ARGOS THERAPEUTICS INC

FORM 10-K
(Annual Report)

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

FORM 10-K

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

For the fiscal year ended December 31, 2017

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

Commission File Number 001-35443

ARGOS THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware 56-2110007
(State or other jurisdiction of incorporation or organization) (I.R.S. Employer
Identification No.)

4233 Technology Drive
Durham, North Carolina 27704
(Address of principal executive offices) (Zip Code)

Registrant’s telephone number, including area code: (919) 287-6300

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 Section 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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post 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 registrant’s knowledge, in definitive proxy 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 ☒  (Do not check if a smaller reporting company)  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 ☒

As of June 30, 2017 (the last business day of the registrant’s most recently completed second fiscal quarter), the aggregate market value of the registrant’s common stock held by non-affiliates was approximately $7.5 million based upon the closing price for shares of the registrant’s common stock of $7.262 as reported by The Nasdaq Global Market on that date.

As of February 28, 2018, there were 7,909,765 shares outstanding of the registrant’s common stock, par value $0.001 per share.
ARGOS THERAPEUTICS, INC.
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For the Year Ended December 31, 2017
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Argos Therapeutics®, Argos® and Arcelis™, the Argos Therapeutics logo and other trademarks or service marks of Argos appearing in this Annual Report on Form 10-K are the property of Argos Therapeutics, Inc. The other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

Unless otherwise indicated, all information in this Annual Report on Form 10-K gives effect to a 1-for-20 reverse stock split of Argos’s common stock that became effective on January 18, 2018.

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This Annual Report on Form 10-K, including “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations,” contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “predict,” “project,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the progress and timing of our development and commercialization activities;
- the timing and conduct and design of our Phase 3 ADAPT clinical trial of rocapuldencel-T in combination with sunitinib / standard-of-care for the treatment of metastatic renal cell carcinoma, or mRCC, including the completion of the trial and the availability of the data from the trial, and our discussions with the U.S. Food and Drug Administration regarding the ADAPT trial and the pathway to registration for rocapuldencel-T;
- the timing and conduct of our planned investigator-initiated Phase 2 clinical trial of rocapuldencel-T, including the timing of the initiation, enrollment and completion of the trial and the availability of data from the trial;
- the timing and conduct of the ongoing investigator-initiated Phase 2 clinical trial of AGS-004 for HIV eradication and the planned investigator-initiated Phase 2 clinical trial of AGS-004 for long-term viral control in pediatric patients, including the timing of the initiation, enrollment and the completion of the trials and the availability of data from the trials;
- our ability to obtain U.S. and foreign marketing approval for rocapuldencel-T for the treatment of mRCC and for AGS-004 for the treatment of HIV, and the ability of these product candidates to meet existing or future regulatory standards;
- the potential benefits of our Arcelis precision immunotherapy technology platform and our Arcelis-based product candidates;
- our intellectual property position and strategy;
- our expectations related to the sufficiency of our cash, cash equivalents and short-term investments;
- the accuracy of our estimates of the size and characteristics of the markets that may be addressed by our product candidates;
- our ability to establish and maintain collaborations for the development and commercialization of our product candidates;
- developments relating to our competitors and our industry; and
- the impact of government laws and regulations.

We have based these forward-looking statements largely on our current plans, intentions, expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in “Item 1A. Risk Factors,” that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.
You should read this Annual Report on Form 10-K with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of filing of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements, except as required by applicable law.

This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. This Annual Report on Form 10-K also includes data based on our own internal estimates. While we believe these industry publications and third party research, surveys and studies are reliable, we have not independently verified such data.
Item 1. Business

We are an immuno-oncology company focused on the development and commercialization of individualized immunotherapies for the treatment of cancer and infectious diseases based on our proprietary precision immunotherapy technology platform called Arcelis.

Our most advanced product candidate is rocapuldencel-T (formerly referred to as AGS-003), which we are developing for the treatment of metastatic renal cell carcinoma, or mRCC, and other cancers. We are conducting a pivotal Phase 3 clinical trial of rocapuldencel-T plus sunitinib (or another targeted therapy) vs. sunitinib (or another targeted therapy) monotherapy for the treatment of newly diagnosed mRCC. We refer to this trial as the ADAPT trial. We dosed the first patient in the ADAPT trial in May 2013 and completed enrollment of the trial in July 2015.

Under the protocol for the trial, a series of interim analyses have been conducted by the independent data monitoring committee, or IDMC, for the trial to evaluate safety, efficacy and futility. The most recent interim analysis was conducted in February 2017 (data cut-off as of February 3, 2017) after 75% of the originally targeted pre-specified number of 290 events for the analysis of the original primary endpoint of overall survival had occurred. At this interim analysis, the IDMC concluded that the trial was unlikely to demonstrate a statistically significant improvement in overall survival in the combination treatment arm, utilizing the intent-to-treat population, the original primary endpoint. The IDMC therefore recommended that the trial be discontinued for futility. The IDMC also noted that rocapuldencel-T had been generally well-tolerated in the trial.

Notwithstanding the IDMC recommendation, we considered the data too immature to observe the delayed treatment effect often observed with immunotherapy and decided to continue to conduct the trial pending further review and analysis of the data and discussions with the U.S. Food and Drug Administration, or FDA. This determination was made after discussion of the results of the interim analysis with the ADAPT trial principal investigators. In determining to continue the trial, we considered, among other factors, the degree of maturity of the data set at the time of the interim analysis, the mechanism of action of rocapuldencel-T, which involves the induction of long-term memory immune responses, and the IDMC’s assessment of the safety profile of rocapuldencel-T. This determination was also supported by the extended durability of tumor responses observed in patients treated with rocapuldencel-T plus sunitinib in the trial. At the time of the IDMC’s February 2017 interim analysis, the median duration of follow-up was 20 months and more than half the patients in both treatment groups were still alive.

In May 2017, we met with the FDA to discuss the ADAPT trial and the future direction of the rocapuldencel-T program. Following that meeting, we determined to continue the ADAPT trial until at least the pre-specified number of 290 events occurs and to submit to the FDA a protocol amendment to increase the pre-specified number of events for the primary analysis of overall survival in the trial beyond 290 events. We believe that extending our evaluation of rocapuldencel-T beyond 290 events in the trial could enhance our ability to observe rocapuldencel-T’s expected delayed treatment effect.

We are currently finalizing an amendment to the ADAPT protocol, including an amended primary endpoint analysis, and plan to submit it to the FDA prior to the interim data analysis planned for the second quarter of 2018, at which time approximately 55 new events (deaths) are expected to have occurred subsequent to the February 2017 interim analysis. We are planning to include the following four co-primary endpoints in the amended ADAPT protocol:

- Overall survival for all randomized patients when approximately 375 events have occurred (under the same analysis that was originally planned for 290 events);
- The percentage of patients surviving at least five years;
- Overall survival for patients who remained alive at the time of the February 2017 interim analysis, to be evaluated when approximately 155 new events have occurred; and
- Overall survival for all patients for whom at least 12 months of follow-up is available (excluding patients who died or were lost to follow-up within the first 12 months after enrollment).

In connection with our amendment of the ADAPT protocol, the special protocol assessment, or the SPA, for the ADAPT trial ceased to be in effect. Additionally, we are developing a protocol for a Phase 2 clinical trial of rocapuldencel-T in combination with a checkpoint inhibitor for the treatment of patients with mRCC, but we do not intend to initiate this trial unless and until we obtain financing to fund the trial.

In addition, we are developing AGS-004, our second Arcelis-based product candidate, for the treatment of HIV. We have completed Phase 1 and Phase 2 trials funded by government grants and a Phase 2b trial that was funded in full by the National Institutes of Health, or NIH, and the National Institute of Allergy and Infectious Diseases, or NIAID. We are currently supporting an ongoing investigator-initiated clinical trial of AGS-004 in adult HIV patients evaluating the use of AGS-004 in combination with vorinostat, a latency reversing drug, for HIV eradication and plan to support an investigator-initiated Phase 2 clinical trial of AGS-004 evaluating AGS-004 for long-term viral control in pediatric patients provided that results from our investigator-initiated clinical trial in adult HIV patients are favorable and government funding is obtained.
Our Arcelis Platform

Our proprietary Arcelis precision immunotherapy technology platform utilizes biological components from a patient’s own cancer cells or virus to generate individualized immunotherapies. These immunotherapies employ specialized white blood cells called dendritic cells to activate an immune response specific to the patient’s own disease. Arcelis is based on the work of Dr. Ralph Steinman, winner of the 2011 Nobel Prize in medicine for the discovery of the role of dendritic cells in the immune system. We believe that our Arcelis-based immunotherapies may be applicable to a wide range of cancers and infectious diseases and have the following attributes that we consider critical to a successful immunotherapy:

- target a patient’s disease-specific antigens, including mutated antigens, or neoantigens, to elicit a potent immune response that is specific to the patient’s own disease;
- overcome the immune suppression that exists in cancer and infectious disease patients;
- induce memory T-cells, a specialized type of immune cell that is known to correlate with improved clinical outcomes for cancer and HIV patients;
- have minimal toxicity; and
- can be produced using a centralized manufacturing process.

Despite our setback with respect to rocapuldencel-T, we continue to believe that our immunotherapies combine the advantages of other approaches to immunotherapy, including approaches to facilitate antigen recognition and approaches to overcome immune suppression such as checkpoint inhibition, while addressing limitations that these approaches present.

Our Development Programs

The following table summarizes our development programs for rocapuldencel-T and AGS-004.

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>Primary Indication</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rocapuldencel-T</td>
<td>mRCC</td>
<td>• Ongoing ADAPT trial; enrollment completed in July 2015; IDMC recommended study discontinuation for futility in February 2017; ongoing discussions with FDA regarding protocol amendment and statistical analysis plan; interim analysis planned for second quarter of 2018</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Planned Phase 2 clinical trial in combination with a checkpoint inhibitor expected to open for enrollment as early as the first half of 2019 subject to supportive data from the ADAPT trial and discussions with the FDA and our obtaining financing to fund the trial.</td>
</tr>
<tr>
<td>AGS-004</td>
<td>HIV</td>
<td>• Ongoing second stage of investigator-initiated clinical trial in combination with vorinostat for HIV eradication</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Planned investigator-initiated Phase 2 clinical trial for long-term viral control in pediatric patients provided that results from ongoing trial in adult HIV patients are favorable and government funding and necessary approvals are obtained</td>
</tr>
</tbody>
</table>

We hold all commercial rights to rocapuldencel-T and AGS-004 in all geographies other than rights to rocapuldencel-T in Russia and the other states comprising the Commonwealth of Independent States, which we exclusively licensed to Pharmstandard International S.A., or Pharmstandard, rights to rocapuldencel-T for the treatment of mRCC in South Korea, which we exclusively licensed to Green Cross Corp., or Green Cross, and rights to rocapuldencel-T in China, Hong Kong, Taiwan and Macau, which we exclusively licensed to Lumy (Hong Kong) Co. Ltd., or Lumy HK. We have granted to MEDcell Co., Ltd., a wholly-owned subsidiary of Medinet Co. Ltd., hereinafter referred to together as “Medinet,” an exclusive license to manufacture rocapuldencel-T for the treatment of mRCC in Japan.
We are developing rocapuldencel-T for the treatment of mRCC and other cancers. We are conducting the ADAPT trial of rocapuldencel-T plus sunitinib / targeted therapy for the treatment of newly diagnosed mRCC. We dosed the first patient in the ADAPT trial in May 2013. In July 2015 we completed enrollment in the ADAPT trial, enrolling 462 patients with the goal of generating 290 events for the original primary endpoint of overall survival. We enrolled these patients at 107 clinical sites in North America, Europe and Israel. Under the ADAPT trial protocol, these patients were randomized between the rocapuldencel-T plus sunitinib / targeted therapy combination arm and sunitinib / targeted therapy alone control arm on a two-to-one basis.

In February 2017, the IDMC for the ADAPT trial recommended that the trial be discontinued for futility based on its planned interim data analysis. The IDMC concluded that the trial was unlikely to demonstrate a statistically significant improvement in overall survival in the combination treatment arm, utilizing the intent-to-treat population at the pre-specified number of 290 events (deaths), the original primary endpoint of the study. Notwithstanding the IDMC’s recommendation, we determined to continue to conduct the trial while we analyzed interim data from the trial. Following a meeting with the FDA, we determined to continue the ADAPT trial until at least the pre-specified number of 290 events occurs and to submit to the FDA a protocol amendment to increase the pre-specified number of events for the primary analysis of overall survival in the trial beyond 290 events. We believe that extending our evaluation of rocapuldencel-T beyond 290 events in the trial could enhance our ability to observe rocapuldencel-T’s expected delayed treatment effect.

We are currently finalizing an amendment to the ADAPT protocol, including an amended primary endpoint analysis, and plan to submit it to the FDA prior to the interim data analysis planned for the second quarter of 2018, at which time approximately 55 new events (deaths) are expected to have occurred subsequent to the February 2017 interim analysis. We are planning to include the following four co-primary endpoints in the amended ADAPT protocol:

- Overall survival for all randomized patients when approximately 375 events have occurred (under the same analysis that was originally planned for 290 events);
- The percentage of patients surviving at least five years;
- Overall survival for patients who remained alive at the time of the February 2017 interim analysis, to be evaluated when approximately 155 new events have occurred; and
- Overall survival for all patients for whom at least 12 months of follow-up is available (excluding patients who died or were lost to follow-up within the first 12 months after enrollment).

In connection with our amendment of the ADAPT protocol, the SPA, for the ADAPT trial ceased to be in effect. Additionally, we are developing a protocol for a Phase 2 clinical trial of rocapuldencel-T in combination with a checkpoint inhibitor for the treatment of patients with mRCC, but we do not intend to initiate this trial unless and until we obtain financing to fund the trial.

**AGS-004**

We are developing AGS-004 for the treatment of HIV and are focusing this program on the use of AGS-004 in combination with other therapies for the eradication of HIV. We believe that by combining AGS-004 with therapies that are being developed to expose the virus in latently infected cells to the immune system, we can potentially eradicate the virus. The current standard of care, antiretroviral drug therapy, or ART, can reduce levels of HIV in a patient’s blood, increase the patient’s life expectancy and improve the patient’s quality of life. However, ART cannot eliminate the virus, which persists in latently infected cells, remains undetectable by the immune system and can recur. In addition, ART requires daily, life-long treatment and can have significant side effects.

We are supporting an investigator-initiated clinical trial of AGS-004 in up to 12 adult HIV patients to evaluate the use of AGS-004 in combination with vorinostat, a latency reversing therapy, for the eradication of HIV at the University of North Carolina. This trial is being conducted in two stages. Stage 1 of this trial has been completed and was designed to study immune response kinetics to AGS-004 in patients on continuous ART. These data were used to better define the optimal dosing strategy in combination with the latency reversing therapy vorinostat in the ongoing Stage 2. Some patients in Stage 1 have rolled over into Stage 2. The patient clinical costs for the first stage of this trial were funded by Collaboratory of AIDS Researchers for Eradication, or CARE. The NIH Division of AIDS has approved $6.6 million in funding for the second stage of this trial.

We also plan to determine whether to explore the use of AGS-004 monotherapy to provide long-term control of HIV viral load in otherwise immunologically healthy patients and eliminate their need for ART. Accordingly, if initial data from Stage 2 of the ongoing adult eradication study are favorable and government funding and necessary approvals are obtained, we expect to support an investigator-initiated Phase 2 clinical trial of AGS-004 monotherapy in pediatric patients infected with HIV who have otherwise healthy immune systems and have been treated with ART since birth or shortly thereafter and, as a result, are lacking the antiviral memory T-cells to combat the virus. The commencement of this trial is subject to supportive data obtained from the adult eradication trial and approval of the protocol by the principal investigator(s), institutional review boards, the IMPAACT Network leadership and the FDA and to the agreement by the NIH to fund the trial costs not related to AGS-004 manufacturing.
Our goal is to become a leading biopharmaceutical company focused on discovering, developing and commercializing individualized immunotherapies for the treatment of a wide range of cancers and certain infectious diseases. Key elements of our strategy, all subject to the availability of financing, are as follows:

- complete clinical development and seek marketing approval of rocapuldencel-T for the treatment of mRCC, subject to our ongoing analysis of the preliminary ADAPT trial data set and our discussions with the FDA;
- expand clinical development of rocapuldencel-T including in mRCC in combination with a checkpoint inhibitor and in other advanced solid tumors;
- commercialize rocapuldencel-T in North America independently and with third parties outside North America;
- establish a facility or otherwise arrange for the commercial manufacture of our products based on our Arcelis platform;
- continue clinical development of AGS-004 for the treatment of HIV, potentially through government funding or other third party funding, and collaborate with third parties for commercialization on a worldwide basis; and
- enter into arrangements with third parties both to assist in the development and commercialization of our product candidates, particularly in international markets, and to in-license product candidates in order to expand our pipeline; and
- pursue expansion of our broad intellectual property protection for our Arcelis precision immunotherapy technology platform, product candidates and proprietary manufacturing processes through U.S. and international patent filings and maintenance of trade secret confidentiality.

Immunotherapy to Treat Cancer and Infectious Diseases

Cancer cells occur frequently in the human body, yet are effectively controlled by T-cells in the immune system, which recognize proteins produced by the cancer cells, known as antigens, as abnormal and kill the associated cancer cells. Two specific types of T-cells are necessary for an effective anti-cancer immune response: CD8+ T-cells, which kill cancer cells, and CD4+ T-cells, which provide a “help” signal that activates and directs the CD8+ T-cell response. Cancer cells utilize several strategies to escape detection by the immune system and T-cells. For example, cancer cells secrete factors that act systemically to prevent T-cells from responding to activation signals, resulting in the inability of T-cells to carry out their role of killing cancer cells. Chronic viral infections such as HIV or hepatitis C present the same challenges to the immune system as cancer because the immune system must overcome this disease-induced immune suppression to recognize and respond to virus-infected cells. Immunotherapy is intended to stimulate and enhance the body’s natural mechanism for recognizing and killing cancer cells and virus-infected cells. Current immunotherapeutic approaches to treat cancer can generally be separated into two different mechanisms of action: approaches to facilitate antigen recognition and approaches to overcome immune suppression.

Approaches to Facilitate Antigen Recognition

Cancer immunotherapies that use an antigen-based approach are designed to stimulate an immune response against one or more tumor-associated antigens. In most cases, the tumor-associated antigens that are being targeted are non-mutated, or normal, antigens, which are usually well tolerated by the immune system. In the context of cancer, these normal antigens are either produced at abnormally high levels or predominantly in tumor cells, or both. The goal of antigen-based immunotherapies is to activate the patient’s own immune system to seek out and kill the cancer cells that carry the targeted antigen. A limited number of antigen-based immunotherapies have been approved by the FDA such as Provenge (sipuleucel-T) for metastatic castrate-resistant prostate cancer, Kymriah (tisagenlecleucel) for B-cell precursor acute lymphoblastic leukemia, and Yescarta (axicabtagene ciloleucel) for certain types of large B-cell lymphomas. Because these immunotherapies are designed to target specific antigens, they are less likely to have toxicity than traditional cancer therapies. However, antigen-based immunotherapies based on shared or commonly overexpressed antigens may have limited efficacy because they are only able to target one or a limited number of antigens, which may or may not be present in the patient’s cancer cells, and do not capture mutated antigens specific to that patient’s tumor that can drive tumor growth.
Approaches to Overcome Immune Suppression

Immunotherapies that rely on approaches to overcome immune suppression are designed to block signaling pathways that prevent T-cell activation and function. The class of monoclonal antibody-based immunotherapies known as checkpoint inhibitors are being developed on the basis of this approach. For example, Bristol-Myers Squibb’s first FDA-approved immunotherapy Yervoy (ipilimumab), a treatment for patients with unresectable or metastatic melanoma, is designed to act by blocking the function of a protein expressed in activated T-cells called CTLA4, which acts as a T-cell “off” switch. By blocking the function of CTLA4, the patient’s T-cells can become activated, resulting in an immune response against tumors. Another pathway that immunotherapies are being developed to address is the PD-1/PD-L1 pathway. In this pathway, activated T-cells expressing the protein PD-1 are disabled when binding occurs between PD-1 and its ligand, PD-L1, which is expressed on tumor cells. Approved anti-PD-1/PD-L1 pathway checkpoint inhibitors and those being developed are designed to interrupt this pathway by binding to the PD-1 protein or the PD-L1 ligand to prevent them from binding with each other. Two anti-PD-1/PD-L1 pathway checkpoint inhibitors, Bristol-Myers Squibb’s nivolumab (Opdivo) and Merck’s pembrolizumab (Keytruda), are FDA approved for patients with several types of cancers, including, in the case of nivolumab, second line therapy of patients with mRCC. Positive results of a Phase 3 trial combining nivolumab and ipilimumab in front-line treatment of metastatic renal carcinoma have also been recently reported. However, not all patients respond to anti-PD-1/PD-L1 checkpoint inhibitors, and, in most cases, patients whose tumors predominantly express PD-L1 are most likely to respond. Immunotherapies that use checkpoint inhibition have demonstrated the ability to effectively overcome immunosuppression and enable T-cells to function against tumor cells and potentially virus-infected cells. However, these therapies are administered systemically to enable T-cells to function and are not designed to target tumor-specific differences, such as the unique mutations of an individual’s tumor. This lack of specificity can negatively impact healthy tissue and cause significant side effects.

Designing Immunotherapies Using Our Arcelis Platform

We believe that our proprietary Arcelis precision immunotherapy technology platform enables us to produce individualized immunotherapies that can combine the advantages of these approaches to immunotherapy while addressing the limitations and disadvantages of these approaches. We have designed our Arcelis platform to create product candidates which have attributes that we believe are critical to a successful immunotherapy:

1. **Target disease-specific antigens, including mutated antigens.** The immunotherapy should target antigens, including unique mutated antigens, associated with the patient’s disease. We believe that immunotherapies that target only non-mutated, or commonly shared, tumor-associated antigens will, in many cases, be limited in terms of efficacy as non-mutated antigens are generally poor at stimulating immune responses. Our Arcelis precision immunotherapy technology platform uses messenger RNA, or mRNA, from the patient’s own cancer or virus to yield an individualized immunotherapy that contains the patient’s disease-specific antigens, including mutated antigens, and is designed to elicit a potent immune response specific to the patient’s own disease.

2. **Overcome disease-induced immune suppression.** The immunotherapy must be able to generate an effective immune response in patients whose immune systems are compromised by their disease. Both tumors and HIV are known to impair the functionality of CD4+ T helper cells, which aid their escape from CD8+ T-cell attack. Our Arcelis-based immunotherapies do not require fully functioning CD4+ helper T-cells to mount an immune response with effective anti-tumor or anti-viral activity as we add the protein known as CD40 ligand, or CD40L, to provide the signaling that the CD4+ helper T-cells would otherwise provide.

3. **Induce memory T-cells.** The immunotherapy should be able to induce specific T-cells, such as CD8+CD28+ memory T-cells, which are known to correlate with improved clinical outcomes for cancer and HIV patients. These memory T-cells are long lived and necessary for a durable immune response. Our Arcelis process produces dendritic cells that secrete IL-12, which is necessary to induce and expand patient-specific CD8+CD28+ memory T-cells. These memory T-cells are able to seek out and kill cancer or virus-infected cells that express the antigens identical to those displayed on the surface of the dendritic cells.
• Have minimal toxicity. The immunotherapy should have minimal toxicity, which would potentially enable it to be combined with other therapies for cancer and infectious diseases. The mechanism of action of Arcelis-based products induces patient- and disease-specific memory T-cells. The antigen source and the dendritic cells that are both used for the therapy are both derived from the individual patient. This target customization and specificity is less likely to impact healthy tissue and cause toxicity. Our Arcelis-based product candidates have been well tolerated in clinical trials in more than 375 patients with no serious adverse events attributed to our immunotherapies.

Our Arcelis precision immunotherapy technology platform is focused on dendritic cells which present antigens to the attention of the human immune system, including, in particular, T-cells, and are critical to the immune system’s recognition of proteins derived from cancer cells or virus-infected cells. Dendritic cells are capable of internalizing cancer or virus protein antigens and displaying fragments of these protein antigens on their surface as small peptides. The dendritic cells then present these peptide antigens to T-cells. This allows the T-cells to bind to these peptide antigens and, in the case of cancer, target and kill cancer cells expressing these antigens and, in the case of infectious disease, target and kill virus-infected cells to control the spread of infectious virus.
The following graphic illustrates the processes comprising our Arcelis precision immunotherapy platform:

**ARCELIS: PATENTED HIGH-YIELD PROCESS**

At the clinical site. As shown in the graphic above, the manufacture of our Arcelis-based immunotherapies requires two components derived from the patient:

- A disease sample: In the case of cancer, the sample consists of tumor cells, and in the case of infectious disease, the sample consists of blood containing the virus. The disease sample is generally collected at the time of diagnosis or initial treatment.

- Monocytes: Monocytes are a type of white blood cell, which are obtained through a laboratory procedure called leukapheresis that occurs after diagnosis and at least three weeks prior to initiating treatment with our immunotherapy.

At the manufacturing facility. The tumor cells or the blood sample and the leukapheresis product are shipped to the manufacturing facility following collection at the clinical site. After receipt of these components at the facility, we take the following steps:

- We isolate the patient’s disease mRNA, which carries the genetic information to recreate the patient’s disease antigens, from the disease sample and amplify the mRNA so that only a small disease sample is required to manufacture the immunotherapy.

- Separately, we extract the monocytes from the leukapheresis product and culture them using a proprietary process to produce matured dendritic cells.
We then combine the matured dendritic cells with a solution of the patient’s isolated mRNA and a proprietary synthetic CD40L RNA. We apply a brief electric pulse to the solution in a process referred to as electroporation, which enables the patient’s mRNA and the CD40L RNA to pass into, or load, the dendritic cells. The dendritic cells process the CD40L RNA into CD40L protein, enabling the dendritic cells to secrete IL-12, a cytokine required to induce and expand CD8+CD28+ memory T-cells.

We then further culture the mRNA-loaded dendritic cells so that these cells allow for antigen expression from the patient’s mRNA and presentation in the form of peptides on the surface of the dendritic cells. These mature, loaded dendritic cells are formulated using the patient’s plasma that was collected during the leukapheresis to become the Arcelis-based product. Typically, several years of doses are produced for each patient.

After verifying the quality of the product, we vial, cryogenically freeze and then ship individual patient doses to the clinic, where each is thawed and administered by intradermal injection.

Patient treatment. Upon injection into the skin of the patient, the mature, loaded dendritic cells are intended to migrate to the lymph nodes near the site of the injection. It is at these lymph nodes that the dendritic cells come into contact with T-cells. This interaction with the loaded dendritic cells is intended to cause a measurable increase in patient- and disease-specific memory T-cells.

We believe that our Arcelis precision immunotherapy technology platform allows us to create individualized immunotherapies that may be capable of treating a wide range of cancers and infectious diseases using a centralized manufacturing process. Specifically, our Arcelis platform typically allows us to:

- produce several years of customized therapy on average for a patient from a small disease sample and a single leukapheresis from that patient;
- produce additional years of therapy for a patient at a later date with an additional leukapheresis enabling the collection of additional monocytes, but without requiring an additional disease sample from the patient;
- use a single manufacturing facility for North America, which is possible because our Arcelis process can utilize monocytes obtained through leukapheresis within four days of the procedure, and doses of our immunotherapies can be shipped frozen in a cryoshipper that can maintain the target temperature for at least ten days;
- cryopreserve the multiple doses generated from the single manufacturing process for each patient in a direct injectable formulation that allows the doses to remain stable and usable for up to five years; and
- produce immunotherapies that can be administered by intradermal injection in an outpatient procedure.

**Rocapuldencel-T for the Treatment of Metastatic Renal Cell Carcinoma and Other Cancers**

We are developing rocapuldencel-T for use in combination with sunitinib (or another targeted therapy) for the treatment of mRCC. Sunitinib is an oral small molecule drug sold under the trade name Sutent and is the current standard of care for initial treatment, or first-line treatment, of mRCC following diagnosis. In April 2012, the FDA notified us that we have obtained fast track designation for rocapuldencel-T for the treatment of mRCC.

We are conducting the ADAPT Phase 3 trial of rocapuldencel-T plus sunitinib (or another targeted therapy) compared to sunitinib (or another targeted therapy) monotherapy for the treatment of newly diagnosed mRCC. In July 2015 we completed enrollment in the ADAPT trial, enrolling 462 patients with the goal of generating 290 events for the original primary endpoint of overall survival. In February 2017, the IDMC for the ADAPT trial recommended that the trial be discontinued for futility based on its planned interim data analysis. The IDMC concluded that the trial was unlikely to demonstrate a statistically significant improvement in overall survival in the combination treatment arm, utilizing the intent-to-treat population at the pre-specified number of 290 events (deaths), the original primary endpoint of the study. Notwithstanding the IDMC’s recommendation, we determined to continue to conduct the trial while we analyzed interim data from the trial.
In May 2017, we met with the FDA to discuss the ADAPT trial and the future direction of the rocapuldencel-T program. Following that meeting, we determined to continue the ADAPT trial until at least the pre-specified number of 290 events occurs and to submit to the FDA a protocol amendment to increase the pre-specified number of events for the primary analysis of overall survival in the trial beyond 290 events. We believe that extending our evaluation of rocapuldencel-T beyond 290 events in the trial could enhance our ability to observe rocapuldencel-T’s expected delayed treatment effect.

