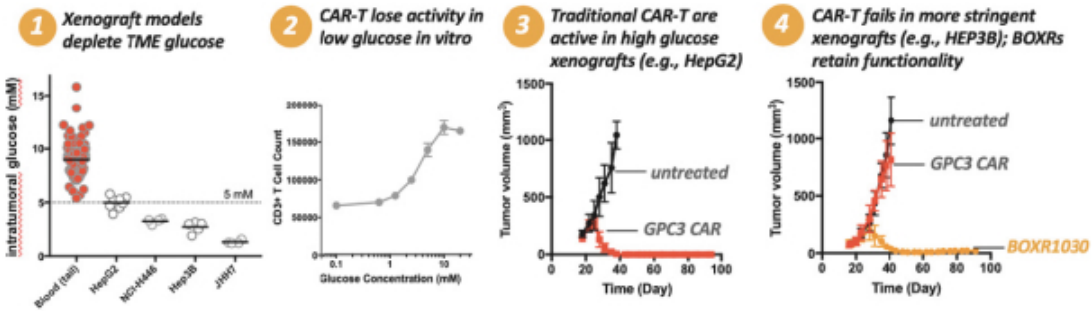


Figure 7. BOXR Experiments

To summarize, we have identified several BOXR lead candidates across two different engineered T cell technologies (universal ACTR and target specific CAR-T cells) that can enhance T cell activity within our preclinical model systems that represent well-validated obstacles in the TME.

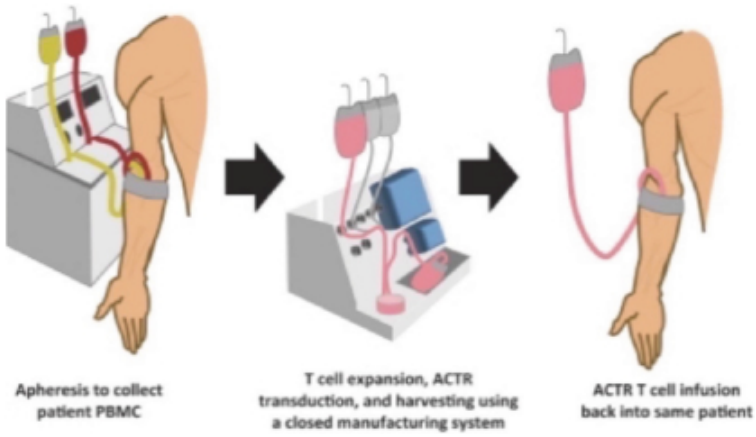
Product Development and Manufacturing

We have developed a T cell manufacturing process is designed as an automated, closed system that uses a serum-free growth medium and other materials that are readily available from qualified suppliers. Because ACTR is a platform technology that can target a wide variety of antigens using a single viral vector, we are refining a platform manufacturing process that is expected to address multiple indications with little or no modification. We understand that the T cell therapy field, including manufacturing and analytical technology, is evolving rapidly and have invested in process development tools, such as high-throughput liquid handling and flow cytometry, design of experiments, and data analysis software in order to map the design space and develop multiple options for processing that can be rapidly deployed to exploit new indications or new discoveries.

In our process, patients initially undergo a laboratory procedure in which white blood cells are removed from the bloodstream (known as leukapheresis), to yield peripheral blood mononuclear cells (PBMCs) that serve as the starting point for ACTR T cell manufacture. Collected PBMCs are transferred to a central GMP manufacturing facility, where they are enriched, activated, and cultured to promote optimal T cell functionality. T cells are then transduced with a non-replicating gamma-retroviral vector containing the ACTR transgene. The culture is incubated for several days to allow the T cell population to expand to the desired dose level. Once expansion has completed, cells are harvested, formulated, packaged, and cryopreserved for shipment back to the clinic for infusion into the same patient from whom the white blood cells were removed. ACTR is currently administered as a single infusion, following preparatory lymphodepletion.

ACTR product is dosed based on the total number of cells expressing the ACTR transgene. The manufacturing process can take from six days to 12 days, depending on the desired dose for a given patient. This manufacturing timeline is typical for the therapeutic T cell industry and can potentially be further optimized. ACTR product is tested using a panel of release assays that assess the safety and suitability of the product candidate for clinical trials. Suitability is controlled through specifications that include the purity of the T cell population and the quantity of ACTR T cells in the final product. Safety is controlled via specifications on appearance, endotoxin, and the absence of microbial contamination and replication-competent viral vector.

An illustration of the manufacturing process is shown in the graphic below:



Commercialization Plan

We currently have no sales, marketing, or commercial product distribution capabilities and have no experience as a company in marketing products. We intend to expand our global commercialization capabilities over time.

As a first step, we plan to establish a U.S.-focused specialty sales and marketing organization in advance of receipt of regulatory approval of our first ACTR product. We believe that in the United States we can address physicians who treat our proposed clinical indications with a direct specialty sales force. Our commercial strategy for markets outside the United States may include the use of strategic partners or the establishment of our own commercial capabilities. We plan to further evaluate these alternatives as we approach approval of our first ACTR product.

We intend to leverage the infrastructure developed for our first approved ACTR product to facilitate commercialization of any additional product candidates for which we gain approval. In addition, we will build upon physicians' familiarity and experience with the first ACTR product to accelerate adoption of subsequent combinations. As additional product candidates advance through our pipeline, our commercial plans may change. In particular, some of our pipeline assets target potentially large solid tumor cancer indications. The potentially large amount of data, the size of the development programs, as well as the size of the target market and thus that of a commercial infrastructure and manufacturing capacity to address such market, may all influence our U.S., European Union (EU), and rest-of-world strategies.

For co-developed products under our collaboration with Seattle Genetics, if successful we will co-commercialize them with Seattle Genetics in the United States, and Seattle Genetics will commercialize them outside of the United States.

Intellectual Property

Intellectual property is an important component of our assets. We are working to establish both strong patent protection and trade secrets to position us as a leader in the practice of ACTR technology. Our efforts include our proprietary technology development as well as licensing patent rights from third parties. In doing so, we have strived to ensure our ability to operate freely within the complex patent landscape of cell therapy. To date, we have patents issued from our in-licensed portfolio in AU, EP (validated in DE, FR, and GB), JP, US, and SG. No other patents have issued from the patent applications that we own or in-license. We are working to

establish strong patent protection and trade secrets to position us as a leader in the practice of the ACTR and BOXR technology. In December 2018, the United States Patent and Trademark Office issued US patent 10,144,770, entitled "Chimeric Receptors and Uses Thereof in Immune Therapy." The '770 patent covers design and use of the ACTR technology. Unum has exclusive, worldwide rights to the '770 patent under the terms of its license agreement with the National University of Singapore and St. Jude Children's Research Hospital. In addition to the '770 patent covering ACTR in the United States, previously granted patents protect the technology in Europe, Japan, and other important territories. Additional filed patent applications cover both the ACTR platform as well as specific product candidates. We are simultaneously seeking patent protection for the BOXR technology platform and have completed filings for several patent applications covering different aspects of the technology. In our efforts to both patent Unum inventions and license additional technologies, we have focused on trying to ensure our ability to operate freely within the complex patent landscape of cell therapy.

The ACTR platform was initially conceived and developed in the laboratories of our scientific founder, Dr. Dario Campana, who was working initially as an investigator at St. Jude Children's Research Hospital (St. Jude's) and subsequently at the National University of Singapore (NUS). The original patent application describing ACTR087 was filed in 2013. A worldwide, exclusive license to the patent rights resulting from this work was executed between us, St. Jude's, and NUS in 2014.

Our further work at encompassing a broad range of ACTR constructs was completed and described in subsequent patent applications filed in 2014. Additional patent applications filed by us between 2014 and 2018 encompass the following additional technological innovations and product-related claims:

- engineered ACTR constructs that specifically engage synthetic (i.e., not endogenous) antibodies.
- targeting non-traditional tumor-target antigens with ACTR (e.g., peptides bound to MHC).
- using ACTR with mixtures of antibodies to simultaneously target multiple antigens or epitopes.
- methods of using ACTR and rituximab to treat lymphoma.
- methods of using ACTR and other antibodies to treat other cancer indications.
- next-generation ACTR constructs with improved functionality in solid tumor cancers.
- ACTR constructs in combination with bolt-on transgenes to improve activities of T cells under stringent *in vitro* and *in vivo* conditions.

Our strategy is to pursue a variety of claims intended to provide multiple layers of protection. These include:

- pursuing (and have obtained) broad claims in the U.S. for the ACTR concept (which we define as a chimeric receptor with the functional properties of Fc binding, T cell co-stimulation, and TCR signaling activity).
- pursuing claims to specific compositions of matter in connection with particular ACTR constructs (including specific protein and nucleic acid sequences).
- different methods of delivering ACTR to T cells, including viral vectors and mRNA.
- methods of using the ACTR platform in combination with antibodies to specified tumor-target antigens to treat disease.
- methods of using specific ACTR constructs in combination with specific monoclonal antibodies to specific tumor-target antigens to treat disease.
- Methods of using ACTR constructs in combination with bolt-on transgenes to improve T cell activity in stringent conditions.

We have obtained granted patents in the in-licensed portfolio in a number of jurisdictions, including AU, EP, JP, US, and SG. Other patent applications that we own or license are still in the early stages of prosecution. Examination of most of the patent applications that we own has not yet commenced, because they are either provisional applications, Patent Cooperation Treaty (PCT) applications, or entered into national phrase just recently. We will need to decide whether and where to pursue protection for the inventions disclosed in these provisional and PCT applications before applicable statutory deadlines, our applications will only be examined in jurisdictions where we elect to pursue protection, and we will only have the opportunity to attempt to obtain patents in such jurisdictions where we elect to pursue protection.

Under the terms of our agreement with NUS and St. Jude's, we have the right to review and comment on all correspondence and proposed responses to office actions and to provide consultation and input on all strategic decisions with respect to filing, prosecution, and maintenance of the licensed patents. We are seeking protection across a range of commercially important territories, including countries in North America, Europe, and Asia.

Our ACTR therapies require the use of commercially available antibodies (e.g., rituximab and trastuzumab, as used in our current clinical trials) or antibodies in preclinical or clinical development (e.g., SEA-BCMA, as used in our current clinical trials) for targeting cancer cells. These commercially available antibodies and antibodies in preclinical/clinical development are developed by third parties. More specifically, rituximab is jointly marketed by Biogen Inc. (Biogen) and Genentech, Inc. (Genentech) (a subsidiary of The Roche Group (Roche)); trastuzumab is marketed by Genentech (Roche); and SEA-BCMA is being developed by Seattle Genetics.

We do not own intellectual property, including patents, over these commercially available antibodies and antibodies in preclinical/clinical development *per se*. For commercially available antibodies, such as rituximab and trastuzumab, we rely on our ability to purchase them on commercially reasonable terms for the clinical trials and their availability for commercialized product. For antibodies in preclinical/clinical development, such as SEA-BCMA, we have formed a strategic partnership with Seattle Genetics under which we have access to the antibodies for clinical trials and development of commercial products.

With respect to rituximab (Rituxan®), Biogen's Form 10-K filed on February 4, 2015 states:

> We have several U.S. patents and patent applications, and numerous corresponding foreign counterparts, directed to anti-CD20 antibody technology, including RITUXAN. The principal patents with claims to RITUXAN or its uses expire in the U.S. between 2015 and 2018 and expired in the rest of the world in 2013, subject to any available patent term extensions. In addition, we and our collaborator Genentech, have additional patents and patent applications directed to anti-CD20 antibodies and their uses to treat various diseases. Genentech has principal responsibility for managing the intellectual property portfolio for RITUXAN and the other anti-CD20 antibodies under our agreements with Genentech.

With respect to trastuzumab (Herceptin®), the latest publicly available information from Genentech in its Form 10-K filed on February 20, 2009 listed the following last-to-expire, product-specific U.S. patents:

Product	Last-to-Expire Product-Specific U.S. Patents	Year of Expiration
Herceptin	6,339,142	2019
	6,407,213	2019
	7,074,404	2019

With respect to SEA-BCMA, Seattle Genetics has not provided any information regarding any relevant patents and patent applications publicly.

The effective term for individual patents varies based upon a number of factors including the date of patent application filing and the date of patent issuance, the territory within which protection is sought, and certain adjustments to patent term tied to regulatory review. Patents in both the U.S. and many other territories generally have an effective term of 20 years from the earliest filing date. Based on its initial filing date, should any patents issue from the ACTR core patent family, the 20-year term of such patents would be expected to expire in 2034. The actual protection afforded by any patents that may issue, if any patents do issue, is expected to vary across different ACTR plus antibody products and depends upon the claimed territory, the scope of claim coverage, the availability of extensions due to regulatory review, validity and enforceability of the claims, and a number of additional factors.

We are not currently a party and have not been a party to any legal proceedings involving patent rights.

The intellectual property value of companies like ours is intrinsically uncertain and involves complex legal and scientific questions. Competitors may commercialize products that infringe our intellectual property if we are unable to both obtain and enforce patent claims protecting our inventions. Our currently pending and future patent applications may not be granted. If granted, our patents may be challenged, invalidated, or circumvented, thereby limiting our ability to stop competitors from marketing related products. Future changes to patent laws (or their interpretation) may limit our ability to protect our inventions and to enforce our patent rights. Any such changes may adversely impact the value ascribed to our intellectual property. Others with related but distinct technology may have freedom to operate and effectively compete with us. Moreover, patents issued to competitors may limit or prevent our ability to practice the ACTR technology and to commercialize ACTR products. In addition, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent.

We seek to protect our technology and product candidates, in part, by entering into confidentiality agreements with those who have access to our confidential information, including our employees, contractors, consultants, collaborators, and advisors. We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in these individuals, organizations, and systems, agreements or security measures may be breached and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or may be independently discovered by competitors. To the extent that our employees, contractors, consultants, collaborators, and advisors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For this and more comprehensive risks related to our proprietary technology, inventions, improvements and products, please see the section on “Risk Factors—Risks Related to Intellectual Property.”

Our trademark portfolio currently contains registrations in China, EUTM, Japan, Singapore, and the United States as well as a registration at WIPO under the Madrid Protocol.

Licenses and Third-Party Research Collaborations

Strategic Collaboration with Seattle Genetics

In June 2015, we entered into a collaboration agreement with Seattle Genetics to identify, research, develop, and commercialize novel antibody-coupled ACTR therapies incorporating Seattle Genetics’ antibodies for the treatment of cancer. We formed a strategic partnership with Seattle Genetics because of its leadership in the discovery, development, and manufacturing of antibody-based therapies for cancer. Under this agreement, we are actively working on developing ACTR combination therapies for two target antigens. The first product candidate under our collaboration is ACTR087 used in combination with SEA-BCMA, targeting the BCMA antigen. We

have not yet disclosed the target antigen of the second product candidate under our collaboration. Under the agreement, Seattle Genetics had an option to nominate a third antigen; this option expired unexercised in June 2017.

Under the terms of the collaboration, Unum will conduct preclinical research and clinical development activities through Phase I clinical trials, and Seattle Genetics will provide all of the funding for those activities. We will work together to co-develop and fund product candidates after Phase I clinical trials unless either company opts out of further development and commercialization activities. Seattle Genetics has the option to opt-out from further development and commercialization activities for each of the two product candidates under the collaboration during two specified periods subsequent to Phase I clinical development. We have an option to opt-out from further development and commercialization activities for each of the two product candidates under the collaboration during a specified period subsequent to Phase II clinical development. If neither party elects to opt-out of further development and commercialization activities, we will co-commercialize any successful developed product candidates and share equally any profits and losses on any co-developed product candidates in the United States. Seattle Genetics retains exclusive commercial rights outside of the United States.

Through December 31, 2018, we had received $25.0 million in upfront payments, $5.0 million in equity investment in our Series B preferred stock financing, and $14.2 million in research and development funding under our collaboration agreement. As of December 31, 2018, we were eligible to receive future collaboration and milestone payments of up to an aggregate of $400.0 million, payments of which are due upon the achievement of specified development, regulatory, and commercial milestones or the occurrence of specific events. During the term of the agreement, we will share equally all profits and losses related to the commercialization of any co-developed products in the United States. We are entitled to receive tiered royalties in the high single digit to mid-teens percentages on net sales achieved outside of the United States for each co-developed product.

Unless earlier terminated, our collaboration agreement will expire on a product-by-product basis in the United States on the date on which neither party is researching, developing or commercializing such product. Outside of the United States, our collaboration agreement will expire on a product-by-product and country-by-country basis at the end of the applicable royalty term for such product in such country. The royalty term will be in effect beginning at the first commercial sale of a product and ending upon the later to occur of (i) expiration of the last valid claim within any patent right that we or Seattle Genetics has that would be infringed by the manufacture, use, sale, offer for sale, or importation of such product in such country, (ii) the end of any regulatory exclusivity periods that apply to the manufacture, use, sale, offer for sale, or importation of such product in such country, or (iii) ten years from the first commercial sale of such product in such country.

License Agreement with National University of Singapore and St. Jude Children's Research Hospital

In August 2014, we entered into a license agreement with the National University of Singapore (NUS) and St. Jude's that grants us an exclusive, worldwide, sublicensable license to certain patent rights and to intellectual property rights related to certain know-how to develop, make, and commercialize licensed products and to perform services for all therapeutic and diagnostic uses. The agreement was subsequently amended twice. The patent applications covered by this agreement are directed to specific ACTR constructs, including ACTR087 and their use in immunotherapy. Pursuant to this license agreement, we have rights to one pending U.S. non-provisional patent application and the corresponding Patent Cooperation Treaty counterpart application, and other counterpart patent applications in jurisdictions outside the United States. The U.S. provisional applications under this license agreement have expired.

In 2014, we made payments of $0.1 million. We are required to pay license maintenance fees on each anniversary of the effective date of the agreement that escalate from less than $0.1 million for each of the first seven years to $0.1 million on the eighth anniversary and each year thereafter. The license agreement requires us to pay tiered royalties ranging in the low single-digit percentages based on annual net sales of licensed products.

In the case that multiple royalty streams are required, due to multiple licenses required for marketed products or services, royalty fees for this technology may be reduced. We may also be obligated to pay up to a maximum of 5.5 million Singapore dollars (equivalent to approximately $4.06 million as of December 31, 2018) in one-time clinical and regulatory milestones related to the development of the first licensed product to hit such milestones. Licensed products could include at least ACTR087. In addition, we are required to pay a low double-digit percentage of certain payments that we receive, if these qualify as sublicensing income, as defined in the license agreement. Through December 31, 2018, we had paid a total of $0.1 million.

The license agreement will expire, on a country-by-country basis until the last to expire of the patents and patent applications covering such licensed product or service. NUS may terminate the license agreement within 60 days after written notice in the event of a breach of contract. NUS may also terminate the agreement upon written notice in the event of our bankruptcy, liquidation, or insolvency. In addition, we have the right to terminate this agreement in its entirety at will upon 90 days' advance written notice to NUS. However, if we have commenced the commercialization of licensed products, we can only terminate at will if we cease all development and commercialization of licensed products.

Competition

The biotechnology and pharmaceutical industries, including the oncology subsector, are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on intellectual property. Any candidates that we successfully develop and commercialize will have to compete with any existing therapies as well as therapies that may be developed in the future. While we believe our ACTR platform and scientific expertise provide us with competitive advantages, we face substantial competition from many different sources, including large and specialty pharmaceutical companies and biotechnology companies, academic research institutions and governmental agencies, and public and private research institutions.

Due to their promising clinical therapeutic effect in clinical trials, we anticipate substantial direct competition from other organizations developing advanced T cell therapies and other types of oncology therapies. In particular, we expect to compete with:

- Companies genetically engineering T cells with CARs that are reactive to tumor associated antigens. In particular, Kite Pharma, Inc. (a Gilead Sciences, Inc. company), Juno Therapeutics, Inc. (a Celgene Corporation company), Novartis AG, and bluebird bio, Inc. In addition, some companies, such as Cellectis SA, are developing allogeneic cell therapies that could compete with our products.
- Companies genetically engineering T cells with TCRs that are reactive to tumor associated antigens. In particular, Adaptimmune Therapeutics plc, Kite Pharma, Inc. (a Gilead Sciences, Inc. company), and Juno Therapeutics, Inc (a Celgene Corporation company).
- Companies developing bi-specific antibodies that bring T cells and tumor cells into close proximity with each other. In particular, Macrogenics, Inc., Amgen Inc., Roche Holding AG, and Genmab A/S.
- Companies developing other immune cells that can be targeted using antibodies, such as NantKwest, Inc.

We believe that other known types of immunotherapies, such as certain check-point inhibitors, may be used in conjunction with ACTR platform to increase efficacy. However, we cannot predict whether other types of immunotherapies may be developed and show greater efficacy and we may have direct and substantial competition from such immunotherapies in the future. Such immunotherapies are being pursued by several biotech companies as well as by large-cap pharma. Many of our current or potential competitors, 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. Mergers and acquisitions in the pharmaceutical, biotechnology, and gene therapy 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 product candidates.

Government Regulation

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

Licensure and Regulation of Biologics in the United States

In the United States, our candidate products are regulated as biological products (biologics), under the Public Health Service Act (PHSA), and the Federal Food, Drug, and Cosmetic Act (FDCA), and their implementing regulations. The failure to comply with the applicable U.S. requirements at any time during the product development process, including non-clinical testing, clinical testing, or the approval process or post-approval process, may subject an applicant to delays in the conduct of a study, regulatory review and approval, and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the U.S. Food and Drug Administration's (FDA), refusal to allow an applicant to proceed with clinical testing, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, and civil or criminal investigations and penalties brought by the FDA or the Department of Justice (DOJ), or other governmental entities.

An applicant seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps:

- non-clinical laboratory tests, animal studies, and formulation studies performed in accordance with the FDA's good laboratory practice (GLP) regulations, where required;
- submission to the FDA of an investigational new drug application (IND) for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an institutional review board (IRB) representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency, and purity of the product candidate for each proposed indication, in accordance with good clinical practices (GCP);
- preparation and submission to the FDA of a biologic license application (BLA), for a biologic product requesting marketing for one or more proposed indications, including submission of detailed information on the manufacture and composition of the product in clinical development and proposed labeling;
- FDA acceptance and review of the BLA, which might include review by an FDA advisory committee;
- one or more FDA inspections of the manufacturing facility or facilities, including those of third parties, at which the product, or components thereof, are produced to assess compliance with current good manufacturing practices (cGMP) requirements and to assure that the facilities, methods, and controls are adequate to preserve the product's identity, strength, quality, and purity;

- any FDA audits of the non-clinical studies and clinical trial sites to assure compliance with GLPs and GCPs, respectively, and the integrity of clinical data in support of the BLA;
- payment of user fees and securing FDA approval of the BLA and licensure of the new biologic product; and
- compliance with any post-approval requirements, including the potential requirement to implement a risk evaluation and mitigation strategy (REMS) and any post-approval studies required by the FDA as a condition of approval.