We are currently finalizing an amendment to the ADAPT protocol, including an amended primary endpoint analysis, and plan to submit it to the FDA prior to the interim data analysis planned for the second quarter of 2018, at which time approximately 55 new events (deaths) are expected to have occurred subsequent to the February 2017 interim analysis. We are planning to include the following four co-primary endpoints in the amended ADAPT protocol:

- Overall survival for all randomized patients when approximately 375 events have occurred (under the same analysis that was originally planned for 290 events);
- The percentage of patients surviving at least five years;
- Overall survival for patients who remained alive at the time of the February 2017 interim analysis, to be evaluated when approximately 155 new events have occurred; and
- Overall survival for all patients for whom at least 12 months of follow-up is available (excluding patients who died or were lost to follow-up within the first 12 months after enrollment).

In connection with our amendment of the ADAPT protocol, the SPA, for the ADAPT trial ceased to be in effect. Additionally, we are developing a protocol for a Phase 2 clinical trial of rocapuldencel-T in combination with a checkpoint inhibitor for the treatment of patients with mRCC, but we do not intend to initiate this trial unless and until we obtain financing to fund the trial.

Renal Cell Carcinoma

RCC is the most common type of kidney cancer. The American Cancer Society, or ACS estimates that there were approximately 63,000 new cases of kidney cancer and approximately 14,000 deaths from this disease in the United States in 2016. The National Comprehensive Cancer Network, or NCCN estimates that 90% of kidney cancer cases are RCC. For patients with RCC that had metastasized by the time RCC was first diagnosed, a condition referred to as newly diagnosed mRCC, the five-year survival rate has historically been approximately 12%.

ACS statistics indicate that approximately 25% of newly diagnosed RCC patients present with mRCC in the United States. Additional patients who were initially diagnosed with earlier stage RCC may also progress to mRCC as these patients suffer relapses. The NCCN estimates between 20% to 30% of patients with early stage RCC will relapse within three years of surgical excision of the primary tumor. Although the National Cancer Institute, or NCI, does not provide prevalence of RCC by stage, based on the NCCN’s three-year relapse rate, we estimate that there may be up to an additional 10,000 to 15,000 cases of mRCC identified annually in the United States. Combining newly diagnosed mRCC patients with patients who relapse, we estimate that there may be between 20,000 to 25,000 new cases of mRCC in the United States each year. We estimate, based on publicly available information, including 2013 quarterly and annual reports of companies that market other therapies approved for mRCC, that the current worldwide mRCC market for these other therapies exceeds $2 billion.

Physicians generally diagnose mRCC by examining a tumor biopsy under a microscope. Upon evaluation of the visual appearance of the tumor cells, a pathologist will classify the mRCC into clear cell or non-clear cell types. According to the NCCN, approximately 80% of all RCC diagnoses are clear cell RCC. Because clear cell types are the most common type of tumor cell, most of the more recently approved therapies for mRCC have limited their clinical trials to patients with the clear cell type of tumor cell. However, the FDA has not limited the approval of these therapies to clear cell types of mRCC, so they may be used for both clear cell and non-clear cell types.

mRCC Patient Classification

Upon diagnosis, the prognosis for patients with mRCC is classified into three overall disease risk profiles — favorable, intermediate and poor — using objective prognostic risk factors. These risk factors were originally developed by researchers at Memorial Sloan Kettering Cancer Center and subsequently revised by Dr. Daniel Heng from the University of Calgary’s Baker Cancer Center and contributors from the International Metastatic Renal Cell Carcinoma Database Consortium, or the Consortium, based on clinical data from patients treated with sunitinib and other therapies. These risk factors, which we refer to as the Heng risk factors, have been correlated to adverse overall survival in mRCC and include:

- time from diagnosis to the initiation of systemic therapeutic treatment of less than one year, which is indicative of more aggressive disease. We refer to this risk factor as the less than one year to treatment risk factor;
- low levels of hemoglobin, a protein in the blood that carries oxygen;
• elevated corrected calcium levels;
• diminished overall patient performance status or physical functioning;
• elevated levels of neutrophils, a type of white blood cell; and
• elevated platelet count.

Patients exhibiting zero risk factors at the time of treatment are included in the favorable risk group; patients exhibiting one or two risk factors are included in the intermediate risk group; and patients exhibiting three or more risk factors are included in the poor risk group. Even when treated with standard of care therapies such as sunitinib, patients in the intermediate risk group have an expected survival of less than two years, and patients in the poor risk group have an expected survival of less than one year. In January 2013, Dr. Heng published in *Lancet Oncology* the following data from the Consortium database regarding overall survival of mRCC patients in these three risk groups treated with sunitinib and other therapies:

- in 157 favorable risk patients, the median overall survival was 43.2 months;
- in 440 intermediate risk patients, the median overall survival was 22.5 months; and
- in 252 poor risk patients, the median overall survival was 7.8 months.

**Current Treatment**

The initial treatment for most mRCC patients when the primary tumor is intact is surgical removal of the tumor, usually requiring partial or complete removal of the affected kidney, referred to as nephrectomy. The NCCN generally recommends systemic treatment with approved therapies for mRCC patients following nephrectomy for patients whose tumors have metastasized or for patients who present with mRCC upon diagnosis or as a result of a relapse from an earlier stage of RCC.

Historically, mRCC has been treated with non-specific, cytokine-based immunotherapies such as interferon α and IL-2, which have demonstrated a clinical benefit in a small percentage of mRCC patients. However, these therapies lack specificity and have been demonstrated to have severe toxicities, which can lead to cardiopulmonary, neuropsychiatric, dermatologic, renal, hepatic and hematologic side effects and limits their use. For example, although high-dose IL-2 is the only therapy to have demonstrated durable complete mRCC remissions, its toxicity restricts its use to a small minority of patients and for a short duration.

Several targeted therapies, such as Sutent (sunitinib), Votrient (pazopanib), Torisel (temsirolimus), Nexavar (sorafenib), Avastin (bevacizumab) plus interferon-α, Afinitor (everolimus), Inlyta (axitinib), Opdivo (nivolumab) and Cabometyx (cabozantinib) are approved for the treatment of mRCC. While most of these targeted therapies have been evaluated in first-line treatment of mRCC, Sutent demonstrated a higher rate of progression free survival and overall survival in its pivotal Phase 3 clinical trial than that shown by the other targeted therapies in their pivotal Phase 3 clinical trials. According to an independent market research survey conducted during the second half of 2014 of 87 US-based medical oncologists and new prescription data (IMS), Sutent was the first-line drug of choice for approximately half of newly treated advanced RCC patients. In addition, the data showed that the use of Votrient was increasing as initial therapy for advanced RCC.

Although most of these targeted therapies have demonstrated prolonged progression free survival as compared to interferon-α, they are rarely associated with durable remissions or enhanced long-term survival, particularly in patients who are classified as intermediate or poor risk at the time of treatment. In addition, each of these targeted therapies has shortcomings that limit their use in the treatment of mRCC, including significant toxicities, such as neutropenia and other hematologic toxicities, fatigue, diarrhea, hand-foot syndrome, hypertension and other cardiovascular effects. The overlapping and combined toxicities of the targeted therapies have prevented their use in combination therapies. For instance, researchers conducting a Phase 1 clinical trial of the combination of sunitinib and temsirolimus discontinued the trial due to toxicities. We believe that the inability to date to combine these therapies without additive toxicity and the absence of durable remissions and prolonged survival in patients with intermediate and poor risk disease indicates there is an unmet need for novel therapeutic approaches for mRCC that can improve efficacy without adding any appreciable toxicity. We determined to conduct the ADAPT trial based on our earlier belief that the combination of rocapuldencel-T with sunitinib or other therapies had the potential to address this unmet need.
Development Status

We are conducting our pivotal Phase 3 ADAPT trial of rocapuldencel-T. We have previously conducted three clinical trials of rocapuldencel-T and its predecessor product, including a Phase 2 trial and two Phase 1 trials. To date, we have administered rocapuldencel-T to over 300 patients in these trials. We submitted to the FDA an investigational new drug application, or IND, for rocapuldencel-T in March 2003. Additionally, we are developing a protocol for a Phase 2 clinical trial of rocapuldencel-T in combination with a checkpoint inhibitor for the treatment of patients with mRCC, but we do not intend to initiate this trial unless and until we obtain financing to fund the trial.

Phase 3 ADAPT Trial of rocapuldencel-T

Overview

The ADAPT trial is a randomized, multicenter, open label trial comparing combination therapy with rocapuldencel-T and sunitinib (or another targeted therapy) to monotherapy with sunitinib (or another targeted therapy) for the treatment of newly diagnosed metastatic renal cell carcinoma (mRCC). A total of 462 previously untreated patients were enrolled in the ADAPT trial and randomized 2:1 between combination treatment with rocapuldencel-T and sunitinib (combination arm) vs. sunitinib monotherapy (control arm) after undergoing cytoreductive nephrectomy. For both arms, the protocol permits switching to other standard-of-care treatments for mRCC for reasons such as intolerance to therapy or disease progression. The original primary efficacy endpoint for the study is a statistically significant improvement in overall survival in the combination treatment utilizing the intent to treat population at the pre-specified number of 290 events (deaths). Secondary efficacy endpoints include progression-free survival, objective response rate and disease control rate, and an exploratory efficacy endpoint of immune response. We dosed the first patient in May 2013 and completed enrollment in July 2015 at 107 sites across North America, Europe and Israel.

In February 2017, the IDMC for the ADAPT trial recommended that the trial be discontinued for futility based on its planned interim data analysis. The IDMC concluded that the trial was unlikely to demonstrate a statistically significant improvement in overall survival in the combination treatment arm, utilizing the intent-to-treat population at the pre-specified number of 290 events (deaths), the original primary endpoint of the study. Notwithstanding the IDMC’s recommendation, we determined to continue to conduct the trial while we analyzed interim data from the trial. Following a meeting with the FDA, we determined to continue the ADAPT trial until at least the pre-specified number of 290 events occurs, and to submit to the FDA a protocol amendment to increase the pre-specified number of events for the primary analysis of overall survival in the trial beyond 290 events. We believe that extending our evaluation of rocapuldencel-T beyond 290 events in the trial could enhance our ability to observe rocapuldencel-T’s expected delayed treatment effect.

We are currently finalizing an amendment to the ADAPT protocol, including an amended primary endpoint analysis, and plan to submit it to the FDA prior to the interim data analysis planned for the second quarter of 2018, at which time approximately 55 new events (deaths) are expected to have occurred subsequent to the February 2017 interim analysis. We are planning to include the following four co-primary endpoints in the amended ADAPT protocol:

- Overall survival for all randomized patients when approximately 375 events have occurred (under the same analysis that was originally planned for 290 events);
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In connection with our amendment of the ADAPT protocol, the SPA, for the ADAPT trial ceased to be in effect. Additionally, we are developing a protocol for a Phase 2 clinical trial of rocapuldencel-T in combination with a checkpoint inhibitor for the treatment of patients with mRCC, but we do not intend to initiate this trial unless and until we obtain financing to fund the trial.

ADAPT Trial Design

Our design for the ADAPT trial required enrollment of adult patients who have been newly diagnosed with mRCC with primary tumor intact and metastatic disease following nephrectomy, who have predominantly clear cell RCC based upon the tumor collected at nephrectomy, and who have not received any prior therapies for RCC. Participating patients were required to be suitable candidates for sunitinib therapy and have either poor risk or intermediate risk disease at presentation, with the less than one year to treatment risk factor and not more than two Heng risk factors in total. As part of the ADAPT trial design, the two arms of the trial were balanced based upon known prognostic risk factors. Patients were stratified by number of Heng risk factors (1, 2, 3 or 4) as well as whether they had measurable versus non-measurable metastatic disease following nephrectomy. The patient population in the ADAPT trial is generally comparable to the patient population treated in our Phase 2 combination therapy clinical trial. Approximately 77% of the patients enrolled in the ADAPT trial are intermediate risk patients (1-2 risk factors) and 23% are poor risk (3-4 risk factors). The average age of patients in the study is 60, with approximately 74% of the patients being male and approximately 95% of the patients being caucasian.
Under the ADAPT trial protocol, patients in the combination arm are dosed with rocapuldencel-T once every three weeks for five doses, followed by a booster dose every three months beginning six weeks after the fifth dose. In accordance with its label, sunitinib dosing is administered in six-week cycles, consisting of four weeks on drug and two weeks on drug holiday. Rocapuldencel-T dosing is initiated at the end of the initial six-week sunitinib cycle. The first dose of rocapuldencel-T is administered prior to the start of sunitinib dosing in the second sunitinib cycle. This dosing regimen is identical to the dosing regimen used in our Phase 2 combination therapy clinical trial of rocapuldencel-T and sunitinib, except that the start of the sixth dose is scheduled for six weeks following the fifth dose to better provide patients the opportunity to receive a total of eight doses across 48 weeks. Patients in the control arm receive sunitinib on the same dosing schedule as patients receive sunitinib in the combination arm.

Under the ADAPT trial protocol, rocapuldencel-T is administered for at least 48 weeks so that patients receive at least eight doses of rocapuldencel-T. Dosing will cease prior to 48 weeks if two events of disease progression or unacceptable toxicity occur or upon the joint decision of the patient and the investigator. If after 48 weeks of dosing of rocapuldencel-T a patient has stable disease or is responding to treatment, dosing will continue once every three months until disease progression. If an investigator determines to discontinue sunitinib, either due to disease progression or toxicity, the investigator can, at any time during the ADAPT trial after the first six-week cycle of sunitinib, initiate second-line therapy with one of the other approved therapies, including pazopanib, axitinib, nivolumab, everolimus or temsirolimus. In the event of discontinuation of sunitinib for patients in the combination arm, such patients would continue with rocapuldencel-T dosing in combination with the second-line therapy. In our Phase 2 combination therapy clinical trial, dosing ceased upon the first event of disease progression and second-line therapy was not permitted.

A graphic of the trial design is shown below:

**Phase 3 ADAPT Trial Design**

![Diagram of trial design]

1 Other therapies may be substituted for Sunitinib for intolerance or progression

**February 2017 Interim Analysis**

As noted above, following the February 2017 interim analysis the IDMC recommended that the ADAPT trial be discontinued for futility. While data on the original primary endpoint of the trial, overall survival in the intent-to-treat population, did not pass the futility test, we conducted several additional analyses, including an analysis of the overall survival in the first one-third of patients enrolled in the study and certain immune monitoring data that we believe suggest that rocapuldencel-T may potentially have a beneficial effect in a significant number of patients and may be working through its intended mechanism of action. A review of the data from the February 2017 interim analysis is provided below.
**Original Primary Endpoint - Overall Survival in the Intent-to-Treat Population**

At the time of the interim analysis after 75% of the targeted number of 290 events had occurred and using a data cut-off of February 3, 2017, the median overall survival for the combination treatment arm was estimated to be 27.7 months (95% Confidence Interval (CI): 23.0, 35.9) compared to 32.4 months (95% CI: 22.5, -) for the control arm in the intent-to-treat population. The hazard ratio was 1.10 (95% CI: 0.83, 1.46), which was greater than the pre-defined futility boundary for the February 2017 interim analysis of 0.98. A Kaplan-Meier plot of this data is provided below:

**Kaplan-Meier Analysis of Overall Survival in Intent-to-Treat Population**

Of note, baseline demographics and subsequent therapies were generally comparable across the two treatment arms.

**Overall Survival in the Modified Intent-to-Treat Population**

There were 39 patients in the combination treatment arm and 14 patients in the control arm who did not receive treatment. These patients did not receive treatment for a variety of reasons including death before initiation of treatment, withdrawal of consent, and, in the combination arm, failure to manufacture rocapuldencel-T. We analyzed the original primary endpoint of overall survival in both treatment arms excluding these patients, which we refer to as the modified intent-to-treat population (mITT). At the time of the interim analysis and using the February 3, 2018 data cut-off date, the estimated median overall survival for the combination treatment arm was 30.4 months (95% CI: 25.8, -) compared to 32.5 months (95% CI: 23.0, -) for the control arm in the mITT population. The hazard ratio was .97 (95% CI: 0.72, 1.33) in the mITT population.

**Post Hoc Analysis of Survival Data for the First One-Third of Enrolled Patients**

Subsequent to the IDMC meeting, to explore the hypothesis that longer follow-up time may provide useful information to identify a potential beneficial effect of rocapuldencel-T, we conducted a post-hoc subgroup analysis of overall survival in the first one-third of patients enrolled in the study (n=154). In these patients, for whom generally the longest follow-up data was available, the estimated median overall survival for the combination arm was 30.1 months (95% CI: 25.8, -) compared to 22.2 months (95% CI: 17.2, -) for the control arm. The hazard ratio in this post-hoc subgroup analysis was 0.88 (95% CI: 0.56, 1.36). A Kaplan-Meier plot of this data is provided below:
Objective Response Rate Data

As of the February 3, 2017 data cut-off date for the February 2017 interim analysis, 42.7% of the 307 patients in the combination treatment arm demonstrated an objective response by RECIST criteria, a secondary endpoint in the trial, as compared with 39.4% of the 155 patients in the control arm.

Duration of Response Data

Patients in the combination treatment arm who demonstrated an objective response had a median duration of response of 8.4 months compared to 6.3 months for patients in the control arm. Additionally, 16% of those patients with an objective response in the combination treatment arm had durable responses lasting at least 30 months compared to 7% of those who had an objective response in the control arm. Also, as of the date of the interim analysis, all of the patients in the combination arm who had achieved a duration of response of at least 30 months had maintained those responses through 36 months. Also of note, at the time of the data cut-off for the February 2017 interim analysis, no patients in the control arm had yet achieved a durable response lasting 36 months or longer.

<table>
<thead>
<tr>
<th>Objective Response Rate</th>
<th>Combination Arm</th>
<th>Control Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT Population</td>
<td>n=307</td>
<td>n=155</td>
</tr>
<tr>
<td>Best Overall Response, n (%)</td>
<td>9 (2.9%)</td>
<td>3 (1.9%)</td>
</tr>
<tr>
<td>Complete Response (CR)</td>
<td>122 (39.7%)</td>
<td>50 (37.4%)</td>
</tr>
<tr>
<td>Partial Response (PR)</td>
<td>121 (39.4%)</td>
<td>57 (36.3%)</td>
</tr>
<tr>
<td>Stable Disease (SD)</td>
<td>30 (9.3%)</td>
<td>10 (6.5%)</td>
</tr>
<tr>
<td>Not Evaluable (NE)</td>
<td>26 (8.1%)</td>
<td>27 (17.4%)</td>
</tr>
<tr>
<td>Objective Response Rate (CR + PR) n (%)</td>
<td>(37.1, 45.4)</td>
<td>(31.6, 47.2)</td>
</tr>
<tr>
<td>Objective Response Rate (CR + PR + SD), n (%)</td>
<td>(77.7, 86.5)</td>
<td>(88.8, 92.5)</td>
</tr>
</tbody>
</table>

Duration of response data is summarized in the graph below. For each time point, the graph shows the percentage of patients with a durable response lasting at least as long as the indicated time. For example, for the 131 patients in the combination arm who had an objective response, 60 of those 131 patients (46%) had a duration of response lasting 12 months or longer, 43 of those 131 patients (33%) had a duration of response lasting 18 months or longer, 27 of those 131 patients (21%) had a duration of response lasting 24 months or longer, and 21 of those 131 patients (16%) had a duration of response lasting 36 months or longer. Note that patients who had a response of at least a certain number of months are also included in the data points for having achieved a duration of response for all previous time points indicated.
Duration of Response Data

Progression-Free Survival Data

At the time of the interim analysis, the median progression-free survival for the combination treatment arm was 6.0 months (95% CI: 5.8, 6.7) compared to 7.8 months (95% CI: 5.9, 9.3) for the control arm in the ITT population. The hazard ratio was 1.15 (95% CI: 0.92, 1.44).

Immune Response Data

Subsequent to the IDMC meeting, we conducted a pre-defined analysis of immune responses, an exploratory efficacy endpoint, using multi-parametric flow cytometry. To analyze immune response, blood samples were collected from patients in the combination treatment arm enrolled at sites in the United States who provided consent for immune monitoring. Of the 146 subjects tested for immune responses, the number of subjects that met the criterion for inclusion in the pre-defined subgroup of immune responders were analyzed. Comparing the measured immune responses after 3, 5 and 7 doses to the immune measurement at visit 2 (immediately before initiation of dosing), 72% met the criterion after 3 doses (n=136), 72% met the criterion after 5 doses (n=134), and 82% met the criterion after seven doses (n=98), suggesting that Rocapuldencel-T is having its intended effect of stimulating an immune response in the majority of patients. Immune responders are defined as patients who have an increase of more than two standard deviations from the patient-specific baseline in the number of memory T cells (CD8+/CD28+/CD45RA-) at one or more time points.

Median overall survival at the time of the February interim analysis had not yet been reached in the subgroup of immune responders (95% CI: 30.1, [-]). Additionally, consistent with the mechanism of action of rocapuldencel-T, for those subjects who received at least seven doses of rocapuldencel-T, there was a statistically significant correlation between survival and the change in the number of antigen-specific memory T-cells from baseline (Spearman's Rho = 0.40; p<0.0001) in patients for whom immune response data has been analyzed (including both immune responders and non-responders, n=72).

The relationship between the immune response, as measured by the increase in the number of antigen-specific memory T-cells from baseline per milliliter of blood, and survival, is shown in the graph below. For those 25 patients with the greatest increase in the number of antigen-specific memory T-cells from baseline, no patient deaths had been recorded as of the time of the February 2017 interim analysis.
Importantly, the number of antigen-specific memory T-cells was found to increase only after administration of rocapuldencel-T, and in those subjects who received at least seven doses of rocapuldencel-T (n= 100) out of the 146 subjects analyzed for immune response, the average number of antigen-specific memory T-cells after the seventh dose was approximately double the number observed before treatment. This increase was found to be statistically significant (p<0.0001).
**IL-12 Secretion Data**

A pre-specified analysis was conducted to evaluate the relationship between the amount of IL-12 secreted by each patient's specific immunotherapy and that patient's survival. Samples from patients in the combination arm enrolled at North American sites who provided consent for immune monitoring (n=179) were divided into two groups: those with above the median amount of IL-12, and those with below the median amount of IL-12. Comparison of the Kaplan-Meier curves for these two groups revealed that those with higher than median levels of IL-12 generally demonstrated improved survival. Additionally, there was a statistically significant correlation between the level of IL-12 and survival (Spearman's Rho = 0.27; p<0.0002). There was also a statistically significant correlation between the level of IL-12 and the change from baseline in antigen-specific memory T-cells for patients who received at least seven doses of rocapuldencel-T (n=95; Spearman's Rho = 0.43; p<0.0001).

**Regulatory T-Cell Data**

A pre-specified analysis was conducted to evaluate the relationship between the percentage of regulatory T-cells at baseline and survival for patients in both arms of the trial enrolled. Samples from patients in the combination treatment arm enrolled at North American sites who provided consent for immune monitoring (n=176) were divided into two groups: those with above median percentage of regulatory T-cells at baseline, and those with below median percentage of regulatory T-cells at baseline. Comparison of the Kaplan-Meier curves for these two groups revealed that those with higher than median percentage of regulatory T-cells at baseline demonstrated improved survival. This finding was in contrast to the control arm (n=79), where a greater percentage of regulatory T-cells at baseline was associated with poorer survival. One hypothesis that could potentially explain this result is that rocapuldencel-T may be acting to convert regulatory T-cells to effector T-cells.

**Other Development Activities.** We are developing a protocol for a Phase 2 clinical trial of rocapuldencel-T in combination with a checkpoint inhibitor for patients with mRCC, which we do not intend to initiate unless and until we obtain financing to fund such trial. We believe that rocapuldencel-T may be capable of treating a wide range of cancers and we are evaluating or plan to evaluate rocapuldencel-T in clinical trials in additional cancer indications. Development of rocapuldencel-T in these other indications will in part depend upon our ongoing review of the ADAPT study data and discussions with the FDA, and subject to us obtaining the financing necessary to support such trials.
Phase 2 Combination Therapy Clinical Trial
From July 2008 to October 2009, we enrolled 21 newly diagnosed mRCC patients in a single arm, multicenter, open label Phase 2 clinical trial of rocapuldencel-T in combination with sunitinib. We conducted this clinical trial at nine clinical sites in the United States and Canada. Our design for the trial required adult patients with previously untreated mRCC, no prior nephrectomy or at least one accessible lesion for biopsy, a histologically confirmed predominantly clear cell tumor, and suitability for sunitinib therapy. The primary endpoint of the trial was complete response rate. Secondary endpoints included progression free survival, overall survival, safety, clinical benefit rate and immune response.

Patients in the trial generally received one initial six-week cycle of sunitinib, consisting of four weeks on drug and two weeks on drug holiday, prior to initiating the combined treatment with rocapuldencel-T. Patients then received a dose of rocapuldencel-T every three weeks for a total of five doses, while also continuing three additional six-week cycles of sunitinib. This 24-week induction phase was followed by a booster phase during which patients received a dose of rocapuldencel-T once every three months and continued to receive sunitinib in six-week cycles until disease progression.

The following table summarizes certain key data from the 11 intermediate risk and 10 poor risk patients enrolled in the Phase 2 combination therapy clinical trial.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>(N=21)</th>
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<tbody>
<tr>
<td>Median OS (1)</td>
<td>30.2 months</td>
</tr>
<tr>
<td>Median PFS (2)</td>
<td>11.2 months</td>
</tr>
<tr>
<td>Complete response (3)</td>
<td>0 patients</td>
</tr>
<tr>
<td>Partial response (4)</td>
<td>9 patients</td>
</tr>
<tr>
<td>Stable disease (5)</td>
<td>4 patients</td>
</tr>
<tr>
<td>Immune response</td>
<td>CD8+ CD28+ memory T-cells correlated with OS, PFS and reduced metastatic tumor burden; IL-2 and interferon-γ (IFN-γ) recovery</td>
</tr>
</tbody>
</table>

(1) Overall survival, or OS, is the length of time from the initiation of treatment to the patient’s death.
(2) Progression free survival, or PFS, is the length of time from treatment initiation to the worsening of the patient’s disease or the patient’s death.
(3) Complete response is the disappearance of all measurable target lesions and non-target lesions.
(4) Partial response is the overall tumor regression based on a decrease of at least 30% in the overall amount of measurable tumor mass in the body and improvement or no change in non-target lesions.
(5) Stable disease is neither sufficient decrease in tumor size to qualify as a partial response nor sufficient increase in tumor size to qualify as disease progression.

Particular observations from these data and the trial, which have informed our further clinical development of rocapuldencel-T, include:

**Efficacy Analysis**

- Seven patients survived for more than 4.5 years following enrollment in this trial. Two of these patients remained alive as of December 31, 2016 and both have had a sustained clinical response spanning nearly eight years and remain on rocapuldencel-T in combination with continued targeted therapy.

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Five poor risk patients did not receive five doses of rocapuldencel-T due to early disease progression. Median overall survival in the 16 patients who received at least five doses of rocapuldencel-T was 36.0 months.

Median overall survival in the 11 intermediate risk patients was 61.9 months. Median overall survival in the 10 poor risk patients was 9.1 months.

The following graphic shows data and follow-up as of December 31, 2015, the number of months that each patient in the Phase 2 clinical trial survived from the time of enrollment in the trial.

- Of the nine patients who exhibited a partial response, five patients exhibited partial responses during the 24-week induction phase, including two patients who exhibited partial responses prior to initiation of treatment with rocapuldencel-T. The other three patients exhibited partial responses after prolonged dosing with rocapuldencel-T during the booster phase. We do not believe that these late occurring partial responses have been observed in clinical trials of sunitinib alone. As a result, we believe that these late responses may relate to the immunologic effects of prolonged rocapuldencel-T dosing and rocapuldencel-T’s effect on CD8+ CD28+ memory T-cells.

- We observed a statistically significant correlation between increased progression free survival and prolonged survival (p<0.001). Statistical significance is determined by methods that establish the p-value of the results. Typically, results are considered statistically significant if they have a p-value of 0.05 or less, meaning that there is less than a one-in-20 likelihood that the observed results occurred by chance.

**Immune Response Analysis**

- In the 14 patients in the trial who received at least five doses of rocapuldencel-T and could be evaluated for memory T-cell response, we observed a statistically significant correlation between the increase in the number of CD8+ CD28+ memory T-cells over the initial five doses of rocapuldencel-T and survival (p<0.002), progression free survival (p<0.031) and reduced metastatic tumor burden (p<0.045). The following graphics show, for each of these 14 patients, the increase in their tumor-specific memory T-cells that they exhibited as measured immediately prior to their first dose of rocapuldencel-T and immediately following the patient’s fifth dose of rocapuldencel-T, or the absence of such increase, as compared to such patient’s survival.
• Rocapuldencel-T was found to have positive impact on immune cell function and restoration of cellular immunity in a majority of patients, including an increase in levels of IL-2 and IFN-γ.

Safety
• The adverse events in this trial associated with rocapuldencel-T were generally only mild injection site reactions, while the toxicities associated with sunitinib were consistent with those expected from treatment with sunitinib alone.

The original design for the Phase 2 clinical trial called for the recruitment of 50 patients to generate 38 fully evaluable patients. However, in October 2009, we terminated enrollment in this trial early due to a lack of funding. As a result, only 21 patients were enrolled and received at least one dose of rocapuldencel-T. In addition, the trial was originally designed to enroll patients with favorable and intermediate risk disease profiles. Instead, the actual population enrolled consisted entirely of patients with intermediate or poor risk disease profiles who had the less than one year to treatment risk factor. Because the patient population had poorer prognoses when they entered the trial than we expected and we did not have a sufficient number of evaluable patients, we did not perform the statistical analysis to determine whether the primary endpoint of complete response rate was achieved. As a result, if we submit a biologics license application, or BLA to the FDA for rocapuldencel-T, we expect the data from this trial to be considered by the FDA for the purpose of evaluating the safety and feasibility of rocapuldencel-T, but that it will only have a limited impact on the FDA’s ultimate assessment of the efficacy of rocapuldencel-T.
Based on our experience with the Phase 2 clinical trial, we concluded that the secondary endpoints in the trial, progression free survival and overall survival, along with immune response, were the appropriate endpoints to consider for measuring the efficacy of rocapuldencel-T in combination with sunitinib in patients with mRCC in our pivotal Phase 3 clinical trial.

Rocapuldencel-T Phase 2 Combination Therapy Clinical Trial, as Compared to Independent Third Party mRCC Data. At ASCO in June 2013, Dr. Heng presented data from the Consortium database regarding overall survival and progression free survival for intermediate and poor risk patients treated with sunitinib and other targeted therapies, including data with respect to 1,189 intermediate and poor risk patients with the less than one year to treatment risk factor.

Using the overall survival data from the Consortium database presented in June 2013 and published in April 2014, a summary comparison of this data with our Phase 2 clinical trial of rocapuldencel-T in combination with sunitinib is set forth in the graphic below. This graphic compares the median overall survival data from the Consortium intermediate and poor risk patients with the less than one year to treatment risk factor with the median overall survival data from the 21 patients in our Phase 2 clinical trial of rocapuldencel-T in combination with sunitinib, all of whom had the less than one year to treatment risk factor. A majority of the Consortium patients and the patients in our Phase 2 clinical trial had one or more additional risk factors.


Progression free survival for intermediate and poor risk patients in the Consortium database with the less than one year to treatment risk factor was 5.6 months, as compared to the 11.2 months of median progression free survival that we observed in the 21 patients in our Phase 2 clinical trial of rocapuldencel-T in combination with sunitinib.
Although we believe comparisons between our data and these collections of data are useful in evaluating the overall results of our Phase 2 clinical trial, the treatment of the Consortium patients was conducted at different sites, at different times and in different patient populations than the treatment in our Phase 2 combination therapy trial. The treatment also differed because certain of the Consortium patients received therapies other than sunitinib as first-line treatment. All of the patients in our Phase 2 clinical trial received sunitinib as first-line treatment. Our ongoing pivotal Phase 3 combination therapy clinical trial of rocapuldencel-T is the first trial that we have conducted that directly compares rocapuldencel-T and sunitinib or other targeted therapies as a combination therapy against sunitinib as monotherapy. Results of this head-to-head comparison in our phase 3 ADAPT trial differed significantly from the comparisons presented above and elsewhere in this Annual Report on Form 10-K.

**AGS-004 for the Treatment of Human Immunodeficiency Virus**

We are developing AGS-004, our second Arcelis-based product candidate, for the treatment of HIV. We have completed three clinical trials of AGS-004. These include Phase 1 and Phase 2 clinical trials that were funded by government grants and a Phase 2b trial that was funded in full by the NIH.

Based on the clinical data that we have generated to date, we have determined to focus our development program on the use of AGS-004 in combination with other therapies to achieve complete virus eradication and the use of AGS-004 monotherapy to provide long-term control of HIV viral load in immunologically healthy patients and eliminate their need for ART.

**Human Immunodeficiency Virus**

HIV is characterized by a chronic viral infection and an associated deterioration of immune function. Specifically, the virus disables and kills crucial human immune cells called CD4+ T-cells. CD4+ T-cells are necessary to generate and maintain antiviral T-cells, including the CD8+CD28+ memory T cells that aid in the killing of virus-infected cells. Over time, this viral impact on an infected person’s immune system outpaces the body’s natural ability to replace CD4+ T-cells and immunodeficiency results. As a result, the longer a person has been infected with the virus, the more functionally impaired these cells become.

At the same time, HIV infection causes the immune cells in HIV patients, including CD4+ T-cells and CD8+ T-cells that are not killed by the virus, to be in a chronic state of activation. The persistent state of immune activation in HIV patients results in chronic inflammation. We believe that this inflammation plays a role in the elevated rates of age-related comorbidities, including malignancies and cardiovascular disease observed in HIV patients. In addition, the activation of the CD4+ T-cells supports virus replication which leads to the production of new virus and increased viral load.

HIV is a persistent virus that can rapidly adapt to its environment by mutating and creating HIV variants that are drug resistant and can evade immune attack. As a result, there are a large number of mutated variants of HIV existing in any one infected individual and no two individuals have identical viral sequences.

According to the World Health Organization, the number of people living with HIV in the world was approximately 35 million in 2013. The Centers for Disease Control and Prevention estimates that more than 1.2 million people are currently living with HIV in the United States and the number of new cases of HIV infection in the United States is expected to remain constant at approximately 50,000 cases per year.

**Current treatments for HIV.** In 1996, triple combinations of oral medications known as ART were demonstrated to substantially reduce the levels of virus in the blood of patients with HIV. Since then, the introduction of new drug classes of ART and combination drug treatment strategies has enhanced treatment for HIV.
ART in HIV-infected patients can decrease levels of HIV in the blood to below the limits of detection, increase life expectancy and improve quality of life. However, there continues to be an unmet need for HIV therapies for the following reasons:

- ART can have significant side effects. The most recent U.S. guidelines on ART treatment contain a number of tables of adverse effects of combination regimens and how to manage them. Some combinations present potentially life-threatening complications and other complications that are chronic, cumulative and overlapping, and sometimes irreversible.

- ART requires life-long daily treatment. The risks of long-term daily administration of ART remain unknown but are potentially significant. In addition, the requirement for life-long daily treatment has made strict adherence to the treatment regime difficult. Poor compliance has led to the development of drug resistant HIV variants that are ineffectively controlled by the available armamentarium of ART.

- ART cannot eradicate the virus and, therefore, does not cure HIV-infected patients. For example, up to 20% of patients receiving ART fail to achieve normal CD4+ T-cell counts, resulting in a continued weakened immune system. In addition, certain patients are not able to achieve effective control of the virus using current treatment regimens. ART cannot eradicate the virus because the virus persists in latently infected cells. These cells, which constitute the HIV latent reservoir, do not consistently express HIV antigens in a manner or a compartment that permits effective control. Instead, these cells serve as a source privileged from ART control for virus replication and viral rebound in the absence of ART. Following discontinuation of treatment with ART, HIV viral levels return to levels observed prior to treatment with ART within 12 weeks of treatment interruption.

**AGS-004 Opportunity**

We believe, based on the mechanism of action of AGS-004 and the clinical data that we have generated, that AGS-004 has the potential to address this unmet need for the following reasons:

- **Potential to Eradicate HIV in Combination with Latency Reversing Drugs**. A number of companies and academic groups are evaluating drugs that can potentially activate the latently infected cells to increase viral antigen expression and make the cells vulnerable to elimination by the immune system. We believe that treating HIV-infected patients, who are being successfully treated with ART, with a combination of AGS-004 and one of these latency reversing drugs could lead to activation of antigen expression from the latently infected cells along with a potent memory T-cell response that is specific to the patient’s own unique viral antigens. We believe that this approach could potentially result in complete eradication of the patient’s virus.

- **Long-Term Viral Load Control in Immunologically Healthy Patients**. We believe that AGS-004 may allow for long-term virus control and eliminate the need for life-long treatment with ART in infected patients who have minimal immune suppression but no T-cell response against their virus. We have designed AGS-004 to induce CD8+ CD28+ memory T-cells that are specific to the patient’s own unique viral antigens, do not require CD4+ T-cell help to kill viral cells and do not result in CD4+ T-cell activation which typically increases viral replication and viral load. As reported in *Clinical & Experimental Immunology*, researchers have demonstrated that elevated levels of CD8+CD28+ memory T-cells in the blood are a statistically significant predictor of long-term non-progression in HIV-infected patients not treated with ART drugs. As a result, we believe that inducing these memory T-cells may lead to viral control. Patients with minimal immune suppression and no T-cell response include pediatric patients who have been successfully treated with ART drugs since birth or shortly thereafter and have generally healthy immune systems.

- **Minimal Toxicity**. AGS-004 has been well tolerated in clinical trials with no serious adverse events being attributed to it. As a result, we believe we can combine AGS-004 with other HIV therapies without additional toxicities.

- **Lack of Chronic Inflammation**. We have designed AGS-004 to elicit a patient-specific and disease-specific immune response that does not cause any additional inflammation. In our clinical trials of AGS-004, AGS-004 has not induced changes in markers that are associated with chronic inflammation in HIV patients.
AGS-004 is an individualized immunotherapy based on our Arcelis precision immunotherapy technology platform. It is produced by electroporating dendritic cells with mRNA encoding for patient-specific HIV antigens that have been derived from a patient’s virus-infected blood and with RNA that encodes the CD40L protein. The process for producing AGS-004 is the same process as is used to produce rocapuldencel-T, with the one key difference being that rocapuldencel-T contains all of the antigens from a patient’s tumor cells while AGS-004 contains potentially all variants unique to each individual patient of four selected HIV antigens (Gag, Nef, Vpr and Rev). We designed AGS-004 to include these antigens because immunity to them has been observed in long-term non-progressors and elite controllers, two groups of rare patients able to control virus replication without ART. Because no two patients share identical HIV antigen sequences and there are a large number of mutated variants of HIV existing in each infected patient, by using mRNA that is specific to the patient’s virus and that captures potentially all of the unique patient-specific variants of each antigen in the sample obtained, we believe our immunotherapy maximizes the relevance of the immune responses induced in each patient.

We have conducted three clinical trials of AGS-004, which include:

- a phase 2b clinical trial of AGS-004;
- a phase 2a clinical trial of AGS-004; and
- a phase 1 clinical trial of AGS-004.

We submitted to the FDA an IND for AGS-004 in August 2008.

We are focusing our development program for AGS-004 on the use of AGS-004 in combination with latency reversing therapies to achieve complete virus eradication. Latently infected cells differ from other infected cells in that the HIV genome is permanently integrated into the chromosomal DNA of the latently infected cells. These latently infected cells persist long-term and constitute the HIV latent reservoir, which serves as a source privileged from ART control for virus replication and viral rebound in the absence of antiretroviral therapy. As a result, demonstration that latently infected cells can be targeted by immune responses induced by AGS-004 is essential to our development strategy pertaining to virus eradication.

**Adult Eradication Trial.** We are supporting an investigator-initiated clinical trial of AGS-004 in 12 adult HIV patients who are being treated with ART to evaluate the use of AGS-004 to eradicate the virus. The trial is being conducted by co-investigator Dr. David Margolis, Professor of Medicine at the University of North Carolina. Dr. Margolis is the leader of CARE, and has been a pioneer in the research of HIV latent reservoir reversing treatments. The trial is being conducted in two stages. Stage 1 of this trial has been completed and was designed to study immune response kinetics to AGS-004 in patients on continuous ART. These data were used to better define the optimal dosing strategy in combination with the latency reversing therapy vorinostat in the ongoing Stage 2. The patient clinical costs for Stage 1 of this trial were funded by CARE. The NIH Division of AIDS has approved $6.6 million in funding to be provided directly to the University of North Carolina for the Stage 2 of this trial.

**Planned Pediatric Functional Cure Trial.** We believe that a patient population that could benefit from AGS-004 monotherapy consists of 14+ year old, HIV-infected individuals who have been treated with ART since birth or shortly thereafter. These individuals are characterized by having very small HIV latent reservoirs and otherwise healthy immune systems, while lacking antiviral CD8+ CD28+ memory T-cell responses. We believe that successfully inducing antiviral CD8+ CD28+ memory T-cell responses in these patients could allow for long-term viral load control and eliminate the need for life-long antiretroviral therapy. We plan to determine whether to support an investigator-initiated Phase 2 clinical trial of AGS-004 in pediatric patients infected with HIV who have otherwise healthy immune systems and have been treated with ART since birth or shortly thereafter and, as a result, are lacking the antiviral memory T-cells to combat the virus. The commencement of this trial is subject to supportive data obtained from the adult eradication trial and approval of the protocol by the principal investigator(s), institutional review boards, the IMPAACT Network leadership and the FDA and to the agreement by the NIH to fund the trial costs not related to AGS-004 manufacturing to evaluate the use of AGS-004 monotherapy to allow for long-term control of viral load and eliminate the need for ART. We are currently developing the clinical protocol for this trial to immunize pediatric HIV patients who were infected at birth and treated with antiretroviral therapy at or near birth. We are developing this clinical protocol in collaboration with Drs. Katherine Luzuriaga, University of Massachusetts, and Deborah Persaud, John Hopkins Medical Center, both specializing in pediatric virology.
Phase 2b Clinical Trial. In January 2015, we completed a randomized, placebo controlled, double blind Phase 2b clinical trial of AGS-004 in chronically infected patients on ART that we opened for enrollment in July 2010. We designed this trial to confirm the data obtained in an earlier Phase 2a clinical trial in which AGS-004 led to a reduction in virus replication. We initially planned to enroll 42 chronically infected patients in the Phase 2b trial at nine clinical sites in the United States and Canada with the intent to generate 36 events for the primary endpoint analysis. However, due to a higher than anticipated dropout rate by patients who were unable to complete the full 12 week treatment interruption period provided for by the trial, we needed to enroll 53 patients in the trial to generate 36 events for the primary endpoint analysis. These patients were randomized between AGS-004 treatment and a placebo control on a two-to-one basis.

HIV infection is classified as “chronic” or “acute” based on how long the patient has been infected prior to starting ART. Patients with chronic HIV infection are patients who have initiated ART after at least six months from the time of initial infection. Patients with acute HIV infection are patients who have initiated ART less than 45 days after initial infection. This trial enrolled adult patients with chronic HIV-1 infection and undetectable viral loads as a result of treatment with ART. Patients also had to have adequate CD4+ T-cell counts and a pre-ART plasma viral sample to be used to manufacture AGS-004.

In this trial, patients first received intradermal doses of AGS-004 or placebo every four weeks for a total of four doses, together with their ART. Following the fourth dose of AGS-004 or placebo, patients discontinued their ART but continued to receive AGS-004 or placebo every four weeks for 12 weeks. We refer to this period as the treatment interruption period. Patients who demonstrated control of viral replication under 10,000 copies/ml and maintained CD4+ T-cell counts above 350 cells/mm$^3$ could remain off ART and continue their treatment interruption past 12 weeks. Following the end of treatment interruption, all patients were eligible for continued treatment with the combination of AGS-004 and ART. A schematic of the trial design is shown below.

**Phase 2b Study Design for the Chronically Infected Cohort**

The primary endpoint of the trial was a comparison of the median viral load in the AGS-004-treated patients with the median viral load in patients receiving placebo after 12 weeks of ART treatment interruption. Under this protocol, the primary endpoint required that there was a $\geq 1.1 \log_{10}$ difference in median viral load between the AGS-004-treated cohort compared to the placebo-treated cohort. A $1.1 \log_{10}$ reduction means a 92% lower virus concentration in the AGS-004-treated cohort compared to the placebo-treated cohort. Secondary endpoints included comparisons between AGS-004-treated patients and the patients receiving placebo with respect to change in viral load from pre-ART to the end of 12 weeks of treatment interruption, duration of treatment interruption, changes in CD4+ T-cell counts and safety.
In September 2011, we added to the trial a single arm, open-label, unblinded cohort of up to 12 patients with acute HIV-1 infection and undetectable viral loads as a result of treatment with ART. We evaluated AGS-004 in this patient population to assess AGS-004 in patients who initiated ART during the acute phase of infection and as a result may have sustained less immune damage. Patients in this cohort were dosed in the same manner as patients in the chronically infected arm of the clinical trial. However, in this cohort, patients had to demonstrate a positive CD8+ CD28+ anti-HIV memory T-cell response in order to become eligible to enter the 12 week treatment interruption period. The primary endpoints for this cohort included the time to detectable viral load during the ART interruption period and comparison of changes in CD4+ T-cell counts during the ART interruption period between the acute cohort and the chronic cohort. Six patients were enrolled in this cohort. All six patients demonstrated a positive CD8+ CD28+ memory T-cell response and initiated treatment interruption. For the five of six patients that re-initiated ART after treatment interruption, there were no significant declines in CD4+ T cells between the interruption date and the re-initiation date. All six patients experienced viral rebound during treatment interruption with the times to detectable viral load ranging from two to eight weeks and the duration of treatment interruption for those patients who reinitiated ART ranged from approximately one month to approximately nine months. In addition, three of six patients had a decrease in circulating CD4+ T cells containing HIV DNA of 25%, 47% and 63%, respectively, when measured after three doses of AGS-004 while on ART.

In the Phase 2b trial, 54 patients received the full four doses of AGS-004 or placebo during the first four weeks together with their ART. Of these patients, 36 patients continued on AGS-004 or placebo for the full 12-week treatment interruption period, 23 of whom received AGS-004.

In January 2015, we announced top-line results from the trial. The primary endpoint of the trial was not achieved.

However, we believe that data from the trial provided evidence of the ability of AGS-004 to induce memory T-cell responses which may have directly impacted the latent viral reservoir. Of the evaluated 22 patients who received AGS-004 and completed the 12-week treatment interruption period, 15 patients, or approximately 70 percent, had positive antiviral memory T-cell responses prior to beginning the treatment interruption versus zero percent of placebo patients. Within the AGS-004 treatment group, those patients that had antiviral memory T-cell responses had significantly fewer CD4+ T-cells with integrated HIV DNA when compared to non-responders. These findings relate directly to the utilization of AGS-004 in our ongoing adult eradication study and our planned pediatric study, where one of the key objectives is to decrease the latent HIV reservoir.

Safety analysis

In this trial, AGS-004 was well tolerated. No AGS-004-related serious adverse events were reported. The most common adverse event was mild injection site reactions. During the antiretroviral treatment interruption, no notable differences in incidence of adverse events occurred compared to when patients were receiving AGS-004 in combination with antiretroviral drug therapy.

NIH and NIAID Contract. Our development of AGS-004 has received significant funding from the U.S. federal government. In September 2006, we entered into a multi-year research contract with the NIH and the National Institute of Allergy and Infectious Diseases, or NIAID, to design, develop and clinically test an autologous HIV immunotherapy capable of eliciting therapeutic immune responses. We are using funds from this contract to develop AGS-004. Under this contract, as it has been amended, the NIH and the NIAID have committed to fund up to $39.8 million, including reimbursement of our direct expenses and allocated overhead and general and administrative expenses of up to $38.4 million and payment of specified amounts totaling up to $1.4 million upon our achievement of specified development milestones. We have recorded total revenue of $38.3 million through December 31, 2017 under the NIH agreement. As of December 31, 2017, there was up to $1.5 million of potential revenue remaining to be earned under the agreement. This commitment extends until July 2018.

We have agreed to a statement of work under the contract, and are obligated to furnish all the services, qualified personnel, material, equipment, and facilities, not otherwise provided by the U.S. government, needed to perform the statement of work. In accordance with the laws applicable to government intellectual property rights under federal contracts, we have a right under our contract with the NIH to elect to retain title to inventions conceived or first reduced to practice under the NIH and NIAID contract, subject to the right of the U.S. government to a royalty-free license to practice or have practiced for or on behalf of the United States the subject invention throughout the world. The government also has special statutory “march-in” rights to license or to require us to license such inventions to third parties under limited circumstances. In addition, we may not grant to any person the exclusive right to use or sell any such inventions in the United States unless such person agrees that any products embodying the subject invention or produced through the use of the subject invention will be manufactured substantially in the United States.
We currently manufacture our Arcelis-based products, including rocapuldencel-T and AGS-004, for research and development purposes and for use in our clinical trials at our facilities in Durham, North Carolina, which we refer to as our Technology Drive and Patriot Center facilities. These facilities include manufacturing suites for the production of products using our Arcelis technology platform. We have designed these suites to comply with the FDA’s current good manufacturing practice, or cGMP, requirements.

In January 2017, we entered into a ten-year lease agreement with two five-year renewal options for 40,000 square feet of manufacturing and office space at the Center for Technology Innovation, or CTI, on the Centennial Campus of North Carolina State University in Raleigh, North Carolina. We had intended to utilize this facility to manufacture rocapuldencel-T to support submission of a BLA to the FDA and to support initial commercialization of rocapuldencel-T.

In addition, to provide for capacity expansion beyond the initial few years following potential launch of rocapuldencel-T, we had planned to buildout and equip a second facility, which we refer to as the Centerpoint facility. In August 2014, we entered into a ten-year lease agreement with renewal options. Under the lease agreement, we agreed to lease certain land and an approximately 125,000 square-foot building to be constructed in Durham County, North Carolina. We initially intended this facility to house our corporate headquarters and commercial manufacturing before we entered into the lease for the CTI facility. The shell of the new facility was constructed on a build-to-suit basis in accordance with agreed upon specifications and plans and was completed in June 2015. However, the build-out and equipping of the interior of the facility was suspended as we pursued financing arrangements to support the further buildout of the facility.

Due to the IDMC recommendation in February 2017 to discontinue the ADAPT trial, we reassessed our manufacturing plans. We determined to use our Technology Drive and Patriot Center facilities for the manufacture of rocapuldencel-T and AGS-004, respectively, to support our ongoing clinical trials and any likely near-term clinical trials that we may initiate and initiated discussions with the landlords of the CTI facility and the Centerpoint facility regarding our leases. In March 2017, the landlord of our CTI facility notified us that it was terminating the lease due to nonpayment of invoices for up-fit costs, effective immediately, and in March 2017 we entered into a lease termination agreement with the landlord. In November 2017, we and TKC Properties, the landlord of the Centerpoint facility, entered into a lease termination agreement in connection with the sale by TKC of the facility to a third party.

We expect that we would establish both manual and automated manufacturing processes in our commercial manufacturing facilities if we determine to build out such facilities. We had decided to delay the implementation of our automated manufacturing process until after initial commercialization of rocapuldencel-T, and thus planned to seek marketing approval of rocapuldencel-T and, if approved, to initially commercially supply rocapuldencel-T using our manual manufacturing process. Prior to implementing commercial manufacturing of rocapuldencel-T, we would be required to demonstrate that our commercial manufacturing facility is constructed and operated in accordance with current good manufacturing practice. We would also be required to show the comparability between rocapuldencel-T that we produce using the manual processes in our current facility and rocapuldencel-T produced using the manual process in our new facility.

We have granted exclusive manufacturing rights for rocapuldencel-T to Pharmstandard in Russia and the other states comprising the Commonwealth of Independent States, to Green Cross in South Korea, to Medinet in Japan and to Lummy HK in China, Hong Kong, Taiwan and Macau. We have also agreed to enter into an agreement with Pharmstandard for the manufacture of rocapuldencel-T in the European market.
Sales and Marketing

We hold exclusive commercial rights to all of our product candidates in all geographies other than rights to rocapuldencel-T in Russia and the other states comprising the Commonwealth of Independent States, which are held by Pharmstandard, rights to rocapuldencel-T for the treatment of mRCC in South Korea, which are held by Green Cross and rights to rocapuldencel-T in China, Hong Kong, Taiwan and Macau, which are held by Lummy HK. We have granted to Medinet an exclusive license to manufacture in Japan rocapuldencel-T for the treatment of mRCC.

We currently intend to retain North American marketing rights for rocapuldencel-T and any future oncology products that we may develop. To maximize the value of these rights, we would expect to build a commercial infrastructure for such products comprised of medical, marketing and sales teams as well as a customer service function to manage patient access and logistics partners associated with rocapuldencel-T production and distribution. Our commercial infrastructure would also include personnel who manage reimbursement activities with third party payors, such as managed care organizations, group purchasing organizations, oncology group networks and government accounts. We currently do not have any commercial capabilities or in-house personnel specializing in these functions. Outside North America, we plan to seek to enter into collaboration agreements with other pharmaceutical or biotechnology firms to commercialize rocapuldencel-T.

For AGS-004, we plan to seek to enter into collaboration agreements with other pharmaceutical or biotechnology firms to commercialize this product candidate on a worldwide basis.

Competition

The biotechnology and pharmaceutical industries are highly competitive. There are many pharmaceutical companies, biotechnology companies, public and private universities and research organizations actively engaged in the research and development of products that may be similar to or competitive with our products. There are a number of multinational pharmaceutical companies and large biotechnology companies currently marketing or pursuing the development of products or product candidates targeting the same indications as our product candidates. It is probable that the number of companies seeking to develop products and therapies for the treatment of unmet needs in these indications will increase. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approaches, and others are based on entirely different approaches.

Many of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Our competitors’ drugs may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render our product candidates obsolete or non-competitive. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. We expect any products that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition and the availability of reimbursement from government and other third party payors.

mRCC

Historically, mRCC was treated with chemotherapy, radiation and hormonal therapies, as well as cytokine-based therapies such as interferon-alpha and IL-2. More recently, the FDA has approved several targeted therapies as monotherapies for mRCC, including Nexavar (sorafenib), marketed by Bayer Healthcare Pharmaceuticals, Inc. and Onyx Pharmaceuticals, Inc.; Sutent (sunitinib) and Inlyta (axitinib), marketed by Pfizer, Inc.; Avastin (bevacizumab), marketed by Genentech, Inc., a member of the Roche Group; Votrient (pazopanib) and Afinitor (everolimus), marketed by Novartis Pharmaceuticals Corporation; Torisel (temsirolimus), marketed by Pfizer and most recently, Opdivo (nivolumab), marketed by Bristol-Myers Squibb and Cabometyx (cabozantinib), marketed by Exelixis, for second-line mRCC. In addition, we estimate that there are numerous therapies for mRCC in clinical development by many public and private biotechnology and pharmaceutical companies targeting numerous different cancer types and stages. A number of these are in late stage development including Opdivo (nivolumab) plus Yervoy (ipilimumab) in combination for first-line mRCC, for which favorable data have been reported in a Phase 3 trial. In addition, if a standalone therapy for mRCC were developed that demonstrated improved efficacy over currently marketed first-line therapies with a favorable safety profile and without the need for combination therapy, such a therapy might pose a significant competitive threat to rocapuldencel-T.
**Other Oncology Indications**

We estimate that there are numerous other cancer immunotherapy products in clinical development by many public and private biotechnology and pharmaceutical companies targeting numerous different cancer types. A number of these product candidates are in late-stage clinical development or have recently been approved in different cancer types including two recently approved checkpoint inhibitor-based immunotherapies, nivolumab which is marketed by Bristol-Myers Squibb and pembrolizumab, which is marketed by Merck. These newer immunotherapies are in addition to the targeted therapies, chemotherapeutics, radiation therapy, hormonal therapies and cytokine-based therapies used in the treatment in a wide range of oncology indications.

**HIV**

There are numerous FDA-approved treatments for HIV, primarily antiretroviral therapies, marketed by large pharmaceutical companies. In addition, generic competition has recently developed as patent exclusivity periods for older drugs have expired, with more than 15 generic bioequivalents currently on the market. The presence of these generic drugs is resulting in price pressure in the HIV therapeutics market. Currently, there are no approved therapies for the eradication of HIV. We expect that major pharmaceutical companies that currently market antiretroviral therapy products or other companies that are developing HIV product candidates may seek to develop products for the eradication of HIV.

**Intellectual Property**

Our success depends in part on our ability to obtain and maintain proprietary protection for our products and product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We are seeking a range of patent and other protections for our product candidates and platform technology. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

**Patents**

We own or exclusively license 16 U.S. patents and three U.S. patent applications, as well as approximately 55 foreign counterparts, covering our Arcelis precision immunotherapy technology platform and Arcelis-based product candidates.

We use our Arcelis precision immunotherapy technology platform to generate individualized mRNA-loaded dendritic cell immunotherapies. As described above, the process of obtaining a disease sample and dendritic cells from a patient, using those materials to manufacture an individualized drug product and shipping the drug product to the clinical site for use in the treatment of the patient involves many important steps. These steps include:

- amplifying mRNA from a disease sample obtained from the patient;
- differentiating dendritic cell precursors (monocytes) isolated from the patient into immature dendritic cells;
- maturing the immature dendritic cells in culture and loading the mature dendritic cells with the amplified mRNA and CD40L protein; and
- formulating the matured, loaded dendritic cells in the patient’s plasma with cryoprotectants to protect the cells in the resulting drug product when the drug product is frozen and thawed.

We have sought to protect these steps or the equipment related to carrying out one or more of these steps through patents or trade secrets. We have also sought to protect the resultant drug product through patents.

These patents and patent applications are directed to one or more aspects of our Arcelis precision immunotherapy technology platform or Arcelis-based products. Specifically, these patents and patent applications are collectively directed to:

- Arcelis-based compositions of matter and products;
• methods of manufacturing Arcelis-based products;
• methods of using Arcelis-based products for treatment of tumors;
• compositions that we use in the manufacture of Arcelis-based AGS-004 products; and
• equipment would be used for assisting the automated manufacture of Arcelis-based products.