Non-clinical Studies and Investigational New Drug Application

Before testing any biologic product candidate in humans, the product candidate must undergo non-clinical testing. Non-clinical tests include laboratory evaluations of product chemistry, formulation, and stability, as well as animal studies to evaluate the potential for efficacy and toxicity for eventual use in humans. The conduct of the non-clinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP requirements. The results of the non-clinical tests, together with manufacturing information, analytical data, any available literature and plans for clinical trials, among other things are submitted to the FDA as part of an IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trial can begin.

As a result, submission of the IND may result in the FDA not allowing the trial to commence or allowing the trial to commence on the terms originally specified by the sponsor in the IND. If the FDA raises concerns or questions either during this initial 30-day period, or at any time during the IND process, it may choose to impose a partial or complete clinical hold. This order issued by the FDA would delay either a proposed clinical trial or cause suspension of an ongoing study, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigation may proceed. This could cause significant delays or difficulties in completing planned clinical trials in a timely manner. The FDA also may impose clinical holds on a biologic product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only recommence under terms authorized by the FDA.

Human Clinical Trials in Support of a BLA

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

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of the BLA so long as the clinical trial is well-designed and well-conducted in accordance with GCP, including review and approval by an independent ethics committee, and the FDA is able to validate the study data through an onsite inspection, if necessary.

Further, each clinical trial must be reviewed and approved by an institutional review board (IRB), either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, and the safety of human

subjects. An IRB must operate in compliance with FDA regulations. The FDA, IRB, or the clinical trial sponsor, including at the recommendation of a data monitoring committee, if applicable, may suspend or discontinue a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements or the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group may recommend continuation of the study as planned, changes in study conduct, or cessation of the study at designated check points based on access to certain data from the study.

Clinical trials typically are conducted in three sequential phases, which may overlap or be combined. Additional studies may be required after approval.

- *Phase I* clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics in healthy humans or, on occasion, in patients with the target disease or condition, such as cancer patients.
- *Phase II* clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications, and determine dose tolerance and optimal dosage. Multiple Phase II clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase III clinical trials.
- *Phase III* clinical trials proceed if the Phase II clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase III clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy, and further test for safety in an expanded and diverse patient population generally at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase III trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a biologic.

In some cases, the FDA may approve a BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase IV clinical trials. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase IV clinical trial requirement or to request a change in the product labeling. Failure to exhibit due diligence with regard to conducting Phase IV clinical trials could result in withdrawal of approval for products.

Clinical trials at each phase of development may not be completed successfully within any specified period, or at all.

In addition to the regulatory requirements summarized above for clinical trials taking place within the United States, clinical trials containing gene therapy products historically have also been subject to review by the NIH Office of Biotechnology Activities' (OBA's) Recombinant DNA Advisory Committee (RAC). In August 2018, the NIH published a notice of the Federal Register to seek public comment on its proposal to amend the NIH Guidelines to further streamline oversight for human gene transfer clinical research protocols and reduce duplicative reporting requirements while focusing the NIH Guidelines more specifically on biosafety issues associated with research involving recombinant or synthetic nucleic acid molecules. The notice included proposed amendments to eliminate RAC review and reporting requirements to NIH for human gene transfer

research protocols and to modify the roles and responsibilities of investigators, institutions, Institutional Biosafety Committees (IBCs), the RAC, and the NIH to be consistent with these goals. Pursuant to the NIH Guidelines, research involving recombinant or synthetic nucleic acid molecules must be approved by an IBC, i.e. a local institutional committee that reviews and oversees basic and clinical research conducted at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment. During the comment period and effective August 2018, the NIH stated it will no longer accept new human gene transfer protocols for the protocol registration process under the NIH Guidelines, or convene the RAC to review individual human gene transfer protocols. The NIH Office of Science Policy also will no longer accept annual reports, safety reports, amendments or other documentation for any previously registered human gene transfer protocols under the NIH Guidelines. The roles and responsibilities of IBCs at the local level will continue as described in the NIH Guidelines. Such trials remain subject to FDA and other clinical trial regulations, and only after FDA, IBC and other relevant approvals are in place can these protocols proceed. Finally, IBCs and IRBs will no longer be required to submit documentation to the NIH assessing whether a particular protocol meets the criteria for RAC review.

Compliance with cGMP Requirements

Before approving a BLA, the FDA typically will 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 full compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing control for products like biologics whose attributes cannot be precisely defined.

Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Manufacturers may have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated.

Review and Approval of a BLA

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

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

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

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of non-clinical studies and clinical trial sites to assure compliance with GLPs and GCPs, respectively, the FDA may issue an approval letter, denial letter, or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. If the application is not approved, the FDA may issue a complete response letter, which will contain the conditions that must be met in order to secure final approval of the application, and when possible will outline recommended actions the sponsor might take to obtain approval of the application. Sponsors that receive a complete response letter may submit to the FDA information that represents a complete response to the issues identified by the FDA. Such resubmissions are classified under PDUFA as either Class 1 or Class 2. The classification of a resubmission is based on the information submitted by an applicant in response to an action letter. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has two months to review a Class 1 resubmission and six months to review a Class 2 resubmission. The FDA will not approve an application until issues identified in the complete response letter have been addressed. The FDA issues a denial letter if it determines that the establishment or product does not meet the agency's requirements.

The FDA may also refer the application to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved. In particular, the FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

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

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

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, and priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or

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

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act (FDASIA). This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Products designated as breakthrough therapies may be eligible for rolling review. In addition, the FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, as part of the 21st Century Cures Act, Congress amended the FDCA to create an expedited program for regenerative medicine therapies, which include cell therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products. Regenerative medicine therapies do not include those human cells, tissues, and cellular and tissue-based products regulated solely under section 361 of the Public Health Service Act and 21 CFR Part 1271. The program is intended to facilitate efficient development and expedite review of regenerative medicine therapies. A sponsor may request that FDA grant regenerative medicine advanced therapy designation concurrently with or after submission of an IND as an amendment. FDA has 60 calendar days after receipt of the designation request to determine whether the product meets the criteria. Qualifying criteria for a regenerative medicine advanced therapy designation are that the product: (1) meets the definition of regenerative medicine therapy; (2) is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) preliminary clinical evidence indicates that the regenerative medicine therapy has the potential to address unmet medical needs for such condition. The features of this designation include all of the benefits of the fast track and breakthrough therapy designation programs.

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

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate

clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality (IMM) and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval, and do not receive either more or less favorable review from the FDA based on such designation.

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

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

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

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA has imposed as part of the approval process. The sponsor will be required to report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information, comply with requirements concerning advertising and promotional labeling, as well as maintain certain records. 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 prescription drug program fees. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A biologic product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official lot release, the manufacturer must submit samples of each lot, together with a release protocol showing a

summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency, and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the 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 trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

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

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Pharmaceutical products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Orphan Drug Designation

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the biologic for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for tax credits and market exclusivity for seven years following the date of the product's marketing approval if granted by the FDA for the first drug with such designation. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development (OOPD) at the FDA based on acceptable confidential requests made under the regulatory provisions. The product must then go through the review and approval process like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first drug. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

The period of exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the indication for which the product has been designated. The FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use. The FDA cannot, however, approve the same product made by another manufacturer for the same indication during the market exclusivity period unless it has the consent of the sponsor or the sponsor is unable to provide sufficient quantities.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCIA). The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. To date, multiple biosimilar products have been approved by the FDA for use in the United States. No interchangeable biosimilars, however, have been approved. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

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

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own non-clinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars 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.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, as amended, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time. By its terms, PREA does not apply to any biologic for an indication for which orphan drug designation has been granted, unless the FDA issues regulations stating otherwise or as described below for a molecularly targeted pediatric cancer investigation.

Pursuant to the FDA Reauthorization Act of 2017, a BLA, submitted after August 18, 2020 for a biologic intended for the treatment of an adult cancer and that is directed at a molecular target that FDA determines to be

substantially relevant to the growth or progression of a pediatric cancer, must contain reports of molecularly targeted pediatric cancer investigations. These investigations are designed to yield clinically meaningful pediatric study data, gathered using appropriate formulations for each age group for which the study is required, regarding dosing, safety, and preliminary efficacy to inform potential pediatric labeling. Applications for products for which orphan drug designation was previously granted will no longer be exempt from PREA and will be required to include these pediatric investigations, unless the investigations are waived or deferred.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

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

Patent Term Restoration and Extension

A patent claiming a new biologic product may be eligible for a limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, which permits a patent restoration of up to five years for patent term lost during product development and FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of an IND and the submission date of a BLA, plus the time between the submission date of a BLA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Regulation and Procedures Governing Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company also must comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the EU, generally follows the same lines as in the United States. It entails satisfactory completion of non-clinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application (MAA), and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on GCP, a system for the approval of clinical trials in the EU has been implemented through national legislation of

the member states. Under this system, an applicant must obtain approval from the competent national authority of an EU member state in which the clinical trial is to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. Furthermore, the applicant may only start a clinical trial at a specific trial site after the independent ethics committee has issued a favorable opinion. The clinical trial application (CTA) must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. It is expected that the new Clinical Trials Regulation (EU) No 536/2014 will apply in 2019 with a three-year transition period. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new regulation, which will be directly applicable in all member states, aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications.

Marketing Authorization

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

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use (CHMP) established at the EMA is responsible for conducting an initial assessment of a product. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

Regulatory Data Protection in the European Union

In the European Union, new chemical entities approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During the additional two-year period of market

exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, non-clinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk benefit balance by the EMA or by the competent authority of the authorizing member state. To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety, and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the EU market (in the case of the centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion, and sale of the medicinal product. These include compliance with the EU's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's GMP requirements and comparable requirements of other regulatory bodies in the EU, which mandate the methods, facilities, and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. Finally, the marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union under Directive 2001/83EC, as amended.

Coverage, Pricing, and Reimbursement

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

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover any product candidates we may develop could reduce physician utilization of such product candidates once approved and have a material adverse effect on our sales, results of operations, and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The containment of healthcare costs also has become a priority of federal, state, and foreign governments and the prices of pharmaceuticals, including biologics, have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for any product candidates we may develop will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of any product candidates we may develop to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

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

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of pharmaceutical products that are granted regulatory approval. Arrangements with providers, consultants, third-party payors, and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians, and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things: knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent; making a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to CMS, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

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

We will be required to spend substantial time and money to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations. Violations of these laws can subject us to

criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, and exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and reputational harm, we may be required to curtail or restructure our operations. Moreover, we expect that there will continue to be federal and state laws and regulations, proposed and implemented, that could impact our future operations and business.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government healthcare programs. Among the provisions of the ACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price" (AMP) for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable products to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient products to be covered under Medicare Part D; (which was increased to 70% as of January 1, 2019 under the Bipartisan Budget Act of 2018);
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board (IPAB) which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products. The ACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription product spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Members of the United States Congress and the Trump Administration have expressed an intent to pass legislation or adopt executive orders to fundamentally change or repeal parts of the Affordable Care Act. While Congress has not passed repeal legislation to date, the 2017 Tax Reform Act includes a provision repealing the individual insurance coverage mandate included in the Affordable Care Act, effective January 1, 2019. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the Affordable Care Act. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the Affordable Care Act for plans sold through such marketplaces.

It remains to be seen whether there will be further changes to the Affordable Care Act as a result of new legislation or further executive, administrative or judicial action. The impact that any such further action will have on the availability of healthcare and containing or lowering the cost of healthcare including the cost of pharmaceutical and biological products is unclear. The full impact of the Affordable Care Act and the political uncertainty surrounding it on our business also remains unclear.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

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

Additional Regulation

In addition to the foregoing, state, and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act, and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling, and disposal of various biologic, chemical, and radioactive substances used in, and wastes generated by, operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. Equivalent laws have been adopted in third countries that impose similar obligations.

Employees

As of December 31, 2018, we had 56 employees, approximately 66% of whom have an M.D., Ph.D., or other advanced degree. All of our employees are in Cambridge, Massachusetts. None of our employees are represented by a labor union or covered under a collective bargaining agreement. We consider our employee relations to be good.

Facilities

Our corporate headquarters are located in Cambridge, Massachusetts, where we lease approximately 33,500 square feet of office and laboratory space pursuant to a lease agreement commencing in July 2015 and expiring in April 2023. This facility houses our research, clinical, regulatory, commercial, and administrative personnel. We believe that our existing facilities are adequate for our near-term needs, but expect to need additional space as we grow. We believe that suitable additional or alternative space would be available as required in the future on commercially reasonable terms.

Legal Proceedings

From time to time, we may be involved in various claims and legal proceedings relating to claims arising out of our operations. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors. We are not currently a party to any legal proceedings.

Corporate History

We were incorporated under the laws of the State of Delaware in March 2014. On April 3, 2018, we completed our initial public offering (IPO) of our common stock and issued and sold 5,770,000 shares of our common stock at a public offering price of $12.00 per share, resulting in net proceeds of approximately $61.5 million, after deducting underwriting discounts and commissions and other offering costs. In addition, we completed a concurrent private placement of $5.0 million of shares of common stock at the public offering price of $12.00 per share, or 416,666 shares, with Seattle Genetics (the Concurrent Private Placement). On April 25, 2018, we issued and sold an additional 215,000 shares of our common stock at the IPO price of $12.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock, resulting in additional net proceeds of $2.4 million to us, after deducting underwriting discounts and commissions.

Implications of Being an Emerging Growth Company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended (JOBS Act). As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure about our executive compensation arrangements;
- no non-binding advisory votes on executive compensation or golden parachute arrangements; and
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of our IPO; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission (SEC). We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this Annual Report on Form 10-K. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock.

We have irrevocably elected to "opt out" of the exemption for the delayed adoption of certain accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Available Information

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

ITEM 1A. RISK FACTORS

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 3 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Business and Industry

We have incurred net losses in every year since our inception and anticipate that we will continue to incur net losses in the future.

We are a clinical-stage biopharmaceutical company with a limited operating history. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception in March 2014. Our net loss was $34.5 million for the year ended December 31, 2018 and $25.5 million for the year ended December 31, 2017.

As of December 31, 2018, we had an accumulated deficit of $92.1 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, product candidates.

Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Our ACTR T cell product candidates represent a novel approach to cancer treatment, which creates significant challenges for us.

Our ACTR T cell product candidates involve (1) harvesting T cells from the patient's blood via leukapheresis, (2) genetically engineering the T cells to incorporate the ACTR transgene, (3) expanding the number of engineered T cells to the desired dose level and (4) infusing the engineered ACTR T cells back into the patient with or following the administration of the antibody. Advancing this novel and personalized investigational therapy creates significant challenges for us, including:

- educating medical personnel about the administration of the ACTR-combination therapy;
- educating medical personnel regarding the potential side effect profile of our product candidates, such as the potential adverse side effects related to cytokine release syndrome, neurotoxicity or autoimmune or rheumatologic disorders;
- administering chemotherapy to patients in advance of administering our product candidates, which may increase the risk of adverse side effects;
- sourcing clinical and, if approved, commercial, supplies for the materials used to manufacture and process our product candidates;
- manufacturing viral vectors to deliver ACTR to T cells;
- developing a robust and reliable ACTR T cell manufacturing process, including efficiently managing shipment of patient cells from and to clinical sites, minimizing potential contamination to the cell product and effectively scaling manufacturing capacity to meet demand;
- managing costs of inputs and other supplies while scaling production;
- using medicines to manage adverse side effects of our product candidates, which may not adequately control the side effects and/or may have a detrimental impact on the efficacy of the treatment;
- obtaining and maintaining regulatory approval from the U.S. Food and Drug Administration (FDA); and
- establishing sales and marketing capabilities upon obtaining any regulatory approval to gain market acceptance of a novel therapy.

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

- We have made a large number of ACTR constructs and used preclinical tests to select product candidates to advance into clinical testing. The preclinical tests are limited in their ability to predict behavior in patients. As we gain clinical experience with ACTR, new learnings may prompt us to select other ACTR constructs for clinical development.

- We have used a retroviral vector to deliver ACTR to T cells. In the future, we may find that a lentiviral vector offers advantages. Switching from retroviral to lentiviral delivery would necessitate additional process development and clinical testing and delay existing product candidates.
- The process by which patient cells are converted into an ACTR T cell has many steps that can influence quality and activity. We have explored a subset of variables and expect to continue to improve and optimize the manufacturing process. Depending upon the nature of the process changes, we may be compelled to perform bridging studies and/or to re-start clinical development, causing delays in time to market and potentially introducing a risk of failure if new processes do not perform as expected.

Our business is highly dependent on the success of our lead lymphoma product candidate, ACTR707 used in combination with rituximab, our other ACTR-antibody combination that we develop, other ACTR-antibody combinations that we may develop, and potential BOXR product candidates that we develop.

Our business and future success depend on our ability to obtain regulatory approval of and then successfully commercialize our lead product candidate, ACTR707 used in combination with rituximab, other product combinations that we develop using antibodies in combination with ACTR087 or ACTR707, and BOXR 1030 and other product candidates that we develop using our BOXR platform. All of our product candidates, including ACTR707 used in combination with rituximab, are in the early stages of development and will require additional clinical and nonclinical development, regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. In addition, because most of our product candidates are based on our ACTR platform, if both ACTR087 and ACTR707 constructs encounter safety, efficacy, or manufacturing problems, developmental delays, regulatory, or commercialization difficulties or other problems, our development plans and business would be significantly harmed. For example, our Phase I clinical trial for ACTR087 used in combination with rituximab was placed on clinical hold in December 2017 pending submission of certain information relating to the trial. Following review of this information by the FDA, the clinical hold was removed in February 2018.

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

Before obtaining regulatory approvals for the commercial sale of our product candidates, including for our lead lymphoma product candidate ACTR707 used in combination with rituximab, any ACTR T cell product candidates used in combination with other antibodies, or any BOXR product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are both safe and effective for use in each target indication. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process, and, because our product candidates are in an early stage of development, there is a high risk of failure and we may never succeed in developing marketable products. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy, insufficient durability of efficacy, or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence clinical trials are never approved as products.

Any clinical trials that we may conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates. If the results of our ongoing or future clinical trials are inconclusive with respect to the efficacy of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for such product candidates. In

some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants.

We designed our Phase I clinical trials of ACTR087 and ACTR707, each used in combination with rituximab, called ATTCK-20-2 and ATTCK-20-03, respectively, primarily to assess safety and efficacy in adult patients with r/r NHL. We recently selected ACTR707 used in combination with rituximab to be the lead lymphoma product candidate to advance to further clinical development. However, the preliminary results from the ATTCK-20-03 Phase I clinical trial may not be indicative of the final analysis of this Phase I clinical trial, especially given the small number of patients that have dosed in this trial. In addition, the Phase I results may not predict results for any further clinical testing of either ACTR087 or ACTR707 used in combination with rituximab or other product candidates that we have developed, such as ACTR087 used in combination with SEA-BCMA and ACTR T cells in combination with trastuzumab for the treatment of patients with HER2+ advanced cancers, or may develop in the future, using antibodies in combination with ACTR087 and ACTR707 or in different indications.

As of the most recent data cutoff date for the ATTCK-20-2 trial of November 1, 2018, approximately 12% (two out of 17) of ACTR087-treated patients in ATTCK-20-2 experienced ACTR087-related severe cytokine release syndrome (CRS) and 6% (one out of 17) of patients experienced severe ACTR087-related neurotoxicity, which was fatal. Of the two events of CRS, one patient subsequently experienced a fatal case of enterococcal sepsis considered related to ACTR087 and one patient subsequently experienced a fatal case of sepsis considered not related to ACTR087. These were the events that resulted in the FDA placing this trial on clinical hold in December 2017 pending submission of certain information relating to the ATTCK-20-2 clinical trial. The clinical hold was removed in February 2018, following review of this information by the FDA. Several protocol and dosing changes were made in early 2018, which we expect to reduce the incidence of severe adverse events and better manage those events that do occur. We recently selected ACTR707 used in combination with rituximab to be the lead lymphoma product candidate for further clinical development, and, as a result, we intend to conclude enrollment in the ATTCK-20-2 study in the first half of 2019. However, if severe safety events are observed in patients treated in spite of the modifications outlined above, the FDA may determine, at any time, that there is an unacceptable safety risk for patients and we may be required to stop the trial prior to the conclusion of the planned enrollment.

In addition, even if the ATTCK-20-03 trial and other currently ongoing or planned trials, such as ATTCK-17-01 Phase I clinical trial or ATTCK-34-01, are successfully initiated and/or completed, as applicable, clinical data are often susceptible to varying interpretations and analyses, and we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. For instance, although our lead product candidates will be dosed in refractory patients with antibodies that the patients have already received, we plan to test future product candidates in patients that have never received the co-administered antibody in prior treatment and with antibodies that have never been independently evaluated for safety or efficacy. As a result, it may be difficult to demonstrate that the ACTR construct, rather than the antibody alone, is causing an observed effect. We cannot guarantee that the FDA will view the ACTR construct as having efficacy even if positive results are observed in these clinical trials. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, approval of our product candidates may be significantly delayed, or we may be required to expend significant additional resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates.

We cannot guarantee that our ACTR product candidates or BOXR technology will show any functionality in the solid tumor environment.

While we plan to develop product candidates for use in solid tumor cancers, including ACTR707 used in combination with trastuzumab for HER2+ cancers, we cannot guarantee that our product candidates will show

any functionality in the solid tumor environment. The cellular environment in which solid tumor cancers exist is inimical to T cells due to several factors including: (1) immunosuppressive cells (e.g., regulatory T cells (Tregs), myeloid derived suppressor cells (MDSCs)), (2) immunosuppressive enzymes and signaling molecules (e.g., IDO1, TGF-beta), (3) limited nutrients (e.g., oxygen, glucose), and (4) toxic metabolites (e.g., reactive oxygen species, lactic acid). Together, these factors can limit the ability of T cells, including ACTR T cells, both to penetrate into the solid tumor and to function properly once there. As a result of these and other solid tumor challenges, our product candidates may not demonstrate efficacy in solid tumors. For example, our ACTR-based product candidates may not be able to access the solid tumor, and even if they do, they may not be able to exert anti-tumor effects in an immunosuppressive tumor microenvironment. In addition, the safety profile of our product candidates may differ in a solid tumor setting. If we are unable to make our product candidates function in solid tumor cancers, our development plans and business may be significantly harmed. We have preliminary preclinical data on the BOXR platform that we believe improves the functionality of T cells, enabling them to be more efficient in solid tumor cancers. However, the preclinical data we have are very new and require additional development to determine the viability of the construct. Additionally, we have chosen our lead BOXR product candidate, BOXR1030, but it is still in preclinical development and we cannot guarantee it will show safety and efficacy in solid tumors, and we may not be able to choose additional nominees or further develop BOXR technology unless we obtain additional financing.

Since the number of patients that we have dosed, or plan to dose, in our ongoing or planned Phase I clinical trials is small, the results from such clinical trials, once completed, may be less reliable than results achieved in larger clinical trials, which may hinder our efforts to obtain regulatory approval for our product candidates.