We believe that all of the above aspects of our Arcelis precision immunotherapy technology platform are required to successfully and efficiently produce our Arcelis-based product candidates and are covered by a combination of our patents, patent applications, trade secrets and know-how. The U.S. patents expire between 2021 and 2029, and the U.S. patent applications, if issued, would expire between 2025 and 2028, the counterpart patents in Europe and Japan expire between 2021 and 2027, and the counterpart patent applications in Europe, if issued, would expire between 2025 and 2027. Included in these patents and patent applications are:

• seven U.S. patents and corresponding patent application in Europe and patent in Japan collectively directed towards an automated apparatus for the manipulation of nucleic acids in a closed container, components thereof and related methods of use. The U.S. and Japanese patents expire in 2027, and the patent application in Europe, if issued, would expire in 2027.

• one U.S. patent and corresponding European and Japanese patents collectively directed towards cryoconserved dendritic cells and related methods of manufacture. The U.S., European and Japanese patents expire in 2021.

• four U.S. patents and two U.S. patent applications, two corresponding European patents, two corresponding Japanese patents and a corresponding patent application in Europe collectively directed towards methods of maturing dendritic cells and the composition of matter of dendritic cells that have undergone this maturation process. The U.S. patents expire in 2026 and the U.S. applications, if issued, would expire in 2025, the European patents expire in 2025 and 2027, the Japanese patents expire in 2025 and 2027 and the patent application in Europe, if issued, would expire in 2025.

• one U.S. patent and corresponding patents in Europe and Japan collectively directed towards methods of manufacture of dendritic cells from monocytes stored for more than six hours and up to four days without freezing and the composition of matter of dendritic cells that have been manufactured from these monocytes. The U.S. patent will expire in 2029, and patents in Europe and Japan will expire in 2026.

• two U.S. patents, two patents in Europe and one patent in Japan are collectively directed towards the composition of matter of AGS-004 and related methods of manufacture. The U.S. patents expire in 2026. The European and Japanese patents will expire in 2025.

• one U.S. patent and one U.S. patent application are directed towards the composition of matter and related methods of use of some of the primers that we use in the manufacture of AGS-004. The U.S. patent and U.S. patent application, if issued, will expire in 2028.

In addition, if the use of Arcelis-based products for the treatment of RCC and HIV are approved by the FDA, then, depending upon factors such as the timing and duration of FDA review and the timing and conditions of FDA approval, as well as factors such as patent claim scope, some of our issued U.S. patents (or patents that may issue from our pending U.S. patent applications) may be eligible for limited patent term extension under the Hatch-Waxman Act.
Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. For example, significant aspects of the process by which we manufacture or plan to automate manufacturing of our Arcelis-based drug product candidates are based on unpatented trade secrets and know-how. Trade secrets and know-how can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how 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 be independently discovered by competitors. To the extent that our consultants, contractors or collaborators 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.

Development and Commercialization Agreements

An important part of our business strategy is to enter into arrangements with third parties both to assist in the development and commercialization of our product candidates, particularly in international markets, and to in-license product candidates in order to expand our pipeline.

Pharmstandard. In August 2013, in connection with the purchase of shares of our series E preferred stock by Pharmstandard, we entered into an exclusive royalty-bearing license agreement with Pharmstandard. Under this license agreement, we granted Pharmstandard and its affiliates a license, with the right to sublicense, to develop, manufacture and commercialize rocapuldencel-T and other products for the treatment of human diseases, which are developed by Pharmstandard using our individualized immunotherapy platform, in the Russian Federation, Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Turkmenistan, Ukraine and Uzbekistan, which we refer to as the Pharmstandard Territory. We also provided Pharmstandard with a right of first negotiation for development and commercialization rights in the Pharmstandard Territory to specified additional products we may develop.

Under the terms of the license agreement, Pharmstandard licensed us rights to clinical data generated by Pharmstandard under the agreement and granted us an option to obtain an exclusive license outside of the Pharmstandard Territory to develop and commercialize improvements to our Arcelis technology generated by Pharmstandard under the agreement, a non-exclusive worldwide royalty-free license to Pharmstandard improvements to manufacture products using our Arcelis technology and a license to specified follow-on licensed products generated by Pharmstandard outside of the Pharmstandard Territory, each on terms to be negotiated upon our request for a license. In addition, Pharmstandard agreed to pay us pass-through royalties on net sales of all licensed products in the low single digits until it has generated a specified amount of aggregate net sales. Once the net sales threshold is achieved, Pharmstandard will pay us royalties on net sales of specified licensed products, including rocapuldencel-T, in the low double digits below 20%. These royalty obligations last until the later of the expiration of specified licensed patent rights in a country or the twelfth anniversary of the first commercial sale in such country on a country by country basis and no further royalties on specified other licensed products. After the net sales threshold is achieved, Pharmstandard has the right to offset a portion of the royalties Pharmstandard pays to third parties for licenses to necessary third party intellectual property against the royalties that Pharmstandard pays to us.

The agreement will terminate upon expiration of the royalty term, upon which all licenses will become fully paid up perpetual exclusive licenses. Either party may terminate the agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy and we may terminate the agreement if Pharmstandard challenges or assists a third party in challenging specified patent rights of ours. If Pharmstandard terminates the agreement upon our material breach or bankruptcy, Pharmstandard is entitled to terminate our licenses to improvements generated by Pharmstandard, upon which we may come to rely for the development and commercialization of rocapuldencel-T and other licensed products outside of the Pharmstandard Territory, and Pharmstandard is entitled to retain its licenses from us and to pay us substantially reduced royalty payments following such termination.

In November 2013, we entered into an agreement with Pharmstandard under which Pharmstandard purchased additional shares of our series E preferred stock. Under this agreement, we agreed to enter into a manufacturing rights agreement for the European market with Pharmstandard and that the manufacturing rights agreement would provide for the issuance of warrants to Pharmstandard to purchase 24,989 shares of our common stock at an exercise price of $116.40 per share. As of February 1, 2018, we had not entered into this manufacturing rights agreement or issued the warrants.
Pharmstandard and Actigen. On February 1, 2018, we entered into an option agreement with Pharmstandard and Actigen Limited to evaluate, with an option to license, certain patent rights and know-how related to a group of fully human PD1 monoclonal antibodies and related technology held by Actigen. Actigen previously granted Pharmstandard an option to exclusively license these patent rights. Under the option agreement, Pharmstandard granted to us (i) an exclusive license for evaluation purposes only to make, have made, use and import the PD1 monoclonal antibodies covered by these patent rights (but not offer to sell or sell products and processes covered by or incorporating the patent rights) for a period of one year from the date of the agreement and (ii) an option exercisable during the one-year period to obtain an exclusive license (with the right to sublicense) under the patent rights to make, have made, use, offer for sale, sell and import (with a right to grant sublicenses) the PD1 monoclonal antibodies for all prophylactic, therapeutic and diagnostic uses and for all human diseases and conditions in the United States and Canada. The parties have agreed that, if we exercise the option during the option exercise period, the parties will negotiate in good faith a license agreement on the terms and conditions outlined in the option agreement, including payments by us to Pharmstandard of (i) an upfront license fee of $3.6 million, payable upon execution of the license agreement in our common stock, (ii) various development and regulatory milestone payments totaling $8.5 million, and (iii) upper single digit percentage royalties on net sales of any pharmaceutical product or therapeutic regimen incorporating the licensed PD1 monoclonal antibodies that will apply on a country-by-country basis until the later of the last to expire patent or ten years from the date of first commercial sale, against which the first $5.0 million of our development expenditures will be credited as prepaid royalties.

In consideration for the rights granted under the option agreement, we agreed to issue to Pharmstandard, on or before April 2, 2018, 169,014 shares of our common stock, the value of which will be creditable against the upfront license fee if we entered into a license agreement. Unless earlier terminated by any party for uncured material breach or by us without cause upon thirty days prior written notice, the option agreement will terminate upon the later of the end of the option exercise period if we decide not to exercise the option or sixty days after we exercise the option.

Green Cross. In July 2013, in connection with the purchase of our series E preferred stock by Green Cross, we entered into an exclusive royalty-bearing license agreement with Green Cross. Under this agreement we granted Green Cross a license to develop, manufacture and commercialize rocapuldencel-T for mRCC in South Korea. We also provided Green Cross with a right of first negotiation for development and commercialization rights in South Korea to specified additional products we may develop.

Under the terms of the license, Green Cross has agreed to pay us $0.5 million upon the initial submission of an application for regulatory approval of a licensed product in South Korea, $0.5 million upon the initial regulatory approval of a licensed product in South Korea and royalties ranging from the mid-single digits to low double digits below 20% on net sales until the fifteenth anniversary of the first commercial sale in South Korea. In addition, Green Cross has granted us an exclusive royalty free license to develop and commercialize all Green Cross improvements to our licensed intellectual property in the rest of the world, excluding South Korea, except that, as to such improvements for which Green Cross makes a significant financial investment and that generate significant commercial benefit in the rest of the world, we are required to negotiate in good faith a reasonable royalty that we will be obligated to pay to Green Cross for such license. Under the terms of the agreement, we are required to continue to develop and to use commercially reasonable efforts to obtain regulatory approval for rocapuldencel-T in the United States.

The agreement will terminate upon expiration of the royalty term, which is 15 years from the first commercial sale, upon which all licenses will become fully paid up perpetual non-exclusive licenses. Either party may terminate the agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy and we may terminate the agreement if Green Cross challenges or assists a third party in challenging specified patent rights of ours. If Green Cross terminates the agreement upon our material breach or bankruptcy, Green Cross is entitled to terminate our licenses to improvements and retain its licenses from us and to pay us substantially reduced milestone and royalty payments following such termination.

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Medinet. In December 2013, we entered into a license agreement with Medinet. Under this agreement, we granted Medinet an exclusive, royalty-free license to manufacture in Japan rocapuldec-T and other products using our Arcelis technology solely for the purpose of the development and commercialization of rocapuldec-T and these other products for the treatment of mRCC. We refer to this license as the manufacturing license. In addition, under this agreement, we granted Medinet an option to acquire a nonexclusive, royalty-bearing license under our Arcelis technology to sell in Japan rocapuldec-T and other products for the treatment of mRCC. We refer to the option as the sale option and the license as the sale license.

The sale option expired on April 30, 2016. As a result, Medinet may only manufacture rocapuldec-T and these other products for us or our designee. We have agreed to negotiate in good faith a supply agreement under which Medinet would supply us or our designee with rocapuldec-T and these other products for development and sale for the treatment of mRCC in Japan. During the term of the manufacturing license, we may not manufacture rocapuldec-T or these other products for us or any designee for development or sale for the treatment of mRCC in Japan.

In consideration for the manufacturing license, Medinet paid us $1.0 million. Medinet also loaned us $9.0 million in connection with us entering into the agreement. We have agreed to use these funds in the development and manufacturing of rocapuldec-T and the other products. Medinet also agreed to pay us milestone payments of up to a total of $9.0 million upon the achievement of developmental and regulatory milestones and $5.0 million upon the achievement of a sales milestone related to rocapuldec-T and these products.

We borrowed the $9.0 million pursuant to an unsecured promissory note that bears interest at a rate of 3.0% per annum. The principal and interest under the note are due and payable on December 31, 2018. Under the terms of the note and the manufacturing license agreement, any milestone payments related to the developmental and regulatory milestones that become due will be applied first to the repayment of the loan. We have achieved $5.0 in milestones. As a result, the outstanding principal of the loan has been reduced to $4.0 million as of February 1, 2018. We have the right to prepay the loan at any time. If we do not repay the loan by December 31, 2018, then we have agreed to grant to Medinet a non-exclusive, royalty-bearing license to make and sell Arcelis products in Japan for the treatment of cancer. In such event, the amounts owing under the loan as of December 31, 2018 may constitute pre-paid royalties under the license or would be due and payable. We do not expect to pay the amounts owing under the loan by December 31, 2018. Royalties under this license would be paid until the expiration of the licensed patent rights in Japan at a rate to be negotiated. If we cannot agree on the royalty rate, we have agreed to submit the matter to arbitration.

Under the agreement, we had the right to revoke both the manufacturing license and the sale license to be granted to Medinet, or the sale license only. On February 14, 2018, we notified Medinet that we irrevocably agreed to have no further right to exercise our right under the license agreement to revoke the manufacturing and the sale license, or the sale license only.

The agreement will terminate upon expiration of the royalty term, upon which all licenses will become fully paid up, perpetual non-exclusive licenses. Either party may terminate the agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy, and we may terminate the agreement if Medinet challenges or assists a third party in challenging specified patent rights of ours. If Medinet terminates the agreement upon our material breach or bankruptcy, Medinet is entitled to terminate our licenses to improvements and retain its royalty-bearing licenses from us.

Lummy. On April 7, 2015, we and Lummy HK entered into a license agreement pursuant to which we granted to Lummy HK an exclusive license under the Arcelis technology, including patents, know-how and improvements to manufacture, develop and commercialize products for the treatment of cancer in China, Hong Kong, Taiwan and Macau. Lummy HK also has a right of first negotiation with respect to a license under the Arcelis technology for the treatment of infectious diseases in China, Hong Kong, Taiwan and Macau. This agreement was subsequently amended in December 2016, October 2017 and March 2018.

Under the terms of the license agreement, the parties will share relevant data, and we will have a right to reference Lummy HK data for purposes of its development programs under the Arcelis technology. In addition, Lummy HK has granted to us an exclusive, royalty-free license under and to any and all Lummy HK improvements to the Arcelis technology conceived or reduced to practice by Lummy HK and Lummy HK data to develop and/or commercialize products outside China, Hong Kong, Taiwan and Macau, an exclusive, royalty-free license under and to any and all INDs and other regulatory approvals and Lummy HK trademarks used for an Arcelis-Based Product to develop and/or commercialize an Arcelis-Based Product outside China, Hong Kong, Taiwan and Macau and a non-exclusive, worldwide, royalty-free license under any Lummy HK improvements and Lummy HK data to manufacture Arcelis-Based Products anywhere in the world. Lummy HK has the right to reference our data, INDs and other regulatory filings and submissions for the purpose of developing and obtaining regulatory approval of licensed products in China, Hong Kong, Taiwan and Macau.
Pursuant to the license agreement, Lummy HK will pay us royalties on net sales and up to an aggregate of $22.3 million upon the achievement of manufacturing, regulatory and commercial milestones, $2.55 million of which has been earned as of March 31, 2018. On October 18, 2017, we entered into a second amendment to the license agreement and Lummy HK paid us $1.5 million upon the achievement of a manufacturing milestone in October 2017. The milestone payment was made in consideration of the successful initiation of transfer of technology related to the manufacturing of rocapuldencel-T. On March 23, 2018, we entered into a third amendment to the license agreement pursuant to which Lummy agreed to pay us a $1.05 million milestone.

The license agreement will terminate upon expiration of the last to expire royalty term for all Arcelis-Based Products, with each royalty term being the longer of the expiration of the last valid patent claim covering the applicable Arcelis-Based Product and 10 years from the first commercial sale of such Arcelis-Based Product. Either party may terminate the license agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy. We may terminate the license agreement if Lummy HK challenges or assists a third party in challenging specified patent rights of ours. If Lummy HK terminates the license agreement upon our material breach or bankruptcy, Lummy HK is entitled to terminate the licenses it granted to us and retain its licenses from us with respect to Arcelis-Based Products then in development or being commercialized, subject to Lummy HK’s continued obligation to pay royalties and milestones with respect to such Arcelis-Based Products.

**Invetech**. In October 2014, we entered into a development agreement with Invetech Pty Ltd, or Invetech. The development agreement supersedes and replaces the development agreement entered into by the parties as of July 2005. Under the development agreement, Invetech agreed to continue to develop and provide prototypes of the automated production system to be used for the manufacture of our Arcelis-based products, or the Production Systems. Development services will be performed on a proposal by proposal basis. Invetech had agreed to defer 30% of its fees, with such deferral not to exceed $5.0 million.

The development agreement requires the parties to discuss in good faith Invetech’s supply of Production Systems for use in manufacturing commercial product. We have an obligation to purchase $25.0 million worth of Production Systems, components, subsystems and spare parts for commercial use. Once that obligation has been satisfied, we have the right to have a third party supply Production Systems for use in manufacturing commercial product, provided that Invetech has a right of first refusal with respect to any offer by a third party and we may not accept an offer from a third party unless that offer is at a price that is less than that offered by Invetech and otherwise under substantially the same or better terms. We will own all intellectual property arising from the development services (with the exception of existing Invetech intellectual property incorporated therein, under which we will have a license). The term of the development agreement will continue until the completion of the development of the Production Systems. The development agreement can be terminated early by either party because of a technical failure or by us without cause.

In September, 2017, we entered into a satisfaction and release agreement with Invetech. Under this agreement, we agreed to make, issue and deliver to Invetech (i) a cash payment of $500,000, (ii) 57,142 shares of our common stock and (iii) an unsecured convertible promissory note in the original principal amount of $5.2 million on account of and in full satisfaction and release of all payment obligations to Invetech arising under the development agreement prior to the date of the satisfaction and release agreement.

**Saint-Gobain**. In January 2015, we entered into a development agreement with Saint-Gobain Performance Plastics Corporation, or Saint-Gobain, that was subsequently amended in 2015, 2016 and 2017. Under the agreement, Saint-Gobain agreed to develop a range of disposables for use in our automated production systems to be used for the manufacture of our Arcelis-based products. We had also agreed separately to purchase $3.5 million in disposables under the agreement during 2017. The Saint-Gobain agreement requires the parties to execute a commercial supply agreement under which Saint-Gobain would become the exclusive supplier of disposables for the manufacture of our products treating solid tumors for no less than fifteen years. The Saint-Gobain agreement will continue until December 31, 2019, but can be terminated earlier by written agreement of the parties because of a material default, including the failure to execute the commercial supply agreement, or a failure to achieve a performance milestone.
In November, 2017, we entered into a satisfaction and release agreement with Saint-Gobain. Under this agreement, we agreed to make, issue and deliver to Saint-Gobain (i) a cash payment of $500,000, (ii) 34,499 shares of our common stock, (iii) an unsecured convertible promissory note in the original principal amount of $2.4 million, and (iv) certain specified equipment originally provided to us under the development agreement, on account of and in full satisfaction and release of all payment obligations to Saint-Gobain arising under the development agreement, including the development fees and charges owed by us to Saint-Gobain.

Cellscript. In December 2015, we entered into a development and supply agreement with Cellscript, LLC. Under the agreement, Cellscript has agreed to develop cGMP processes for the manufacture and production of CD40L RNA, a ribonucleic acid used in the production of our Arcelis-based products, and to manufacture and produce CD40L RNA.

In consideration for these development and production services, we have agreed to pay Cellscript total fees of $4.6 million. Upon the execution of the agreement, we made an initial payment to Cellscript of $2.0 million through the issuance to Cellscript of 45,309 shares of our common stock. The balance of these fees are payable to Cellscript, at our option, in cash, common stock or a combination of cash and common stock upon the achievement of development milestones. Any shares of common stock issued pursuant to the agreement are subject to a lock-up period of 180 days from the date of issuance of such shares to Cellscript.

Under the terms of the agreement, Cellscript shall be the sole and exclusive manufacturer and supplier to us of CD40L RNA, and we will make agreed upon cash payments to Cellscript for CD40L RNA produced for us during the term of the Agreement. Under the agreement, Cellscript shall also be our sole and exclusive supplier of enzymes and various kits comprising enzymes for transcription, capping and/or polyadenylation of RNA. We will make agreed upon cash payments to Cellscript for each kit that is purchased under the agreement.

The agreement will continue until the earlier of (i) June 30, 2018 or (ii) the effective date of a commercial supply agreement negotiated in good faith by the parties, but can be earlier terminated by either party due to a material breach or upon bankruptcy of the other party.

Government Regulation

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

U.S. Drug and Biological Product Approval Process

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. Biologic products are licensed for marketing under the Public Health Service Act, or PHSA. The failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA’s refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug or biological product may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA’s good laboratory practice, or GLP, regulations;
• submission to the FDA of an IND which must become effective before human clinical trials may begin;
• approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
• performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug or biological product for each indication;
• submission to the FDA of a new drug application, or NDA, for a drug product or a BLA for a biologic;
• satisfactory completion of an FDA advisory committee review, if applicable;
• satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP, and to assure that the facilities, methods and controls are adequate to preserve the drug’s identity, strength, quality and purity;
• FDA review and approval of the NDA or BLA; and
• compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies and the IND. Before an applicant begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess its potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved NDA. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold or partial hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials. Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB’s requirements or if the product candidate has been associated with unexpected serious harm to patients. Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee, or DSMB.
Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- **Phase 1:** The drug or biological candidate product is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- **Phase 2:** The drug or biological candidate product is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- **Phase 3:** The drug or biological candidate product is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate’s safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group and to further document a clinical benefit in the case of drugs approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB’s requirements or if the drug has been associated with unexpected serious harm to patients.

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

**Special Protocol Assessment.** The SPA process is designed to facilitate the FDA’s review and approval of drug and biological products by allowing the FDA to evaluate the proposed design and size of Phase 3 clinical trials that are intended to form the primary basis for determining a drug or biological product’s efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the trial protocol and respond to a sponsor’s questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis, within 45 days of receipt of the request. The FDA ultimately assesses whether the trial protocol design and planned analysis of the trial adequately address objectives in support of a regulatory submission. All agreements and disagreements between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Even if the FDA agrees to the design, execution and analyses proposed in protocols reviewed under an SPA, the FDA may revoke or alter its agreement under the following circumstances:

- public health concerns emerge that were unrecognized at the time of the protocol assessment;
- a sponsor fails to follow a protocol that was agreed upon with the FDA;
- the relevant data, assumptions, or information provided by the sponsor in a request for SPA change are found to be false statements or misstatements or are found to omit relevant facts; or
- the FDA and the sponsor agree in writing to modify the trial protocol and such modification is intended to improve the study.
Marketing Approval. Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product’s chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA or BLA requesting approval to market the product for one or more indications. Every new product must be the subject of an approved application before it may be commercialized in the United States. Under federal law, the submission of most applications is subject to an application user fee, which for federal fiscal year 2018 is $2,421,495 for an application requiring clinical data. The sponsor of an approved application is also subject to an annual program fee, which for fiscal year 2018 is $304,162. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, as amended and reauthorized, an NDA, BLA or supplement to an NDA or BLA for certain types of new drug or biological products must contain data that are adequate to assess the safety and effectiveness of the drug or biological 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. 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. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

The FDCA requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, or other clinical development programs.

The FDA also could require submission of a risk evaluation and mitigation strategy, or REMS, plan to mitigate any identified or suspected serious risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs and BLAs within the first 60 days after submission before accepting them for filing to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA or BLA to determine, among other things, whether the product is safe and effective (described as safe, pure and potent for BLAs) and the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product’s continued safety, purity and potency. The FDA is required to refer an application for a novel drug or biological product to an advisory committee or explain why such referral was not made. 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.

Before approving an NDA or 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 compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and integrity of the clinical data submitted.

The testing and approval process requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to develop our product candidates and secure necessary governmental approvals, which could delay or preclude us from marketing our products.
If the FDA’s evaluation of the NDA or BLA and inspection of the manufacturing facilities and clinical trial sites are favorable, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA or BLA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. If and when those conditions have been met to the FDA’s satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug or biological product with specific prescribing information for specific indications. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

Even if the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug’s safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some 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.

**Special FDA Expedited Review and Approval Programs.**

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 fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation. The FDA may also approve certain products on an accelerated basis. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious aspect of a serious or life-threatening disease or condition and will fill an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product’s application before the application is complete.

Under the provisions of the Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted in 2012, a sponsor also can request designation of a product candidate as a “breakthrough therapy.” A breakthrough therapy is defined as a drug or biological product that is intended, alone or in combination with one or more other drugs or biological 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 are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

In addition, the FDA may give a priority review designation to drugs or biological products that provide safe and effective therapy where no satisfactory alternative exists or a significant improvement compared to marketed products in the treatment, diagnosis or prevention of a disease. For products regulated by the Center for Biologics Evaluation and Research, or CBER, the product must be intended to treat a serious or life threatening disease or condition. A priority review means that the targeted time for the FDA to review an application is six months, rather than ten months. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.
With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Finally, 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 and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Post-Approval Requirements. Any drug or biological products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA or BLA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product’s safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the drug or biologic.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs and biological products are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer’s tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.
Once 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, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of 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. Drugs 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.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products.

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

**Biosimilars and Non-Patent Exclusivity.** The 2010 Patient Protection and Affordable Care Act, which was signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 or BPCIA. That Act established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. As of January 1, 2018, the FDA has approved nine biosimilar products for use in the United States. No interchangeable biosimilars, have been approved. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Additional guidances are expected to be finalized by FDA in the near term.

Under the Act, 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 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. We believe that our investigational products, if approved via full BLAs, will be considered “reference products” that are entitled to both four-year and twelve-year exclusivity under the BPCIA. 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 preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars 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 Exclusivity**. Pediatric exclusivity is another type of non-patent 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 or patent protection, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an application 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.

**Orphan Drug Designation and Exclusivity**. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug (including a biologic) intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or 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 in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full NDA or full BLA, to market the same drug for the same indication for seven years. For purposes of small molecule drugs, the FDA defines “same drug” as a drug that contains the same active moiety and is intended for the same use as the previously approved orphan drug. For purposes of large molecule drugs, the FDA defines “same drug” as a drug that contains the same principal molecular structural features, but not necessarily all of the same structural features, and is intended for the same use as the drug in question. Notwithstanding the above definitions, a drug that is clinically superior to an orphan drug will not be considered the “same drug” and thus will not be blocked by orphan drug exclusivity.

Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different indications. If a product designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity. Orphan exclusivity will also not bar approval of another product under certain circumstances, including if a subsequent product with the same product for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

**The 21st Century Cures Act.** On December 13, 2016, the 21st Century Cures Act, or Cures Act, was enacted into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increasing funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act, or PHSA, to reauthorize and expand funding for the NIH. The Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges the NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.
With amendments to the FDCA and the PHSA, Title I of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain products intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for product applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires the FDA to evaluate the potential use of “real world evidence” to help support approval of new indications for approved products; provides a new “limited population” approval pathway for antibiotic and antifungal products intended to treat serious or life-threatening infections; and authorizes the FDA to designate a product as a “regenerative advanced therapy,” thereby making it eligible for certain expedited review and approval designations.

**Health care Law and Regulation**

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

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and 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 health care 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, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.

- the federal Health Insurance Portability and Accountability Act of 1996, or 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 health care benefit program or making false statements relating to health care matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing · or covering up a material fact or making any materially false statement in connection with the delivery of or payment for health care benefits, items or services;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, 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

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to health care items or services that are reimbursed by non-government third-party payors, including private insurers.
Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pharmaceutical Insurance Coverage and Health Care Reform

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is 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 marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor’s decision to provide coverage for a product does not imply that an adequate reimbursement rate will be 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.

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

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

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drug agents or biologic agents, which is apportioned among these entities according to their market share in certain government health care programs;

- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
• a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D;

• extension of manufacturers’ Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;

• a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, instilled, implanted or injected;

• expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers’ Medicaid rebate liability;

• expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

• new requirements under the federal Physician Payments Sunshine Act for drug manufacturers to report information related to payments and other transfers of value made to physicians and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members;

• a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

• creation of the Independent Payment Advisory Board, which, if and when impaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs; and

• establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and will stay in effect through 2024 unless additional Congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

These healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices or the frequency with which products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. In May 2017, the U.S. House of Representatives passed legislation known as the American Health Care Act of 2017. In the U.S., Senate legislation has been proposed to replace the ACA known as the Better Care Reconciliation, to repeal the ACA without companion legislation to replace it, or to enact a “skinny” version of the Better Care Reconciliation Act of 2017. In addition, the Senate considered proposed healthcare reform legislation known as the Graham-Cassidy bill. None of these measures was passed by the U.S. Senate.
The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 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 or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction (CSR) payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

More recently, with enactment of the Tax Cuts and Jobs Act of 2017 in December 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Foreign Regulation

Although we do not currently market any of our products outside the United States and have no current plans to engage in product commercialization outside the United States, we may decide to do so in the future. In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods, and may be otherwise complicated by some of our products and product candidates being controlled substances. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.
Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. Sales of any of our product candidates, if approved, will depend, in part, on the extent to which the costs of the products will be covered by third party payors, including government health programs such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product once coverage is approved. Third party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the approved drugs for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, we 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. Our product candidates may not be considered medically necessary or cost-effective. A payor’s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at an appropriate return on investment. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals such as the drug product candidates that we are developing and could adversely affect our net revenue and results.

Pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug 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. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drug products will allow favorable reimbursement and pricing arrangements for any of our products.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on drug pricing. Coverage policies, third party reimbursement rates and drug pricing regulation may change at any time. In particular, the PPACA and a related reconciliation bill, which we collectively refer to as the Affordable Care Act or ACA, contain provisions that may reduce the profitability of drug products, including, for example, increased rebates for covered outpatient drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries, and annual fees based on pharmaceutical companies’ share of sales to federal health care programs. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.
New Legislation and Regulations

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of products regulated by the FDA. For example, the FDASIA and PPACA provisions discussed above were enacted in 2012 and 2010, respectively.

Numerous statements made by President Trump and members of the U.S. Congress indicate that it is likely that legislation will be passed by Congress and signed into law by President Trump that repeals the PPACA, in whole or in part, and/or introduces a new form of health care reform. It is unclear at this point what the scope of such legislation will be and when it will become effective. Because of the uncertainty surrounding this replacement health care reform legislation, we cannot predict with any certainty the likely impact of the PPACA’s repeal or the adoption of any other health care reform legislation on our business. Whether or not there is alternative health care legislation enacted in the United States, there is likely to be significant disruption to the health care market in the coming months and years.