A study design that is considered appropriate for regulatory approval includes a sufficiently large sample size with appropriate statistical power, as well as proper control of bias, to allow a meaningful interpretation of the results. The preliminary results of trials with smaller sample sizes can be disproportionately influenced by the impact the treatment had on a few individuals, which limits the ability to generalize the results across a broader community, thus making the study results less reliable than studies with a larger number of patients. As a result, there may be less certainty that such product candidates would achieve a statistically significant effect in any future clinical trials. If we conduct any future clinical trials, we may not achieve a statistically significant result or the same level of statistical significance, if any, that we may have seen in prior clinical trials. Additionally, our inability to dose a sufficient number of patients in our clinical trials could result in significant delays and could require us to abandon one or more clinical trials altogether. Delays in our clinical trials may result in increased development costs for our drug candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

We may not be able to file investigational new drug applications (INDs) or IND amendments or clinical trial authorization applications (CTAs) to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA or other regulatory authorities may not permit us to proceed.

We expect to leverage the ACTR and BOXR platforms by submitting additional INDs or CTAs in the future for ACTR T cell and BOXR product candidates used in combination with other monoclonal antibodies. In addition, however, our timing of filing on future product candidates is dependent on further research. We cannot be sure that submission of an IND or CTA will result in the FDA or other regulatory authority allowing further clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND or CTA, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs or CTAs.

We have limited experience as a company conducting clinical trials or managing a manufacturing facility for our product candidates.

We have limited experience as a company in conducting clinical trials. In part because of this lack of experience, we cannot be certain that our ongoing clinical trials will be completed on time or if the planned clinical trials will begin or be completed on time, if at all. Large-scale trials would require significant additional financial and management resources and reliance on third-party clinical investigators, contract research organizations (CROs), or consultants. Relying on third-party clinical investigators or CROs may force us to encounter delays that are outside of our control.

In the future, we also intend to operate our own manufacturing facility, which will require significant resources, and we have limited experience as a company in expanding or managing a manufacturing facility. In part because of this lack of experience, we cannot be certain that our manufacturing facility will be completed on time, if at all, or if the planned clinical trials will begin or be completed on time, if at all. In part because of our inexperience, we may have unacceptable or inconsistent product quality success rates and yields, and we may be unable to maintain adequate quality control, quality assurance and qualified personnel. In addition, if we switch from one manufacturing facility to our own manufacturing facility for one or more of our product candidates in the future, we may need to conduct additional preclinical studies to bridge our modified product candidates to earlier versions. Failure to successfully create and operate our proposed manufacturing facility could adversely affect the commercial viability of our product candidates.

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

Undesirable side effects caused by our product candidates could cause us or regulatory authorities, including institutional review boards (IRBs), to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of subjects and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the drug. Because of our dose escalation design for our clinical trials, undesirable side effects could also result in an expansion in the size of our clinical trials, increasing the expected costs and timeline of our clinical trials. Additionally, results of our trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics.

In certain trials of CAR-based products, which also use an engineered T cell, side effects, such as CRS and neurotoxicity, arose that resulted in risk, injury, or death to the patients. We observed some of these side effects in the second dose level of our Phase I clinical trial of ACTR087 used in combination with rituximab, called ATTCK-20-2. These events resulted in the FDA placing the trial on clinical hold pending submission of certain information relating to the ATTCK-20-2 clinical trial. The clinical hold was removed in February 2018, following review of this information by the FDA. We will likely continue to observe some or all of these side effects in our clinical trials at additional dosage levels. We have established safety management and monitoring guidelines for clinical investigators to detect and treat potential side effects. However, there is no guarantee that these medical interventions will be effective in preventing negative effects to the patient. Additionally, if we continue to observe severe side effects in our clinical trials, our ongoing clinical trials may be halted or put on an additional clinical hold prior to completion if there is an unacceptable safety risk for patients.

Autoimmune reaction triggered by an interaction between a patient's naturally occurring antibodies and ACTR T cells is a theoretical safety risk unique to the ACTR approach. If a patient's self-generated antibodies were directed to a target expressed on the surface of cells in normal tissue (i.e., autoantibodies), ACTR would be directed to attack these tissues, potentially resulting in off-tumor effects. These autoantibodies may be present whether or not the patient has an active autoimmune disease. In our clinical testing, we have taken steps to minimize the likelihood of this happening (e.g., excluding patients with a history of autoimmune disease from our trials and screening for the presence of certain autoantibodies). To date, we have not observed any autoimmune adverse effects in clinical testing of ACTR. There is no guarantee, however, that we will not

observe autoimmune reactions in the future and no guarantee that if we do, that we will be able to implement interventions to address the risk.

If unacceptable toxicities arise in the development of our product candidates, we could suspend or terminate our trials or the FDA or comparable foreign regulatory authorities, or local regulatory authorities such as IRBs, could order us to cease clinical trials. Competent national health authorities, such as the FDA, could also deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from T cell therapy are not normally encountered in the general patient population and by medical personnel. We expect to have to train medical personnel using ACTR or BOXR to understand the respective side effect profiles of ACTR and BOXR for all clinical trials and upon any commercialization of any product candidates, if approved. Inadequate training in recognizing or managing the potential side effects of ACTR or BOXR could result in patient deaths. Any of these occurrences may harm our business, financial condition and prospects significantly.

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

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

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

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

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

Clinical trials are expensive, time-consuming, and difficult to design and implement.

Human clinical trials are expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. Because our product candidates are based on new technology and engineered on a patient-by-patient basis, we expect that they will require extensive research and development and have substantial manufacturing and processing costs. In addition, costs to treat patients with relapsed or refractory cancer and to treat potential side effects that may result from our product candidates can be significant. Accordingly, our clinical trial costs are likely to be significantly higher than those for more conventional therapeutic technologies or drug product candidates. In addition, our proposed personalized product candidates involve several complex and costly manufacturing and processing steps, the costs of which will be borne by us.

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

Cancer therapies are sometimes characterized as first line, second line, or third line, and the FDA often approves new therapies initially only for a particular line of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, usually chemotherapy, antibody drugs, tumor-targeted small molecules, hormone therapy, radiation therapy, surgery, or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules, or a combination of these. Third line therapies can include hematopoietic stem cell transplantation in certain cancers, chemotherapy, antibody drugs, and small molecule tumor-targeted therapies, more invasive forms of surgery, and new revolutionary technologies. We expect to initially seek approval of our product candidates in most instances at least as a third line therapy, for use in patients with relapsed or refractory metastatic cancer. Subsequently, for those products that prove to be sufficiently safe and beneficial, if any, we would expect to seek approval as a second line therapy and potentially as a first line therapy, but there is no guarantee that our product candidates, even if approved as a third or subsequent line of therapy, would be approved for an earlier line of therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive a particular line of therapy and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new therapies may change the estimated incidence or prevalence of these cancers. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates. For instance, we expect ACTR087 and ACTR707, each used in combination with rituximab, to initially target a small patient population that suffers from r/r NHL. Even if we obtain significant market share for our product candidates within our addressable patient population, because the potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications, including use as first or second line therapy.

We may choose not to develop a potential product candidate, or we may suspend, deprioritize or terminate one or more discovery programs or preclinical or clinical product candidates or programs.

At any time and for any reason, we may determine that one or more of our discovery programs or preclinical or clinical product candidates or programs does not have sufficient potential to warrant the allocation of resources toward such program or product candidate. Accordingly, we may choose not to develop a potential product candidate or elect to suspend, deprioritize or terminate one or more of our discovery programs or preclinical or clinical product candidates or programs. For example, we have determined to conclude enrollment in our ATTCK-20-2 study in the first half of 2019 as a result of emerging clinical data from our Phase I

ATTCK-20-03 trial, the continuing progress in our ATTCK-20-03 trial, and our desire to efficiently manage resources for our clinical programs. If we suspend, deprioritize or terminate a program or product candidate in which we have invested significant resources, we will have expended resources on a program or product candidate that will not provide a full return on our investment and may have missed the opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or product candidates.

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

We have developed a pipeline of product candidates and intend to pursue clinical development of additional product candidates that combine ACTR T cells with different antibodies and target different tumor types. Developing, obtaining regulatory approval for and commercializing additional product candidates will require substantial additional funding beyond the net proceeds from our initial public offering (IPO) and concurrent private placement with Seattle Genetics, Inc. (Concurrent Private Placement), and is prone to the risks of failure inherent in medical product development. We cannot provide you any assurance that we will be able to successfully advance any of these additional product candidates through the development process.

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

ACTR therapies rely on the use of antibodies to target specific cancers, which are developed by third parties. We are limited in our ability to apply ACTR to a wider range of potential target cancers by our ability to partner for or acquire these antibodies on commercially reasonable terms.

ACTR therapies require the use of tumor-specific antibodies, which guide the ACTR and bind to the antigens on the surface of a tumor, to target specific types of cancers. Many of our current and proposed clinical trials rely on the use of commercially available and well-understood antibodies, such as rituximab and trastuzumab. Our ability to develop and commercialize our ACTR T cells used in combination with rituximab, trastuzumab, or any other FDA-approved antibody will depend on our ability to purchase such antibodies on commercially reasonable terms for the clinical trials and their availability for the commercialized product, if approved.

We also plan to expand the use of our ACTR platform in combination with one or more other antibodies that have not yet been approved for marketing by the FDA or similar regulatory authorities outside of the United States, as planned with our product candidate ACTR087 used in combination with SEA-BCMA in adult patients with r/r multiple myeloma. Our ability to develop product candidates using unapproved antibodies will rely on our ability to acquire such antibodies through partnerships or collaborations on commercially reasonable terms. However, we cannot be certain that potential future collaborations will provide us with a steady supply of antibodies that we can utilize in combination with ACTR to develop future product candidates. If we are unable to enter into such strategic collaborations on commercially reasonable terms or fail to realize the benefits of any such collaboration, we may be limited to using approved antibodies in combination with ACTR087, ACTR707, or any other future ACTR construct we may develop.

We have entered into a collaboration agreement with Seattle Genetics, Inc. (Seattle Genetics), pursuant to which Seattle Genetics will generate antibodies against two target antigens to use in combination with ACTR T cells to develop future product candidates. Under the agreement, Seattle Genetics had the option to elect a third target antigen, but its option expired unexercised in June 2017. We cannot be certain that the collaboration agreement with Seattle Genetics will provide us with antibodies that we can successfully combine with ACTR T cells.

The failure to enter into a successful collaboration or the expense of purchasing an approved antibody may delay our development timelines, increase our costs and jeopardize our ability to develop ACTR087, ACTR707, or any other future ACTR construct we may develop as a commercially viable drug, which could result in delays in product development and harm our business.

ACTR therapies rely on the use of antibodies to target specific cancers, which the FDA may revoke approval for or may not approve, independent of the safety or efficacy of our ACTR T cells.

We have developed, are developing, and intend to develop product candidates using ACTR087 or ACTR707 used in combination with one or more currently approved antibodies, such as rituximab for r/r NHL and trastuzumab for HER2+ cancers. If the FDA or similar regulatory authorities outside of the United States revoke approval of any antibodies we use in combination with ACTR087, ACTR707 or any ACTR T cell product, we will not be able to market any products made in combination with such revoked antibodies.

If safety or efficacy issues arise with any of these antibodies, we could experience significant regulatory delays, and the FDA or similar regulatory authorities outside of the United States may require us to redesign or terminate the applicable clinical trials. In addition, the approval of ACTR in combination with an antibody may require clinical trials to demonstrate the safety and efficacy of the therapeutic antibody on its own. If the antibodies we use in combination with ACTR087, ACTR707, or any other future ACTR construct we may develop are replaced as the standard of care for the indications we choose to target, the FDA or similar regulatory authorities outside of the United States may require us to conduct additional clinical trials. In addition, if manufacturing or other issues result in a shortage of supply of the antibodies with which we determine to combine with ACTR087, ACTR707, or any other future ACTR construct we may develop, we may not be able to complete clinical development of ACTR087, ACTR707, or any other future ACTR construct we may develop on our current timeline or at all.

Even if ACTR087, ACTR707, or any other future ACTR construct we may develop were to receive marketing approval or be commercialized for use in combination with other existing antibodies, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of an antibody used in combination with ACTR087, ACTR707, or any other future ACTR construct we may develop, or that safety, efficacy, manufacturing or supply issues could arise with these existing antibodies. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks, such as revocation of regulatory approval for one part of the combination therapy, if we develop any of our other product candidates for use in combination with other antibodies. This could result in our own products being removed from the market or being less successful commercially.

We also plan to consider ACTR087, ACTR707 or any other future ACTR product in combination with one or more other antibodies that have not yet been approved for marketing by the FDA or similar regulatory authorities outside of the United States, as planned with our product candidate ACTR087 used in combination with SEA-BCMA in adult patients with r/r multiple myeloma. We will not be able to market and sell ACTR087, ACTR707 or any other future ACTR product in combination with any such unapproved antibodies that do not ultimately obtain marketing approval, either as a standalone or used in combination with our ACTR T cells. If the FDA or similar regulatory authorities outside of the United States determine that we need to demonstrate the separate safety or efficacy of the applicable antibodies, or if safety, efficacy, manufacturing, or supply issues arise with the antibodies we choose to evaluate in combination with ACTR087, ACTR707 or any other future ACTR construct we may develop, we may be unable to obtain approval of or market ACTR087, ACTR707 or any other future ACTR construct we may develop.

If the FDA or similar regulatory authorities outside of the United States revoke their approval or do not approve these other antibodies, or if safety, efficacy, manufacturing, or supply issues arise with the antibodies we choose to evaluate in combination with ACTR087, ACTR707 or any other future ACTR construct we may develop, we may be unable to obtain approval of or market ACTR087, ACTR707 or any other future ACTR construct we may develop.

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

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

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

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

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

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

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

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

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

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

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

Specifically, by genetically engineering T cell products, we face significant competition in both the CAR technology and TCR space from multiple companies, including Kite Pharma, Inc. (a Gilead Sciences, Inc. company), Juno Therapeutics, Inc. (a Celgene Corporation company), Novartis AG, and bluebird bio, Inc. Even if we obtain regulatory approval of our product candidates, the availability and price of our competitors' products could limit the demand and the price we are able to charge for our product candidates. We may not be able to implement our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug or biologic products or choose to reserve our product candidates for use in limited circumstances.

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

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

We conduct our operations at our facility in Cambridge, Massachusetts. This region is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all.

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

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

As of December 31, 2018, we had 56 employees. As our development and commercialization plans and strategies develop, and as we transition into operating as a public company, we expect to need additional managerial, operational, sales, marketing, financial and other personnel, as well as additional facilities to expand our operations. Future growth would impose significant added responsibilities on members of management, including:

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

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

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

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, or we are not able to effectively build out new facilities to accommodate this expansion, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

We have entered into a strategic collaboration with Seattle Genetics and may form or seek collaborations or strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such alliances or licensing arrangements.

We may form or seek strategic alliances, create joint ventures or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any future product candidates that we may develop. In particular, we may seek to enter into collaborations to give us access to antibodies to use in combination with our ACTR platform. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. For example, we entered into a collaboration agreement with Seattle Genetics pursuant to which Seattle Genetics has agreed to generate antibodies against two target antigens and we are responsible for creating ACTR T cells to pair with these antibodies to create combination product candidates. However, there are ways in which Seattle Genetics may elect to opt-out from further development and commercialization of the resulting product candidates. If Seattle Genetics elects to exercise one of these options our timelines could be delayed and our business otherwise adversely affected, and we cannot be certain that we will achieve the revenue or specific net income that we anticipate.

In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy and obtain marketing approval.

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

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

- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

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

If we fail to obtain additional financing, we may be unable to complete the development and commercialization of our product candidates.

Our operations have consumed substantial amounts of cash since inception. As of December 31, 2018, we had working capital of $56.1 million and capital resources consisting of cash and cash equivalents and marketable securities of $78.6 million. We expect to continue to spend substantial amounts to continue the clinical and preclinical development of our product candidates, including our current and planned clinical trials for ACTR087 and ACTR707, each used in combination with rituximab. If approved, we will require significant additional amounts in order to launch and commercialize our product candidates.

Our operating plan includes our efforts to advance our lead lymphoma product candidate ACTR707 used in combination with rituximab for adult patients with r/r B cell non-Hodgkin lymphoma through the completion of the dose escalation and the cohort expansion parts of the Phase I clinical trial; to advance our second lymphoma product candidate, ACTR087 used in combination with rituximab for adult patients with r/r non-Hodgkin lymphoma, through the conclusion of the Phase I clinical trial in the first half of 2019; to fund a Phase I clinical trial of ACTR707 used in combination with trastuzumab for patients with HER2+ cancers; and to develop product candidates in earlier stages of development, including BOXR 1030, and any additional product candidates that we select, to expand headcount and internal capabilities, and for working capital and other general corporate purposes. However, we know that our existing cash, cash equivalents, and marketable securities, and our available borrowings under our loan and security agreement will not be sufficient to complete our planned Phase I clinical trial of ACTR707 used in combination with trastuzumab for patients with HER2+ cancers and we will need to raise additional funds to complete this trial, or to progress into clinical development any additional product candidates that we may select. Additionally, changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may require additional capital for the further development and commercialization of our product candidates and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Our license agreements may also be terminated if we are unable to meet the payment obligations under the agreements. We could be required to seek collaborators for our product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to our product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

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

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

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

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

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

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

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

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

Our operations, and those of our CROs, commercial manufacturing organizations (CMOs), and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural

or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce and process our product candidates on a patient-by-patient basis. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

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

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to: comply with the regulations of the FDA and other similar foreign regulatory bodies, provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws and regulations will increase significantly, and our costs associated with compliance with such laws and regulations are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other third-party payors that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;

- the federal Physician Payment Sunshine Act, created under the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act of 2010, collectively, the Affordable Care Act, and its implementing regulations, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the United States Department of Health and Human Services (HHS) information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

In 2016, the European Union adopted a new regulation governing data practices and privacy called the General Data Protection Regulation (European Union) 2016/679, or GDPR, which became effective on May 25, 2018. The GDPR applies to any company established in the European Economic Area, or EEA (being the European Union plus Norway, Iceland and Liechtenstein) as well as to those outside the EEA if they collect and use personal data in connection with the offering of goods or services to individuals in the European Union or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, mandatory data breach notification requirements and onerous new obligations on services providers. Non-compliance with the GDPR may result in monetary penalties of up to e20.0 million or 4% of worldwide revenue, whichever is higher. Notably, on January 21, 2019, Google was fined almost $57.0 million by French regulators for violating the transparency/information requirements and consent rules under the GDPR.

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

Upon the closing of the IPO, we adopted a code of business conduct and ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

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

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if our product

candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

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

Failure to obtain or retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with corporate collaborators. Although we have clinical trial insurance, our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act (TCJA) that significantly reforms the Internal Revenue Code of 1986, as amended. The TCJA, 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; limitation of the deduction for net operating losses and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such tax losses may be carried forward indefinitely); 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 generally referred to as "orphan drugs". The tax rate change resulted in (i) a reduction in the gross amount of our deferred tax assets recorded as of December 31, 2017, without an impact on the net amount of our deferred tax assets, which are recorded with a full valuation allowance, and (ii) no income tax expense or benefit being recognized as of the enactment date of the TCJA. We continue to examine the impact this tax reform legislation may have on our business. However, the effect of the TCJA on us and our affiliates, whether adverse or favorable, is uncertain and may not become evident for some period of time. You are urged to consult your tax adviser regarding the implications of the TCJA on an investment in our common stock.

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

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change taxable income may be limited. As a result of our most recent private placements, IPO, and other transactions that have occurred over the past three years, we may have experienced, an "ownership change." We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As of December 31, 2018, we had U.S. federal and state net operating loss carryforwards of $69.8 million and $71.7 million, respectively, and U.S. federal and state research and development tax credit carryforwards of $4.0 million, and $0.9 million respectively, which could be limited if we experience an "ownership change." The reduction of the corporate tax rate under the TCJA may cause a reduction in the economic benefit of our net operating loss carryforwards and other deferred tax assets available to the us. Under the TCJA, net operating losses generated after December 31, 2017 will not be subject to expiration.

The terms of our loan and security agreement may restrict our ability to engage in certain transactions and subject our assets to collateralization.

In January 2017, we entered into a loan and security agreement with Pacific Western Bank (PWB). Pursuant to the terms of the loan and security agreement, subject to certain exceptions, we cannot engage in certain transactions without PWB's prior written consent, which shall not be unreasonably withheld. Such transactions include:

- disposing of our business or certain assets;
- changing our business, management, ownership or business locations;
- incurring additional debt or liens or making payments on other debt;
- making certain investments and declaring dividends;
- acquiring or merging with another entity;
- engaging in transactions with affiliates; or
- encumbering intellectual property.

If PWB does not provide its consent to such actions, we could be prohibited from engaging in transactions that could be beneficial to our business and our stockholders unless we were to repay the loans, which may not be desirable or possible. The loan and security agreement is collateralized by a pledge of substantially all of our assets, except for our intellectual property. If we were to default under the loan and security agreement, including for an inability to repay amounts as they become due, and we were unable to obtain a waiver for such a default, PWB would have a right to accelerate our obligation to repay the entire loan and foreclose on these assets in order to satisfy our obligations under the loan and security agreement. In addition, PWB would also have the right to place a hold on our accounts maintained at PWB and refuse to fund any then unfunded commitments under the loan and security agreement. Any such action on the part of PWB against us could have a materially adverse impact on our business, financial condition and results of operations.

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

As widely reported, global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If

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

As of December 31, 2018, we had cash, cash equivalents, and marketable securities of $78.6 million and available borrowings under our loan and security agreement of $15.0 million. While we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents and marketable securities since December 31, 2018, no assurance can be given that further deterioration of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or our ability to meet our financing objectives. Furthermore, our stock price may decline due in part to the volatility of the stock market and the general economic downturn.

We face risks arising from the results of the public referendum held in United Kingdom and its membership in the European Union.

The ongoing developments following from the United Kingdom's public referendum vote to exit from the European Union could cause disruptions to and create uncertainty surrounding our business, including affecting our relationships with existing and potential suppliers, manufacturers, and other third parties. Negotiations have commenced to determine the terms of the United Kingdom's future relationship with the European Union, including the terms of trade between the United Kingdom and the European Union. The effects of Brexit will depend upon any agreements the United Kingdom makes to retain access to European Union markets either during a transitional period or more permanently. The measures could potentially have corporate structural consequences, adversely change tax benefits or liabilities in these or other jurisdictions and could disrupt some of the markets and jurisdictions in which we operate. In addition, Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which European Union laws to replace or replicate. In addition, the announcement of Brexit has caused significant volatility in global stock markets and currency exchange rate fluctuations, including the strengthening of the USD against some foreign currencies, and the Brexit negotiations may continue to cause significant volatility. The progress and outcomes of Brexit negotiations also may create global economic uncertainty. Any of these effects of Brexit, among others, could materially adversely affect the business, business opportunities, and financial condition of our company.

Risks Related to Our Reliance On Third Parties

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

We depend and will depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs and strategic partners to conduct our preclinical studies and clinical trials under agreements with us. We expect to have to negotiate budgets and contracts with CROs, trial sites and CMOs which may result in delays to our development timelines and increased costs. We will rely heavily on these third parties over the course of our clinical trials, and we control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these clinical trials and the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our

regulatory responsibilities. We and these third parties are required to comply with good clinical practices (GCPs), which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP regulations. In addition, our clinical trials must be conducted with biologic product produced under current good manufacturing practices (cGMP) regulations and will require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

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

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

We expect to rely on third parties to manufacture our clinical product supplies, and we may rely on third parties for at least a portion of the manufacturing process of our product candidates, if approved. Our business could be harmed if those third parties fail to provide us with sufficient quantities of clinical product supplies or product candidates or fail to do so at acceptable quality levels or prices.

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and must currently rely on outside vendors to manufacture supplies and process our product candidates, which is and will need to be done on a patient-by-patient basis. We have not yet caused our product candidates to be manufactured or processed on a commercial scale and may not be able to do so for any of our product candidates.

Although in the future we do intend to develop our own manufacturing facility, we also intend to use third parties as part of our manufacturing process and may, in any event, never be successful in developing our own manufacturing facility. Our anticipated reliance on a limited number of third-party manufacturers exposes us to the following risks:

- We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA must inspect any manufacturers for current cGMP compliance as part of our marketing application. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, the production of our product candidates.

- In order to utilize an additional manufacturer of our product candidates, we will be required to demonstrate comparability of the drug product produced by such a manufacturer to the FDA's satisfaction before releasing the product for clinical use.
- Our manufacturers may have little or no experience with autologous cell products, which are products made from a patient's own cells, and therefore may require a significant amount of support from us in order to implement and maintain the infrastructure and processes required to manufacture our product candidates.
- Our third-party manufacturers might be unable to timely manufacture our product candidates, to produce comparable products or conduct consistent testing across sites, or produce the quantity and quality required to meet our clinical and commercial needs, if any.
- Our third-party suppliers or collaborators from whom we receive our antibodies used in combination with our ACTR T cells may be unable to timely manufacture or provide the applicable antibody or produce the quantity and quality required to meet our clinical and commercial needs.
- Contract manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately.
- Our future contract manufacturers may not perform as agreed, may not devote sufficient resources to our product candidates or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store, and distribute our products, if any.
- Manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.
- We may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our product candidates.
- Our third-party manufacturers could breach or terminate their agreements with us.
- Raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available or may not be suitable or acceptable for use due to material or component defects.
- Our contract manufacturers and critical reagent suppliers may be subject to inclement weather, as well as natural or man-made disasters.
- Our contract manufacturers may have unacceptable or inconsistent product quality success rates and yields, and we have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel.

Each of these risks could delay or prevent the completion of our clinical trials or the approval of any of our product candidates by the FDA, result in higher costs or adversely impact commercialization of our product candidates. In addition, we will rely on third parties to perform certain specification tests on our product candidates prior to delivery to patients. If these tests are not appropriately done and test data are not reliable, patients could be put at risk of serious harm and the FDA could place significant restrictions on our company until deficiencies are remedied.

The manufacture of biological drug products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls.

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

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

In addition, because our product candidates are all based upon the ACTR construct, any problems we encounter with manufacturing the ACTR construct would likely affect all of our products, if approved, and product candidates, increasing the impact of any manufacturing issues we encounter and potentially adversely affecting our ability to attain or maintain profitable operations.

ACTR and BOXR therapies rely on the availability of specialty raw materials, which may not be available to us on acceptable terms or at all.

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

In addition, some of our raw materials are currently available from a single supplier, or a small number of suppliers. The type of cell culture media and cryopreservation buffer that we currently use in our manufacturing process for ACTR087 and ACTR707 are each only available from a single supplier. In addition, the cell processing equipment and tubing that we use in our current manufacturing process is only available from a single supplier. We also use certain biologic materials, including certain activating antibodies, that are available from multiple suppliers, but each version may perform differently, requiring us to characterize them and potentially modify some of our protocols if we change suppliers. We cannot be sure that these suppliers will remain in business, or that they will not be purchased by one of our competitors or another company that is not interested in continuing to produce these materials for our intended purpose. Accordingly, if we no longer have access to these suppliers, we may experience delays in our clinical or commercial manufacturing which could harm our business or results of operations.

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

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our third-party manufacturers. Our manufacturers are subject to

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

Risks Related to Government Regulation

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

We have not previously submitted a Biologics License Application (BLA) to the FDA or similar approval applications to comparable foreign authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety, purity and potency for each desired indication. The BLA must also include significant information regarding the manufacturing controls for the product. We expect the novel nature of our product candidates to create further challenges in obtaining regulatory approval. For example, the FDA has no experience with commercial development of ACTR therapies for cancer. Accordingly, the regulatory approval pathway for our product candidates may be uncertain, complex, expensive and lengthy, and approval may not be obtained.

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

- the availability of financial resources to commence and complete the planned trials;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval at each clinical trial site by an IRB or ethics committee;
- recruiting suitable patients to participate in a trial;
- having patients complete a trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- adding new clinical trial sites; or
- manufacturing sufficient quantities of qualified materials under cGMPs and applying them on a subject by subject basis for use in clinical trials.

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

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

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

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

The FDA may disagree with our regulatory plan and we may fail to obtain regulatory approval of our product candidates.

We plan to advance our lead lymphoma product candidate, ACTR707 used in combination with rituximab, for the treatment of adult patients with r/r NHL through Phase I clinical trial. If we believe the Phase I data are compelling, we plan to advance that product candidate in further clinical development for the treatment of adult patients with r/r NHL and to discuss with the FDA the potential to move to a registration trial in r/r NHL upon completion of the current Phase I clinical trial of that product candidate. However, the general approach for FDA approval of a new biologic or drug is dispositive data from two well-controlled, Phase III clinical trials of the relevant biologic or drug in the relevant patient population. Phase III clinical trials typically involve hundreds of patients, have significant costs and take years to complete. The FDA may not believe our accelerated approval strategy to move directly to a registration trial for ACTR used in combination with rituximab in r/r NHL upon completion of the current Phase I clinical trial is warranted and may require a Phase III clinical trial or trials prior to approval.

Our clinical trial results may also not support approval. In addition, 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 number, design, or implementation of our clinical trials, including whether we have identified an appropriate surrogate marker or intermediate clinical endpoint to support an accelerated approval pathway;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our product candidates are safe, pure and potent, or effective, for any of their proposed indications;
- 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 may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of a BLA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Any of these factors, many of which are beyond our control, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects.

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

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

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

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

Any regulatory approvals that we receive for our product candidates will require surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a risk evaluation and mitigation strategy in order to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;

- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

In addition, if we were able to obtain accelerated approval of ACTR087 or ACTR707 used in combination with an antibody or BOXR1030, the FDA would require us to conduct a confirmatory study to verify the predicted clinical benefit and additional safety studies. The results from the confirmatory study may not support the clinical benefit, which would result in the approval being withdrawn.

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

The use of engineered T cells as a potential cancer treatment is a recent development and may not become broadly accepted by physicians, patients, hospitals, cancer treatment centers and others in the medical community. Various factors will influence whether our product candidates are accepted in the market, including:

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

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

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

Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete.

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

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

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

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

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

Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates.

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

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

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

Members of the United States Congress and the Trump Administration have expressed an intent to pass legislation or adopt executive orders to fundamentally change or repeal parts of the Affordable Care Act. While Congress has not passed repeal legislation to date, the 2017 Tax Reform Act includes a provision repealing the individual insurance coverage mandate included in the Affordable Care Act, effective January 1, 2019. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the Affordable Care Act. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act of 2017, the remaining provisions of the Affordable Care Act are invalid as well. The Texas District Court Judge, as well as the Trump Administration and the Centers for Medicare & Medicaid Services, or CMS, have stated that the ruling will have no immediate effect. In December 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. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which

may have the effect of relaxing the essential health benefits required under the Affordable Care Act for plans sold through such marketplaces. There may be further changes to the Affordable Care Act as a result of new legislation or further executive, administrative or judicial action.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012 (the ATRA), which delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. In March 2013, the President signed an executive order implementing sequestration, and in April 2013, the 2% Medicare payment reductions went into effect. The ATRA also, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

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

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

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contained further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. 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, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. On January 31, 2019, the HHS Office of Inspector General, proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Further, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to 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 pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future, including repeal, replacement or significant revisions to the Affordable Care Act. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

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

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

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

Regulatory requirements in the United States and abroad governing gene therapy products have changed frequently and may continue to change in the future. FDA established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research to consolidate the review of gene therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee, among others, to advise this review. Prior to initiating a clinical study, because of our use of a viral vector for production of our ACTR T cells, our clinical protocols have been subject to review by the NIH's Recombinant DNA Advisory Committee (RAC). A Federal Register Notice in August 2018 proposed to remove this requirement for most gene therapy studies and the NIH is not currently requiring RAC review for such studies, which we interpret will include studies that use ACTR T cell products. Adverse developments in clinical trials of genetically modified cell therapies conducted by other sponsors may cause FDA or other oversight bodies to change the requirements for clinical investigation and/or marketing authorization of any of our product candidates at any time.

Risks Related to Our Intellectual Property

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

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others.

Under our collaboration agreement with Seattle Genetics for the development and commercialization of novel therapies for cancer, we depend on a license from Seattle Genetics for use of their proprietary antibodies. Additionally, aspects of the ACTR technology are subject to a license from St. Jude Children's Research Hospital (St. Jude's) and the National University of Singapore (NUS).

We are currently, and expect in the future to be, party to material license or collaboration agreements. These agreements typically impose numerous obligations, such as diligence and payment obligations. Any termination of these licenses could result in the loss of significant rights and could harm our ability to commercialize our product candidates. These licenses do and future licenses may include provisions that impose obligations and restrictions on us. For example, our license agreement with St. Jude's and NUS imposes some limitations on our ability to assign the license to a party other than an affiliate. This could delay or otherwise negatively impact a transaction that we may wish to enter into.

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

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

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

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

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

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

Currently, we have obtained one European patent, which is validated in Germany, France, and Great Britain, and one Japanese patent from our in-licensed patent portfolio. No other patents have issued from the patent applications that we own or in-license. We anticipate additional patent applications will be filed both in the United States and in other countries, as appropriate. However, we cannot predict:

- if and when patents will issue;
- the degree and range of protection any issued patents will afford us against competitors including whether third parties will find ways to invalidate or otherwise circumvent our patents;

- whether any of our intellectual property will provide any competitive advantage;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications; or
- whether we will need to initiate or defend litigation or administrative proceedings which may be costly whether we win or lose.

Composition of matter patents for biological and pharmaceutical products, such as ACTR-based product candidates, are generally considered to be the strongest form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. We have obtained issuances of composition of matter claims in one European patent from the licensed-in portfolio. We, however, cannot be certain that the claims in our pending patent applications covering composition of matter of our product candidates will be considered patentable by the United States Patent and Trademark Office (USPTO), or by patent offices in foreign countries, or that the claims in any of our issued patents will be considered patentable by courts in the United States or foreign countries. Method of use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may induce or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. Furthermore, for United States 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, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Various post grant review proceedings, such as inter partes review and post grant review, are available for any interested third party to challenge the patentability of claims issued in patents to us. While these post grant review proceedings have been used less frequently to invalidate biotech patents, they have been successful regarding other technologies, and these relatively new procedures are still changing, and those changes might affect future results.

In addition to the protection afforded by patents, we seek to rely on trade secret protection, confidentiality agreements, and license agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our product discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. Although we require all of our employees to assign their inventions to us, and require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the

United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

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

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, reexamination, and post grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others.

Third parties may assert that we are employing their proprietary technology without authorization. Generally, conducting clinical trials and other development activities in the United States is not considered an act of infringement. If and when ACTR087 or another product candidate is approved by the FDA, a third party may then seek to enforce its patent by filing a patent infringement lawsuit against us. While we do not believe that any claims that could otherwise materially adversely affect commercialization of our product candidates, if approved, are valid and enforceable, we may be incorrect in this belief, or we may not be able to prove it in a litigation. In this regard, patents issued in the U.S. by law enjoy a presumption of validity that can be rebutted only with evidence that is "clear and convincing," a heightened standard of proof. There may be third-party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, we may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, constructs or molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, could involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license

would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly.

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

Presently we have rights to certain intellectual property, through licenses from third parties and under patent applications that we own or will own, related to ACTR087, ACTR707, and BOXR constructs, and certain other product candidates. Because additional product candidates may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, while we have patent rights or are pursuing patent rights directed to certain ACTR constructs and BOXR constructs we may not be able to obtain intellectual property to broad ACTR constructs and BOXR constructs in certain jurisdictions.

Our product candidates may also require specific formulations to work effectively and efficiently and these rights may be held by others. Similarly, efficient production or delivery of our product candidates may also require specific compositions or methods, and the rights to these may be owned by third parties. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. Moreover, the specific antibodies that will be used with our product candidates may be covered by the intellectual property rights of others.

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

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

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

Post-grant proceedings, including interference proceedings, provoked by third parties or brought by the USPTO may be necessary to determine the validity or priority of inventions with respect to our patents or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business

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

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

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

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

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

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In

addition, the United States continues to adapt to wide-ranging patent reform legislation that became effective starting in 2012. Moreover, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Changes in the laws and regulations governing patents in other jurisdictions could similarly have an adverse effect on our ability to obtain and effectively enforce our patent rights.

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

Certain of our key patent families (covering the ACTR087 construct) have been filed in the United States, as well as in numerous jurisdictions outside the United States, and we plan to similarly pursue subgeneric claims prior to expiration of applicable deadlines (including a patent family covering the ACTR707 construct). However, we have less robust intellectual property rights outside the United States, and, in particular, we may not be able to pursue generic coverage of the ACTR platform outside of the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Most of our patent portfolio is at the very early stage. We will need to decide whether and in which jurisdictions to pursue protection for the various inventions in our portfolio prior to applicable deadlines.

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

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

We generally enter into confidentiality and intellectual property assignment agreements with our employees, consultants, and contractors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, those agreements may not be honored and may not effectively assign intellectual property rights to us. Moreover, there may be some circumstances, where we are unable to negotiate for such ownership rights. Disputes regarding ownership or inventorship of

intellectual property can also arise in other contexts, such as collaborations and sponsored research. If we are subject to a dispute challenging our rights in or to patents or other intellectual property, such a dispute could be expensive and time consuming. If we were unsuccessful, we could lose valuable rights in intellectual property that we regard as our own.

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

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

Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.

The degree of future protection afforded by our intellectual property rights, whether owned or in-licensed, is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- pending patent applications that we own or license may not lead to issued patents;
- patents, should they issue, that we own or license, may not provide us with any competitive advantages, or may be challenged and held invalid or unenforceable;
- others may be able to develop and/or practice technology that is similar to our technology or aspects of our technology but that is not covered by the claims of any of our owned or in-licensed patents, should any such patents issue;
- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we (or our licensors) might not have been the first to make the inventions covered by a pending patent application that we own or license;
- we (or our licensors) might not have been the first to file patent applications covering a particular invention;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;
- we may not be able to obtain and/or maintain necessary licenses on reasonable terms or at all;
- third parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights, or any rights at all, over that intellectual property;
- we may not be able to maintain the confidentiality of our trade secrets or other proprietary information;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business and results of operation.

Risks Related to Ownership of our Common Stock

An active trading market for our common stock may not be sustained.

Our common stock began trading on the Nasdaq Global Select Market on March 29, 2018. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares may not be sustained, which could put downward pressure on the market price of our common stock and thereby affect the ability of our stockholders to sell their shares at attractive prices, at the times that they would like to sell them, or at all.

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

The trading price of our common stock is likely to continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K, these factors include:

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

- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or immunotherapy in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and The Nasdaq Global Select Market and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. If the market price of our common stock does not exceed your purchase price, you may not realize any return on your investment in us and may lose some or all of your investment. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would harm our business, operating results, or financial condition.

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

We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, pursuant to our loan and security agreement with PWB, we are prohibited from paying cash dividends without PWB's prior written consent, and any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock, which may never occur.

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

Our executive officers, directors, and 5% stockholders beneficially owned over 64% of our voting stock as of December 31, 2018. These stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

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

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act (JOBS Act) enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended (Sarbanes-Oxley Act), reduced disclosure obligations regarding executive compensation in this Annual Report on Form 10-K and our periodic reports and proxy statements, and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years following the year in which we completed our IPO, although circumstances could cause us to lose that status earlier. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of our IPO, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in this Annual Report on Form 10-K and our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected to "opt out" of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, changes in rules of U.S. generally accepted accounting principles or their interpretation, the adoption of new guidance, or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations.

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

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

and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

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

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

The lock-up entered into during our IPO lapsed on September 24, 2018. If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after other legal restrictions on resale entered into during our IPO lapse, the trading price of our common stock could decline.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our 2018 Stock Option and Incentive Plan (2018 Plan) will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act of 1933, as amended (the Securities Act). If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The holders of 13,646,028 shares of our common stock as of December 31, 2018, are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our 2018 Plan, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

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

Pursuant to the 2018 Plan, our management is authorized to grant stock options to our employees, directors, and consultants. The number of shares initially reserved for issuance under the 2018 Plan is 2,547,558 plus the 1,030,234 shares of common stock remaining available for issuance under the 2015 Stock Incentive Plan (2015 Plan). Additionally, the shares of common stock underlying any awards that are forfeited, canceled, held back

upon exercise or settlement of an award to satisfy the exercise price or tax withholding, repurchased or are otherwise terminated by us under the 2018 Plan or the 2015 Plan will be added back to the shares of common stock available for issuance under the 2018 Plan. As of December 31, 2018, 2,793,738 shares remained available for future issuance under the 2018 Plan. The number of shares of our common stock reserved for issuance under the 2018 Plan shall be cumulatively increased on January 1, 2019 and each January 1 thereafter by 4% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year or a lesser number of shares determined by our board of directors. Unless our board of directors elects not to increase the number of shares available for future grant each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

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

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

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

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer, or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

Our amended 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 the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, any action to interpret, apply, enforce, or determine the validity of our certificate of incorporation or bylaws or any action asserting a claim against us that is governed by the internal affairs doctrine. The choice of 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. Alternatively, if a court were to find the choice of forum provision contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

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

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. In connection with our IPO, we began the process of documenting, reviewing, and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act, which will require annual management assessment of the effectiveness of our internal control over financial reporting. We have begun recruiting additional finance and accounting personnel with certain skill sets that we need as a public company.

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

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

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company, the trading price for our stock would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our principal executive office is located at 200 Cambridge Park Drive, Suite 3100, Cambridge, Massachusetts 02140 where we lease approximately 33,500 square feet of office and laboratory space pursuant to a lease agreement expiring in April 2023.

We believe that our current facilities are adequate to meet our immediate needs.

ITEM 3. LEGAL PROCEEDINGS

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

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades under the symbol "UMRX" on the Nasdaq Global Select Market and has been publicly traded since March 29, 2018. Prior to this time, there was no public market for our common stock.

Holders of Our Common Stock

As of February 28, 2019, there were approximately 7 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

Dividends

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

Securities authorized for issuance under equity compensation plans

Information about our equity compensation plans will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

Recent Sales of Unregistered Equity Securities

We did not sell any of our unregistered securities during the three months ended December 31, 2018.

Use of Proceeds from Initial Public Offering

Our initial public offering of common stock, or the IPO, was effected through a Registration Statement on Form S-1 (File No. 333-223414) that was declared effective by the Securities and Exchange Commission, or SEC, on March 28, 2018. The net offering proceeds to us, after deducting underwriting discounts and offering expenses, were approximately $63.9 million. We received proceeds of $5.0 million from our concurrent private placement of 416,666 shares of common stock with Seattle Genetics. None of the net proceeds were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates, other than payments in the ordinary course of business to officers for salaries and to non-employee directors as compensation for board or board committee service. As of December 31, 2018, we estimate that we have used approximately $27.8 million of the net proceeds from our IPO and concurrent private placement for clinical development of our product candidates and research activities and for working capital and other general corporate purposes. We have invested the unused net proceeds from the offering in marketable securities and money market accounts. Our planned use of the net proceeds from the IPO and concurrent private placement as described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on March 29, 2018 have been modified as a result of our decision to conclude enrollment in the ATTCK-20-2 study in the first half of 2019. We currently anticipate that the net proceeds will fund operating expenses and capital expenditures requirements into early 2021.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period from October 1, 2018 to December 31, 2018.

ITEM 6. SELECTED FINANCIAL DATA

We are a smaller reporting company, as defined in Rule 12b-2 of the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this item.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

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

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of novel immunotherapy products designed to harness the power of a patient's immune system to cure cancer. Our proprietary technologies include a universal, engineered cell therapy, referred to as Antibody-Coupled T cell Receptor (ACTR), that is intended to be used in combination with a wide range of tumor-specific antibodies to target different tumor types. In addition, we have developed a second novel technology, Bolt-On Chimeric Receptor (BOXR), for improving T cell functionality in solid tumor cancer applications by overcoming immunosuppressive tumor microenvironments. BOXR T cells may be directed to attack tumor cells using a variety of targeting strategies and our efforts to date have demonstrated activity using either ACTR or scFv-based CAR receptors. Our vision is to use our ACTR and BOXR product candidates to transform cancer treatment and deliver patient cures in many different hematologic and solid tumor cancers, improving upon current therapies.

We have a broad product pipeline that includes five programs. Four clinical-stage programs are based on the ACTR platform, composed of either ACTR087 or ACTR707 T cells co-administered with approved and investigational antibodies. ACTR087 is our original ACTR construct, comprising the ectodomain of CD16, the costimulatory domain of 4-1BB, and the signaling domain of CD3-zeta. ACTR707 is a modified ACTR construct selected for improved performance across a number of dimensions, including increased proliferation, cytokine secretion, and persistence in a repeat stimulation test. ACTR707 differs from ACTR087 in terms of its costimulatory domain (CD28) and other structural components. Our most advanced programs are comprised of ACTR087 or ACTR707 used in combination with rituximab to treat adult patients with relapsed or refractory CD20+ non-Hodgkin lymphoma (r/r NHL). These combinations are being tested in two ongoing, multi-center, open-label Phase I clinical trials called ATTCK-20-2 and ATTCK-20-03.

We completed patient enrollment and dosing of ACTR707 in combination with rituximab in the first two dose levels of the ATTCK-20-03 trial and presented preliminary data from these dose levels at the Sixtieth annual American Society of Hematology (ASH) meeting in December 2018 (2018 ASH Meeting). We have subsequently completed enrollment of patients in the third dose level of this trial and initiated enrollment at the fourth dose level. In 2019, we expect to define a recommended phase II dose (RP2D) based upon analysis of the cohorts tested during the dose escalation phase of the trial and to begin to confirm this recommended dose in an expansion cohort.