In addition to potential for new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted, or FDA regulations, guidance, policies or interpretations changed or what the impact of such changes, if any, may be.

Segment and Geographic Information

Operating segments are defined as components of an enterprise engaging in business activities from which it may earn revenues and incur expenses, for which discrete financial information is available and whose operating results are regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. We view our operations and manage our business in one operating segment and all of our operations are in North America.

Employees

As of February 28, 2018, we had 39 employees, including 11 in research and development, 1 in clinical development, 16 in manufacturing and 11 in general and administrative functions. None of our employees is subject to a collective bargaining agreement or represented by a labor or trade union. We believe that our relations with our employees are good.

Corporate Information

We were incorporated in the State of Delaware on May 8, 1997. Our principal executive offices are located at 4233 Technology Drive, Durham, North Carolina 27704, and our telephone number is (919) 287-6300.

Available Information

We file with the Securities and Exchange Commission, or SEC, annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy and information statements and amendments to reports filed or furnished pursuant to Sections 13(a), 14 and 15(d) of the Securities Exchange Act of 1934, as amended. The public may obtain these filings at the SEC’s Public Reference Room at 100 F Street, NE, Washington, DC 20549 or by calling the SEC at 1-800-SEC-0330. The SEC also maintains a website at http://www.sec.gov that contains reports, proxy and information statements and other information regarding Argos and other companies that file materials with the SEC electronically. As soon as practicable after filing with the SEC, copies of our reports on Forms 10-K, Forms 10-Q and Forms 8-K may also be obtained, free of charge, electronically through the investor relations portion of our web site, www.argostherapeutics.com/investor-relations/sec-filings/default.aspx.
We webcast any earnings calls we have on our investor relations website. Additionally, we provide notifications of news or announcements regarding our financial performance, including SEC filings, investor events and press and earnings releases, on the investor relations portion of our website. Further corporate governance information, including our corporate governance guidelines, board committee charters, Code of Business Conduct and Ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, or persons performing similar functions, is also available on our investor relations website under the heading “Corporate Governance.” The contents of our website are not intended to be incorporated by reference into this Annual Report on Form 10-K or in any other report or document we file with the SEC.
Item 1A. Risk Factors

We operate in a dynamic and rapidly changing business environment that involves multiple risks and substantial uncertainty. The following discussion addresses risks and uncertainties that could cause, or contribute to causing, actual results to differ from expectations in material ways. In evaluating our business, investors should pay particular attention to the risks and uncertainties described below and in other sections of this Annual Report on Form 10-K and in our subsequent filings with the SEC. These risks and uncertainties, or other events that we do not currently anticipate or that we currently deem immaterial also may affect our results of operations, cash flows and financial condition. The trading price of our common stock could also decline due to any of these risks, and you could lose all or part of your investment.

Risks Related to the Development and Regulatory Approval of Our Product Candidates

We have depended heavily on the success of our two product candidates, rocapuldencel-T and AGS-004. Clinical trials of our product candidates may not be successful. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We currently have no products approved for sale. We have invested a significant portion of our efforts and financial resources in the development of rocapuldencel-T for the treatment of metastatic renal cell carcinoma, or mRCC, and other cancers and AGS-004 for the treatment of HIV.

Our ability to generate product revenues, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful development and commercialization of rocapuldencel-T and AGS-004 and any other product candidates we develop, if we determine to proceed with its development. The success of our product candidates will depend on several factors, including the following:

• successful completion of clinical trials, including clinical results that are statistically significant as well as clinically meaningful in the context of the indications for which we are developing our product candidates;

• receipt of marketing approvals from the FDA and similar regulatory authorities outside the United States;

• establishing a facility for the commercial manufacture of products based on our Arcelis precision immunotherapy technology platform;

• maintaining patent and trade secret protection and regulatory exclusivity for our product candidates, both in the United States and internationally;

• launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;

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• commercial acceptance of our products, if and when approved, by patients, the medical community and third party payors;
• obtaining and maintaining healthcare coverage and adequate reimbursement;
• effectively competing with other therapies; and
• a continued acceptable safety profile of the products following any marketing approval.

In February 2017, we announced that the Independent Data Monitoring Committee, or IDMC, for our pivotal Phase 3 ADAPT clinical trial of rocapuldencel-T in combination with sunitinib / standard-of-care for the treatment of mRCC recommended that the trial be discontinued for futility based on its planned interim data analysis. The IDMC concluded that the trial was unlikely to demonstrate a statistically significant improvement in overall survival in the combination treatment arm, utilizing the intent-to-treat population at the pre-specified number of 290 events (deaths), the original primary endpoint of the study. Notwithstanding the IDMC’s recommendation, we determined to continue to conduct the trial while we analyzed interim data from the trial. Following a meeting with the FDA, we determined to continue the ADAPT trial until at least the pre-specified number of 290 events occurs and to submit to the FDA a protocol amendment to increase the pre-specified number of events for the primary analysis of overall survival in the trial beyond 290 events. We believe that extending our evaluation of rocapuldencel-T beyond 290 events in the trial could enhance our ability to observe rocapuldencel-T’s expected delayed treatment effect.

We are currently finalizing an amendment to the ADAPT protocol, including an amended primary endpoint analysis, and plan to submit it to the FDA prior to the interim data analysis planned for the second quarter of 2018, at which time approximately 55 new events (deaths) are expected to have occurred subsequent to the February 2017 interim analysis. We are planning to include the following four co-primary endpoints in the amended ADAPT protocol:

- Overall survival for all randomized patients when approximately 375 events have occurred (under the same analysis that was originally planned for 290 events);
- The percentage of patients surviving at least five years;
- Overall survival for patients who remained alive at the time of the February 2017 interim analysis, to be evaluated when approximately 155 new events have occurred; and
- Overall survival for all patients for whom at least 12 months of follow-up is available (excluding patients who died or were lost to follow-up within the first 12 months after enrollment).

In connection with our amendment of the ADAPT protocol, the special protocol assessment, or the SPA, for the ADAPT trial ceased to be in effect. The FDA also may not accept our proposed protocol amendment, including the amended primary endpoint analysis.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

*If clinical trials of our product candidates, such as our ADAPT trial of rocapuldencel-T, fail to demonstrate safety and efficacy to the satisfaction of the FDA or similar regulatory authorities outside the United States or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.*

Before obtaining regulatory approval for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more of our clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.
To date, we have not completed a randomized clinical trial of rocapuldencel-T against a placebo or a comparator therapy. Our phase 2 trial of rocapuldencel-T was a single arm trial in which only 21 patients received the combination of rocapuldencel-T and sunitinib. Our ADAPT trial of rocapuldencel-T is a randomized trial designed to compare directly the combination of rocapuldencel-T and sunitinib or another therapy to treatment with sunitinib or another therapy monotherapy. Under the original protocol for the trial, the data from the trial needed to demonstrate an increase in median overall survival of approximately six months for the rocapuldencel-T plus sunitinib / targeted therapy arm as compared to the sunitinib / targeted therapy monotherapy control arm at 290 events (deaths) in the intent to treat population in order to show statistical significance and achieve the original primary endpoint of the trial.

Based on the February 2017 interim analysis, the IDMC concluded that the trial was unlikely to demonstrate a statistically significant improvement in overall survival in the combination treatment arm, utilizing the intent-to-treat population, the original primary endpoint of the trial. However, even demonstration of statistical significance and achievement of the primary endpoint of the trial would not assure approval by the FDA or similar regulatory authorities outside the United States. Notwithstanding the IDMC’s recommendation, we determined to continue the ADAPT trial until at least the pre-specified number of 290 events occurs and to submit to the FDA a protocol amendment to increase the pre-specified number of events for the primary analysis of overall survival in the trial beyond 290 events. We believe that extending our evaluation of rocapuldencel-T beyond 290 events in the trial could enhance our ability to observe rocapuldencel-T’s expected delayed treatment effect.

We are currently finalizing an amendment to the protocol for the ADAPT trial, including an amended primary endpoint analysis, and plan to submit it to the FDA prior to the interim data analysis planned for the second quarter of 2018, at which time approximately 55 new events (deaths) are expected to have occurred subsequent to the February 2017 interim analysis. We are planning to include the following four co-primary endpoints in the amended ADAPT protocol:

- Overall survival for all randomized patients when approximately 375 events have occurred (under the same analysis that was originally planned for 290 events);
- The percentage of patients surviving at least five years;
- Overall survival for patients who remained alive at the time of the February 2017 interim analysis, to be evaluated when approximately 155 new events have occurred; and
- Overall survival for all patients for whom at least 12 months of follow-up is available (excluding patients who died or were lost to follow-up within the first 12 months after enrollment).

In connection with our amendment of the ADAPT protocol, the SPA, for the ADAPT trial ceased to be in effect. The FDA has not advised us whether our proposed protocol amendment, including the amended primary endpoint analysis, would be acceptable to the FDA. As a result, even if we achieve each of the co-primary endpoints in the trial, there can be no assurance that the FDA or similar regulatory authorities outside the United States would grant marketing approval of rocapuldencel-T. In originally designing the ADAPT trial we considered other reported clinical trials and data from the International Metastatic Renal Cell Carcinoma Database Consortium, or the Consortium. However, results from two different trials or between a trial and an analysis of a treatment database often cannot be reliably compared. Accordingly, patients in our ADAPT trial who received treatment with sunitinib / targeted therapy monotherapy had not had, as of the February 2017 interim analysis, results similar to patients studied in other clinical trials of sunitinib or to patients in the Consortium database who were treated with sunitinib or other therapies. If the patients in our ADAPT trial who received sunitinib / targeted therapy monotherapy have results which are better than the results that occurred in other clinical trials of sunitinib or the results described in the Consortium database, we may not demonstrate a sufficient clinical benefit from rocapuldencel-T in combination with sunitinib and other therapies to allow the FDA to approve rocapuldencel-T for marketing. Moreover, if the patients in our ADAPT trial who received the combination of rocapuldencel-T and sunitinib / targeted therapy have results which are worse than the results that occurred in our Phase 2 clinical trial, we may not demonstrate a sufficient benefit from the combination therapy to allow the FDA to approve rocapuldencel-T for marketing.

For drug and biological products, the FDA typically requires the successful completion of two adequate and well-controlled clinical trials to support marketing approval because a conclusion based on two such trials will be more reliable than a conclusion based on a single trial. In the case of rocapuldencel-T, we intended to seek approval based upon the results of a single pivotal Phase 3 clinical trial, our ADAPT trial, because rocapuldencel-T is intended for life threatening disease. The FDA reviewed our plans to conduct our ADAPT trial under its SPA process. In February 2013, the FDA advised us in a letter that it had completed its review of our plans under the SPA process. The FDA also informed us that in order for a single trial to support approval of an indication, the trial must be well conducted, and the results of the trial must be internally consistent, clinically meaningful and statistically persuasive. In connection with our amendment of the ADAPT protocol to increase the pre-specified number of events for the primary analysis of overall survival in the trial beyond 290 events, the SPA for the ADAPT trial ceased to be in effect.

As a general matter, if we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements;
- be subject to restrictions on how the product is distributed or used; or
- have the product removed from the market after obtaining marketing approval.
If we experience any of a number of possible unforeseen events in connection with our clinical trials, potential marketing or commercialization of our product candidates could be delayed or prevented.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive regulatory approval or commercialize our product candidates. For example, in February 2017, we announced that the IDMC for our pivotal Phase 3 ADAPT clinical trial of rocapuldencel-T in combination with sunitinib/standard-of-care for the treatment of mRCC had recommended that the trial be discontinued for futility based on its planned interim data analysis. Unforeseen events that could delay or prevent our ability to receive regulatory approval or commercialize our product candidates include:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate; for example, in our Phase 2b clinical trial of AGS-004, we experienced a higher dropout rate than we anticipated due to the higher than expected number of patients who did not complete the full 12 week antiretroviral treatment interruption required by the protocol for the trial;
- our third party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may decide, or regulators or institutional review boards may require us or our investigators to, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate; and
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

In addition, the patients recruited for clinical trials of our product candidates may have a disease profile or other characteristics that are different than we expect and different than the clinical trials were designed for, which could adversely impact the results of the clinical trials. For instance, our Phase 2 combination therapy clinical trial of rocapuldencel-T in combination with sunitinib was originally designed to enroll patients with favorable disease risk profiles and intermediate disease risk profiles with a primary endpoint of complete response rate. However, the actual trial population consisted entirely of patients with intermediate disease risk profiles and poor disease risk profiles. This is a population for which published research has shown that sunitinib alone, as well as other of the therapies for mRCC, rarely if ever produce complete responses in mRCC, and in our Phase 2 clinical trial in this population, the combination therapy of rocapuldencel-T and sunitinib did not show a complete response rate that met the endpoint of the trial.

Our product development costs will also increase if we experience delays in testing or obtaining marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. For example, in response to our submission of an investigational new drug application, or IND, for AGS-004, the FDA raised safety concerns regarding the analytical treatment interruption contemplated by our protocol for our Phase 2 clinical trial of AGS-004, and required a one-year safety follow-up after the final dose for each patient. This resulted in the need for an amendment to the trial protocol and a four-month delay prior to initiating the Phase 2 clinical trial in the United States. In addition, the IDMC for our pivotal Phase 3 ADAPT clinical trial of rocapuldencel-T in combination with sunitinib/standard-of-care for the treatment of mRCC recommended that the trial be discontinued for futility based on its planned interim data analysis. Notwithstanding the IDMC’s recommendation, we determined to continue to conduct the trial while we analyzed interim data from the trial. Following a meeting with FDA in May 2017, we determined to continue the ADAPT trial until at least the pre-specified number of 290 events occurs and to submit to the FDA a protocol amendment to increase the pre-specified number of events for the primary analysis of overall survival in the trial beyond 290 events. We believe that extending our evaluation of rocapuldencel-T beyond 290 events in the trial could enhance our ability to observe rocapuldencel-T’s expected delayed treatment effect.

We are currently finalizing an amendment to the ADAPT protocol, including an amended primary endpoint analysis, and plan to submit it to the FDA prior to the interim data analysis planned for the second quarter of 2018, at which time approximately 55 new events (deaths) are expected to have occurred subsequent to the February 2017 interim analysis. We are planning to include the following four co-primary endpoints in the amended ADAPT protocol:

- Overall survival for all randomized patients when approximately 375 events have occurred (under the same analysis that was originally planned for 290 events);
- The percentage of patients surviving at least five years;
- Overall survival for patients who remained alive at the time of the February 2017 interim analysis, to be evaluated when approximately 155 new events have occurred; and
- Overall survival for all patients for whom at least 12 months of follow-up is available (excluding patients who died or were lost to follow-up within the first 12 months after enrollment).

In connection with our amendment of the ADAPT protocol, the special protocol assessment, or the SPA, for the ADAPT trial ceased to be in effect. The FDA also may not accept our proposed protocol amendment, including the amended primary endpoint analysis.
In addition to additional costs, significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to commercialize our product candidates and may harm our business and results of operations.

*If we experience delays or difficulties in the enrollment of patients in our clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.*

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In particular, the recommendation by the IDMC that the ADAPT study be terminated for futility may negatively impact our ability to enroll patients in future clinical trials of rocapuldencel-T.

Our competitors may have ongoing clinical trials for product candidates that could be competitive with our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors’ product candidates. For example, during the Phase 1/2 monotherapy clinical trial of rocapuldencel-T that we conducted, our ability to enroll patients in the trial was adversely affected by the FDA’s approval of sorafenib and sunitinib, because patients did not want to receive, and physicians were reluctant to administer, rocapuldencel-T as an experimental monotherapy once new therapies that showed efficacy in clinical trials were introduced to the market and became widely available.

Patient enrollment is affected by other factors including:

- severity of the disease under investigation;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

The actual amount of time for full enrollment of our clinical trials could be longer than planned. Enrollment delays in any of our clinical trials may result in increased development costs for our product candidates, which would cause the value of the company to decline and limit our ability to obtain additional financing. Our inability to enroll a sufficient number of patients for any of our other clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

*We are developing AGS-004 for use in combination with latency reversing drugs to eradicate HIV. If latency reversing drugs are not successfully developed for HIV on a timely basis or at all, we will be unable to develop AGS-004 for this use or will be delayed in doing so. In addition, because there are currently no products approved for HIV eradication, we cannot be certain of the clinical trials that we will need to conduct or the regulatory requirements that we will need to satisfy in order to obtain marketing approval of AGS-004 for this purpose.*
We are focusing our development program for AGS-004 on the use of AGS-004 in combination with latency reversing drugs, including vorinostat, to eradicate HIV. We plan to rely on these latency reversing drugs because we recognize that the ultimate objective of virus eradication is unlikely to be achieved with immunotherapy alone because the immune system is not able to recognize the HIV virus in latently infected cells with a low level or lack of expression of HIV antigens.

Several companies and academic groups are evaluating latency reversing drugs that can potentially activate latently infected cells to increase viral antigen expression and make the cells vulnerable to elimination by the immune system. We are not a party to any arrangements with these companies or academic groups. If these companies or academic groups determine not to develop latency reversing drugs for this purpose because the drugs do not sufficiently increase viral antigen expression or have unacceptable toxicities, or these companies or academic groups otherwise determine to collaborate with other developers of immunotherapies on a combination therapy for complete virus eradication, we will not be able to complete our AGS-004 development program. In addition, if these companies or academic groups do not proceed with such development on a timely basis, our AGS-004 program correspondingly would be delayed.

A number of the latency reversing drugs being evaluated for use in HIV patients are currently approved in the United States and elsewhere for use in the treatment of specified cancer indications. For instance, vorinostat is approved for cutaneous T-cell lymphoma. If these drugs are not approved by the FDA or equivalent foreign regulatory authorities for use in HIV, the FDA and these other regulatory authorities may not approve AGS-004 without the latency reversing drug having received marketing approval for HIV. If the FDA and these other regulatory authorities approve AGS-004 without the approval of the latency reversing drug for HIV, the use of AGS-004 in combination with the latency reversing drug for virus eradication would require sales of the latency reversing drug for off-label use. In such event, the success of the combination of AGS-004 and the latency reversing drug would be subject to the willingness of physicians, patients, healthcare payors and others in the medical community to use the latency reversing drug for off-label use and of government authorities and third party payors to pay for the combination therapy. In addition, we would be limited in our ability to market the combination for its intended use if the latency reversing drug were to be used off-label.

Currently, there are no products approved for the eradication of HIV. As a result, we cannot be certain as to the clinical trials we will need to conduct or the regulatory requirements that we will need to satisfy in order to obtain marketing approval of AGS-004 for the eradication of HIV.

**If serious adverse or inappropriate side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.**

All of our product candidates are still in preclinical or clinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. In addition, such effects or characteristics could cause an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates, require us to conduct additional clinical trials or other tests or studies, and could result in a more restrictive label, or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities.

**Our Arcelis-based product candidates are immunotherapies that are based on a novel technology utilizing a patient’s own tissue. This may raise development issues that we may not have anticipated or be able to resolve, regulatory issues that could delay or prevent approval or personnel issues that may prevent us from further developing and commercializing our product candidates.**

Rocapuldencel-T and AGS-004 are based on our novel Arcelis precision immunotherapy technology platform. In the course of developing this platform and these product candidates, we have encountered difficulties in the development process. For example, we terminated the development of MB-002, the predecessor to rocapuldencel-T, when the results from the initial clinical trial of MB-002 indicated that the product candidate only corrected defects in the production of one of two critical cytokines required for effective immune response. In addition, in February 2017, the IDMC for our ADAPT clinical trial of rocapuldencel-T in combination with sunitinib / standard-of-care recommended that the trial be discontinued for futility based on its planned interim data analysis. There can be no assurance that additional development problems will not arise in the future which we may not have anticipated or be able to resolve or which may cause significant delays in development.
In addition, regulatory approval of novel product candidates such as our Arcelis-based product candidates manufactured using novel manufacturing processes such as ours can be more expensive and take longer than for other, more well-known or extensively studied pharmaceutical or biopharmaceutical products, due to our and regulatory agencies’ lack of experience with them. The FDA has only approved a few individualized immunotherapy products to date. This lack of experience may lengthen the regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to significant post-approval limitations or restrictions.

The novel nature of our product candidates also means that fewer people are trained in or experienced with product candidates of this type, which may make it difficult to find, hire and retain capable personnel for research, development and manufacturing positions.

**Development of our individualized Arcelis-based product candidates is subject to significant uncertainty because each product candidate is derived from source material that is inherently variable. This variability could reduce the effectiveness of our Arcelis-based product candidates, delay any FDA approval of any of our Arcelis-based product candidates, cause us to change our manufacturing methods and adversely affect the commercial success of any approved Arcelis-based products.**

The disease samples from the patients to be treated with our Arcelis-based products vary from patient to patient. This inherent variability may adversely affect our ability to manufacture our products because each tumor or virus sample that we receive and process will yield a different product. As a result, we may not be able to consistently produce a product for every patient and we may not be able to treat all patients effectively. Such inconsistency could delay FDA or other regulatory approval of our Arcelis-based product candidates or, if approved, adversely affect market acceptance and use of our Arcelis-based products. If we have to change our manufacturing methods to address any inconsistency, we may have to perform additional clinical trials, which would delay FDA or other regulatory approval of our Arcelis-based product candidates and increase the costs of development of our Arcelis-based product candidates.

The inherent variability of the disease samples from the patients to be treated with our Arcelis-based products may further adversely affect our ability to manufacture our products because variability in the source material for our product candidates, such as tumor cells or viruses, may cause variability in the composition of other cells in our product candidates. Such variability in composition or purity could adversely affect our ability to establish acceptable release specifications and the development and regulatory approval processes for our product candidates may be delayed, which would increase the costs of development of our Arcelis-based product candidates.

**If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.**

Failure to obtain regulatory approval for any of our product candidates will prevent us from commercializing the product candidate. We have not received regulatory approval to market any of our product candidates in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain regulatory approvals and expect to rely on third party contract research organizations to assist us in this process. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each therapeutic indication to establish the product candidate’s safety and efficacy. Securing FDA approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use.
The process of obtaining regulatory approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. To date, the FDA has only approved a few individualized immunotherapy products. Changes in clinical guidelines or regulatory approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA has substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of a product candidate. Any regulatory approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

**Failure to obtain regulatory approval in international jurisdictions would prevent our product candidates from being marketed abroad.**

We are a party to arrangements with third parties, and intend to enter into additional arrangements with third parties, under which they would market our products outside the United States. In order to market and sell our products in the European Union and many other jurisdictions, we or such third parties must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

**A fast track designation by the FDA may not actually lead to a faster development, regulatory review or approval process.**

If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address an unmet need for this condition, the treatment sponsor may apply for FDA fast track designation. In April 2012, the FDA notified us that we obtained fast track designation for rocapuldencel-T for the treatment of mRCC. Fast track designation does not ensure that we will experience a faster development, regulatory review or approval process compared to conventional FDA procedures. Additionally, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.
The efforts of the Trump Administration to pursue regulatory reform may limit the FDA’s ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

The Trump Administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA’s ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, President Trump issued an executive order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the “two-for-one” provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and on February 2, 2017, the administration indicates that the “two-for-one” provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA’s ability to exercise its regulatory authority. If these executive actions impose constraints on FDA’s ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses for at least the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $74.8 million for the year ended December 31, 2015, $53.0 million for the year ended December 31, 2016 and $40.6 million for the year ended December 31, 2017. As of December 31, 2017, we had an accumulated deficit of $372.6 million. As a result of our historical operating losses and expected future negative cash flows from operations, we have concluded that there is substantial doubt about our ability to continue as a going concern. To date, we have financed our operations primarily through public offerings of common stock, private placements of common stock, preferred stock and warrants, convertible debt financings, debt from financial institutions, government contracts, government and other third party grants and license and collaboration agreements. We have devoted substantially all of our efforts to research and development, including clinical trials. We have not completed development of any product candidates.

We have devoted a significant portion of our financial resources to the development of rocapuldencel-T and expect this to continue as we continue the ADAPT trial. The continued development of rocapuldencel-T will necessarily impact the amount of expenses we incur and the size of our operating losses for the foreseeable future.

As we proceed with the development of our product candidates, including rocapuldencel-T, provided we are able to raise the capital necessary to fund such development, we anticipate that our expenses will increase substantially if and as we:

- continue our ADAPT trial of rocapuldencel-T for the treatment of mRCC or initiate other clinical trials of rocapuldencel-T for the treatment of mRCC;
- continue to support the ongoing investigator-initiated clinical trial of AGS-004;
- support any planned investigator-initiated clinical trials of rocapuldencel-T and AGS-004;
- initiate and conduct additional trials of rocapuldencel-T and AGS-004 for the treatment of cancers and HIV;
- seek regulatory approvals for our product candidates that successfully complete clinical trials;
• establish a facility for the commercial manufacture of products based on our Arcelis precision immunotherapy technology platform;
• establish a sales, marketing and distribution infrastructure to commercialize products for which we may obtain regulatory approval;
• maintain, expand and protect our intellectual property portfolio;
• continue our other research and development efforts;
• hire additional clinical, quality control, scientific and management personnel; and
• add operational, financial and management information systems and personnel, including personnel to support our product development and planned commercialization efforts.

To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This development and commercialization will require us to be successful in a range of challenging activities, including successfully completing preclinical testing and clinical trials of our product candidates, obtaining regulatory approval for these product candidates, building out and equipping a commercial manufacturing facility and manufacturing, marketing and selling those products for which we may obtain regulatory approval. We are only in the preliminary stages of some of these activities. We may never succeed in these activities and may never generate revenues that are significant or large enough to achieve profitability.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, expand our business, maintain our research and development efforts or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We are in the process of making a determination as to the next steps for the rocapuldecel-T clinical program. In February 2017, the IDMC for the ADAPT trial recommended that the trial be discontinued for futility based on its planned interim data analysis. The IDMC concluded that the trial was unlikely to demonstrate a statistically significant improvement in overall survival in the combination treatment arm, utilizing the intent-to-treat population at the pre-specified number of 290 events (deaths), the original primary endpoint of the study. Notwithstanding the IDMC’s recommendation, we determined to continue to conduct the trial while we analyzed interim data from the trial. Following a meeting with the FDA, we determined to continue the ADAPT trial until at least the pre-specified number of 290 events occurs, and have submitted to the FDA a protocol amendment to increase the pre-specified number of events for the primary analysis of overall survival in the trial beyond 290 events. We are engaged in discussions with the FDA regarding our development program for rocapuldecel-T and the ADAPT protocol.

We may also consider changes to our current business strategy and future operations. We are reviewing alternatives with a goal of maximizing the value of our company. We could determine to engage in one or more potential transactions, such as the sale of our company, a strategic partnership with one or more parties or the licensing, sale or divestiture of some of our assets or proprietary technologies, or to continue to operate our business in accordance with our existing business strategy. Pending any decision to change strategic direction, we are continuing to conduct our ongoing clinical trials while managing our cash position. We cannot provide any commitment as to the timing of our determination or the strategy we may adopt. If we determine to change our business strategy or to seek to engage in a strategic transaction, our future business, prospects, financial position and operating results could be significantly different than those in historical periods or projected by our management. Because of the significant uncertainty regarding our future plans, we are not able to accurately predict the impact of a potential change in our existing business strategy.
We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce, terminate or eliminate our product development programs, including establishing a commercial manufacturing facility or our commercialization efforts and to take other actions to reduce our operating expenses.

We have no external sources of funds other than our contract with the NIH and NIAID for the development of AGS-004, and we expect our expenses to increase in connection with our ongoing activities, particularly as we continue our ADAPT trial of rocapuldencel-T for the treatment of mRCC; and if we decide to initiate other clinical trials of rocapuldencel-T for mRCC, support ongoing investigator-initiated clinical trial of AGS-004; support planned investigator-initiated clinical trials of rocapuldencel-T and AGS-004; initiate and conduct additional clinical trials of rocapuldencel-T and AGS-004 for the treatment of cancers and HIV; undertake development of the group of PD1 monoclonal antibodies which we recently secured an exclusive option to in-license, if we decide to exercise that option; and seek regulatory approval for our product candidates and establish a commercial manufacturing facility or otherwise arrange for commercial manufacturing. In addition, if we obtain regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding if we wish to continue our operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, terminate or eliminate our product development programs or our commercialization efforts and to take other actions to reduce our operating expenses.

We have outstanding debt payable to Pharmstandard International S.A., or Pharmstandard, a collaborator and our largest stockholder, in the aggregate principal amount of $6.0 million; Invitech Pty Ltd, or Invitech, in the aggregate principal amount of $5.2 million; Saint-Gobain Performance Plastics Corporation, or Saint-Gobain, in the aggregate principal amount of $2.4 million; and Medinet Co. Ltd., or Medinet, in the aggregate principal amount of $4.0 million.

We do not currently have sufficient cash resources to pay all of our accrued obligations in full or to continue our business operations beyond the end of 2018. Therefore, we will need to raise additional capital prior to such time in order to continue to operate our business beyond that time. Alternatively, we may seek to engage in one or more potential transactions, such as the sale of our company, a strategic partnership with one or more parties or the licensing, sale or divestiture of some of our assets or proprietary technologies, but there can be no assurance that we will be able to enter into such a transaction or transactions on a timely basis or on terms that are favorable to us, or at all. Under these circumstances, we may instead determine to dissolve and liquidate our assets or seek protection under the bankruptcy laws. If we decide to dissolve and liquidate our assets or to seek protection under the bankruptcy laws, it is unclear to what extent we will be able to pay our obligations, and, accordingly, it is further unclear whether and to what extent any resources will be available for distributions to stockholders.