In the fourth quarter of 2017, we completed patient enrollment and dosing of ACTR087 in combination with rituximab in the dose escalation phase of the ATTCK-20-2 trial, and in the second quarter of 2018 we initiated the cohort expansion phase of the trial using an optimized dose of ACTR087. We completed enrollment in the

cohort expansion phase of the ATTCK-20-2 study in the first quarter of 2019. Preliminary data from the dose escalation phase of the ATTCK-20-2 trial were presented in December 2017 at the Fifty-ninth annual ASH meeting (2017 ASH Meeting). In both Phase I trials, we believe that we have demonstrated clinical proof of concept, as evidenced by ACTR T cell expansion and persistence, a favorable tolerability profile at defined dose levels, and anti-tumor activity. Based on emerging clinical data from the Phase I ATTCK-20-03 trial, the continuing progress in that trial, and our desire to efficiently manage resources, we have selected ACTR707 used in combination with rituximab to be the lead lymphoma program for advancement to further clinical development.

Our third program, ACTR087 used in combination with SEA-BCMA, is the first program resulting from our strategic collaboration with Seattle Genetics, Inc. (Seattle Genetics). We are currently enrolling and dosing adult patients with r/r multiple myeloma in a Phase I multi-center trial, ATTCK-17-01. We reported initial data from the first three cohorts of this trial at the 2018 ASH Meeting. We are currently enrolling and dosing patients in the fourth cohort and expect to continue dose escalation during 2019.

Our fourth program is ACTR707 used in combination with trastuzumab. We have an active IND to evaluate ACTR707 used in combination with trastuzumab as a potential treatment for advanced HER2+ solid tumor cancers, and in December 2018 we initiated a Phase I multi-center trial called ATTCK-34-01 testing this regimen in patients with HER2+ solid tumor cancers. We plan to enroll patients into this dose escalation trial throughout 2019.

Our fifth program is derived from our BOXR platform and is designated BOXR1030. BOXR1030 is comprised of a GPC3 CAR T cell therapy that includes an undisclosed bolt-on transgene expected to improve T cell metabolism and, preserve functionality in the environment of highly glycolytic tumors. We have initiated formal preclinical development activities, including safety testing and GMP process development, to prepare for future clinical testing.

In the longer term, we aim to leverage our ACTR and BOXR platforms to develop a broad range of programs to address many different hematologic and solid tumor cancers.

Since our inception in 2014, we have focused significant efforts and financial resources on building our ACTR and BOXR platforms, establishing and protecting our intellectual property portfolio, conducting research and development of our product candidates, manufacturing drug product material for use in preclinical studies and clinical trials, staffing our company, and raising capital. We do not have any products approved for sale and have not generated any revenue from product sales. To date, we have funded our operations primarily with proceeds from the sales of preferred stock, our initial public offering of common stock and concurrent private placement (as further discussed below), and payments received under our collaboration agreement with Seattle Genetics. On April 3, 2018, we completed our initial public offering (IPO) of our common stock and issued and sold 5,770,000 shares of our common stock at a public offering price of $12.00 per share, resulting in net proceeds of approximately $61.5 million, after deducting underwriting discounts and commissions and other offering costs. In addition, we completed a concurrent private placement of $5.0 million of shares of common stock at the public offering price of $12.00 per share, or 416,666 shares, with Seattle Genetics (Concurrent Private Placement).

In connection with our IPO, we issued and sold an additional 215,000 shares of our common stock on April 25, 2018, pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock at the public offering price of $12.00 and received additional net proceeds of $2.4 million, after deducting underwriting discounts and commissions.

Since our inception, we have incurred significant operating losses. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. Our net losses were $34.5 million and $25.5 million

for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, we had an accumulated deficit of $92.1 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We expect that our expenses and capital requirements will increase substantially in connection with our ongoing activities, particularly if and as we:

- conduct additional clinical trials for our product candidates;
- continue to discover and develop additional product candidates;
- acquire or in-license other product candidates and technologies;
- maintain, expand, and protect our intellectual property portfolio;
- hire additional clinical, scientific, and commercial personnel;
- establish manufacturing capabilities in-house;
- establish a commercial manufacturing source and secure supply chain capacity sufficient to provide commercial quantities of any product candidates for which we may obtain regulatory approval;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain regulatory approval; and
- add operational, financial, and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, as well as to support our transition to a public reporting company.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for our product candidates. If we obtain regulatory approval for any of our product candidates and do not enter into a commercialization partnership, we expect to incur significant expenses related to developing our internal commercialization capability to support product sales, marketing, and distribution. Further, as a result of the IPO, we expect to incur additional costs associated with operating as a public company.

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

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve or maintain profitability. Even if we are able to generate 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 unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2018, we had cash, cash equivalents, and marketable securities of $78.6 million and available borrowings under our loan and security agreement of $15.0 million. We expect that our cash, cash equivalents and marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements into early 2021, without considering available borrowings under our loan and security agreement. See “—Liquidity and Capital Resources”.

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 the sale of products in the near future. If our development efforts for our product candidates are successful and result in regulatory approval or additional license or collaboration agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from additional collaboration or license agreements that we may enter into with third parties. We expect that our revenue for the next several years will be derived primarily from a collaboration we entered into with Seattle Genetics in June 2015 as well as any additional collaborations that we may enter into in the future. We cannot provide assurance as to the timing of future milestone or royalty payments or that we will receive any of these payments at all.

The Company has a collaboration agreement with Seattle Genetics whereby the parties agreed to jointly develop two product candidates incorporating our ACTR platform and Seattle Genetics' antibodies. Under the collaboration agreement, the Company conducts preclinical research and clinical development activities related to the two specified product candidates through Phase I clinical development, and Seattle Genetics provides the funding for those activities.

Effective January 1, 2018, we adopted a new revenue recognition standard, which changed the manner in which we recognize revenue from our collaboration agreement with Seattle Genetics. Under the new standard, we recognize revenue from the collaboration agreement using the cost-to-cost method, which we believe best depicts the transfer of control to the customer, in contrast to recognizing revenue on a straight-line basis over the estimated 58-month performance period under the previous standard.

Under the collaboration agreement with Seattle Genetics, we recognized revenue of $9.7 million and $8.4 million for the years ended December 31, 2018 and 2017, respectively, related to the upfront payment received from Seattle Genetics under our collaboration agreement as well as reimbursements of research and development costs.

Operating Expenses

Research and Development Expenses

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

- employee-related expenses, including salaries, related benefits, and stock-based compensation expense for employees engaged in research and development functions;
- expenses incurred in connection with the preclinical and clinical development of our product candidates, including under agreements with third parties, such as consultants and contractors and contract research organizations (CROs);
- the cost of manufacturing drug products for use in our preclinical studies and clinical trials, including under agreements with third parties, such as consultants and contractors and contract manufacturing organizations (CMOs);
- laboratory supplies and animal care;
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and insurance; and
- payments made under third-party licensing agreements.

Our research and development costs include costs for the development of product candidates that we are jointly developing with Seattle Genetics and for which we receive reimbursement as specified in the agreement.

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

Our direct external research and development expenses are tracked on a program-by-program basis and consist of costs, such as fees paid to consultants, contractors, CMOs, and CROs in connection with our preclinical and clinical development activities. We do not allocate employee costs, costs associated with our discovery efforts, laboratory supplies, and facilities, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple product development programs and, as such, are not separately classified.

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

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the progress of the development efforts of parties with whom we have entered, or may enter, into collaboration arrangements;
- our ability to maintain our current research and development programs and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the successful completion of clinical trials with safety, tolerability, and efficacy profiles that are satisfactory to the U.S. Food and Drug Administration (FDA) or any comparable foreign regulatory authority;
- the receipt of regulatory approvals from applicable regulatory authorities;
- the success in establishing and operating a manufacturing facility, or securing manufacturing supply through relationships with third parties;
- our ability to obtain and maintain patents, trade secret protection, and regulatory exclusivity, both in the United States and internationally;
- our ability to protect our rights in our intellectual property portfolio;
- the commercialization of our product candidates, if and when approved;
- the acceptance of our product candidates, if approved, by patients, the medical community, and third-party payors;
- competition with other products; and
- a continued acceptable safety profile of our therapies following approval.

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

General and Administrative Expenses

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

Other Income (Expense)

Interest Income

Interest income consists of interest earned on our cash equivalents and marketable securities balances. Our interest income has not been significant due to low interest earned on invested balances.

Other Income, Net

Other income, net consists of miscellaneous income and expense unrelated to our core operations, primarily income from subleasing a portion of our headquarters facilities.

Income Taxes

Since our inception, we have not recorded any current or deferred tax benefit for the net losses we have incurred in each year or for our earned research and development tax credits, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating loss carryforwards and tax credits will not be realized. As of December 31, 2018, we had U.S. federal and state net operating loss carryforwards of $69.8 million and $71.7 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2035. The 2018 federal net operating loss of $39.6 million is available to be carried forward indefinitely but can only offset 80% of taxable income per year. As of December 31, 2018, we also had U.S. federal and state research and development tax credit carryforwards of $4.0 million and $0.9 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2034 and 2030, respectively. As of December 31, 2018, the Company has Massachusetts investment tax credits of $0.2 million which generally have a 3 year carryover period.

We have recorded a full valuation allowance against our net deferred tax assets at each balance sheet date.

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017:

	Year Ended December 31,	
	2018	2017
	(in thousands)	
Collaboration revenue	$ 9,734	$ 8,360
Operating expenses:		
Research and development	38,285	29,832
General and administrative	7,454	4,680
Total operating expenses	45,739	34,512
Loss from operations	(36,005)	(26,152)
Other income (expense):		
Interest income	1,153	386
Other income, net	320	274
Total other income, net	1,473	660
Net loss	$ (34,532)	$ (25,492)

Collaboration Revenue

Collaboration revenue recognized during the years ended December 31, 2018 and 2017 of $9.7 million and $8.4 million, respectively, was related to our collaboration agreement with Seattle Genetics. Effective January 1, 2018, we adopted the new revenue recognition standard, which changed the manner in which we recognize revenue from our collaboration agreement with Seattle Genetics. Under the new standard, we recognize revenue from the collaboration agreement by applying the cost-to-cost method, in contrast to recognizing revenue on a straight-line basis over the estimated 58-month performance period under the previous standard.

Research and Development Expenses

	Year Ended December 31,		
	2018	2017	Change
	(in thousands)		
Direct research and development expenses by program:			
ACTR087 used in combination with rituximab	$ 4,194	$ 6,457	$(2,263)
ACTR707 used in combination with rituximab	5,207	2,179	3,028
ACTR087 used in combination with SEA-BCMA	4,032	1,884	2,148
ACTR707 used in combination with trastuzumab	1,387	—	1,387
Unallocated expenses:			
Personnel related (including stock-based compensation)	12,065	10,058	2,007
Laboratory supplies, facility related and other	11,400	9,254	2,146
Total research and development expenses	$ 38,285	$ 29,832	$ 8,453

Research and development expenses were $38.3 million for the year ended December 31, 2018, compared to $29.8 million for the year ended December 31, 2017. The decrease in direct external costs related to our

ACTR087 used in combination with rituximab program of $2.3 million was primarily due to a decrease in manufacturing costs given the lower planned enrollment levels compared to 2017. The increase in direct external costs related to our ACTR707 used in combination with rituximab program of $3.0 million was primarily due to an increase in clinical trial costs and manufacturing costs related to our Phase I clinical trial, which commenced in the fourth quarter of 2017. The increase in direct external costs incurred for our ACTR087 used in combination with SEA-BCMA program primarily related to increased clinical trial and manufacturing costs related to our Phase I clinical trial which commenced in the first quarter of 2018, partially offset by a decrease in consulting costs related to the IND filing in 2017. We are developing our ACTR087 used in combination with SEA-BCMA product candidate in conjunction with Seattle Genetics. We incurred costs related to our ACTR707 used in combination with trastuzumab program in connection with our IND filing and start-up costs for our Phase I clinical trial which we initiated in the fourth quarter of 2018.

The increase in personnel-related costs of $2.0 million included in unallocated expenses was primarily a result of an increase in stock-based compensation expense as well as increased overall compensation. Personnel-related costs for the years ended December 31, 2018 and 2017 included stock-based compensation expense of $2.2 million and $1.2 million, respectively. The increase in stock-based compensation expense was primarily related to additional employee stock options and a higher value of our common stock. The increase in laboratory supplies, facility-related, and other costs of $2.1 million was primarily due to increased costs related to scaling our manufacturing processes.

General and Administrative Expenses

General and administrative expenses for the years ended December 31, 2018 were $7.5 million, compared to $4.7 million for the year ended December 31, 2017. The increase in general and administrative expenses was primarily due to an increase in personnel-related costs of $1.0 million, increased professional and consulting fees of $1.0 million, and an increase in facility related and other costs of $0.8 million. The increase in personnel-related costs was primarily due to increased stock-based compensation expense due to additional stock option grants and an increased per share value of our common stock as well as increased overall compensation. The increase in professional and consulting fees was primarily due to an increase in various advisory fees, including those related to legal, accounting, investor relations and recruiting fees, associated with operating as a public company. The increase in facility related and other costs was primarily due to increased insurance expense associated with operating as a public company.

Interest Income

Interest income for the year ended December 31, 2018 was $1.2 million, compared to $0.4 million for the year ended December 31, 2017. Interest income increased primarily as a result of higher invested balances due to cash proceeds received from our IPO and Concurrent Private Placement.

Other Income, Net

Other income, net for the years ended December 31, 2018 and 2017 was $0.3 million in each year. We had subleases for a portion of our facilities in both periods. Our last sublease ended in 2018.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have generated limited revenue to date from funding arrangements with our collaboration partner. We have not yet commercialized any of our product candidates and we do not expect to generate revenue from sales of any product candidates for several years, if at all. Prior to our IPO, we had funded our operations with proceeds from the sales of preferred stock and payments received under our collaboration agreement.

On April 3, 2018, we completed our IPO, and issued and sold 5,770,000 shares of common stock at a public offering price of $12.00 per share, resulting in net proceeds of $61.5 million after deducting underwriting

discounts and commissions and other offering costs. We also completed the Concurrent Private Placement and sold 416,666 shares of common stock at a public offering price of $12.00 per share, resulting in proceeds of $5.0 million. On April 25, 2018, we issued and sold an additional 215,000 shares of our common stock at the IPO price of $12.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock, resulting in additional net proceeds of $2.4 million after deducting underwriting discounts and commissions.

As of December 31, 2018, we had cash, cash equivalents, and marketable securities of $78.6 million and available borrowings under our loan and security agreement of $15.0 million.

Cash Flows

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

	Year Ended December 31,	
	2018	2017
	(in thousands)	
Cash used in operating activities	$ (32,489)	$ (25,835)
Cash provided by (used in) investing activities	(10,531)	13,588
Cash provided by (used in) financing activities	70,346	(729)
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 27,326	$ (12,976)

Operating Activities

During the year ended December 31, 2018, operating activities used $32.5 million of cash, primarily resulting from our net loss of $34.5 million and from net cash used by changes in our operating assets and liabilities of $2.2 million, partially offset by net non-cash charges of $4.2 million. Net cash used by changes in our operating assets and liabilities for the year ended December 31, 2018 consisted primarily of a $3.8 million decrease in deferred revenue, after the impact of the adoption of the new revenue standard (ASC 606), a $0.8 million increase in accounts receivable, a $0.3 million increase in prepaid expenses and other current assets and a $0.4 million increase in other assets, all partially offset by a $3.3 million increase in accounts payable and accrued expenses and other current liabilities.

During the year ended December 31, 2017, operating activities used $25.8 million of cash, primarily resulting from our net loss of $25.5 million and net cash used by changes in our operating assets and liabilities of $2.9 million, partially offset by net non-cash charges of $2.5 million. Net cash used by changes in our operating assets and liabilities for the year ended December 31, 2017 consisted primarily of a $3.9 million decrease in deferred revenue and an increase of $0.2 million in prepaid expenses and other current assets, partially offset by a $1.1 million increase in accounts payable and accrued expenses and other current liabilities.

In June 2015, we received an upfront payment of $25.0 million from Seattle Genetics under our collaboration agreement. At that time, we recorded the $25.0 million as deferred revenue, to be subsequently recognized as revenue over our period of performance. Changes in deferred revenue in all periods were due to the initial recording of and increases to the amount of deferred revenue from payments from Seattle Genetics for reimbursements of research and development costs as well as the subsequent recognition as revenue of a portion of the deferred revenue.

Changes in accounts payable, accrued expenses, and prepaid expenses and other current assets and other assets in all periods were generally due to growth in our business, the advancement of our product candidates, and the timing of vendor invoicing and payments.

Investing Activities

During the year ended December 31, 2018, net cash used in investing activities was $10.5 million, consisting of net purchases of marketable securities of $10.0 million and purchases of property and equipment of $0.5 million.

During the year ended December 31, 2017, net cash provided by investing activities was $13.6 million, consisting primarily of net maturities and sales of marketable securities of $14.5 million, partially offset by purchases of property and equipment of $0.9 million.

Financing Activities

During the year ended December 31, 2018, net cash provided by financing activities was $70.3 million, consisting primarily of proceeds from our IPO in April 2018, net of underwriting discounts and commissions, of $66.8 million and proceeds from our concurrent private placement of $5.0 million, partially offset by payments of offering costs related to our IPO of $2.1 million.

During the year ended December 31, 2017, we used $0.8 million of cash to pay offering costs related to our IPO.

Loan and Security Agreement

In January 2017, we entered into a loan and security agreement (the Loan Agreement) with Pacific West Bank (PWB), which provides for term loan borrowings of up to $15.0 million through January 19, 2019. Borrowings under the Loan Agreement bear interest at a variable annual rate equal to the greater of (i) the prime rate plus 0.25% or (ii) 3.75%, and are payable over an interest-only period until January 19, 2019, followed by a 24-month period of equal monthly payments of principal and interest. All amounts outstanding as of the maturity date of January 19, 2021 become immediately due and payable.

In connection with the Loan Agreement, we agreed to enter into warrant agreements with PWB pursuant to which warrants will be issued to purchase a number of shares of our capital stock equal to 1% of the amount of each term loan borrowing under the Loan Agreement, divided by the applicable exercise price.

No amounts had been borrowed as term loans under the Loan Agreement as of December 31, 2018. In January 2019, we amended the Loan Agreement to extend the available date for borrowings from January 19, 2019 to June 30, 2019 and extend the interest only period from January 19, 2019 to June 30, 2020, with the possibility of further extension to March 31, 2021 if certain equity financing considerations are met. Additionally, the loan repayment period will be over a 24-month period following the end of the interest-only period.

Borrowings under the Loan Agreement are collateralized by substantially all of our assets, except for our intellectual property. Under the Loan Agreement, we have agreed to affirmative and negative covenants to which we will remain subject until maturity. These covenants include limitations on our ability to incur additional indebtedness and engage in certain fundamental business transactions, such as mergers or acquisitions of other businesses. There are no financial covenants associated with the Loan Agreement. Events of default under the Loan Agreement include failure to make payments when due, insolvency events, failure to comply with covenants, and material adverse effects with respect to us.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials for our product candidates in development. In addition, as

a result of the IPO, we are incurring additional costs associated with operating as a public company. The timing and amount of our operating expenditures will depend largely on:

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

As of December 31, 2018, we had cash, cash equivalents, and marketable securities of $78.6 million and available borrowings under our Loan Agreement of $15.0 million. We expect that our cash, cash equivalents and marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements into early 2021, without considering available borrowings under our Loan Agreement. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect.

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

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, 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 Note 2 to our consolidated financial statements included in this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Collaboration Agreements

We follow the accounting guidance for collaboration agreements, which requires that certain transactions between us and collaborators are recorded in our consolidated statements of operations and comprehensive loss on either a gross basis or net basis, depending on the characteristics of the collaborative relationship, and requires enhanced disclosure of collaborative relationships. We evaluate our collaboration agreements for proper classification in our consolidated statements of operations and comprehensive loss based on the nature of the underlying activity. If payments to and from collaborative partners are not within the scope of other authoritative accounting literature, the consolidated statements of operations classification for the payments is based on a reasonable, rational analogy to authoritative accounting literature that is applied in a consistent manner. When we have concluded that we have a customer relationship with one of our collaborators, such as that with Seattle Genetics, we follow the guidance in Accounting Standards Codification (ASC) Topic 606, *Revenue from Contracts with Customers* (ASC 606), effective as of January 1, 2018.

Revenue Recognition of Collaboration Agreements

On January 1, 2018, we adopted ASC 606, which amended revenue recognition principles and provides a single, comprehensive set of criteria for revenue recognition within and across all industries. The new revenue standard provides a five-step framework whereby revenue is recognized when control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of the new revenue standard, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when collectability of the consideration to which we are entitled in exchange for the goods or services we transfer to the customer is determined to be probable.

At contract inception, once the contract is determined to be within the scope of the new revenue standard, we assess whether the goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation. Goods and services that are determined not to be distinct are combined with other promised goods and services until a distinct bundle is identified. In determining whether goods or services are distinct, management evaluates certain criteria, including whether (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (capable of being distinct) and (ii) the good or service is separately identifiable from other goods or services in the contract (distinct in the context of the contract).

At the inception of an arrangement that includes options for a customer to purchase additional services or products at agreed upon prices in the future, we evaluate whether each option provides a material right. An option that provides a material right will be accounted for as a separate performance obligation.

We then determine the transaction price, which is the amount of consideration we expect to be entitled from a customer in exchange for the promised goods or services, for each performance obligation and recognize the associated revenue as each performance obligation is satisfied. Our estimate of the transaction price for each contract includes all variable consideration to which we expect to be entitled. Variable consideration includes payments in the form of collaboration payments, regulatory milestone payments, commercial milestone payments, and royalty payments. For collaboration, regulatory milestone, and commercial milestone payments, we evaluate whether it is probable that the consideration associated with each milestone will not be subject to a significant reversal in the cumulative amount of revenue recognized. Amounts that meet this threshold are included in the transaction price using the most likely amount method, whereas amounts that do not meet this threshold are considered constrained and excluded from the transaction price until they meet this threshold. At the end of each subsequent reporting period, we re-evaluate the probability of a significant reversal of the cumulative revenue recognized for our milestones, and, if necessary, adjusts our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis. We exclude sales-based royalties until the sale occurs.

The new revenue standard requires us to allocate the arrangement consideration on a relative standalone selling price basis for each performance obligation after determining the transaction price of the contract and identifying the performance obligations to which that amount should be allocated. The relative standalone selling price is defined in the new revenue standard as the price at which an entity would sell a promised good or service separately to a customer. If other observable transactions in which we have sold the same performance obligation separately are not available, we are required to estimate the standalone selling price of each performance obligation. Key assumptions to determine the standalone selling price may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success. A performance obligation is satisfied and revenue is recognized when “control” of the promised good or service is transferred, either over time or at a point in time, to the customer. A customer obtains control of a good or service if it has the ability to (1) direct its use and (2) obtain substantially all of the remaining benefits from it.

If a contract should be accounted for as a combined performance obligation, we determine the period over which the performance obligations will be performed and revenue will be recognized. We will recognize revenue using the cost-to-cost method, which we believe best depicts the transfer of control to the customer. Under the cost-to-cost method, the extent of progress towards completion is measured based on the ratio of actual costs incurred to the total estimated costs expected upon satisfying the identified performance obligation. Under this method, revenue will be recorded as a percentage of the estimated transaction price based on the extent of progress towards completion. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which we are expected to complete our performance obligations under an arrangement. The estimate of our measure of progress and estimate of variable consideration to be included in the transaction price will be updated at each reporting date as a change in estimate. The amount of transaction price allocated to the satisfied portion of the performance obligation, based on our measure of progress, will be recognized immediately on a cumulative catch-up basis, resulting in an adjustment to revenue in the period of change. The amount related to the unsatisfied portion will be recognized as that portion is satisfied over time.

Amounts received prior to satisfying the revenue recognition criteria listed above are recorded as deferred revenue in the accompanying consolidated balance sheets. Amounts expected to be recognized as revenue within 12 months of the balance sheet date are classified as current deferred revenue. Amounts not expected to be recognized as revenue within the following 12 months of the balance sheet date are classified as deferred revenue, net of current portion. We recognize deferred revenue by first allocating from the beginning deferred

revenue balance to the extent that the beginning deferred revenue balance exceeds the revenue to be recognized. Billings during the period are added to the deferred revenue balance to be recognized in future periods. To the extent that the beginning deferred revenue balance is less than revenue to be recognized during the period, billings during the period are allocated to revenue. In the event that a collaboration agreement was to be terminated and we had no further performance obligations, we would recognize as revenue any portion of the 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.

Amounts are recorded as accounts receivable when our right to consideration is unconditional. We do not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less or the amount is immaterial.

Prior to January 1, 2018, under the previous revenue recognition standard in effect, we recognized revenue from our collaboration agreement with Seattle Genetics on a straight-line basis over the estimated period of performance, which was the term of our preclinical research and clinical development activities related to the two specified product candidates through Phase I clinical development. As payments from Seattle Genetics were earned related to our preclinical research and clinical development activities through Phase I clinical development, we recognized as revenue the portion of the payments equal to the percentage of the elapsed research and development term to the total estimated research and development term, with the remaining portion of consideration received being recognized over the remaining estimated period of performance on a straight-line basis. Our estimate of the period of performance was approximately 58 months.

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

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

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CMOs and CROs that supply, conduct, and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our

understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been 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 employees and directors based on their fair value on the date of the grant and recognize compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. We apply the straight-line method of expense recognition to all awards with only service-based vesting conditions and would apply the graded-vesting method to all awards with performance-based vesting conditions or to awards with both service-based and performance-based vesting conditions.

For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed. At the end of each financial reporting period prior to the completion of the service, the fair value of these awards is remeasured 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-based award 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 common stock options, the risk-free interest rate for a period that approximates the expected term of our common stock options, and our expected dividend yield.

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 in the rules and regulations of the SEC.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report.

Inflation Risk

During the last two years, inflation and changing prices have not had a material effect on our business. We are unable to predict whether inflation or changing prices will materially affect our business in the foreseeable future.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are a smaller reporting company, as defined in Rule 12b-2 of the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this item.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

UNUM THERAPEUTICS INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Unum Therapeutics Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Unum Therapeutics Inc. and its subsidiary (the "Company") as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, of redeemable convertible preferred stock and stockholders' equity (deficit), and of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Change in Accounting Principle

As discussed in Note 2 to the consolidated financial statements, the Company changed the manner in which it accounts for revenues from contracts with customers in 2018.

Basis for Opinion

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

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

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

Emphasis of Matter

As discussed in Note 1 to the consolidated financial statements, the Company will require additional financing to fund future operations. Management's evaluation of the events and conditions and management's plans to mitigate this matter are also described in Note 1.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 28, 2019

We have served as the Company's auditor since 2015.

UNUM THERAPEUTICS INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 55,671	$ 28,270
Marketable securities	22,923	12,691
Accounts receivable	1,668	830
Prepaid expenses and other current assets	740	513
Restricted cash	—	75
Total current assets	81,002	42,379
Property and equipment, net	3,251	4,108
Restricted cash	1,255	1,255
Deferred offering costs	—	1,373
Other assets	419	—
Total assets	$ 85,927	$ 49,115
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 1,519	$ 1,346
Accrued expenses and other current liabilities	5,477	2,953
Deferred revenue	17,949	6,891
Total current liabilities	24,945	11,190
Deferred rent	748	906
Deferred revenue, net of current portion	—	8,714
Total liabilities	25,693	20,810
Commitments and contingencies (Note 12)		
Redeemable convertible preferred stock (Series A and B), $0.001 par value; no shares and 20,791,407 shares authorized at December 31, 2018 and 2017, respectively; no shares and 20,771,850 shares issued and outstanding at December 31, 2018 and 2017, respectively	—	77,151
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value; 10,000,000 shares and no shares authorized at December 31, 2018 and 2017, respectively; no shares issued or outstanding	—	—
Common stock, $0.001 par value; 150,000,000 shares and 60,040,000 shares authorized at December 31, 2018 and 2017, respectively; 30,057,970 shares and 10,201,690 shares issued and outstanding at December 31, 2018 and 2017, respectively	30	10
Additional paid-in capital	152,275	2,499
Accumulated other comprehensive loss	(12)	(16)
Accumulated deficit	(92,059)	(51,339)
Total stockholders' equity (deficit)	60,234	(48,846)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 85,927	$ 49,115

The accompanying notes are an integral part of these consolidated financial statements.

UNUM THERAPEUTICS INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share amounts)

	Year Ended December 31,	
	2018	2017
Collaboration revenue	$ 9,734	$ 8,360
Operating expenses:		
Research and development	38,285	29,832
General and administrative	7,454	4,680
Total operating expenses	45,739	34,512
Loss from operations	(36,005)	(26,152)
Other income (expense):		
Interest income	1,153	386
Other income, net	320	274
Total other income, net	1,473	660
Net loss	(34,532)	(25,492)
Accretion of redeemable convertible preferred stock to redemption value	(16)	(65)
Net loss attributable to common stockholders	$ (34,548)	$ (25,557)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.39)	$ (2.51)
Weighted average common shares outstanding, basic and diluted	24,895,670	10,191,807
Comprehensive loss:		
Net loss	$ (34,532)	$ (25,492)
Other comprehensive income (loss):		
Unrealized gains on marketable securities, net of tax of $0	4	8
Total other comprehensive income (loss)	4	8
Comprehensive loss	$ (34,528)	$ (25,484)

The accompanying notes are an integral part of these consolidated financial statements.

UNUM THERAPEUTICS INC.
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balances at December 31, 2016	20,771,850	$ 77,086	10,190,228	$ 10	$ 1,163	$ (24)	$ (25,847)	$ (24,698)
Issuance of common stock upon exercise of stock options	—	—	11,462	—	60	—	—	60
Stock-based compensation expense	—	—	—	—	1,341	—	—	1,341
Unrealized gains on marketable securities	—	—	—	—	—	8	—	8
Accretion of redeemable convertible preferred stock to redemption value	—	65	—	—	(65)	—	—	(65)
Net loss	—	—	—	—	—	—	(25,492)	(25,492)
Balances at December 31, 2017	20,771,850	77,151	10,201,690	10	2,499	(16)	(51,339)	(48,846)
Adjustment to retained earnings for change in accounting policy	—	—	—	—	—	—	(6,188)	(6,188)
Accretion of redeemable convertible preferred stock to redemption value	—	16	—	—	(16)	—	—	(16)
Conversion of redeemable convertible preferred stock to common stock	(20,771,850)	(77,167)	13,229,362	13	77,154	—	—	77,167
Issuance of common stock sold in initial public offering, net of underwriting discounts, commissions and offering costs	—	—	5,985,000	6	63,942	—	—	63,948
Proceeds from private placement concurrent with initial public offering	—	—	416,666	1	4,999	—	—	5,000
Issuance of common stock upon exercise of stock options	—	—	225,252	—	609	—	—	609
Stock-based compensation expense	—	—	—	—	3,088	—	—	3,088
Unrealized gains on marketable securities	—	—	—	—	—	4	—	4
Net loss	—	—	—	—	—	—	(34,532)	(34,532)
Balances at December 31, 2018	—	$ —	30,057,970	$ 30	$152,275	$ (12)	$ (92,059)	$ 60,234

The accompanying notes are an integral part of these consolidated financial statements.

UNUM THERAPEUTICS INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2018	2017
Cash flows from operating activities:		
Net loss	$ (34,532)	$ (25,492)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	3,088	1,341
Depreciation and amortization expense	1,321	1,171
Premiums paid on marketable securities	—	(13)
Net amortization (accretion) of premiums (discounts) on marketable securities	(246)	17
Loss on disposal of fixed assets	10	—
Non-cash interest expense	23	20
Changes in operating assets and liabilities:		
Accounts receivable	(838)	98
Prepaid expenses and other current assets	(250)	(237)
Other assets	(419)	—
Accounts payable	367	(31)
Accrued expenses and other current liabilities	2,883	1,168
Deferred rent	(52)	(2)
Deferred revenue	(3,844)	(3,875)
Net cash used in operating activities	(32,489)	(25,835)
Cash flows from investing activities:		
Purchases of property and equipment	(549)	(912)
Purchases of marketable securities	(47,682)	(6,500)
Maturities and sales of marketable securities	37,700	21,000
Net cash provided by (used in) investing activities	(10,531)	13,588
Cash flows from financing activities:		
Proceeds from initial public offering, net of underwriting discounts and commissions	66,793	—
Proceeds from private placement concurrent with initial public offering	5,000	—
Proceeds from issuance of common stock upon stock option exercises	609	60
Payments of initial public offering costs	(2,056)	(789)
Net cash provided by (used in) financing activities	70,346	(729)
Net increase (decrease) in cash, cash equivalents and restricted cash	27,326	(12,976)
Cash, cash equivalents and restricted cash at beginning of period	29,600	42,576
Cash, cash equivalents and restricted cash at end of period	$ 56,926	$ 29,600
Supplemental disclosure of noncash investing and financing information:		
Conversion of convertible redeemable preferred stock into common stock	$ 77,154	$ —
Purchases of property and equipment included in accounts payable	$ —	$ 75
Deferred offering costs included in accounts payable and accrued expenses	$ —	$ 584
Accretion of redeemable convertible preferred stock to redemption value	$ 16	$ 65

The accompanying notes are an integral part of these consolidated financial statements.

UNUM THERAPEUTICS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of the Business and Basis of Presentation

Unum Therapeutics Inc. ("Unum" or the "Company") is a clinical-stage biopharmaceutical company focused on the development and commercialization of novel immunotherapy products designed to harness the power of a patient's immune system to cure cancer. The Company's proprietary technologies include Antibody-Coupled T cell Receptor ("ACTR"), a universal, engineered cell therapy that is intended to be used in combination with a wide range of tumor-specific antibodies to target different tumor types, and Bolt-On Chimeric Receptor ("BOXR"), a novel approach to engineered T cell therapy designed specifically for solid tumor applications. Unum was incorporated in March 2014 under the laws of the State of Delaware.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's drug development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

On March 16, 2018, the Company effected a one-for-1.5701314513884 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of the Company's redeemable convertible preferred stock (see Note 8). Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the redeemable convertible preferred stock conversion ratios.

On April 3, 2018, the Company completed an initial public offering ("IPO") of its common stock and issued and sold 5,770,000 shares of common stock at a public offering price of $12.00 per share, resulting in net proceeds of $61.5 million after deducting underwriting discounts and commissions and other offering costs. In addition, Seattle Genetics, Inc. ("Seattle Genetics") purchased from the Company, concurrently with the IPO in a private placement, $5.0 million of shares of common stock at a price per share equal to the initial public offering price, or 416,666 shares (the "concurrent private placement").

Upon closing of the IPO, the Company's outstanding redeemable convertible preferred stock automatically converted into shares of common stock (see Note 8). Upon conversion of the redeemable convertible preferred stock, the Company reclassified the carrying value of the redeemable convertible preferred stock to common stock and additional paid-in capital.

On April 25, 2018, the Company issued and sold an additional 215,000 shares of its common stock at the IPO price of $12.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock, resulting in additional net proceeds of $2.4 million after deducting underwriting discounts and commissions.

The accompanying consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. Since inception, the Company has funded its operations with the sales of redeemable convertible preferred stock, payments received in connection with a collaboration agreement, and most recently, with proceeds from the IPO and concurrent private placement completed in April 2018. The Company has incurred

recurring losses since inception, including net losses attributable to the Company of $34.5 million for the year ended December 31, 2018. As of December 31, 2018, the Company had an accumulated deficit of $92.1 million. The Company expects to continue to generate operating losses in the foreseeable future. As of March 28, 2019, the issuance date of the consolidated financial statements, the Company expects that its cash, cash equivalents and marketable securities will be sufficient to fund its operating expenses and capital expenditure requirements through at least 12 months from the issuance date of the consolidated financial statements, without considering available borrowings under the Company's loan and security agreement.

The Company will ultimately need to seek additional funding through equity offerings, debt financings, collaborations, licensing arrangements and other marketing and distribution arrangements, partnerships, joint ventures, combinations or divestitures of one or more of its businesses. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into collaborative arrangements or divest its assets. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. Arrangements with collaborators or others may require the Company to relinquish rights to certain of its technologies or product candidates. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate its research and development programs or commercialization efforts, which could adversely affect its business prospects.

The Company's consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP").

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary. All intercompany accounts and transactions have been eliminated in consolidation.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, revenue recognition, the accrual of research and development expenses and the valuation of stock-based awards. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates, as there are changes in circumstances, facts and experience. Actual results may differ from those estimates or assumptions.

Concentrations of Credit Risk and of Significant Suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company maintains most of its cash and cash equivalents at three accredited financial institutions. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on third-party vendors for its product candidates. In particular, the Company relies, and expects to continue to rely, on a small number of vendors to manufacture supplies and process its product candidates for its development programs. These programs could be adversely affected by a significant interruption in the manufacturing process.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated.

After consummation of the equity financing, these costs are recorded in stockholders' equity (deficit) as a reduction of additional paid-in capital generated as a result of the offering. Should the planned equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss.

Debt Issuance Costs

The Company capitalizes certain legal and other third-party fees that are directly associated with obtaining access to capital under credit facilities. Debt issuance costs incurred in connection with obtaining access to capital are recorded in prepaid expenses and other current assets and are amortized over the availability period or term of the credit facility. Debt issuance costs related to a recognized debt liability are recorded as a direct reduction of the carrying amount of the debt liability.

Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase to be cash equivalents.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation and amortization expense is recognized using the straight-line method over the estimated useful life of each asset as follows:

	Estimated Useful Life
Laboratory equipment	5 years
Computer equipment and software	3 years
Furniture and fixtures	5 years
Leasehold improvements	Shorter of life of lease or 10 years

Costs for capital assets not yet placed into service are capitalized as construction-in-progress and depreciated in accordance with the above guidelines once placed into service. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance are charged to expense as incurred.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. An impairment loss would be recognized in loss from operations when estimated undiscounted future cash flows expected to result from the use of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows. The Company did not record any impairment losses on long-lived assets during the years ended December 31, 2018 or 2017.

Fair Value Measurements

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most

advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's cash equivalents and marketable securities are carried at fair value, determined according to the fair value hierarchy described above (see Note 3). The carrying values of the Company's accounts receivable, accounts payable and accrued expenses approximate their fair values due to the short-term nature of these liabilities.

Marketable Securities

The Company's marketable securities, consisting of debt securities, are classified as available-for-sale and are reported at fair value. Unrealized gains and losses on available-for-sale debt securities are reported as a component of accumulated other comprehensive income (loss) in stockholders' equity (deficit). Realized gains and losses and declines in value determined to be other than temporary are based on the specific identification method and are included as a component of other income (expense), net in the consolidated statements of operations and comprehensive loss. The Company classifies its marketable securities with maturities beyond one year as short-term, based on their highly liquid nature and because such marketable securities are available for current operations.

The Company evaluates its marketable securities with unrealized losses for other-than-temporary impairment. When assessing marketable securities for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions in general. If any adjustment to fair value reflects a decline in the value of the investment that the Company considers to be "other than temporary," the Company reduces the investment to fair value through a charge to the statement of operations and comprehensive loss. No such adjustments were necessary during the periods presented.

Classification and Accretion of Redeemable Convertible Preferred Stock

The Company classified redeemable convertible preferred stock outside of stockholders' equity (deficit) because the shares contained certain redemption features that were not solely within the control of the Company. The carrying values of the redeemable convertible preferred stock were accreted to their respective redemption values from the date of issuance through the earliest date of redemption.

Segment Information

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's singular focus is the development and commercialization of immunotherapy products for cancer. All of the Company's tangible assets are held in the United States.

Collaboration Agreements

The Company follows the accounting guidance for collaboration agreements, which requires that certain transactions between the Company and collaborators be recorded in its consolidated statements of operations and comprehensive loss on either a gross basis or net basis, depending on the characteristics of the collaborative relationship, and requires enhanced disclosure of collaborative relationships. The Company evaluates its collaboration agreements for proper classification in its consolidated statements of operations and comprehensive loss based on the nature of the underlying activity. If payments to and from collaborative partners are not within the scope of other authoritative accounting literature, the consolidated statements of operations classification for the payments is based on a reasonable, rational analogy to authoritative accounting literature that is applied in a consistent manner. When the Company has concluded that it has a customer relationship with one of its collaborators, such as that with Seattle Genetics (see Note 6), the Company follows the guidance in Accounting Standards Codification ("ASC") Topic 606, *Revenue From Contracts With Customers* ("ASC 606").

Revenue Recognition of Collaboration Agreements

On January 1, 2018, the Company adopted the new revenue standard, discussed below under the heading "Recently Adopted Accounting Pronouncements", which amended revenue recognition principles and provides a single, comprehensive set of criteria for revenue recognition within and across all industries. The new revenue standard provides a five-step framework whereby revenue is recognized when control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of the new revenue standard, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when collectability of the consideration to which the Company is entitled in exchange for the goods or services it transfers to the customer is determined to be probable.

At contract inception, once the contract is determined to be within the scope of the new revenue standard, the Company assesses whether the goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation. Goods and services that are determined not to be distinct are combined with other promised goods and services until a distinct bundle is identified. In determining whether goods or services are distinct, management evaluates certain criteria, including whether (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (capable of being distinct) and (ii) the good or service is separately identifiable from other goods or services in the contract (distinct in the context of the contract).

At the inception of an arrangement that includes options for a customer to purchase additional services or products at agreed upon prices in the future, the Company evaluates whether each option provides a material right. An option that provides a material right will be accounted for as a separate performance obligation.

The Company then determines the transaction price, which is the amount of consideration it expects to be entitled from a customer in exchange for the promised goods or services, for each performance obligation and recognizes the associated revenue as each performance obligation is satisfied. The Company's estimate of the transaction price for each contract includes all variable consideration to which it expects to be entitled. Variable consideration includes payments in the form of collaboration payments, regulatory milestone payments, commercial milestone payments, and royalty payments. For collaboration, regulatory milestone, and commercial milestone payments the Company evaluates whether it is probable that the consideration associated with each milestone will not be subject to a significant reversal in the cumulative amount of revenue recognized. Amounts that meet this threshold are included in the transaction price using the most likely amount method, whereas amounts that do not meet this threshold are considered constrained and excluded from the transaction price until

they meet this threshold. At the end of each subsequent reporting period, the Company re-evaluates the probability of a significant reversal of the cumulative revenue recognized for its milestones, and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis. The Company excludes sales-based royalties until the sale occurs.

The new revenue standard requires the Company to allocate the arrangement consideration on a relative standalone selling price basis for each performance obligation after determining the transaction price of the contract and identifying the performance obligations to which that amount should be allocated. The relative standalone selling price is defined in the new revenue standard as the price at which an entity would sell a promised good or service separately to a customer. If other observable transactions in which the Company has sold the same performance obligation separately are not available, the Company is required to estimate the standalone selling price of each performance obligation. Key assumptions to determine the standalone selling price may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success. A performance obligation is satisfied and revenue is recognized when "control" of the promised good or service is transferred, either over time or at a point in time, to the customer. A customer obtains control of a good or service if it has the ability to (1) direct its use and (2) obtain substantially all of the remaining benefits from it.

If a contract should be accounted for as a combined performance obligation, the Company determines the period over which the performance obligations will be performed and revenue will be recognized. The Company will recognize revenue using the cost-to-cost method, which it believes best depicts the transfer of control to the customer. Under the cost-to-cost method, the extent of progress towards completion is measured based on the ratio of actual costs incurred to the total estimated costs expected upon satisfying the identified performance obligation. Under this method, revenue will be recorded as a percentage of the estimated transaction price based on the extent of progress towards completion. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which the Company is expected to complete its performance obligations under an arrangement. The estimate of the Company's measure of progress and estimate of variable consideration to be included in the transaction price will be updated at each reporting date as a change in estimate. The amount of transaction price allocated to the satisfied portion of the performance obligation, based on the Company's measure of progress, will be recognized immediately on a cumulative catch-up basis, resulting in an adjustment to revenue in the period of change. The amount related to the unsatisfied portion will be recognized as that portion is satisfied over time.

Amounts received prior to satisfying the revenue recognition criteria listed above are recorded as deferred revenue in the accompanying consolidated balance sheets. Amounts expected to be recognized as revenue within 12 months of the balance sheet date are classified as current deferred revenue. Amounts not expected to be recognized as revenue within the following 12 months of the balance sheet date are classified as deferred revenue, net of current portion. The Company recognizes deferred revenue by first allocating from the beginning deferred revenue balance to the extent that the beginning deferred revenue balance exceeds the revenue to be recognized. Billings during the period are added to the deferred revenue balance to be recognized in future periods. To the extent that the beginning deferred revenue balance is less than revenue to be recognized during the period, billings during the period are allocated to revenue. In the event that a collaboration agreement was to be terminated and the Company had no further performance obligations, the Company would recognize as revenue any portion of the 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. The Company recognized revenue of $9.7 million during the year ended December 31, 2018 from the deferred revenue balance at January 1, 2018. At December 31, 2018, the Company had deferred revenue of $17.9 million related to its collaboration.

Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less. The Company expenses incremental costs of obtaining a

contract as and when incurred if the expected amortization period of the asset that the Company would have recognized is one year or less or the amount is immaterial. The Company has not capitalized any costs to obtain its contract.

Research and Development Costs

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, stock-based compensation and benefits, facilities costs and laboratory supplies, depreciation, manufacturing expenses and external costs of outside vendors engaged to conduct preclinical development activities and clinical trials as well as the cost of licensing technology. Research and development costs include costs for the development of product candidates that the Company is jointly developing with Seattle Genetics and for which it receives reimbursement as specified in the agreement.

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. 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.