In 2017, we received several deficiency letters from the Listing Qualifications Department of The Nasdaq Stock Market notifying us that we were not in compliance with various requirements for continued listing on The Nasdaq Global Market, including the $50 million minimum market value of listed securities requirement, the $1.00 minimum bid price, and the $15 million minimum market value of publicly held shares requirement. In October 2017, we received two letters from The Nasdaq Global Market with respect to these deficiencies providing that, unless we requested a hearing before a Nasdaq Hearing Panel, our common stock would be delisted. In January 2018, we had a hearing before a Listing Qualifications Panel, or the Panel, at which we requested continued listing pending our return to compliance with such requirements. On January 17, 2018, we received a determination from Nasdaq indicating that our listing would be transferred from The Nasdaq Global Market to The Nasdaq Capital Market, provided that we demonstrated, on or before February 2, 2018, a closing bid price of $1.00 or more for a minimum of ten prior consecutive trading days, that, on or before April 24, 2018, we satisfied the $2.5 million stockholders’ equity requirement and demonstrated our ability to maintain compliance with the minimum stockholders’ equity requirement through the end of fiscal 2018, among other actions, and that we continued to meet the requirements for continued listing on The Nasdaq Capital Market. On February 15, 2018, we received formal notice from Nasdaq indicating that we have evidenced full compliance with the minimum $1.00 bid price requirement for continued listing on The Nasdaq Capital Market. We are not currently in compliance with the stockholders’ equity requirement. If we are unable to regain compliance to the satisfaction of the Panel and our common stock is delisted from trading, our ability to raise capital to continue to fund our operations by selling shares and our ability to acquire other companies or technologies by using our shares as consideration will be impaired.

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Our future capital requirements will depend on many factors, including:

- our decision as to our next steps with respect to the development of rocapuldencel-T and our Phase 3 ADAPT clinical trial;
- the progress and results of any investigator initiated clinical trials of rocapuldencel-T that we may support;
- the progress and results of the ongoing investigator-initiated clinical trial of AGS-004 in combination with vorinostat for HIV eradication and the planned investigator-initiated clinical trial of AGS-004 that we support and our ability to obtain additional funding under our NIH and NIAID contract for our AGS-004 program;
- the development, initiation and support of additional clinical trials of rocapuldencel-T in mRCC or other indications and AGS-004 in HIV;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates or for the PD1 monoclonal antibodies which we have an option to in-license, should we decide to exercise our option;
- the costs and timing of establishing a commercial manufacturing facility or of alternative arrangements for commercial manufacturing and any costs and liabilities associated with financing arrangements entered into to fund the costs of these activities;
- the costs, timing and outcome of regulatory submissions and review of our product candidates;
- the costs of commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive regulatory approval;
- the potential need to repay the $4.0 million in principal currently remaining outstanding under the loan under our license agreement with Medinet Co. Ltd. and its wholly-owned subsidiary, MEDcell Co., LTD, which we refer to together as Medinet;
- payments due under our agreement with Medpace for the conduct of the ADAPT clinical trial;
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates be approved by the FDA or a similar regulatory authority outside the United States;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or invest in other businesses, products and technologies;
- our ability to obtain government or other third party funding for the development of our product candidates; and
- our ability to establish collaborations on favorable terms, if at all, particularly arrangements to develop, market and distribute rocapuldencel-T outside North America and arrangements for the development and commercialization of our non-oncology product candidates, including AGS-004.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Additional financing may not be available to us on acceptable terms, or at all.

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Our independent registered public accounting firm included an explanatory paragraph relating to our ability to continue as a going concern in its report on our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017.

Our report from our independent registered public accounting firm for the year ended December 31, 2017 includes an explanatory paragraph stating that our losses from operations and required additional funding to finance our operations raise substantial doubt about our ability to continue as a going concern. If we are unable to obtain sufficient funding, our business, prospects, financial condition and results of operations will be materially and adversely affected, and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding to us on commercially reasonable terms or at all.

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.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, government contracts, government and other third party grants or other third party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders’ ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. For example, since 2016 we have issued and sold securities in several PIPE financings, under a sales agreement with Cowen, and in a public follow-on offering, each of which have resulted in dilution to our existing stockholders. Additionally, during 2017 we issued both secured and unsecured convertible debt and raised equity capital under our sales agreement with Cowen, which have resulted in further dilution to our stockholders.

Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

We may also seek to collaborate with third parties for the manufacturing, development or commercialization of rocapuldencel-T outside of North America. We also may seek government or other third party funding for the continued development of AGS-004 and to collaborate with third parties for the development and commercialization of AGS-004. If we raise additional funds through government or other third party funding, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If the loan from Medinet becomes due and we do not repay it, we have agreed to grant Medinet a non-exclusive, royalty-bearing license to make and sell Arcelis products in Japan for the treatment of cancer.

Our ability to use our net operating loss carry-forwards and tax credit carryforwards may be limited.

The utilization of the net operating loss and tax credit carryforwards may be subject to limitation under the rules regarding a change in stock ownership as determined by the Internal Revenue Code, and state and foreign tax laws. Section 382 of the Internal Revenue Code of 1986, as amended, imposes annual limitations on the utilization of net operating loss carryforwards, other tax carryforwards, and certain built-in losses upon an ownership change as defined under that section. In general terms, an ownership change may result from transactions that increase the aggregate ownership of certain of our stockholders by more than 50 percentage points over a three-year testing period. If we have undergone a Section 382 ownership change, an annual limitation would be imposed on certain of our tax attributes, including net operating loss and capital loss carryforwards, and certain other losses, credits, deductions or tax basis. We believe that we experienced an ownership change during 2014 under Section 382. Due to the Section 382 limitation resulting from the ownership change, $28.2 million of our U.S. federal net operating losses are expected to expire unused. Additionally, our U.S. federal tax credits and state net operating losses may be limited. The amount of U.S. federal net operating losses expected to expire due to the Section 382 limitation has not been recognized in our consolidated financial statements as of December 31, 2017. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carry-forwards and other tax credit carryforwards to offset U.S. federal taxable income may be subject to limitations, which potentially could result in increased future tax liability to us. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain how various states will respond to the newly enacted federal tax law.
Risk Related to the Commercialization of our Product Candidates

"We have no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability."

Our operations to date have been limited to financing and staffing our company, developing our technology and product candidates and establishing collaborations. We have not yet demonstrated an ability to successfully complete a pivotal clinical trial, compile an acceptable regulatory submission, obtain marketing approvals, manufacture a commercial scale product or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

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

Even if rocapuldencel-T or AGS-004 receives regulatory approval, it may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

We have never commercialized a product candidate. Even if rocapuldencel-T or AGS-004 receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. Gaining market acceptance for our Arcelis-based products may be particularly difficult as, to date, the FDA has only approved a few individualized immunotherapies and our Arcelis-based products are based on a novel technology. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our product candidates for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of sales, marketing and distribution support;
- the approval of other new products for the same indications;
- the ability of our product to be combined with emerging standards of care;
- availability and amount of reimbursement from government payors, managed care plans and other third party payors;
- adverse publicity about the product or favorable publicity about competitive products;
- clinical indications for which the product is approved; and
- the prevalence and severity of any side effects.

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If any of our product candidates receives marketing approval and we, or others, later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the product could be compromised.

Clinical trials of our product candidates are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, in a broader patient population or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we may be required to recall the product or change the way the product is administered;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- additional restrictions may be imposed on the distribution or use of the product via a risk evaluation and mitigation strategy, or REMS;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We have only limited commercial capabilities and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization, outsource these functions to third parties or enter into collaborations or other arrangements with third parties for the distribution or marketing of our product candidates should such candidates receive marketing approval.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.
Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- inability to establish customer service and access services, including potential supply chain and specialty pharmacy arrangements.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or doing so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any products that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Many marketed therapies for the indications that we are currently pursuing, or indications that we may in the future seek to address using our Arcelis precision immunotherapy technology platform, are widely accepted by physicians, patients and payors, which may make it difficult for us to replace them with any products that we successfully develop and are permitted to market.

The FDA has approved several targeted therapies as monotherapies for mRCC, including Nexavar (sorafenib), marketed by Bayer Healthcare Pharmaceuticals, Inc. and Onyx Pharmaceuticals, Inc.; Sutent (sunitinib) and Inlyta (axitinib), marketed by Pfizer, Inc.; Avastin (bevacizumab), marketed by Genentech, Inc., a member of the Roche Group; Votrient (pazopanib) and Afinitor (everolimus), marketed by Novartis Pharmaceuticals Corporation; Torisel (temsirolimus), marketed by Pfizer and most recently, Opdivo (nivolumab), marketed by Bristol-Myers Squibb and Cabometyx (cabozantinib), marketed by Exelixis, for second-line mRCC. In addition, we estimate that there are numerous therapies for mRCC in clinical development by many public and private biotechnology and pharmaceutical companies targeting numerous different cancer types and stages. A number of these are in late stage development including Opdivo (nivolumab) plus Yervoy (ipilimumab) in combination for first-line mRCC, which recently demonstrated favorable data compared to sunitinib in a Phase 3 trial. If a standalone therapy for mRCC were developed that demonstrated improved efficacy over currently marketed first-line therapies with a favorable safety profile and without the need for combination therapy, such a therapy might pose a significant competitive threat to rocapuldecne-T.
We are currently conducting our ADAPT trial of rocapuldencel-T plus sunitinib / targeted therapy. We elected to study rocapuldencel-T in clinical trials in combination with sunitinib due in part to sunitinib being the current standard-of-care for first-line treatment of mRCC. Although we do not expect to seek FDA approval of rocapuldencel-T solely in combination with sunitinib and have provided that, under the protocol for the ADAPT trial, investigators may discontinue sunitinib due to disease progression or toxicity and initiate second-line treatment with other approved compatible therapies, if we obtain approval of rocapuldencel-T by the FDA, such FDA approval may be limited to the combination of rocapuldencel-T and sunitinib. In such event, the commercial success of rocapuldencel-T would be linked to the commercial success of sunitinib. As a result, if sunitinib ceases to be the standard-of-care for first-line treatment of mRCC or another event occurs that adversely affects sales of sunitinib, the commercial success of rocapuldencel-T may be adversely affected.

We estimate that there are numerous other cancer immunotherapy products in clinical development by many public and private biotechnology and pharmaceutical companies targeting numerous different cancer types. A number of these product candidates are in late-stage clinical development or have recently been approved in different cancer types, including two recently approved checkpoint inhibitor-based immunotherapies, nivolumab which is marketed by Bristol-Myers Squibb, and pembrolizumab, which is marketed by Merck. These newer immunotherapies are in addition to the targeted therapies, chemotherapeutics, radiation therapy, hormonal therapies and cytokine-based therapies used in the treatment in a wide range of oncology indications.

There are also numerous FDA-approved treatments for HIV, primarily antiretroviral therapies marketed by large pharmaceutical companies. Generic competition has developed in this market as patent exclusivity periods for older drugs have expired, with more than 15 generic drugs currently on the market. The presence of these generic drugs is resulting in price pressure in the HIV therapeutics market and could affect the pricing of AGS-004. Currently, there are no approved therapies for the eradication of HIV. We expect that major pharmaceutical companies that currently market antiretroviral therapy products or other companies that are developing HIV product candidates may seek to develop products for the eradication of HIV.

Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and device industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

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

The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. In the United States, recently passed legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain regulatory approval.
Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

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

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. These risks may be even greater with respect to our Arcelis-based products which are manufactured using a novel technology. None of our product candidates has been widely used over an extended period of time, and therefore our safety data are limited. We derive the raw materials for manufacturing of our Arcelis-based product candidates from human cell sources, and therefore the manufacturing process and handling requirements are extensive and stringent, which increases the risk of quality failures and subsequent product liability claims.

If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
substantial monetary awards to trial participants or patients;

- loss of revenue; and

- the inability to commercialize any products that we may develop.

We currently hold $10.0 million in product liability insurance coverage, which may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage when we begin commercializing our product candidates, if ever. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

*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 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 products.

We have based our research and development efforts on our Arcelis precision immunotherapy technology platform. Notwithstanding our large investment to date and potential future expenditures in our Arcelis precision immunotherapy technology platform, we have not yet developed, and may never successfully develop, any marketed drugs using this approach. As a result of pursuing the development of product candidates using our Arcelis precision immunotherapy platform, we may fail to develop product candidates or address indications based on other scientific approaches that may offer greater commercial potential or for which there is a greater likelihood of success.

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.

**Risks Related to Our Dependence on Third Parties**

*Our reliance on government funding adds uncertainty to our research and commercialization efforts and may impose requirements that increase the costs of commercialization and production of our government-funded product candidates.*

Our current development of AGS-004 for HIV is primarily funded by the NIH. We are dependent upon further government funding for continued development of AGS-004. However, increased pressure on governmental budgets may reduce the availability of government funding for programs such as AGS-004. In addition, contracts and grants from the U.S. government and its agencies include provisions that give the government substantial rights and remedies, many of which are not typically found in commercial contracts, including provisions that allow the government to:

- terminate agreements, in whole or in part, for any reason or no reason;

- reduce or modify the government’s obligations under such agreements without the consent of the other party;

- claim rights, including intellectual property rights, in products and data developed under such agreements;

- impose U.S. manufacturing requirements for products that embody inventions conceived or first reduced to practice under such agreements;
• suspend or debar the contractor or grantee from doing future business with the government or a specific government agency;
• pursue criminal or civil remedies under the False Claims Act, False Statements Act and similar remedy provisions specific to government agreements; and
• limit the government’s financial liability to amounts appropriated by the U.S. Congress on a fiscal-year basis, thereby leaving some uncertainty about the future availability of funding for a program even after it has been funded for an initial period.

Government agreements normally contain additional terms and conditions that may increase our costs of doing business, reduce our profits, and expose us to liability for failure to comply with these terms and conditions. These include, for example:

• specialized accounting systems unique to government contracts and grants;
• mandatory financial audits and potential liability for price adjustments or recoupment of government funds after such funds have been spent;
• public disclosures of certain contract and grant information, which may enable competitors to gain insights into our research program; and
• mandatory socioeconomic compliance requirements, including labor standards, non-discrimination and affirmative action programs and environmental compliance requirements.

We expect to depend on collaborations with third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We intend to commercialize rocapuldencel-T independently in North America and to collaborate with other third parties to manufacture, develop or commercialize rocapuldencel-T outside North America. We have entered into an exclusive license agreement with Pharmstandard for the development and commercialization of rocapuldencel-T in Russia and the other states comprising the Commonwealth of Independent States and an exclusive license agreement with Green Cross Corp., or Green Cross, for the development and commercialization of rocapuldencel-T for the treatment of mRCC in South Korea and an exclusive license agreement with Lummy (Hong Kong) Co. Ltd., or Lummy HK, for the development, manufacture and commercialization of rocapuldencel-T in China, Hong Kong, Taiwan and Macau. We have also entered into a license agreement with Medinet under which we granted Medinet an exclusive license to manufacture in Japan rocapuldencel-T for the purpose of development and commercialization for the treatment of mRCC.

We also plan to seek government or other third party funding for continued development of AGS-004 and to collaborate with third parties to develop and commercialize AGS-004. Our likely collaborators for any development, distribution, marketing, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

Under our existing arrangements we have limited control, and under any additional arrangements we may enter into with third parties we will likely have limited control, over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators’ abilities to successfully perform the functions assigned to them in these arrangements.
Collaborations involving our product candidates would pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator’s strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or, require 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 products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may have the right to conduct clinical trials of our product candidates without our consent and could conduct trials with flawed designs that result in data that adversely affect our clinical trials, our ability to obtain marketing approval for our product candidates or market acceptance of our product candidates;
- collaborators may hold rights that could preclude us from commercializing our products in certain territories. For example, we have granted Medinet an exclusive license to manufacture in Japan rocapuldencel-T for the treatment of mRCC. If we and Medinet are unable to agree to the terms of a supply agreement, we will not be able to sell rocapuldencel-T in Japan unless we repurchase these rights from Medinet;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- 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. For example, in 2009, our collaboration with Kyowa Hakko Kirin Co., Ltd. with respect to rocapuldencel-T and AGS-004 was terminated by our collaborator.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

**If we are not able to establish additional collaborations, we may have to alter any development and commercialization plans.**

Our drug development programs and any potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may collaborate with pharmaceutical and biotechnology companies for the development and commercialization of those product candidates. For example, we have entered into license agreements with third parties to develop, manufacture and/or commercialize rocapuldencel-T in Russia and the other states comprising the Commonwealth of Independent States, South Korea, Japan, China, Hong Kong, Taiwan and Macau, and we may seek to collaborate with other third parties to develop and commercialize rocapuldencel-T in other parts of the world. We also intend to collaborate with third parties to develop and commercialize AGS-004.
We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator’s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under existing license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all.

If we are not able to obtain such funding or enter into collaborations for our product candidates, we may have to curtail the development of such product candidates, reduce or delay a candidate’s development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop these product candidates or bring these product candidates to market and generate product revenue.

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We do not independently conduct clinical trials of our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to perform this function. Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our oversight responsibilities as sponsor of the trial. We remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA and other regulatory authorities require us to comply with standards, commonly referred to as Good Clinical Practice, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

For instance, in December 2015 we received a notice from Health Canada that one of the sites at which we were conducting our Phase 3 ADAPT trial in Canada had been found to be non-compliant with Good Clinical Practice in Canada and that if the issues raised in the notice were not corrected, Health Canada could suspend our authorization to conduct the ADAPT trial at all sites in Canada. We submitted a response to Health Canada and subsequently received a Completion of Response notice from Health Canada stating that our corrective actions were satisfactory and that the matter was officially closed.
We also rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our existing or future distributors could delay clinical development or regulatory approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

**Risks Related to the Manufacturing of Our Product Candidates**

We will need to establish a facility to manufacture our Arcelis-based products on a commercial scale. We do not have experience in manufacturing Arcelis-based products on a commercial scale. If, due to our lack of manufacturing experience, we cannot manufacture our Arcelis-based products on a commercial scale successfully or manufacture sufficient product to meet our expected commercial requirements, our business may be materially harmed.

We currently have manufacturing suites in our Technology Drive and Patriot Center leased facilities in Durham, North Carolina. We manufacture our Arcelis-based product candidates for research and development purposes and for clinical trials at these facilities.

In 2017, we entered into a ten-year lease agreement with two five-year renewal options for 40,000 square feet of manufacturing and office space at the Center for Technology Innovation, or CTI, on the Centennial Campus of North Carolina State University in Raleigh, North Carolina. We had intended to utilize this facility to manufacture rocapuldencel-T to support submission of a BLA to the FDA and to support initial commercialization of rocapuldencel-T.

In addition, to provide for capacity expansion beyond the initial few years following potential launch of rocapuldencel-T, we had planned to build-out and equip a second facility, which we refer to as the Centerpoint facility. In August 2014, we entered into a ten-year lease agreement with renewal options for the Centerpoint facility. Under the lease agreement, we agreed to lease certain land and an approximately 125,000 square-foot building to be constructed in Durham County, North Carolina. We initially intended this facility to house our corporate headquarters and commercial manufacturing before we entered into the lease for the CTI facility. The shell of the new facility was constructed on a build-to-suit basis in accordance with agreed upon specifications and plans and was completed in June 2015. However, the build-out and equipping of the interior of the facility was suspended as we pursued financing arrangements to support the further build out of the facility.

Due to the IDMC recommendation in February 2017 to discontinue the ADAPT trial, we reassessed our manufacturing plans. In March 2017, we entered into a lease termination agreement with the landlord of our CTI facility terminating our lease of the CTI facility as of March 17, 2017. In November 2017, we and the landlord of the Centerpoint facility entered into a lease termination agreement terminating our lease of the Centerpoint facility and the landlord successfully completed the sale of the facility to a third party. We believe that our Technology Drive and Patriot Center facilities are sufficient for the manufacture of rocapuldencel-T and AGS-004 to support our ongoing clinical trials and any likely near-term clinical trials that we may initiate.

We expect that we would establish both manual and automated manufacturing processes in our commercial manufacturing facility if we determine to establish such facility. We had decided to delay the implementation of our automated manufacturing process until after initial commercialization of rocapuldencel-T, and thus planned to seek marketing approval of rocapuldencel-T and, if approved, to initially commercially supply rocapuldencel-T using our manual manufacturing process. Prior to implementing commercial manufacturing of rocapuldencel-T, we would be required to demonstrate that our commercial manufacturing facility is constructed and operated in accordance with current good manufacturing practice. We would also be required to show the comparability between rocapuldencel-T that we produce using the manual processes in our current facility and rocapuldencel-T produced using the manual process in the commercial manufacturing facility.

If we transition to automated manufacturing processes, we expect our automated manufacturing processes will be based on existing functioning prototypes of automated devices for the production of commercial quantities of our Arcelis-based product candidates. These devices can be used to perform substantially all steps required for the manufacture of our Arcelis-based product candidates.
We do not have experience in manufacturing products on a commercial scale. In addition, because we are aware of only a few companies that have manufactured an individualized immunotherapy product for commercial sale, there are limited precedents from which we can learn. We may encounter difficulties in the manufacture of our Arcelis-based products due to our limited manufacturing experience. These difficulties could delay the build-out and equipping of a commercial manufacturing facility and regulatory approval of the manufacture of our Arcelis-based products using the facility, increase our costs or cause production delays or result in us not manufacturing sufficient product to meet our expected commercial requirements, any of which could damage our reputation and hurt our profitability. If we are unable to successfully increase our manufacturing capacity to commercial scale, our business may be materially adversely affected.

If we fail to establish commercial manufacturing operations in compliance with regulatory requirements, or augment our manufacturing personnel, we may not be able to initiate commercial operations or produce sufficient product to meet our expected commercial requirements. We have delayed the implementation of our automated manufacturing process and may not be able to use such process on a timely basis or at all.

In order to meet our business plan, which contemplated manufacturing our product first using manual processes and later using automated processes for the commercial requirements of rocapuldencel-T and any other Arcelis-based product candidates that might be approved, we planned to build out and equip a leased commercial manufacturing facility and add manufacturing personnel in advance of any regulatory submission for approval of rocapuldencel-T. If we determine to continue our plan to establish a commercial manufacturing facility, we will require substantial capital expenditures and additional regulatory approvals. In addition, it will be costly and time consuming to recruit necessary additional personnel.

If we are unable to successfully build out and equip a commercial manufacturing facility in compliance with regulatory requirements or hire and train additional necessary manufacturing personnel appropriately, our filing for regulatory approval of our product candidates may be delayed or denied.

We plan to delay the implementation of our automated manufacturing process until we complete the clinical development of rocapuldencel-T and secure additional funding. Thus, if we are able to successfully complete the clinical development of rocapuldencel-T and obtain marketing approval, we plan to initially commercially supply rocapuldencel-T using manual manufacturing processes. Prior to implementing commercial manufacturing of rocapuldencel-T, we will be required to demonstrate that the commercial manufacturing facility is constructed and operated in accordance with current Good Manufacturing Practice, or cGMP. If we continue the development of rocapuldencel-T, we will also be required to show the comparability between rocapuldencel-T that we produce using the manual processes in our current facility and rocapuldencel-T produced using the manual process in the new facility.

Our implementation of automated processes could take longer, particularly if we are unable to achieve any of the required tasks on a timely basis, or at all. Work under our collaboration with Invetech and Saint-Gobain to develop the equipment and disposables necessary to implement the automated manufacturing processes for Arcelis-based products is not expected to resume until we are able to successfully complete the clinical development of rocapuldencel-T and obtain marketing approval. If Invetech or Saint-Gobain are delayed in resumption of the projects or do not perform as expected under the agreements or the projects with Invetech or Saint-Gobain are unsuccessful for any other reason, our timelines for the implementation of our automated manufacturing processes could be further delayed and our business could be adversely affected.

Prior to implementing the automated manufacturing processes for Arcelis-based products, we will be required to:

- demonstrate that the disposable components and sterilization and packaging methods used in the manufacturing process are suitable for use in manufacturing in accordance with current good manufacturing practice, or cGMP, and current Good Tissue Practices, or cGTP;
- build and validate processing equipment that complies with cGMP and cGTP;
- equip a commercial manufacturing facility to accommodate the automated manufacturing process;
We will need regulatory approval to use the automated manufacturing processes for commercial purposes. If the FDA requires us to conduct a bridging study to demonstrate comparability between rocapuldencel-T that we produce manually and rocapuldencel-T produced using the automated processes, the implementation of the automated manufacturing processes and the filing for such approval will likely be delayed.

If we are unable to successfully implement the automated processes required and demonstrate comparability between the rocapuldencel-T that we produce manually and rocapuldencel-T produced using the automated processes, our filing for regulatory approval of the commercial use of our automated manufacturing processes may be delayed or denied and we may not be able to initiate commercial manufacturing using our automated manufacturing processes. In such event, our commercial manufacturing costs will be higher than anticipated and we may not be able to manufacture sufficient product to meet our expected commercial requirements.

**Lack of coordination internally among our employees and externally with physicians, hospitals and third-party suppliers and carriers, could cause manufacturing difficulties, disruptions or delays and cause us to not have sufficient product to meet our clinical trial requirements or potential commercial requirements.**

Manufacturing our Arcelis-based product candidates requires coordination internally among our employees and externally with physicians, hospitals and third party suppliers and carriers. For example, a patient’s physician or clinical site will need to coordinate with us for the shipping of a patient’s disease sample and leukapheresis product to our manufacturing facility in a timely manner, and we will need to coordinate with them for the shipping of the manufactured product to them. Such coordination involves a number of risks that may lead to failures or delays in manufacturing our Arcelis-based product candidates, including:

- failure to obtain a sufficient supply of key raw materials of suitable quality;
- difficulties in manufacturing our product candidates for multiple patients simultaneously;
- difficulties in obtaining adequate patient-specific material, such as tumor samples, virus samples or leukapheresis product, from physicians;
- difficulties in completing the development and validation of the specialized assays required to ensure the consistency of our product candidates;
- failure to ensure adequate quality control and assurances in the manufacturing process as we increase production quantities;
- difficulties in the timely shipping of patient-specific materials to us or in the shipping of our product candidates to the treating physicians due to errors by third party carriers, transportation restrictions or other reasons;
- destruction of, or damage to, patient-specific materials or our product candidates during the shipping process due to improper handling by third party carriers, hospitals, physicians or us;
- destruction of, or damage to, patient-specific materials or our product candidates during storage at our facilities; and
- destruction of, or damage to, patient-specific materials or our product candidates stored at clinical and future commercial sites due to improper handling or holding by clinicians, hospitals or physicians.
If we are unable to coordinate appropriately, we may encounter delays or additional costs in achieving our clinical and commercialization objectives, including in obtaining regulatory approvals of our product candidates and supplying product, which could materially damage our business and financial position.

**If our existing manufacturing facilities or any commercial manufacturing facility that we use are damaged or destroyed, or production at one of these facilities is otherwise interrupted, our business and prospects would be negatively affected.**

We currently lease two manufacturing facilities. If we establish a commercial manufacturing facility, it will be our only commercial manufacturing facility in North America. If our existing manufacturing facilities or a commercial manufacturing facility that we decide to build out and equip, or the equipment in either of these facilities, is damaged or destroyed, we likely would not be able to quickly or inexpensively replace our manufacturing capacity and possibly would not be able to replace it at all. Any new facility needed to replace either our existing manufacturing facility or a new commercial manufacturing facility would need to comply with the necessary regulatory requirements, need to be tailored to our specialized automated manufacturing requirements and require specialized equipment. We would need FDA approval before selling any products manufactured at a new facility. Such an event could delay our clinical trials or, if any of our product candidates are approved by the FDA, reduce or eliminate our product sales.

We maintain insurance coverage to cover damage to our property and equipment and to cover business interruption and research and development restoration expenses. If we have underestimated our insurance needs with respect to an interruption in our clinical manufacturing of our product candidates, we may not be able to adequately cover our losses.

**Risks Related to Our Intellectual Property**

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

We are a party to a number of intellectual property license agreements with third parties, including with respect to each of recapulencel-T and AGS-004, and we may enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under these licenses, our licensors may have the right to terminate these license agreements, in which event we might not be able to market any product that is covered by these agreements, or to convert the license to a non-exclusive license, which could materially adversely affect the value of the product candidate being developed under the license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms.

*If we are unable to obtain and maintain patent protection for our technology and products, or if our licensors are unable to obtain and maintain patent protection for the technology or products that we license from them, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be adversely affected.*

Our success depends in large part on our and our licensors’ ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We and our licensors have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development efforts before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or products that we license from third parties and are reliant on our licensors. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.
The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our and our licensors’ patent rights are highly uncertain. Our and our licensors’ pending and future patent applications may not result in patents being issued which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Third parties could practice our inventions in territories where we do not have patent protection. Furthermore, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, we own or exclusively license patents relating to our process of manufacturing an individualized drug product. A U.S. patent may be infringed by anyone who, without authorization, practices the patented process in the United States or imports a product made by a process covered by the U.S. patent. In foreign countries, however, importation of a product made by a process patented in that country may not constitute an infringing activity, which would limit our ability to enforce our process patents against importers in that country. Furthermore, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. If competitors are able to use our technologies, our ability to compete effectively could be harmed.

Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, in the United States, the first to invent the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is generally entitled to the patent. Under the America Invents Act, or AIA, enacted in September 2011, the United States moved to a first inventor to file system in March 2013. The United States Patent and Trademark Office only recently finalized the rules relating to these changes and courts have yet to address the new provisions. These changes could increase the costs and uncertainties surrounding the prosecution of our patent applications and the enforcement or defense of our patent rights. Furthermore, we may become involved in interference proceedings, opposition proceedings, or other post-grant proceedings, such as reissue, reexamination or inter parties review proceedings, which may challenge our patent rights or the patent rights of others. An adverse determination in any such proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. The issuance of a patent is not conclusive as to its scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to or stop prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. For example, certain of the U.S. patents we exclusively licensed from Duke University expired in 2016 and the European and Japanese patents exclusively licensed from Duke University expired in April 2017. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.
We may become involved in lawsuits to protect or enforce our patents, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents. To counter such infringement or unauthorized use, we may be required to file infringement claims against third parties, which can be expensive and time consuming. In addition, during an infringement proceeding, a court may decide that the patent rights we are asserting are invalid or 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 proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. 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, our licensors may have rights to file and prosecute such claims and we are reliant on them.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. We cannot ensure that third parties do not have, or will not in the future obtain, intellectual property rights such as granted patents that could block our ability to operate as we would like. There may be patents in the United States or abroad owned by third parties that, if valid, may block our ability to make, use or sell our products in the United States or certain countries outside the United States, or block our ability to import our products into the United States or into certain countries outside the United States.

We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology. For example, third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party’s intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may be unable to obtain any required license on commercially reasonable terms or even obtain a license at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We have research licenses to certain reagents and their use in the development of our product candidates. We would need commercial licenses to these reagents for any of our product candidates that receive approval for sale in the United States. We believe that commercial licenses to these reagents will be available. However, if we are unable to obtain any such commercial licenses, we may be unable to commercialize our product candidates without infringing the patent rights of third parties. If we did seek to commercialize our product candidates without a license, these third parties could initiate legal proceedings against us.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee’s former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.
Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

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

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. The types of protections available for trade secrets are particularly important with respect to our Arcelis precision immunotherapy technology platform’s manufacturing capabilities, which involve significant unpatented know-how. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, sponsored researchers, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Legal Compliance Matters

Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, cGTP requirements, requirements regarding the distribution of samples to physicians and recordkeeping. Even if regulatory approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved label. The FDA imposes stringent restrictions on manufacturers’ communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. In addition, later discovery of previously unknown problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:
• restrictions on such products, manufacturers or manufacturing processes;
• restrictions on the marketing of a product;
• restrictions on product distribution;
• requirements to conduct post-marketing clinical trials;
• warning or untitled letters;
• withdrawal of the products from the market;
• refusal to approve pending applications or supplements to approved applications that we submit;
• recall of products;
• fines, restitution or disgorgement of profits or revenue;
• suspension or withdrawal of regulatory approvals;
• refusal to permit the import or export of our products;
• product seizure; or
• injunctions or the imposition of civil or criminal penalties.

Our relationships with customers and third party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, program exclusion, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

• the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, 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 under federal and state healthcare programs such as Medicare and Medicaid;
• the federal False Claims Act imposes civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
• the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
• the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

• the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, the PPACA, or the Health Care Reform Law will require manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; and

• analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, and 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 drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

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 and may require drug manufacturers to report information related to payments and other transfers of value 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 the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Numerous statements made by President Trump and members of the U.S. Congress indicate that it is likely that legislation will be passed by Congress and signed into law by President Trump that repeals the PPACA, in whole or in part, and/or introduces a new form of health care reform. It is unclear at this point what the scope of such legislation will be and when it will become effective. Because of the uncertainty surrounding this replacement health care reform legislation, we cannot predict with any certainty the likely impact of the PPACA’s repeal or the adoption of any other health care reform legislation on our financial condition or operating results. Whether or not there is alternative health care legislation enacted in the United States, there is likely to be significant disruption to the health care market in the coming months and years.

**Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.**

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.
In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class in certain cases. Cost reduction initiatives and other provisions of this and other more recent legislation could decrease the coverage and reimbursement that is provided for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act or other more recent legislation may result in a similar reduction in payments from private payors.

In March 2010, former President Obama signed into law the Health Care Reform Law, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Health Care Reform Law revises the definition of “average manufacturer price” for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may affect our business practices with health care practitioners. We will not know the full effects of the Health Care Reform Law until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the effect of the Health Care Reform Law, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. In addition, with the new Administration and Congress, there will likely be additional administrative or legislative changes, including modification, repeal, or replacement of all, or certain provisions of, the ACA. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the ACA. The Budget Resolution is not a law; however, it is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the ACA. 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 or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices.

At the same time, Congress has focused on additional legislative changes, including in particular repeal and replacement of certain provisions of the ACA. For example, with enactment of the Tax Cuts and Jobs Act of 2017, in December 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of the Congress has put forth multiple bills designed to repeal or replace and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 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 or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction (CSR) payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.
The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA’s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, as part of the Health Care Reform Law, an abbreviated pathway for the approval of biosimilar and interchangeable biological products was created. The new abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be submitted to the FDA until four years, or approved by the FDA until 12 years, after the original brand product identified as the reference product was approved under a BLA. The new law is complex and is only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact, implementation and meaning is subject to uncertainty. While it is uncertain when any such processes may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that if any of our product candidates were to be approved as biological products under a BLA, such approved products should qualify for the four-year and 12-year periods of exclusivity. However, there is a risk that the U.S. Congress could amend the BPCIA to significantly shorten these exclusivity periods as proposed by President Obama, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and radioactive and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers’ compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.
In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

**Risks Related to Organizational Employee Matters**

*Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.*

We are highly dependent on Jeffrey Abbey, our president and chief executive officer, Charles Nicolette, our vice president of research and development and chief scientific officer, and Richard Katz, our vice president and chief financial officer, as well as the other principal members of our management and scientific teams. Although we have formal employment agreements with each of our executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified personnel is critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel, our setback with respect to rocapuldencel-T, the implementation of our workforce action plan and our limited cash resources. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

**Risks Related to Our Common Stock**

*Our executive officers, directors, affiliates of all officers and directors and other of our affiliates who own our outstanding common stock have the ability to significantly influence matters submitted to stockholders for approval.*

Our executive officers, directors, affiliates of our executive officers and directors and other of our affiliates beneficially own, in the aggregate, shares representing approximately 26.77% of our outstanding common stock as of February 28, 2018. As a result, if these stockholders were to choose to act together, they would be able to significantly influence matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.
Our largest stockholder, Pharmstandard, could exert significant influence over us and could limit your ability to influence the outcome of key transactions, including any change of control.

Our largest stockholder, Pharmstandard, beneficially owns, in the aggregate, shares representing approximately 18.83% of our outstanding common stock as of February 28, 2018. Pharmstandard is also the holder of the $6.0 million principal amount of a secured convertible note that we issued in June 2017, although the ability of Pharmstandard to exercise its conversion option is limited to the extent such exercise would cause Pharmstandard’s ownership in our Company to exceed 39.9%. In addition, two members of our board of directors are closely associated with Pharmstandard. As a result, we expect that Pharmstandard will be able to exert significant influence over our business. Pharmstandard may have interests that differ from your interests, and it may vote in a way with which you disagree and that may be adverse to your interests. The concentration of ownership of our capital stock may have the effect of delaying, preventing or deterring a change of control of our company, could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company and may adversely affect the market price of our common stock.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.
An active trading market for our common stock may not be sustained, and investors may not be able to resell their shares at or above the price they paid. In addition, if we fail to meet the requirements for continued listing on The Nasdaq Capital Market, our common stock could be delisted from trading, which would decrease the liquidity of our common stock and our ability to raise additional capital.

Although our common stock is currently listed on The Nasdaq Capital Market, an active trading market for our shares may not be sustained. If an active market for our common stock is not sustained, it may be difficult for you to sell your shares without depressing the market price for the shares or sell your shares at all. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

In 2017, we received several deficiency letters from the Listing Qualifications Department of The Nasdaq Stock Market notifying us that we were not in compliance with various requirements for continued listing on The Nasdaq Global Market and that, unless we requested a hearing before the Panel, trading of our common stock would be suspended at the opening of business on November 6, 2017. As a result, we requested a hearing, and in January 2018, we had a hearing before the Panel at which we requested the transfer of our listing to The Nasdaq Capital Market and presented our plan to evidence compliance with various requirements for continued listing on The Nasdaq Capital Market. On January 17, 2018, we received a determination from Nasdaq indicating that our listing would be transferred from The Nasdaq Global Market to The Nasdaq Capital Market, provided that we demonstrated, on or before February 2, 2018, a closing bid price of $1.00 or more for a minimum of ten prior consecutive trading days, that, on or before April 24, 2018, we satisfied the $2.5 million stockholders’ equity requirement and demonstrated our ability to maintain compliance with the minimum stockholders’ equity requirement through the end of fiscal 2018, among other actions, and that we continued to meet the requirements for continued listing on The Nasdaq Capital Market. On February 15, 2018, we received formal notice from Nasdaq indicating that we have evidenced full compliance with the minimum $1.00 bid price requirement for continued listing on The Nasdaq Capital Market. We are not currently in compliance with the stockholders’ equity requirement.

If we fail to regain compliance with the conditions set by the Panel or otherwise do not comply with the continued listing requirements of The Nasdaq Capital Market and our common stock is delisted by Nasdaq by the April 24, 2018 deadline, our common stock may be eligible to trade on the OTC Bulletin Board or another over-the-counter market. Any such alternative would likely result in it being more difficult for us to raise additional capital through the public or private sale of equity securities and for investors to dispose of, or obtain accurate quotations as to the market value of, the common stock and could result in a decrease in the trading price of our common stock. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence, and the loss of business development opportunities, some or all of which may contribute to a further decline in our stock price. In addition, there can be no assurance that the common stock would be eligible for trading on any such alternative exchange or markets.

If our stock price continues to be volatile, purchasers of our common stock could incur substantial losses.

Our stock price has been volatile. For example, our stock has traded in a range from a low price per share of $0.81 and a high price per share of $113.66 during the period of from January 1, 2017 through March 30, 2018 on a post-split adjusted basis. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

• our determination with regard to the next steps for our recapindle-T clinical program based on our discussions with the FDA;
• our cash resources;
• results of clinical trials of our product candidates or those of our competitors, such as the interim data analysis that we plan to conduct in the second quarter of 2018;
• the success of competitive products or technologies;
• potential approvals of our product candidates for marketing by the FDA or equivalent foreign regulatory authorities or our failure to obtain such approvals;
• regulatory or legal developments in the United States and other countries;
• the results of our efforts to commercialize our product candidates;
• developments or disputes concerning patents or other proprietary rights;
• the recruitment or departure of key personnel;
• the level of expenses related to any of our product candidates or clinical development programs;
• the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
• actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
• variations in our financial results or those of companies that are perceived to be similar to us;
• changes in the structure of healthcare payment systems;
• market conditions in the pharmaceutical and biotechnology sectors and issuance of new or changed securities analysts’ reports or recommendations;
• general economic, industry and market conditions; and
• the other factors described in this “Risk Factors” section.

In addition, pharmaceutical companies have experienced significant share price volatility in recent years, and securities class action litigation, shareholder derivative litigation, or other proceedings often follow a decline in the market price of a company’s securities. For instance, in March 2017, a purported stockholder of our company filed a putative class action lawsuit against us, our chief executive officer, our chief financial officer, and our vice president of finance generally alleging that the defendants violated the federal securities laws by, among other things, making material misstatements or omissions concerning the progress of the ADAPT Phase 3 clinical trial of rocapuldencel-T, the planned biologics licensing application for rocapuldencel-T and the prospects for approval. This matter was dismissed in September 2017. If we face such litigation or proceedings, it could result in substantial costs and a diversion of management’s attention and resources.

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

As a public company, and particularly after we are no longer an emerging growth company, we will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Capital Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and make some activities more time-consuming and costly.
We cannot predict or estimate the amount of additional costs we may incur to continue to operate as a public company, nor can we predict the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 of the Sarbanes-Oxley Act of 2002 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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

We are an “emerging growth company,” as defined in the JOBS Act, and may remain an emerging growth company for up to five years following our initial public offering in February 2014. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In this Annual Report on Form 10-K for the year ended December 31, 2017, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.
The trading market for our common stock will depend on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us, or provide favorable coverage. If one or more analysts downgrade our stock or change their opinion of our stock to be less favorable, our share price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.
Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We have two facilities located in Durham, North Carolina, where we occupy approximately 20,000 and 16,000 square feet, respectively, of office, laboratory and manufacturing space. Our leases expire in January 2023 and December 2021, respectively. We manufacture our Arcelis-based product candidates for research and development purposes and for clinical trials at these facilities, which we refer to as our Technology Drive and Patriot Center facilities.

Item 3. Legal Proceedings

We are not a party to any legal proceedings and are not aware of any claims or actions pending or threatened against us. In the future, we might from time to time become involved in litigation relating to claims arising from our ordinary course of business.

Item 4. Mine Safety Disclosures

Not Applicable.
Prior to January 19, 2018, our common stock was listed on The Nasdaq Global Market. Since January 19, 2018, our common stock has been listed on The Nasdaq Capital Market. Our common stock trades under the symbol “ARGS”.

The following table sets forth, for the quarterly periods indicated, the high and low intraday sales prices of our common stock as reported by The Nasdaq Global Market or The Nasdaq Capital Market, as applicable:

<table>
<thead>
<tr>
<th>Year ended December 31, 2016</th>
<th>High</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>First quarter</td>
<td>$173.00</td>
<td>$36.60</td>
</tr>
<tr>
<td>Second quarter</td>
<td>$279.40</td>
<td>$95.00</td>
</tr>
<tr>
<td>Third quarter</td>
<td>$141.50</td>
<td>$75.00</td>
</tr>
<tr>
<td>Fourth quarter</td>
<td>$102.00</td>
<td>$69.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year ended December 31, 2017</th>
<th>High</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>First quarter</td>
<td>$113.66</td>
<td>$6.20</td>
</tr>
<tr>
<td>Second quarter</td>
<td>$16.40</td>
<td>$6.66</td>
</tr>
<tr>
<td>Third quarter</td>
<td>$9.40</td>
<td>$3.32</td>
</tr>
<tr>
<td>Fourth quarter</td>
<td>$5.80</td>
<td>$2.62</td>
</tr>
</tbody>
</table>

As of February 28, 2018, there were 7,909,765 outstanding shares and approximately 50 stockholders of record. This number does not include beneficial owners whose shares were held in street name. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Stock Performance Graph

The graph set forth below compares the cumulative total stockholder return on an initial investment of $100 in our common stock between February 7, 2014, the date on which our common stock began trading on The Nasdaq Global Market, and December 31, 2017, with the comparative cumulative total return of such amount on (i) The Nasdaq Composite Index and (ii) The Nasdaq Biotechnology Index over the same period. We have not paid any cash dividends and, therefore, the cumulative total return calculation for us is based solely upon our stock price appreciation or depreciation and does not include any reinvestment of cash dividends. The graph assumes our closing sales price on February 7, 2014 of $160.00 per share as the initial value of our common stock.

The comparisons shown in the graph below are based upon historical data. We caution that the stock price performance shown in the graph below is not necessarily indicative of, nor is it intended to forecast, the potential future performance of our common stock.
Dividends

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business.

Recent Sales of Unregistered Securities

We did not sell any unregistered equity securities during the period covered by this Annual Report on Form 10-K that have not already been reported in a Quarterly Report on Form 10-Q or in a Current Report on Form 8-K.

Purchase of Equity Securities

We did not purchase any of our equity securities during the fourth quarter of the period covered by this Annual Report on Form 10-K.
You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes in “Item 8. Financial Statements and Supplementary Data” and “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations” in this Annual Report on Form 10-K. We have derived the consolidated statements of operations data for the years ended December 31, 2015, 2016 and 2017, and the consolidated balance sheet data as of December 31, 2016 and 2017 from our audited consolidated financial statements included in “Item 8. Financial Statements and Supplementary Data.” The consolidated statements of operations data for the year ended December 31, 2013 and 2014 and the consolidated balance sheet data as of December 31, 2013, 2014 and 2015 were derived from our audited financial statements which are not included in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period. The consolidated financial information reflects a one-for-six reverse stock split of our common stock effected on January 17, 2014 and a one-for-20 reverse stock split of our common stock effected on January 18, 2018, which have been retrospectively applied for all periods presented.

### Consolidated Statements of Operations Data:

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Revenue</strong></td>
<td>$4,421,689</td>
<td>$1,974,019</td>
<td>$518,329</td>
<td>$945,468</td>
<td>$1,899,398</td>
</tr>
<tr>
<td><strong>Operating expenses:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>23,991,151</td>
<td>45,498,916</td>
<td>62,054,823</td>
<td>38,307,236</td>
<td>21,656,096</td>
</tr>
<tr>
<td>General and administrative</td>
<td>4,662,317</td>
<td>8,599,359</td>
<td>11,011,011</td>
<td>14,203,301</td>
<td>12,183,235</td>
</tr>
<tr>
<td>Impairment of property and equipment (1)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>741,114</td>
<td>27,254,385</td>
</tr>
<tr>
<td>Restructuring costs (2)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>6,031,779</td>
</tr>
<tr>
<td>Gain on disposal of impaired property (3)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(2,767,540)</td>
</tr>
<tr>
<td><strong>Operating loss</strong></td>
<td>(24,231,779)</td>
<td>(52,124,256)</td>
<td>(72,547,505)</td>
<td>(52,306,183)</td>
<td>(62,458,557)</td>
</tr>
<tr>
<td><strong>Other income (expense):</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interest income</td>
<td>7,184</td>
<td>66,580</td>
<td>25,382</td>
<td>57,326</td>
<td>64,485</td>
</tr>
<tr>
<td>Interest expense</td>
<td>(4,705)</td>
<td>(1,123,579)</td>
<td>(2,263,599)</td>
<td>(1,774,740)</td>
<td>(1,308,201)</td>
</tr>
<tr>
<td>Gain on early extinguishment of debt (4)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>2,356,478</td>
</tr>
<tr>
<td>Change in fair value of warrant liability (5)</td>
<td>355,352</td>
<td>—</td>
<td>—</td>
<td>1,007,352</td>
<td>20,758,425</td>
</tr>
<tr>
<td>Investment tax credits</td>
<td>—</td>
<td>140,556</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Other (expense) income</td>
<td>(47,615)</td>
<td>(265,239)</td>
<td>(2,799)</td>
<td>(11,865)</td>
<td>9,860</td>
</tr>
<tr>
<td>Other income (expense), net</td>
<td>310,216</td>
<td>(1,181,682)</td>
<td>(2,241,016)</td>
<td>(721,927)</td>
<td>21,881,047</td>
</tr>
<tr>
<td><strong>Net loss</strong></td>
<td>(23,921,563)</td>
<td>(53,305,938)</td>
<td>(74,788,521)</td>
<td>(53,028,110)</td>
<td>(40,577,510)</td>
</tr>
<tr>
<td><strong>Accretion of redeemable convertible preferred stock</strong></td>
<td>4,772,991</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Less: Preferred stock dividend due to exchanges of preferred shares</strong></td>
<td>(14,726,088)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Net loss attributable to common stockholders</strong></td>
<td>(33,874,660)</td>
<td>(54,169,164)</td>
<td>(74,788,521)</td>
<td>(53,028,110)</td>
<td>(40,577,510)</td>
</tr>
<tr>
<td><strong>Basic and diluted net loss attributable to common stockholders per share</strong></td>
<td>(2,947.42)</td>
<td>(62.38)</td>
<td>(73.12)</td>
<td>(33.14)</td>
<td>(13.45)</td>
</tr>
<tr>
<td><strong>Basic and diluted weighted average shares outstanding</strong></td>
<td>11,493</td>
<td>868,383</td>
<td>1,022,862</td>
<td>1,600,286</td>
<td>3,017,409</td>
</tr>
</tbody>
</table>
(1) Represents impairment loss on property and equipment held for sale in the years ended December 31, 2016 and 2017; none present in other periods presented.

(2) Represents costs of a reduction-in-force implemented in the year ended December 31, 2017; none present in other periods presented.

(3) Represents a gain on the disposal of impaired property in the year ended December 31, 2017 in connection with the termination of the Centerpoint facility lease and certain other property from the Saint-Gobain debt restructuring.

(4) Represents the aggregate gain on early extinguishment of debt resulting from the modification of terms of repayment of certain obligations during the year ended December 31, 2017; none present in other periods presented.

(5) Represents gain on change in value of warrants classified as liabilities in the years ended December 31, 2013, 2016 and 2017; we had no such warrants outstanding classified as liabilities during the years ended December 31, 2014 and 2015.

**Consolidated Balance Sheet Data:**

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash, cash equivalents and short-term investments</td>
<td>$46,957,782</td>
<td>$56,239,937</td>
<td>$7,166,304</td>
<td>$52,973,376</td>
<td>$15,188,838</td>
</tr>
<tr>
<td>Total assets</td>
<td>51,131,295</td>
<td>64,366,878</td>
<td>31,037,699</td>
<td>97,204,391</td>
<td>20,777,764</td>
</tr>
<tr>
<td>Total long-term liabilities</td>
<td>10,080,106</td>
<td>29,718,320</td>
<td>51,076,321</td>
<td>60,424,858</td>
<td>20,454,679</td>
</tr>
<tr>
<td>Redeemable convertible preferred stock</td>
<td>113,664,469</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total stockholders' (deficit) equity</td>
<td>(75,776,593)</td>
<td>31,351,804</td>
<td>(28,201,435)</td>
<td>6,169,695</td>
<td>(9,234,080)</td>
</tr>
</tbody>
</table>

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Overview

We are an immuno-oncology company focused on the development and commercialization of individualized immunotherapies for the treatment of cancer and infectious diseases based on our proprietary precision immunotherapy technology platform called Arcelis.

Our most advanced product candidate is rocapuldencel-T, which we are developing for the treatment of metastatic renal cell carcinoma, or mRCC, and other cancers. We are currently conducting a pivotal Phase 3 clinical trial of rocapuldencel-T plus sunitinib or another therapy for the treatment of newly diagnosed mRCC. We refer to this trial as the ADAPT trial. We dosed the first patient in the ADAPT trial in May 2013 and completed enrollment of the ADAPT trial in July 2015. In February 2017, the independent data monitoring committee, or the IDMC, for the ADAPT trial recommended that the trial be discontinued for futility based on its planned interim data analysis. The IDMC concluded that the study was unlikely to demonstrate a statistically significant improvement in overall survival in the combination treatment arm, utilizing the intent-to-treat population at the pre-specified number of 290 events (deaths), the original primary endpoint of the study.

Notwithstanding the IDMC’s recommendation, we determined to continue to conduct the trial while we analyzed interim data from the trial. In May 2017, we met with the FDA to discuss the ADAPT trial and the future direction of the rocapuldencel-T program. Following that meeting, we determined to continue the ADAPT trial until at least the pre-specified number of 290 events occurs, and to submit to the FDA a protocol amendment to increase the pre-specified number of events for the primary analysis of overall survival in the trial beyond 290 events. We believe that extending our evaluation of rocapuldencel-T beyond 290 events in the trial could enhance our ability to observe rocapuldencel-T’s expected delayed treatment effect.

We are currently finalizing an amendment to the ADAPT protocol, including an amended primary endpoint analysis, and plan to submit it to the FDA prior to the interim data analysis planned for the second quarter of 2018, at which time approximately 55 new events (deaths) are expected to have occurred subsequent to the February 2017 interim analysis. We are planning to include the following four co-primary endpoints in the amended ADAPT protocol:

- Overall survival for all randomized patients when approximately 375 events have occurred (under the same analysis that was originally planned for 290 events);
- The percentage of patients surviving at least five years;
- Overall survival for patients who remained alive at the time of the February 2017 interim analysis, to be evaluated when approximately 155 new events have occurred; and
- Overall survival for all patients for whom at least 12 months of follow-up is available (excluding patients who died or were lost to follow-up within the first 12 months after enrollment).

In connection with our amendment of the ADAPT protocol, the special protocol assessment, or the SPA, for the ADAPT trial ceased to be in effect.

Additionally, we are developing a protocol for a Phase 2 clinical trial of rocapuldencel-T in combination with a checkpoint inhibitor for the treatment of patients with mRCC, but we do not intend to initiate this trial unless and until we obtain financing to fund the trial.

We are developing AGS-004, our second Arcelis-based product candidate, for the treatment of HIV. We have completed Phase 1 and Phase 2 trials funded by government grants and a Phase 2b trial that was funded in full by the National Institutes of Health, or NIH, and the National Institute of Allergy and Infectious Diseases, or NIAID. We are currently supporting an ongoing investigator-initiated clinical trial of AGS-004 in adult HIV patients evaluating the use of AGS-004 in combination with vorinostat, a latency reversing drug, for HIV eradication, and plan to support an investigator-initiated Phase 2 clinical trial of AGS-004 evaluating AGS-004 for long-term viral control in pediatric patients provided that results from the investigator-initiated trial in adult HIV patients are favorable and government funding is available.

On March 3, 2017, we entered into a payoff letter with Horizon Technology Finance Corporation and Fortress Credit Co LLC, or the Lenders, under our venture loan and security agreement, or the Loan Agreement, pursuant to which we paid, on March 6, 2017, a total of $23.1 million to the Lenders, representing the principal balance and accrued interest outstanding under the Loan Agreement in repayment of our outstanding obligations under the Loan Agreement. In addition, we issued to the Lenders five year warrants to purchase an aggregate of 5,000 shares of common stock at an exercise price of $26.00 per share in consideration of the Lenders acceptance of $23.1 million as payment in full. Upon the payment of the $23.1 million and the issuance of the warrants pursuant to the payoff letter, all of our outstanding indebtedness and obligations to the Lenders under the Loan Agreement were paid in full, and the Loan Agreement and the notes thereunder were terminated.

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes appearing in “Item 8. Financial Statements and Supplementary Data” in this Annual Report on Form 10-K. In addition to historical information, 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, future financial performance, expense levels and liquidity sources, includes forward-looking statements that involve risks and uncertainties. You should read “Item 1A. Risk Factors” in this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.
In March 2017, we announced that our board of directors approved a workforce action plan designed to streamline operations and reduce operating expenses. During the year ended December 31, 2017, we recognized $1.2 million in severance costs, all of which was paid as of December 31, 2017. We also recognized $3.2 million in stock-based compensation expense from the acceleration of vesting of stock options and restricted stock held by the terminated employees during the year ended December 31, 2017.

In June 2017, we raised net proceeds of $6.0 million through the issuance of a secured convertible note to Pharmstandard International S.A., or Pharmstandard, a collaborator and our largest stockholder, in the aggregate principal amount of $6.0 million.

In August 2017, we entered into an agreement with Medpace, Inc., or Medpace, regarding $1.5 million in deferred fees that we owed Medpace for contract research and development services. Under the agreement we paid $0.85 million of the amount during the third quarter of 2017 and agreed to pay the balance by April 2018.

In September 2017, we entered into a satisfaction and release agreement, or the Invetech Satisfaction and Release Agreement, with Invetech Pty Ltd, or Invetech. Under the Invetech Satisfaction and Release Agreement, we agreed to make, issue and deliver to Invetech (i) a cash payment of $0.5 million, (ii) 57,142 shares of our common stock and (iii) an unsecured convertible promissory note in the original principal amount of $5.2 million on account of and in full satisfaction and release of all of our payment obligations to Invetech arising under our development agreement with Invetech, or the Invetech Development Agreement, prior to the date of the Invetech Satisfaction and Release Agreement, including our obligation to pay Invetech up to a total of $8.3 million in deferred fees, bonus payments and accrued interest.

In November 2017, we entered into a satisfaction and release agreement, or the Saint-Gobain Satisfaction and Release Agreement, with Saint-Gobain Performance Plastics Corporation, or Saint-Gobain. Under the Saint-Gobain Satisfaction and Release Agreement, we agreed to make, issue and deliver to Saint-Gobain (i) a cash payment of $0.5 million, (ii) 34,499 shares of our common stock, (iii) an unsecured convertible promissory note in the original principal amount of $2.4 million, and (iv) certain specified equipment originally provided to us by Saint-Gobain under the development agreement with Saint-Gobain, or the Saint-Gobain Development Agreement, on account of and in full satisfaction and release of all of our payment obligations to Saint-Gobain arising under the Saint-Gobain Development Agreement, prior to the date of the Saint-Gobain Satisfaction and Release Agreement, including the development fees and charges. In connection with entering into the Saint-Gobain Satisfaction and Release Agreement, we and Saint-Gobain entered into an amendment to the Saint-Gobain Development Agreement to extend the term to December 31, 2019.

From June 2017 through December 31, 2017, we raised proceeds of $15.5 million through the issuance of common stock in an at-the-market offering under our original sales agreement with Cowen & Company, LLC, or Cowen. In February 2018, we amended and restated the original sales agreement with Cowen to increase the maximum aggregate offering price of the shares of our common stock which we may sell under the agreement from $30,000,000 to up to $45,000,000. As of March 16, 2018, we raised an additional $7.3 million of proceeds through the sale of our common stock subsequent to December 31, 2017 under the amended and restated sales agreement and $15.8 million remained available for sale under the amended and restated sales agreement.