Research Contract Costs and Accruals

The Company has entered into various research and development contracts with companies both inside and outside of the United States. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies or trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Stock-Based Compensation

The Company measures all stock-based awards granted to employees and directors based on the fair value on the date of grant using the Black-Scholes option-pricing model. Compensation expense of those awards is recognized over the requisite service period, which is generally the vesting period of the respective award. Generally, the Company issues awards with only service-based vesting conditions and records the expense for these awards using the straight-line method. Forfeitures are accounted for as they occur.

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

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

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, 2018 and 2017, the Company's only element of other comprehensive loss was unrealized gains (losses) on marketable securities.

Net Income (Loss) per Share

Prior to the closing of its IPO, the Company followed the two-class method when computing net income (loss) per share, as the Company had issued shares that met the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed. The Company's redeemable convertible preferred stock contractually entitled the holders of such shares to participate in dividends but did not contractually require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reported a net loss, such losses were not allocated to such participating securities, and as a result, basic and diluted net loss per share were the same.

Subsequent to the closing of its IPO, basic net income (loss) per common share is computed by dividing the net income (loss) by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) per common share is computed by dividing net income (loss) by the weighted average number of common shares outstanding for the period, including potential dilutive common shares assuming the dilutive effect of outstanding stock options. Accordingly, in periods in which the Company reported a net loss, dilutive common shares were not assumed to have been issued as their affect was anti-dilutive, and as a result, diluted net loss per common share was the same as basic net loss per common share.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. 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.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Recently Adopted Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2014-09, *Revenue from Contracts with Customers (Topic 606)* ("ASU 2014-09"), which supersedes existing revenue recognition guidance under GAAP. The standard's core principle is that a company will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. The standard outlines a five-step process to achieve this principle, and requires companies to use more judgment and make more estimates than under the previous guidance. The Company determined that these judgments and estimates include identifying performance obligations in the customer contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each separate performance obligation. ASU 2014-09 also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts. In August 2015, the FASB issued ASU 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, which delayed the effective date of ASU 2014-09 such that the standard became effective for public entities for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. The FASB subsequently issued amendments to ASU No. 2014-09 that had the same effective dates and transition requirements as ASU 2014-09, all of which collectively are herein referred to as "ASC 606".

On January 1, 2018, the Company adopted the new revenue standard by applying the modified retrospective method to its collaboration agreement with Seattle Genetics (see Note 6) which was not completed as of January 1, 2018. As a result, while reporting periods beginning on the Company's adoption of the new revenue standard are presented under the new revenue standard, prior period amounts have not been adjusted and continue to be presented under the revenue standard in effect prior to January 1, 2018.

The following table summarizes the cumulative effect to the Company's consolidated balance sheet upon the adoption of the new revenue standard on January 1, 2018 (in thousands):

	Balance at December 31, 2017	Adjustments	Balance at January 1, 2018
Deferred revenue, current and net of current portion	$ 15,605	$ 6,188	$ 21,793
Accumulated deficit	$ (51,339)	$ (6,188)	$ (57,527)

The adjustment is the result of the application of the new revenue standard regarding how entities should measure progress in satisfying performance obligations and the contract's transaction price. Under ASC 606, the Company recognizes revenue using the cost-to-cost method, which it believes best depicts the transfer of control to the customer. In contrast, under the previous revenue standard, the Company recognized revenue on a straight-line basis over the estimated period of performance. In addition, under ASC 606, the estimated transaction price includes variable consideration for payments expected to be earned for preclinical research and clinical development activities through Phase I, which, under the previous standard, the Company was precluded from including in the estimated transaction price until such payments were determinable and due.

The Company accounts for the license, research and development services, and steering committee services under ASC 606 as a single performance obligation under the collaboration agreement, just as it accounted for those items as a single unit of accounting under the previous standard. The options held by Seattle Genetics are expected to continue to be accounted for separately as they do not represent material rights based on the criteria of ASC 606. Further, ASC 606 does not have an impact on the Company's current accounting for milestone or royalty payments.

In accordance with the new revenue standard requirements, the following tables summarize the impact of adoption on the Company's consolidated balance sheets, consolidated statements of operations and comprehensive loss, and consolidated statements of cash flows (in thousands):

Consolidated Balance Sheet

	At December 31, 2018		
	Under Topic 606	Under Topic 605	Effect of Change
Deferred revenue, current portion	$ 17,949	$ 8,110	$ 9,839
Deferred revenue, net of current portion	$ —	$ 2,128	$ (2,128)
Accumulated deficit	$ (92,059)	$ (84,348)	$ (7,711)

Consolidated Statements of Operations and Comprehensive Loss

	Year Ended December 31, 2018		
	Under Topic 606	Under Topic 605	Effect of Change
Collaboration revenue	$ 9,734	$ 11,257	$ (1,523)
Net loss	$ (34,532)	$ (33,009)	$ (1,523)
Net loss attributable to common stockholders	$ (34,548)	$ (33,025)	$ (1,523)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.39)	$ (1.33)	$ (0.06)
Comprehensive loss	$ (34,528)	$ (33,005)	$ (1,523)

Consolidated Statement of Cash Flows

	Year Ended December 31, 2018		
	Under Topic 606	Under Topic 605	Effect of Change
Net loss	$ (34,532)	$ (33,009)	$ (1,523)
Change in deferred revenue	$ (3,844)	$ (5,367)	$ 1,523

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"), to address diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The Company adopted the standard retrospectively for all periods presented on the required effective date of January 1, 2018, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

In November 2016, the FASB issued ASU 2016-18, *Statement of Cash Flows, Restricted Cash*, requiring restricted cash and restricted cash equivalents to be included with cash and cash equivalents on the statement of cash flows when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. The Company adopted this standard during the first quarter of 2018. Restricted cash is now included as a component of cash, cash equivalents, and restricted cash on the Company's consolidated statements of cash flows. The inclusion of restricted cash increased the beginning and ending balances of the consolidated statement of cash flows by $1.3 million for the year ended December 31, 2017.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"), which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. The Company adopted the standard prospectively beginning on the required effective date of January 1, 2018, and its adoption did not have a material impact on the Company's financial position, results of operations or cash flows.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors). The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. The guidance is effective for public entities for annual reporting periods beginning after December 15, 2018 and for interim periods within those fiscal years, and early adoption is permitted. ASU 2016-02 initially required adoption using a modified retrospective approach, under which all years presented in the financial statements would be prepared under the revised guidance. In July 2018, the FASB issued ASU No. 2018-11, *Leases (Topic 842)*, which added an optional transition method under which financial statements may be prepared under the revised guidance for the year of adoption, but not for prior years. Under the latter method, entities will recognize a cumulative catch-up adjustment to the opening balance of retained earnings in the period of adoption. The Company plans to adopt the new leasing standard on January 1, 2019, using a modified retrospective transition approach to be applied to leases existing as of, or entered into after, January 1, 2019. The Company will apply the "package of practical expedients", which permits the Company not to reassess under the new standards for prior conclusions about lease identification, lease classification and initial direct costs. Upon adoption of the new leasing standards, the Company expects to recognize a lease liability of approximately $7.5 million and a related right-of-use asset of approximately $6.6 million on its consolidated balance sheet with the difference being due to the elimination of previously reported deferred rent. The Company does not expect the adoption of the standard to have a material impact on its results of operations or cash flows.

In July 2017, the FASB issued ASU No. 2017-11, *Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480), Derivatives and Hedging (Topic 815) I. Accounting for Certain Financial Instruments with Down Round Features II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception* ("ASU 2017-11"). Part I applies to entities that issue financial instruments such as warrants, convertible debt or convertible preferred stock that contain down-round features. Part II replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. ASU 2017-11 is required to be adopted for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. The Company plans to adopt ASU No. 2017-11 on January 1, 2019 and does not expect the adoption of this guidance to have a material impact on its consolidated financial statements.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation – Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"). ASU 2018-07 is intended to simplify aspects of share-based compensation issued to non-employees by making the guidance consistent with the accounting for employee share-based compensation. ASU 2018-07 is required to be adopted for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. Early adoption is permitted. The Company does not expect the adoption of this guidance to have a material impact on its consolidated financial statements.

3. Marketable Securities and Fair Value Measurements

Marketable securities by security type consisted of the following (in thousands):

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. Treasury bills and notes (due within one year)	$ 22,935	$ —	$ (12)	$22,923
	$ 22,935	$ —	$ (12)	$22,923

	December 31, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. Treasury bills and notes (due within one year)	$ 5,007	$ —	$ (10)	$ 4,997
U.S. government agency bonds (due within one year)	7,700	—	(6)	7,694
	$ 12,707	$ —	$ (16)	$12,691

The following tables present the Company's fair value hierarchy for its cash equivalents and marketable securities, which are measured at fair value on a recurring basis (in thousands):

	Fair Value Measurements at December 31, 2018 Using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ —	$ 52,100	$ —	$ 52,100
Marketable securities:				
U.S. Treasury bills and notes	22,923	—	—	22,923
	$ 22,923	$ 52,100	$ —	$ 75,023

	Fair Value Measurements at December 31, 2017 Using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ —	$ 24,196	$ —	$ 24,196
Marketable securities:				
U.S. Treasury notes	4,997	—	—	4,997
U.S. government agency bonds	—	7,694	—	7,694
	$ 4,997	$ 31,890	$ —	$ 36,887

U.S. Treasury bills and notes were valued based on Level 1 inputs. Money market funds and U.S. government agency bonds were valued by the Company using quoted prices in active markets for similar securities, which represent a Level 2 measurement within the fair value hierarchy.

During the years ended December 31, 2018 and 2017, there were no transfers between Level 1, Level 2 and Level 3.

4. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2018	2017
Laboratory equipment	$ 5,801	$ 5,327
Computer equipment and software	203	218
Furniture and fixtures	317	317
Leasehold improvements	426	426
	6,747	6,288
Less: Accumulated depreciation and amortization	(3,496)	(2,180)
	$ 3,251	$ 4,108

Depreciation and amortization expense was $1.3 million and $1.2 million for the years ended December 31, 2018 and 2017, respectively.

5. Accrued Expenses and Other Current Liabilities

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

	December 31,	
	2018	2017
Accrued employee compensation and benefits	$1,599	$1,315
Accrued external research and development expense	1,799	478
Accrued professional fees	400	980
Other	1,679	180
	$5,477	$2,953

6. Collaboration Agreement

The Company has a collaboration agreement with Seattle Genetics, entered into in 2015, whereby the parties agreed to jointly develop two product candidates incorporating the Company's ACTR platform and Seattle Genetics' antibodies. Under the collaboration agreement, the Company conducts preclinical research and clinical development activities related to the two specified product candidates through Phase I clinical development, and Seattle Genetics provides the funding for those activities. Seattle Genetics will continue development activities of the two specified product candidates in collaboration with the Company unless it exercises one of its two options to opt-out from further development and commercialization activities for each of the two product candidates during specified periods subsequent to Phase I clinical development. In addition, the Company has an option to opt-out from further development and commercialization activities for each of the two product candidates, exercisable during a specified period subsequent to Phase II clinical development. If neither party exercises its options to opt-out from further development and commercialization activities for each product candidate, the parties will work together to co-develop and fund each product candidate after Phase I clinical development and Seattle Genetics will pay the Company specified collaboration and milestone payments upon the occurrence of specified events related to each product candidate. As of December 31, 2018, the Company was eligible to receive future collaboration and milestone payments under the collaboration agreement of up to an aggregate of $400.0 million across the two active product candidates, consisting of $100.0 million of aggregate collaboration payments, $100.0 million of aggregate regulatory milestone payments and $200.0 million of aggregate commercial milestone payments. The individual collaboration payments are payable upon the occurrence of specified clinical development events and range up to $30.0 million per product candidate. The individual

regulatory milestone payments are payable upon the first regulatory approval of each product in the United States and the first regulatory approval of each product in specified territories outside the United States and range up to $35.0 million per product. The individual commercial milestone payments are payable upon the achievement of specified aggregate annual net sales for each product and range up to $60.0 million per product.

In the event that a party exercises its option to opt-out from further development and commercialization of a product candidate, the parties will negotiate in good faith the payment obligations of the continuing party to the opt-out party for that product candidate. Unless either party exercises its right to opt-out from further development and commercialization activities, the Company and Seattle Genetics will co-commercialize and share profits and losses equally on any co-developed products in the United States. Seattle Genetics will retain exclusive commercial rights outside of the United States and is obligated to pay the Company tiered royalties ranging in the high single-digit to mid-teens percentages based on net sales outside of the United States. The royalties are payable on a product-by-product basis and may be reduced in specified circumstances. Seattle Genetics will purchase ACTR T cells from the Company on a cost-plus basis for its commercial supply outside of the United States.

Unless earlier terminated, the collaboration agreement will expire on a product-by-product basis in the United States on the date on which neither party is researching, developing or commercializing such product. Outside of the United States, the collaboration agreement will expire on a product-by-product and country-by-country basis at the end of the applicable royalty term for such product in such country. The royalty term will be in effect beginning at the first commercial sale of a product and ending upon the later to incur of (i) expiration of the last valid claim within any patent right that the Company or Seattle Genetics has that would be infringed by the manufacture, use, sale, offer for sale, or importation of such product in such country, (ii) the end of any regulatory exclusivity periods that apply to the manufacture, use, sale, offer for sale, or importation of such product in such country, or (iii) ten years from the first commercial sale of such product in such country.

The Company evaluated whether the performance obligations under this agreement, including the license, research and development services, steering committee participation, and manufacturing services should be accounted for as a single unit or multiple units of accounting. Because of the risk associated with obtaining approval for commercial sale in the Seattle Genetics territories, manufacturing services associated with commercial supply were considered a contingent deliverable and will be accounted for if and when performed. The Company accounts for the license, research and development services, and steering committee services under ASC 606 as a single performance obligation under the collaboration agreement.

The Company determined that the transaction price includes the $25.0 million upfront payment and the total payments to be earned for preclinical research and clinical development activities. The total transaction price is being recognized as revenue over the performance period using the cost-to-cost method, which the Company believes best depicts the transfer of control to the customer. As payments from Seattle Genetics are earned related to the Company's preclinical research and clinical development activities through Phase I clinical development, the Company recognizes as revenue the portion of the payments equal to the percentage of the cost of completed research and development activities to the cost of the total estimated research and development activities. Any future milestone payments will be recognized, along with the other arrangement consideration, over the remaining estimated period of performance, if any, beginning at the time a milestone payment is earned, with a cumulative catch up being recognized for the completed portion of the estimated research costs.

At the inception of the arrangement, the Company evaluated the separate options held by Seattle Genetics (i) to expand the collaboration to include a third product candidate upon payment of an additional fee and (ii) to continue development activities beyond Phase I clinical development activities and determined that each option was substantive. Each option represents a separate buying decision by Seattle Genetics, is not essential to the functionality of the current deliverables, and was not offered at a substantially discounted price. As each option was deemed to be substantive, the item underlying the option was not considered to be a deliverable at the inception of the arrangement and the incremental fees associated with each option were not included in the initial arrangement consideration. These options will be accounted for as separate units of accounting when, and if, such options are exercised by Seattle Genetics.

Under the collaboration agreement, the Company recognized revenue of $9.7 million and $8.4 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018 and 2017, deferred revenue of $17.9 million and $15.6 million, respectively, was recorded related to this agreement. As noted in Note 2 above, deferred revenue was increased by $6.2 million as of January 1, 2018 upon adoption of ASC 606. As of December 31, 2018, the aggregate amount of the transaction price allocated to the remaining performance obligation for preclinical research and clinical development activities related to the two specified product candidates through Phase I is estimated to be approximately $54.1 million, which is expected to be recognized as revenue through December 31, 2022.

7. Loan and Security Agreement

In January 2017, the Company entered into a loan and security agreement with a lender, the ("Loan Agreement"), which provides for term loan borrowings of up to $15.0 million through January 19, 2019. Borrowings under the loan and security agreement bear interest at a variable annual rate equal to the greater of (i) the prime rate plus 0.25% or (ii) 3.75%, and are payable over an interest-only period until January 19, 2019, followed by a 24-month period of equal monthly payments of principal and interest. All amounts outstanding as of the maturity date of January 19, 2021 become immediately due and payable.

In connection with the loan and security agreement, the Company agreed to enter into warrant agreements with the lender pursuant to which warrants will be issued to purchase a number of shares of the Company's capital stock equal to 1% of the amount of each term loan borrowing under the loan and security agreement, divided by the applicable exercise price.

No amounts have been borrowed as term loans under the loan and security agreement as of December 31, 2018. In January 2019, the Company amended the Loan Agreement to extend the available borrowing date, the interest-only period and the repayment period (see Note 16).

Borrowings under the loan and security agreement are collateralized by substantially all of the Company's assets, except for its intellectual property. Under the loan and security agreement, the Company has agreed to affirmative and negative covenants to which it will remain subject until maturity. These covenants include limitations on the Company's ability to incur additional indebtedness and engage in certain fundamental business transactions, such as mergers or acquisitions of other businesses. There are no financial covenants associated with the loan and security agreement. Events of default under the loan and security agreement include failure to make payments when due, insolvency events, failure to comply with covenants and material adverse effects with respect to the Company.

8. Redeemable Convertible Preferred Stock

The Company had issued Series A redeemable convertible preferred stock (the "Series A preferred stock") and Series B redeemable convertible preferred stock (the "Series B preferred stock"). The Series A preferred stock and the Series B preferred stock are collectively referred to as the "Preferred Stock". The Preferred Stock converted to shares of common stock on a 1:1.5701314513884 basis upon the closing of the IPO on April 3, 2018.

As of December 31, 2017, the Preferred Stock consisted of the following (in thousands, except share amounts):

	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Preference	Common Stock Issuable Upon Conversion
Series A preferred stock	12,297,276	12,297,276	$ 12,267	$ 12,297	7,832,001
Series B preferred stock	8,494,131	8,474,574	64,884	65,000	5,397,361
	20,791,407	20,771,850	$ 77,151	$ 77,297	13,229,362

Prior to the closing of the IPO, the holders of the Preferred Stock had the following rights and preferences:

Voting

The holders of Preferred Stock were entitled to vote, together with the holders of common stock, on matters submitted to stockholders for a vote. The holders of Preferred Stock were entitled to the number of votes equal to the number of common shares into which each such share of Preferred Stock could convert. In addition, the holders of Series A preferred stock, voting exclusively and as a separate class, were entitled to elect two directors of the Company. The holders of Series B preferred stock, voting exclusively and as a separate class, were entitled to elect one director of the Company.

Conversion

Each share of Preferred Stock was convertible at the option of the holder at any time after the date of issuance. Each share of Preferred Stock would have automatically converted into shares of common stock at the applicable conversion ratio then in effect upon the closing of a firm commitment public offering with at least $50.0 million of gross proceeds to the Company. Shares of Series A preferred stock would have automatically converted into shares of common stock at the applicable conversion ratio then in effect upon written consent of the holders of at least 65% of the then-outstanding shares of Series A preferred stock. Shares of Series B preferred stock would have automatically converted into shares of common stock at the applicable conversion ratio then in effect upon written consent of the holders of at least a majority of the then-outstanding shares of Series B preferred stock.

The conversion ratio of each series of Preferred Stock was determined by dividing the Original Issue Price of each series by the Conversion Price of each series. The Original Issue Price was $1.00 per share for Series A preferred stock and $7.67 per share for Series B preferred stock. The Conversion Price at issuance was $1.570131 per share for Series A preferred stock and $12.042908 per share for Series B preferred stock, subject to appropriate adjustment in the event of any stock split, stock dividend, combination or other similar recapitalization and other adjustments as set forth in the Company's certificate of incorporation, as amended and restated.

Dividends

The holders of Preferred Stock were entitled to receive noncumulative dividends if and when declared by the Company's board of directors. The Company could not declare, pay or set aside any dividends on shares of any other series of capital stock of the Company, other than dividends on common stock payable in common stock, unless the holders of the Series A and Series B preferred stock first received, or simultaneously received, a dividend on each outstanding share of Series A and Series B preferred stock in an amount at least equal to the greater of (i) $0.08 per share in the case of Series A preferred stock and $0.61 per share in the case of Series B preferred stock, each subject to appropriate adjustment in the event of any stock split, stock dividend, combination or other similar recapitalization with respect to such shares, and (ii) (A) in the case of a dividend on common stock or any class or series of stock that was convertible into common stock, that dividend per share of Preferred Stock as would equal the product of (1) the dividend payable on each share of such class or series determined, if applicable, as if all shares of such class or series had been converted into common stock and (2) the number of shares of common stock issuable upon conversion of each share of Preferred Stock, or (B) in the case of a dividend on any class or series that was not convertible into common stock, at a rate per share of Preferred Stock determined by (1) dividing the amount of the dividend payable on each share of such class or series of capital stock by the Original Issue Price of such class or series of capital stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination of or other similar recapitalization affecting such shares) and (2) multiplying such fraction by an amount equal to the Original Issue Price of each series of Preferred Stock. If the Company declared, paid or set aside, on the same date, a dividend on shares of more than one class or series of capital stock of the Company, the dividend payable to the holders of the Preferred Stock would have been calculated based upon the dividend on the class or series of capital stock that would have resulted in the highest Preferred Stock dividend. Stockholders were not entitled to any accruing dividends. No dividends had been declared or paid.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution or winding-up of the Company or Liquidating Event (as described below), the holders of shares of Preferred Stock would have received, in preference to the common stockholders, an amount equal to the greater of (i) the Original Issue Price per share of the respective share of Preferred Stock, plus all dividends declared but unpaid on such shares, or (ii) the amount the holders would have received if the Preferred Stock were converted into common stock prior to such liquidation event. In the event that the assets available for distribution to the Company's stockholders had not been sufficient to permit payment to the holders of Preferred Stock in the full amount to which they were entitled, the assets available for distribution would have been distributed on a pro rata basis among the holders of the Series A and Series B preferred stock. After the payment of all preferential amounts to the holders of the Preferred Stock then, to the extent available, the remaining assets available for distribution would have been distributed among the holders of the common stock ratably based on the number of shares of common stock held by each holder.

Unless the holders of at least two-thirds of the then-outstanding shares of Preferred Stock, voting together as a single class on an as-converted basis, elected otherwise, a Liquidating Event would have included a merger or consolidation (other than one in which stockholders of the Company own a majority by voting power of the outstanding shares of the surviving or acquiring corporation) or a sale, lease, transfer, exclusive license or other disposition of all or substantially all of the assets of the Company.

Redemption

At any time on or after June 10, 2020, shares of each of the Series A and Series B preferred stock were subject to mandatory redemption by the Company in three equal annual installments beginning 60 days after receipt of a notice of redemption from the holders of at least two-thirds of the combined voting power of the holders of outstanding shares of Series A and Series B preferred stock, voting together as a single class, in an amount equal to the Original Issue Price per share of each series of Preferred Stock plus any dividends declared but unpaid thereon.

9. Equity

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are not entitled to receive dividends, unless declared by the board of directors.

On March 16, 2018, the Company effected a one-for-1.5701314513884 reverse stock split of its issued and outstanding shares of common stock. Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split.

On April 3, 2018, the Company completed an IPO of its common stock and issued and sold 5,770,000 shares of common stock at a public offering price of $12.00 per share, resulting in net proceeds of $61.5 million after deducting underwriting discounts and commissions and other offering costs. In addition, Seattle Genetics purchased from the Company, concurrently with the IPO in a private placement, $5.0 million of shares of common stock at a price per share equal to the initial public offering price, or 416,666 shares. Upon closing of the IPO, the Company's authorized shares of common stock were increased to 150,000,000 shares. The Company also authorized 10,000,000 shares of undesignated preferred stock.

On April 25, 2018, the Company issued and sold an additional 215,000 shares of its common stock at the IPO price of $12.00 per share pursuant to the underwriters' partial exercise of their option to purchase additional shares of common stock, resulting in additional net proceeds of $2.4 million after deducting underwriting discounts and commissions.

10. Stock-Based Compensation

2015 Stock Incentive Plan

The Company's 2015 Stock Incentive Plan (the "2015 Plan") provided for the Company to grant incentive stock options or nonqualified stock options, restricted stock, restricted stock units and other equity awards to employees, directors and consultants of the Company. The 2015 Plan was administered by the board of directors or, at the discretion of the board of directors, by a committee of the board of directors. The board of directors could also delegate to one or more officers of the Company the power to grant awards to employees and certain officers of the Company. The exercise prices, vesting and other restrictions were determined at the discretion of the board of directors, or its committee if so delegated. Stock options granted under the 2015 Plan with service-based vesting conditions generally vest over four years and expire after ten years. The total number of shares of common stock that could have been issued under the 2015 Plan was 4,144,876 shares. Upon effectiveness of the Company's 2018 Stock Option and Incentive Plan, the ("2018 Plan") in March 2018, the remaining shares available under the 2015 Plan became available for issuance under the 2018 Plan and no future issuance will be made under the 2015 Plan. Additionally, outstanding options under the 2015 Plan that are expired, terminated, surrendered or canceled without having been fully exercised will be available for future issuance under the 2018 Plan.

The exercise price for stock options granted is not less than the fair value of common shares as determined by the board of directors as of the date of grant. Prior to the Company's IPO, the Company's board of directors valued the Company's common stock, taking into consideration its most recently available valuation of common stock performed by third parties as well as additional factors which may have changed since the date of the most recent contemporaneous valuation through the date of grant.

2018 Stock Option and Incentive Plan

On March 16, 2018, the Company's stockholders approved the 2018 Plan, which became effective on March 27, 2018. The 2018 Plan provides for the grant of incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock units, restricted stock awards, unrestricted stock awards, cash-based awards and dividend equivalent rights. The number of shares initially reserved for issuance under the 2018 Plan is 2,800,721 plus the shares of common stock remaining available for issuance under the 2015 Plan. The number of shares reserved shall be cumulatively increased on January 1, 2019 and each January 1 thereafter by 4% of the number of shares of the Company's common stock outstanding on the immediately preceding December 31 or a lesser number of shares determined by the Company's board of directors. The shares of common stock underlying any awards that are forfeited, canceled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, repurchased or are otherwise terminated by the Company under the 2018 Plan or the 2015 Plan will be added back to the shares of common stock available for issuance under the 2018 Plan. As of December 31, 2018, 2,793,738 shares remained available for future issuance under the 2018 Plan. The number of authorized shares reserved for issuance under the 2018 Plan was increased by 1,202,319 shares effective as of January 1, 2019.

2018 Employee Stock Purchase Plan

On March 16, 2018, the Company's stockholders approved the 2018 Employee Stock Purchase Plan (the "ESPP"), which became effective on March 28, 2018. A total of 314,000 shares of common stock were reserved for issuance under this plan. In addition, the number of shares of common stock that may be issued under the ESPP will automatically increase on January 1, 2019, and each January 1 thereafter through January 1, 2027, by the least of (i) 500,000 shares of common stock, (ii) 1% of the number of shares of the Company's common stock outstanding on the immediately preceding December 31 or (iii) such lesser number of shares as determined by the ESPP administrator. The number of authorized shares reserved for issuance under the ESPP was increased by 300,580 shares effective as of January 1, 2019.

Stock Option Valuation

The fair value of stock option grants is estimated using the Black-Scholes option-pricing model. The Company historically had been a private company and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. For options with service-based vesting conditions, the expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

The following table presents, on a weighted average basis, the assumptions used in the Black-Scholes option-pricing model to determine the fair value of stock options granted to employees and directors:

	Year Ended December 31,	
	2018	2017
Risk-free interest rate	2.64%	1.81%
Expected volatility	67.40%	66.77%
Expected dividend yield	—	—
Expected life (in years)	6.07	6.06

The following table summarizes the Company's option activity since December 31, 2017:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2017	3,156,939	$ 4.01		
Granted	929,231	12.00		
Exercised	(225,252)	2.71		
Forfeited	(198,936)	7.54		
Outstanding as of December 31, 2018	3,661,982	$ 5.92	6.2	$ 5,019
Vested and expected to vest as of December 31, 2018	3,661,982	$ 5.92	6.2	$ 5,019
Options exercisable as of December 31, 2018	2,086,919	$ 2.89	5.0	$ 4,873

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had strike prices lower than the fair value of the Company's common stock.

The aggregate intrinsic value of options exercised during the years ended December 31, 2018 and 2017 was $1.6 million and less than $0.1 million, respectively.

The weighted average grant-date fair value of awards granted during the years ended December 31, 2018 and 2017 was $6.50 per share and $5.39 per share, respectively.

As of December 31, 2018, there were outstanding unvested service-based stock options held by non-employees for the purchase of 18,566 shares of common stock.

The Company recorded stock-based compensation expense in the following expense categories of its consolidated statements of operations and comprehensive loss (in thousands):

	Year Ended December 31,	
	2018	2017
Research and development expenses	$ 2,184	$ 1,159
General and administrative expenses	904	182
Total	$ 3,088	$ 1,341

As of December 31, 2018, total unrecognized compensation cost related to the unvested stock-based awards was $8.6 million, which is expected to be recognized over a weighted average period of 2.6 years.

11. Income Taxes

2017 U.S. Tax Reform

On December 22, 2017, the Tax Cuts and Jobs Act (the "TCJA") was signed into United States law. The TCJA includes a number of changes to existing tax law, including, among other things, a permanent reduction in the federal corporate income tax rate from 34% to 21%, effective as of January 1, 2018, as well as 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 tax rate change resulted in (i) a reduction in the gross amount of the Company's deferred tax assets recorded as of December 31, 2017, without an impact on the net amount of its deferred tax assets, which are recorded with a full valuation allowance, and (ii) no income tax expense or benefit being recognized as of the enactment date of the TCJA. The Company finalized its accounting for the income tax effects of TCJA during 2018, with no adjustment to the provisional amounts previously recorded.

Income Taxes

During the years ended December 31, 2018 and 2017, the Company recorded no current or deferred income tax benefits for the net operating losses or research and development tax credits generated in each year due to its uncertainty of realizing a benefit from those items. The Company had no foreign operating losses.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2018	2017
Federal statutory income tax rate	(21.0)%	(34.0)%
State taxes, net of federal benefit	(6.2)	(5.1)
Federal and state research and development tax credits	(4.2)	(7.6)
Federal research and development tax credit add-back	—	2.3
Nondeductible items	0.7	1.3
2017 Tax Acts and Jobs Cut	—	21.9
Increase in deferred tax asset valuation allowance	30.7	21.2
Effective income tax rate	0.0%	0.0%

Net deferred tax assets as of December 31, 2018 and 2017 consisted of the following (in thousands):

	December 31, 2018	December 31, 2017
Deferred tax assets:		
Net operating loss carryforwards	19,189	$ 8,211
Research and development and investment tax credits	4,891	3,467
Deferred revenue	3,294	3,693
Accrued expenses	437	491
Capitalized start-up costs	93	102
Capitalized research and development expense	60	73
Other	933	574
Total deferred tax assets	28,897	16,611
Valuation allowance	(28,897)	(16,611)
Net deferred tax assets	$ —	$ —

As of December 31, 2018, the Company had U.S. federal and state net operating loss carryforwards of $69.8 million and $71.7 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2035. The 2018 federal net operating loss of $39.6 million is available to be carried forward indefinitely but can only offset 80% of taxable income per year. As of December 31, 2018, the Company also had U.S. federal and state research and development tax credit carryforwards of $4.0 million and $0.9 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2034 and 2030, respectively. As of December 31, 2018, the Company has Massachusetts investment tax credits of $0.2 million which generally have a 3 year carryover period.

Utilization of the U.S. federal and state net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, and corresponding provisions of state law, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the federal and state net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, 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 limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2018 and 2017. Management reevaluates the positive and negative evidence at each reporting period.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2018 and 2017 related primarily to the increase in net operating loss carryforwards and research and development tax credit carryforwards, partially offset in 2017 by a decrease in deferred tax assets resulting from the decreased federal corporate tax rate, and were as follows (in thousands):

	Year Ended December 31,	
	2018	2017
Valuation allowance as of beginning of year	$ 16,611	$ 11,208
Decreases recorded as benefit to income tax provision	—	(5,575)
Increases recorded to income tax provision	12,286	10,978
Valuation allowance as of end of year	$ 28,897	$ 16,611

As of December 31, 2018 and 2017, the Company had not recorded any amounts for unrecognized tax benefits. The Company files income tax returns in the U.S. and Massachusetts. The statute of limitations for assessment by the Internal Revenue Service and Massachusetts tax authorities remains open for all years since 2015. The Company's tax attributes related to years prior to 2015 can still be adjusted under audit. No federal or state tax audits are currently in process.

12. Commitments and Contingencies

Operating Leases

The Company leases its facility under a non-cancelable operating lease that expires in April 2023. Under the terms of the lease, the Company secured a $1.3 million letter of credit as security for its leased facility. The underlying cash securing this letter of credit has been classified as non-current restricted cash in the accompanying consolidated balance sheets. The lease includes annual rent escalations, which are accrued, such that rent expense is recognized on a straight-line basis over the terms of occupancy.

Future minimum lease payments under the operating lease as of December 31, 2018 are as follows (in thousands):

Year Ending December 31,	
2019	1,878
2020	1,933
2021	1,989
2022	2,046
2023	689
	$8,535

Rent expense for the years ended December 31, 2018 and 2017 was $1.8 million and $1.8 million, respectively.

In January 2017, the Company entered into a 12-month sublease agreement with a tenant for up to 2,500 square feet of general office and laboratory space at its headquarters. In December 2017, the Company entered into a new sublease agreement with a tenant for approximately 5,000 square feet of general office and laboratory space at its headquarters. The sublease ended in June 2018. The Company recognized $0.3 million and $0.3 million received under the subleases as other income in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2018 and 2017, respectively.

License Agreement

Under its license agreement with National University of Singapore and St. Jude Children's Research Hospital, Inc. (collectively the "Licensors") entered into in 2014, the Company is obligated to pay license maintenance fees on each anniversary of the effective date of the agreement that escalate from less than $0.1 million for each of the first seven years to $0.1 million on the eighth anniversary and each year thereafter. The Company is also obligated to make aggregate milestone payments of up to 5.5 million Singapore dollars (equivalent to approximately $4.0 million as of December 31, 2018) upon the achievement of specified clinical and regulatory milestones and to pay tiered royalties ranging in the low single-digit percentages on annual net sales of licensed products sold by the Company or its sublicensees. The royalties are payable on a product-by-product and country-by-country basis and may be reduced in specified circumstances. Additionally, under certain circumstances, the Company is obligated to pay the Licensors a percentage of amounts received from sublicensees.

The license agreement will expire on a country-by-country basis until the last to expire of the patents and patent applications covering such licensed product or service. The Licensors may terminate the license agreement within 60 days after written notice in the event of a breach of contract. The Licensors may also terminate the agreement upon written notice in the event of the Company's bankruptcy, liquidation, or insolvency. In addition, the Company has the right to terminate this agreement in its entirety at will upon 90 days' advance written notice to the Licensors. However, if the Company has commenced the commercialization of licensed products, the Company can only terminate at will if it ceases all development and commercialization of licensed products.

Manufacturing Commitment

As of December 31, 2018, the Company had non-cancelable minimum purchase commitments under contract manufacturing agreements for payments totaling $1.5 million over the following 12 months.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and its executive officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2018 or 2017.

Legal Proceedings

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

13. 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):

	Year Ended December 31,	
	2018	2017
Numerator:		
Net loss	$ (34,532)	$ (25,492)
Accretion of redeemable convertible preferred stock to redemption value	(16)	(65)
Net loss attributable to common stockholders	$ (34,548)	$ (25,557)
Denominator:		
Weighted average common shares outstanding, basic and diluted	24,895,670	10,191,807
Net loss per share attributable to common stockholders, basic and diluted	$ (1.39)	$ (2.51)

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 common shares 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 common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	December 31,	
	2018	2017
Redeemable convertible preferred shares (as converted to common stock)	—	13,229,362
Stock options to purchase common stock	3,661,982	3,156,939
	3,661,982	16,386,301

14. Retirement Plan

The Company has a defined-contribution plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pre-tax basis. As currently established, the Company is not required to make and to date has not made any contributions to the 401(k) Plan. The Company did not make any matching contributions during the years ended December 31, 2018 or 2017.

15. Selected Quarterly Financial Data (Unaudited)

The following information has been derived from unaudited financial statements that, in the opinion of management, include all recurring adjustments necessary for a fair statement of such information (in thousands except per share data):

	Mar 31, 2017	Jun 30, 2017	Sep 30, 2017	Dec 31, 2017	Mar 31, 2018	Jun 30, 2018	Sep 30, 2018	Dec 31, 2018
Statements of Operations Data:								
Revenue	$ 1,827	$ 2,079	$ 2,331	$ 2,123	$ 2,220	$ 1,666	$ 2,043	$ 3,805
Loss from operations	(6,069)	(6,033)	(7,170)	(6,880)	(6,986)	(9,439)	(10,576)	(9,004)
Net loss	(5,939)	(5,863)	(7,000)	(6,690)	(6,735)	(9,023)	(10,168)	(8,606)
Net loss attributable to common stockholders	(5,955)	(5,880)	(7,016)	(6,706)	(6,751)	(9,023)	(10,168)	(8,606)
Basic and diluted net loss attributable to common stockholders per share:	$ (0.58)	$ (0.58)	$ (0.69)	$ (0.66)	$ (0.66)	$ (0.31)	$ (0.34)	$ (0.29)

16. Subsequent Events

In January 2019, the Company amended the Loan Agreement (see Note 7) to extend the available date for borrowings from January 19, 2019 to June 30, 2019 and extend the interest only period from January 19, 2019 to June 30, 2020, with the possibility of further extension to March 31, 2021 if certain equity financing considerations are met. Additionally, the loan repayment period will be over a 24-month period following the end of the interest-only period.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and President and our Vice President of Finance (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2018. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2018, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Internal Control Over Financial Reporting

Management's Report on Internal Control Over Financial Reporting

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

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended December 31, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item 10 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) 1. *Financial Statements*

For a list of the financial statements included herein, see Index to the Financial Statements on page 113 of this Annual Report on Form 10-K, incorporated into this Item by reference.

2. *Financial Statement Schedules*

Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the financial statements or the notes thereto.

3. *Exhibits*

See the Exhibit Index in Item 15(b) below.

(b) **Exhibit Index.**

Exhibit Number	Description
3.1	Form of Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)
3.2	Form of Amended and Restated Bylaws (incorporated by reference to Exhibit 3.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)
4.1	Form of Stock Purchase Agreement between the Registrant and Seattle Genetics, Inc. (incorporated by reference to Exhibit 4.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)
10.1	Form of Director Indemnification Agreement (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)
10.2	Form of Officer Indemnification Agreement (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)
10.3#	Employment Agreement by and between the Registrant and Charles Wilson (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)
10.4#	Employment Agreement by and between the Registrant and Michael Vasconcelles (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)
10.5#	Employment Agreement by and between the Registrant and Christiana Stamoulis (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)
10.6#	Unum Therapeutics Inc. 2018 Stock Option and Incentive Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)
10.7#	Unum Therapeutics Inc. 2018 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)

Exhibit Number	Description
10.8#	Unum Therapeutics Inc. Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)
10.9	Loan and Security Agreement by and between the Registrant and Pacific Western Bank dated as of January 19, 2017 (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1 (File No. 333-223414) filed March 19, 2018)
10.10*	First Amendment to Loan and Security Agreement with Pacific Western Bank dated as of July 6, 2018
10.11	Second Amendment to Loan and Security Agreement by and between Pacific Western Bank and Registrant dated as of January 18, 2019 (incorporated by reference to Exhibit 10.1 to the Registrant's Form 8-K (File No. 001-38443) filed January 23, 2019)
23.1*	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.
31.1*	Certification of Chief Executive Officer of the Registrant Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Chief Financial Officer of the Registrant Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*†	Certification of Chief Executive Officer of the Registrant Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*†	Certification of Chief Financial Officer of the Registrant Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101INS*	XBRL Instance Document.
101SCH*	XBRL Taxonomy Extension Schema Document.
101CAL*	XBRL Taxonomy Extension Calculation Linkbase Document.
101LAB*	XBRL Taxonomy Extension Labels Linkbase Document.
101PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.
101DEF*	XBRL Taxonomy Extension Definition Linkbase Document.

* Filed herewith.

\# Indicates management contract or compensation plan.

(1) Schedules and exhibits have been omitted from this filing pursuant to Item 601(b)(2) of Regulation S-K. The registrant agrees to furnish supplementally a copy of any omitted schedule or exhibit to the Securities and Exchange Commission upon its request; provided, however, that the registrant may request confidential treatment pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended, for any schedule or exhibit so furnished.

† The certifications attached as Exhibits 32.1 and 32.2 that accompany this Annual Report on Form 10-K, are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of Unum Therapeutics Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 28, 2019

UNUM THERAPEUTICS INC.

By: /s/ Charles Wilson
Charles Wilson, Ph.D.
Chief Executive Officer and President

Pursuant to the requirements of the Securities Act of 1934, this report has been signed by the following persons on behalf of the registrant and in the capacities indicated on March 28, 2019:

Signature	Title(s)
/s/ Charles Wilson Charles Wilson, Ph.D.	Chief Executive Officer, President and Director (Principal Executive Officer)
/s/ John Green John Green	Vice President, Finance (Principal Financial and Accounting Officer)
/s/ Bruce Booth Bruce Booth, DPhil.	Director
/s/ Jörn Aldag Jörn Aldag	Director
/s/ Karen Ferrante Karen Ferrante, M.D.	Director
/s/ Robert J. Perez Robert J. Perez	Director
/s/ Liam Ratcliffe Liam Ratcliffe, M.D., Ph.D.	Director

FIRST AMENDMENT
TO
LOAN AND SECURITY AGREEMENT

This First Amendment to Loan and Security Agreement (this "***Amendment***") is entered into as of July 6, 2018, by and between PACIFIC WESTERN BANK, a California state chartered bank ("***Bank***"), and UNUM THERAPEUTICS, INC. ("***Borrower***"),

RECITALS

Borrower and Bank are parties to that certain Loan and Security Agreement dated as of January 19, 2017 (as amended from time to time, the "**Agreement**"). The parties desire to amend the Agreement in accordance with the terms of this Amendment.

NOW, THEREFORE, the parties agree as follows:

1) Pursuant to Section 6.2(i) of the Agreement (as in effect immediately prior to the effectiveness of this Amendment), Borrower is required to deliver to Bank, within 30 days after the last day of each month, a company prepared consolidated balance sheet, income statement, and statement of cash flows covering Borrower's operations during such period (the "Monthly Financials"). As of the date hereof, Borrower has not delivered to Bank its Monthly Financials for the reporting periods ending April 30, 2018 and May 31, 2018, resulting in violations of the Agreement (the "Monthly Financials Violations"), Bank hereby waives the Monthly Financials Violations.

2) Section 6.2(i) of the Agreement is hereby amended and restated, as follows:

(i) as soon as available, but in any event within 30 days after the end of each calendar month, a company prepared consolidated balance sheet, income statement, and statement of cash flows covering Borrower's operations during such period, in a form reasonably acceptable to Bank and certified by a Responsible Officer; provided, however, that if Borrower's Cash at Bank is greater than two (2) times Borrower's outstanding Indebtedness to Bank, then Borrower shall instead provide to Bank, within five (5) days after the filing thereof, Borrower's periodic financial reporting filed with the Securities and Exchange Commission on Forms 10-K and 10-Q;

3) Unless otherwise defined, all initially capitalized terms in this Amendment shall be as defined in the Agreement. The Agreement, as amended hereby, shall be and remain in full force and effect in accordance with its respective terms and hereby is ratified and confirmed in all respects. Except as expressly set forth herein, the execution, delivery, and performance of this Amendment shall not operate as a waiver of, or as an amendment of, any right, power, or remedy of Bank under the Agreement, as in effect prior to the date hereof. Borrower ratifies and reaffirms the continuing effectiveness of all agreements entered into in connection with the Agreement.

4) Borrower represents and warrants that the representations and warranties contained in the Agreement are true and correct as of the date of this Amendment.

5) This Amendment may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one instrument.

6) As a condition to the effectiveness of this Amendment, Bank shall have received, in form and substance satisfactory to Bank, the following:

   a) this Amendment, duly executed by Borrower;

   b) payment of all Bank Expenses, including Bank's expenses for the documentation of this amendment and any related documents, and any UCC, good standing or intellectual property search or filing fees, which may be debited from any of Borrower's accounts; and

   c) such other documents and completion of such other matters, as Bank may reasonably deem necessary or appropriate.

[Signature Page Follows]

IN WITNESS WHEREOF, the undersigned have executed this Amendment as of the first date above written.

UNUM THERAPEUTICS INC.		**PACIFIC WESTERN BANK**	
By:	/s/ Christiana Stamoulis	By:	/s/ Scott Hansen
Name:	Christiana Stamoulis	Name:	Scott Hansen
Title:	President and CFO	Title:	SVP

[Signature Page to First Amendment to Loan and Security Agreement]

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-224137) of Unum Therapeutics Inc. of our report dated March 28, 2019 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 28, 2019

Exhibit 31.1

CERTIFICATIONS

I, Charles Wilson, certify that:

1. I have reviewed this Annual Report on Form 10-K of Unum Therapeutics Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the Company and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 28, 2019

By: /s/ Charles Wilson
Charles Wilson, Ph.D.
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, John Green, certify that:

1. I have reviewed this Annual Report on Form 10-K of Unum Therapeutics Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the Company and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 28, 2019

By: /s/ John Green
John Green
Vice President, Finance
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,

AS ADOPTED PURSUANT TO

SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Unum Therapeutics Inc. (the "Company") for the fiscal year ended December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Charles Wilson, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 28, 2019

By: /s/ Charles Wilson
Charles Wilson, Ph.D.
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,

AS ADOPTED PURSUANT TO

SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Unum Therapeutics Inc. (the "Company") for the fiscal year ended December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, John Wagner, Chief Financial Officer and Treasurer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 28, 2019

By: /s/ John Green
John Green
Vice President, Finance
(Principal Financial Officer)