In addition, in January 2018 we entered into a stock purchase agreement with Lummy (Hong Kong), Ltd., or Lummy, under which we agreed to issue and sell to Lummy in a private financing 375,000 shares of common stock for an aggregate purchase price of $1.5 million. In March 2018, we and Lummy amended the stock purchase agreement to reduce the aggregate price for the shares to $450,000. Concurrent with such amendment, we entered into an amendment to our license agreement with Lummy pursuant to which Lummy agreed to pay us a $1.05 million milestone payment.
As of December 31, 2017, we had cash and cash equivalents of $15.2 million and working capital of $7.6 million. We do not currently have sufficient cash resources to pay all of our accrued obligations in full or to continue our business operations beyond the end of 2018. Therefore, we will need to raise additional capital prior to such time to continue to operate our business beyond that time. Alternatively, we may seek to engage in one or more potential transactions, such as the sale of our company, a strategic partnership with one or more parties or the licensing, sale or divestiture of some of our assets or proprietary technologies, but there can be no assurance that we will be able to enter into such a transaction or transactions on a timely basis or on terms that are favorable to us. Under these circumstances, we may instead determine to dissolve and liquidate our assets or seek protection under the bankruptcy laws. If we decide to dissolve and liquidate our assets or to seek protection under the bankruptcy laws, it is unclear to what extent we will be able to pay our obligations, and, accordingly, it is further unclear whether and to what extent any resources will be available for distributions to stockholders.

Our consolidated financial statements have been prepared assuming that we will continue as a going concern, which contemplates the realization of assets and the settlement of liabilities and commitments in the normal course of business. As of December 31, 2017, our current assets totaled $17.2 million compared with current liabilities of $9.6 million, and we had cash and cash equivalents of $15.2 million. Based upon our current and projected cash flow, we note there is substantial doubt about our ability to continue as a going concern within one year after the date that these financial statements are issued. The financial statements for the year ended December 31, 2017 do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from uncertainty related to our ability to continue as a going concern.

We have devoted substantially all of our resources to our drug development efforts, including advancing our Arcelis precision immunotherapy technology platform, conducting clinical trials of our product candidates, protecting our intellectual property and providing general and administrative support for these operations. We have not generated any revenue from product sales and, to date, have funded our operations primarily through public offerings of our common stock and warrants, a venture loan, private placements of common stock, preferred stock and warrants, convertible debt financings, government contracts, government and other third party grants and license and collaboration agreements. From inception in May 1997 through December, 2017, we have raised a total of $518.4 million in cash, including:

- $353.2 million from the sale of our common stock, convertible debt, warrants and preferred stock;
- $32.9 million from the licensing of our technology;
- $107.3 million from government contracts, grants and license and collaboration agreements; and
- $25.0 million from the Loan Agreement with the Lenders.

We have incurred losses in each year since our inception in May 1997. Our net loss was $74.8 million, $53.0 million and $40.6 million for the years ended December 31, 2015, 2016, and 2017, respectively. As of December 31, 2017, we had an accumulated deficit of $372.6 million. Substantially all of our operating losses have resulted from costs incurred in connection with our development programs and from general and administrative costs associated with our operations.

If we are able to raise the capital necessary to continue the development of our product candidates, including rocapuldencel-T and AGS-004, we anticipate that our expenses will increase substantially if and as we:

- continue our ongoing ADAPT trial of rocapuldencel-T for the treatment of mRCC or initiate other clinical trials of rocapuldencel-T for the treatment of mRCC;
- continue to support the ongoing investigator-initiated clinical trial of AGS-004;
- support any planned investigator-initiated clinical trials of rocapuldencel-T and AGS-004;
- initiate and conduct additional clinical trials of rocapuldencel-T and AGS-004 for the treatment of cancers and HIV;
• seek regulatory approvals for our product candidates that successfully complete clinical trials;
• establish a facility for the commercial manufacture of our products based on our Arcelis-based precision immunotherapy technology platform;
• establish a sales, marketing and distribution infrastructure to commercialize products for which we may obtain regulatory approval;
• maintain, expand and protect our intellectual property portfolio;
• continue our other research and development efforts;
• hire additional clinical, quality control, scientific and management personnel; and
• add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts.

We have no external committed sources of funds other than our contract with the NIH and NIAID, as described under the section entitled NIH Funding below. We do not expect to generate significant additional funds or product revenue unless and until we successfully complete development, obtain marketing approval and commercialize our product candidates, either alone or in collaboration with third parties, which we expect will take a number of years and is subject to significant uncertainty. Accordingly, we will need to raise additional capital prior to the commercialization of rocapuldencel-T, AGS-004 or any of our other product candidates if we determine to continue our business operation. Until such time, if ever, as we can generate substantial product revenues, we expect to seek to finance our operating activities through a combination of equity offerings, debt financings, government contracts, government and other third party grants or other third party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. However, we may be unable to raise additional funds through these means when needed, on favorable terms or at all.

**NIH Funding**

In September 2006, we entered into a multi-year research contract with the NIH and NIAID to design, develop and clinically test an autologous HIV immunotherapy capable of eliciting therapeutic immune responses. We have used funds from this contract to develop AGS-004, including to fund in full our Phase 2b clinical trial of AGS-004. On June 29, 2016, a contract modification was agreed to that extended the NIH and NIAID’s commitment under the contract to July 31, 2018. We have agreed to a statement of work under the contract, and are obligated to furnish all the services, qualified personnel, material, equipment, and facilities not otherwise provided by the U.S. government needed to perform the statement of work.

Under this contract, as amended, the NIH and NIAID have committed to fund up to a total of $39.8 million, including reimbursement of direct expenses and allocated overhead and general and administrative expenses of up to $38.4 million and payment of other specified amounts totaling up to $1.4 million upon our achievement of specified development milestones. This amount includes a September 2014 modification of the contract under which the NIH and NIAID agreed to fund up to an additional $0.5 million to cover a portion of the manufacturing costs of the planned Phase 2 clinical trial of AGS-004 for long-term viral control in pediatric patients. The NIH’s commitment under the contract extends to July 31, 2018. Since September 2010, we have received reimbursement of our allocated overhead and general and administrative expenses at provisional indirect cost rates equal to negotiated provisional indirect cost rates agreed to with the NIH and NIAID in September 2010. These provisional indirect cost rates are subject to adjustment based on our actual costs pursuant to the agreement with the NIH and NIAID and may result in additional payments to us from the NIH and NIAID to reflect our actual costs since September 2010.

We have recorded revenue of $38.3 million through December 31, 2017 under the NIH and NIAID contract. This contract is the only arrangement under which we have generated substantial revenue. As of December 31, 2017, there was up to $1.5 million of potential revenue remaining to be earned under the agreement with the NIH and NIAID.
An important part of our business strategy has been to enter into arrangements with third parties both to assist in the development and commercialization of our product candidates, particularly in international markets, and to in-license product candidates in order to expand our pipeline.

**Pharmstandard**. In August 2013, in connection with the purchase of shares of our series E preferred stock by Pharmstandard, we entered into an exclusive royalty-bearing license agreement with Pharmstandard. Under this license agreement, we granted Pharmstandard and its affiliates a license, with the right to sublicense, to develop, manufacture and commercialize rocapuldencel-T and other products for the treatment of human diseases, which are developed by Pharmstandard using our individualized immunotherapy platform, in the Russian Federation, Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Turkmenistan, Ukraine and Uzbekistan, which we refer to as the Pharmstandard Territory. We also provided Pharmstandard with a right of first negotiation for development and commercialization rights in the Pharmstandard Territory to specified additional products we may develop.

Under the terms of the license agreement, Pharmstandard licensed us rights to clinical data generated by Pharmstandard under the agreement and granted us an option to obtain an exclusive license outside of the Pharmstandard Territory to develop and commercialize improvements to our Arcelis technology generated by Pharmstandard under the agreement, a non-exclusive worldwide royalty-free license to Pharmstandard improvements to manufacture products using our Arcelis technology and a license to specified follow-on licensed products generated by Pharmstandard outside of the Pharmstandard Territory, each on terms to be negotiated upon our request for a license. In addition, Pharmstandard agreed to pay us pass-through royalties on net sales of all licensed products in the low single digits until it has generated a specified amount of aggregate net sales. Once the net sales threshold is achieved, Pharmstandard will pay us royalties on net sales of specified licensed products, including rocapuldencel-T, in the low double digits below 20%. These royalty obligations last until the later of the expiration of specified licensed patent rights in a country or the twelfth anniversary of the first commercial sale in such country on a country by country basis and no further royalties on specified other licensed products. After the net sales threshold is achieved, Pharmstandard has the right to offset a portion of the royalties Pharmstandard pays to third parties for licenses to necessary third party intellectual property against the royalties that Pharmstandard pays to us.

The agreement will terminate upon expiration of the royalty term, upon which all licenses will become fully paid up perpetual exclusive licenses. Either party may terminate the agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy and we may terminate the agreement if Pharmstandard challenges or assists a third party in challenging specified patent rights of ours. If Pharmstandard terminates the agreement upon our material breach or bankruptcy, Pharmstandard is entitled to terminate our licenses to improvements generated by Pharmstandard, upon which we may come to rely for the development and commercialization of rocapuldencel-T and other licensed products outside of the Pharmstandard Territory, and Pharmstandard is entitled to retain its licenses from us and to pay us substantially reduced royalty payments following such termination.

In November 2013, we entered into an agreement with Pharmstandard under which Pharmstandard purchased shares of our series E preferred stock. Under this agreement, we agreed to enter into a manufacturing rights agreement for the European market with Pharmstandard and that the manufacturing rights agreement would provide for the issuance of warrants to Pharmstandard to purchase 24,989 shares of our common stock at an exercise price of $116.40 per share. As of March 16, 2018, we had not entered into this manufacturing rights agreement or issued the warrants.
On February 1, 2018, we entered into an option agreement with Pharmstandard and Actigen Limited, or Actigen, under which we obtained an exclusive option to license certain patent rights and know-how related to a group of fully human PD1 monoclonal antibodies and related technology held by Actigen. Actigen previously granted Pharmstandard an option to exclusively license these patent rights. Under the option agreement, Pharmstandard granted to us an exclusive license for evaluation purposes only to make, have made, use and import the PD1 monoclonal antibodies covered by these patent rights (but not offer to sell or sell products and processes covered by or incorporating the patent rights) for a period of one year from the date of the agreement and an option exercisable during the option exercise period to obtain an exclusive license (with the right to sublicense) under the patent rights to make, have made, use, offer for sale, sell and import (with a right to grant sublicenses) the PD1 monoclonal antibodies for all prophylactic, therapeutic and diagnostic uses and for all human diseases and conditions in the United States and Canada. The parties have agreed that, if we exercise the option during the option exercise period, the parties will negotiate in good faith a license agreement, on the terms and conditions outlined in the option agreement, including payments by us to Pharmstandard of an upfront license fee of $3.6 million, payable upon execution of the license agreement in our common stock, various development and regulatory milestone payments totaling $8.5 million, and upper single digit percentage royalties on net sales of any pharmaceutical product or therapeutic regimen incorporating the licensed PD1 monoclonal antibodies that will apply on a country-by-country basis until the later of the last to expire patent or ten years from the date of first commercial sale, against which the first $5.0 million of our development expenditures will be credited as prepaid royalties.

In consideration for the rights granted under the option agreement, we agreed to issue to Pharmstandard, on or before April 2, 2018, 169,014 shares of our common stock, the value of which will be creditable against the upfront license fee of $3.6 million if we enter into a license agreement. Unless earlier terminated by any party for uncured material breach or by us without cause upon thirty days prior written notice, the option agreement will terminate upon the later of the end of the option exercise period if we decide not to exercise the option or sixty days after we exercise the option.

Green Cross. In July 2013, in connection with the purchase of our series E preferred stock by Green Cross Corp., or Green Cross, we entered into an exclusive royalty-bearing license agreement with Green Cross. Under this agreement we granted Green Cross a license to develop, manufacture and commercialize rocapuldencel-T for mRCC in South Korea. We also provided Green Cross with a right of first negotiation for development and commercialization rights in South Korea to specified additional products we may develop.

Under the terms of the license, Green Cross has agreed to pay us $0.5 million upon the initial submission of an application for regulatory approval of a licensed product in South Korea, $0.5 million upon the initial regulatory approval of a licensed product in South Korea and royalties ranging from the mid-single digits to low double digits below 20% on net sales until the fifteenth anniversary of the first commercial sale in South Korea. In addition, Green Cross has granted us an exclusive royalty free license to develop and commercialize all Green Cross improvements to our licensed intellectual property in the rest of the world, excluding South Korea, except that, as to such improvements for which Green Cross makes a significant financial investment and that generate significant commercial benefit in the rest of the world, we are required to negotiate in good faith a reasonable royalty that we will be obligated to pay to Green Cross for such license. Under the terms of the agreement, we are required to continue to develop and to use commercially reasonable efforts to obtain regulatory approval for rocapuldencel-T in the United States.

The agreement will terminate upon expiration of the royalty term, which is 15 years from the first commercial sale, upon which all licenses will become fully paid up perpetual non-exclusive licenses. Either party may terminate the agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy and we may terminate the agreement if Green Cross challenges or assists a third party in challenging specified patent rights of ours. If Green Cross terminates the agreement upon our material breach or bankruptcy, Green Cross is entitled to terminate our licenses to improvements and retain its licenses from us and to pay us substantially reduced milestone and royalty payments following such termination.

Medinet. In December 2013, we entered into a license agreement with Medinet. Under this agreement, we granted Medinet an exclusive, royalty-free license to manufacture in Japan rocapuldencel-T and other products using our Arcelis technology solely for the purpose of the development and commercialization of rocapuldencel-T and these other products for the treatment of mRCC. We refer to this license as the manufacturing license. In addition, under this agreement, we granted Medinet an option to acquire a nonexclusive, royalty-bearing license under our Arcelis technology to sell in Japan rocapuldencel-T and other products for the treatment of mRCC. We refer to the option as the sale option and the license as the sale license.
The sale option expired on April 30, 2016. As a result, Medinet has only retained the manufacturing license and may only manufacture rocapuldencel-T and these other products for us or our designee. We have agreed to negotiate in good faith a supply agreement under which Medinet would supply us or our designee with rocapuldencel-T and these other products for development and sale for the treatment of mRCC in Japan. During the term of the manufacturing license, we may not manufacture rocapuldencel-T or these other products for us or any designee for development or sale for the treatment of mRCC in Japan.

In consideration for the manufacturing license, Medinet paid us $1.0 million. Medinet also loaned us $9.0 million in connection with us entering into the agreement. We have agreed to use these funds in the development and manufacturing of rocapuldencel-T and the other products. Medinet also agreed to pay us milestone payments of up to a total of $9.0 million upon the achievement of developmental and regulatory milestones and $5.0 million upon the achievement of a sales milestone related to rocapuldencel-T and these products.

We borrowed the $9.0 million pursuant to an unsecured promissory note that bears interest at a rate of 3.0% per annum. The principal and interest under the note are due and payable on December 31, 2018. Under the terms of the note and the manufacturing license agreement, any milestone payments related to the developmental and regulatory milestones that become due will be applied first to the repayment of the loan. We have achieved $5.0 million in milestones. As a result, the outstanding principal of the loan as of February 1, 2018 has been reduced to $4.0 million. We have the right to prepay the loan at any time. If we have not repaid the loan by December 31, 2018, then we have agreed to grant to Medinet a non-exclusive, royalty-bearing license to make and sell Arcelis products in Japan for the treatment of cancer. In such event, the amounts owing under the loan as of December 31, 2018 may constitute pre-paid royalties under the license or would be due and payable. We do not expect to pay the amounts owing under the loan by December 31, 2018. Royalties under this license would be paid until the expiration of the licensed patent rights in Japan at a rate to be negotiated. If we cannot agree on the royalty rate, we have agreed to submit the matter to arbitration.

Under the agreement, we had the right to revoke both the manufacturing license and the sale license to be granted to Medinet or the sale license only. On February 14, 2018, we notified Medinet that we irrevocably agreed to have no further right to exercise our right under the license agreement to revoke the manufacturing and the sale license, or the sale license only.

The agreement will terminate upon expiration of the royalty term, upon which all licenses will become fully paid up, perpetual non-exclusive licenses. Either party may terminate the agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy, and we may terminate the agreement if Medinet challenges or assists a third party in challenging specified patent rights of ours. If Medinet terminates the agreement upon our material breach or bankruptcy, Medinet is entitled to terminate our licenses to improvements and retain its royalty-bearing licenses from us.

**Lummy**. On April 7, 2015, we and Lummy (Hong Kong) Co. Ltd., or Lummy HK, entered into a license agreement pursuant to which we granted to Lummy HK an exclusive license under the Arcelis technology, including patents, know-how and improvements to manufacture, develop and commercialize products for the treatment of cancer in China, Hong Kong, Taiwan and Macau. Lummy HK also has a right of first negotiation with respect to a license under the Arcelis technology for the treatment of infectious diseases in China, Hong Kong, Taiwan and Macau. This agreement was subsequently amended in December 2016, October 2017 and March 2018.

Under the terms of the license agreement, the parties will share relevant data, and we will have a right to reference Lummy HK data for purposes of its development programs under the Arcelis technology. In addition, Lummy HK has granted to us an exclusive, royalty-free license under and to any and all Lummy HK improvements to the Arcelis technology conceived or reduced to practice by Lummy HK and Lummy HK data to develop and/or commercialize products outside China, Hong Kong, Taiwan and Macau, an exclusive, royalty-free license under and to any and all investigational new drugs, or INDs, and other regulatory approvals and Lummy HK trademarks used for an Arcelis-based product to develop and/or commercialize an Arcelis-based product outside China, Hong Kong, Taiwan and Macau and a non-exclusive, worldwide, royalty-free license under any Lummy HK improvements and Lummy HK data to manufacture Arcelis-based products anywhere in the world. Lummy HK has the right to reference our data, INDs and other regulatory filings and submissions for the purpose of developing and obtaining regulatory approval of licensed products in China, Hong Kong, Taiwan and Macau.
Pursuant to the license agreement, Lummy HK will pay us royalties on net sales and an aggregate of up to $22.3 million upon the achievement of manufacturing, regulatory and commercial milestones. On October 18, 2017, we entered into a second amendment to the license agreement and Lummy HK paid us $1.5 million upon the achievement of a manufacturing milestone in October 2017. On March 23, 2018, we entered into a third amendment to the license agreement pursuant to which Lummy agreed to pay us a $1.05 million milestone.

Of the potential $22.3 million in milestone payments, to date we have earned $2.55 million, of which we have received $1.5 million as of March 31, 2018. The license agreement will terminate upon expiration of the last to expire royalty term for all Arcelis-based products, with each royalty term being the longer of the expiration of the last valid patent claim covering the applicable Arcelis-based product and 10 years from the first commercial sale of such Arcelis-based product. Either party may terminate the license agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy. We may terminate the license agreement if Lummy HK challenges or assists a third party in challenging specified patent rights of ours. If Lummy HK terminates the license agreement upon our material breach or bankruptcy, Lummy HK is entitled to terminate the licenses it granted to us and retain its licenses from us with respect to Arcelis-based products then in development or being commercialized, subject to Lummy HK’s continued obligation to pay royalties and milestones with respect to such Arcelis-based products.

**Invetech**. In October 2014, we entered into the Invetech Development Agreement. Under the Invetech Development Agreement, Invetech had agreed to continue to develop and provide prototypes of the automated production system to be used for the manufacture of our Arcelis-based products. Subsequent to signing the Invetech Development Agreement, Invetech agreed to defer 30% of its fees, up to $5.0 million subject to payments by us in installments over 2017 and 2018.

On September 22, 2017, we entered into the Invetech Satisfaction and Release Agreement. Under the Invetech Satisfaction and Release Agreement, we agreed to make, issue and deliver to Invetech (i) a cash payment of $0.5 million (ii) 57,142 shares of our common stock and (iii) an unsecured convertible promissory note in the original principal amount of $5.2 million on account of and in full satisfaction and release of all of our payment obligations to Invetech arising under the Invetech Development Agreement prior to the date of the Invetech Satisfaction and Release Agreement, including our obligation to pay Invetech up to a total of $8.3 million in deferred fees, bonus payments and accrued interest.

Although we currently have no ongoing activities under the Invetech Development Agreement, the term of the Invetech Development Agreement will continue until the completion of the development of the production systems. The Invetech Development Agreement can be terminated early by either party because of a technical failure or by us without cause. We own all intellectual property arising from the development services with the exception of existing Invetech intellectual property incorporated therein-under which we have a license.

**Saint-Gobain**. In January 2015, we entered into the Saint-Gobain Development Agreement, that was subsequently amended in 2015, 2016 and 2017. Under the Saint-Gobain Development Agreement, Saint-Gobain agreed to develop a range of disposables for use in our automated production systems to be used for the manufacture of our Arcelis-based products. The Saint-Gobain agreement requires the parties to execute a commercial supply agreement under which Saint-Gobain would become the exclusive supplier of disposables for the manufacture of our products treating solid tumors for no less than fifteen years. The Saint-Gobain agreement will continue until December 31, 2019, but can be terminated by written agreement of the parties because of a material default, including the failure to execute the commercial supply agreement, or a failure to achieve a performance milestone.
On November 22, 2017, we entered into the Saint-Gobain Satisfaction and Release Agreement. Under the Saint-Gobain Satisfaction and Release Agreement, we agreed to make, issue and deliver to Saint-Gobain (i) a cash payment of $0.5 million, (ii) 34,499 shares of our common stock (iii) an unsecured convertible promissory note in the original principal amount of $2.4 million, and (iv) certain specified equipment originally provided to us under the development agreement, on account of and in full satisfaction and release of all payment obligations to Saint-Gobain arising under the development agreement, including the development fees and charges owed by us to Saint-Gobain.

**Cellscript.** In December 2015, we entered into a development and supply agreement with Cellscript, LLC, or Cellscript. Under the agreement, Cellscript has agreed to develop cGMP processes for the manufacture and production of CD40L RNA, a ribonucleic acid used in the production of our Arcelis-based products, and to manufacture and produce CD40L RNA.

In consideration for these development and production services, we have agreed to pay Cellscript total fees of $4.6 million. Upon the execution of the agreement, we made an initial payment to Cellscript of $2.1 million through the issuance to Cellscript of 45,309 shares of our common stock. The balance of these fees is payable to Cellscript, at our option, in cash, common stock or a combination of cash and common stock upon the achievement of development milestones. Any shares of common stock issued pursuant to the agreement are subject to a lock-up period of 180 days from the date of issuance of such shares to Cellscript.

Under the terms of the agreement, Cellscript shall be the sole and exclusive manufacturer and supplier to us of CD40L RNA, and we will make agreed upon cash payments to Cellscript for CD40L RNA produced for us during the term of the agreement. Under the agreement, Cellscript shall also be our sole and exclusive supplier of enzymes and various kits comprising enzymes for transcription, capping and/or polyadenylation of RNA. We will make agreed upon cash payments to Cellscript for each kit that is purchased under the agreement.

The agreement will continue until the earlier of June 30, 2018 or the effective date of a commercial supply agreement negotiated in good faith by the parties, but can be earlier terminated by either party due to a material breach or upon bankruptcy of the other party.

**Manufacturing**

We currently have manufacturing suites located at our Technology Drive and Patriot Center leased facilities in Durham, North Carolina. We manufacture our Arcelis-based product candidates for research and development purposes and for clinical trials at these facilities.

In January 2017, we entered into a ten-year lease agreement with two five-year renewal options for 40,000 square feet of manufacturing and office space at the Center for Technology Innovation, or CTI, on the Centennial Campus of North Carolina State University in Raleigh, North Carolina. We provided a security deposit in the amount of $2.4 million as security for obligations under the lease agreement, which was provided in the form of a letter of credit. We had intended to utilize this facility to manufacture rocapuldencel-T to support submission of a biologics license application, or BLA, to the FDA and to support initial commercialization of rocapuldencel-T.

To provide for capacity expansion beyond the initial few years following potential launch of rocapuldencel-T, we also had planned to build-out and equip a second facility, which we refer to as the Centerpoint facility. In August 2014, we entered into a ten-year lease agreement with renewal options. Under the lease agreement, we agreed to lease certain land and an approximately 125,000 square-foot building to be constructed in Durham County, North Carolina. We initially intended this facility to house our corporate headquarters and commercial manufacturing before we entered into the lease for the CTI facility. The shell of the new facility was constructed on a build-to-suit basis in accordance with agreed upon specifications and plans and was completed in June 2015. However, the build-out and equipping of the interior of the facility was suspended as we pursued financing arrangements to support the further build out of the facility.
Due to the recommendation of the IDMC in February 2017 to discontinue the ADAPT study, we have reassessed our manufacturing plans. In March 2017, we entered into a lease termination agreement with the landlord of our CTI facility terminating the lease as of March 17, 2017. From the $2.4 million letter of credit, the landlord drew down $0.7 million to cover unpaid construction costs in March 2017 and $1.7 million in April 2017 for lease termination damages and agreed to return $0.1 million in consideration for being able to salvage some of the construction costs. Pursuant to the lease termination agreement, we have no further obligations under the lease. During the year ended December 31, 2017, we recorded a lease termination fee of $1.6 million that is included in restructuring costs on the statement of operations and Current portion of restructuring liability on the balance sheet. We also recorded an impairment loss on Construction-in-progress on the property of $0.9 million during the year ended December 31, 2017.

In November 2017, we and TKC Properties, the landlord of the Centerpoint facility, entered into a lease termination agreement terminating the lease agreement as of November 21, 2017. In addition, TKC Properties completed the sale of the facility to a third party and we received cash proceeds of approximately $1.8 million. As of December 31, 2017, we recorded $0 for the Centerpoint facility and $0 for the lease liability. Additionally, we are no longer required to maintain restricted cash of approximately $0.7 million as a security deposit.

Financial Overview

Revenue

To date, we have not generated revenue from the sale of any products. During the years ended December 31, 2015, 2016 and 2017, substantially all of our revenue has been derived from our NIH and NIAID contract and a license agreement with Lummy HK. We may generate revenue in the future from government contracts and grants, payments from future license or collaboration agreements and product sales. We expect that any revenue we generate will fluctuate from quarter to quarter.

Research and Development Expenses

Since our inception in 1997, we have focused our resources on our research and development activities, including conducting preclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings for our product candidates. We recognize our research and development expenses as they are incurred. Our research and development expenses consist primarily of:

- salaries and related expenses for personnel in research and development functions;
- fees paid to consultants and clinical research organizations, or CROs, including in connection with our clinical trials, and other related clinical trial fees, such as for investigator grants, patient screening, laboratory work and statistical compilation and analysis;
- commercial manufacturing development consisting of costs incurred under our development agreement with Invetech under which Invetech had agreed to develop and provide prototypes of the automated production system to be used for the manufacture of our Arcelis-based products;
- allocation of facility lease and maintenance costs;
- costs incurred under our development agreement with Saint-Gobain to develop a range of disposables for use in the automated production system;
- depreciation of leasehold improvements, laboratory equipment and computers;
- costs related to production of product candidates for clinical trials;
Our direct research and development expenses consist principally of external costs, such as fees paid to investigators, consultants, central laboratories and CROs, including in connection with our clinical trials, and related clinical trial fees. Commercial manufacturing development costs consist primarily of costs incurred under our development agreement with Invetech to develop and provide prototypes of the automated production system to be used for the manufacture of our Arcelis-based products. We have been developing rocapuldencel-T and AGS-004 in parallel, and typically use our employee and infrastructure resources across multiple research and development programs. We do not allocate salaries, share-based compensation, employee benefit or other indirect costs related to our research and development function to specific product candidates.

The successful development of our clinical and preclinical product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of any of our clinical or preclinical product candidates or the period, if any, in which material net cash inflows from these product candidates may commence. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress, expense and results of our ongoing clinical trials;
- the scope, rate of progress, expense and results of additional clinical trials that we may conduct;
- the scope, rate of progress, expense and results of our commercial manufacturing development efforts;
- other research and development activities; and
- the timing of regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. If the FDA or another regulatory authority were to require us to conduct clinical trials beyond those which we currently anticipate will be required for the completion of clinical development of a product candidate or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development. Particularly in light of the recent recommendation by the IDMC to discontinue the ADAPT study due to futility, we expect that the continued development of rocapuldencel-T, which is contingent upon our ongoing review of the preliminary data set from the ADAPT study and discussions with the FDA regarding the amended protocol, will be significantly more costly, and take a significantly longer period of time, than we had previously anticipated.
Commercial Manufacturing Development

Commercial manufacturing development costs consist primarily of costs incurred under our development agreement with Invotech to develop and provide prototypes of the automated production system to be used for the manufacture of our Arcelis-based products and our development agreement with Saint-Gobain to develop a range of disposables for use in the automated production system.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for employees in executive, operational and finance, information technology and human resources functions. Other significant general and administrative expenses include allocation of facilities costs, professional fees for accounting and legal services, premiums for directors’ and officers’ insurance and other insurance policies, expenses associated with obtaining and maintaining patents, and expenses incurred as a result of operating as a public company.

Interest Income and Interest Expense

Interest income consists of interest earned on our cash, cash equivalents and short-term investments.

Interest expense consists primarily of accrued interest costs related to our debt. During the years ended December 31, 2015, 2016 and 2017, interest expense primarily resulted from interest on the Loan Agreement with the Lenders, our convertible note payable to Pharmstandard, our note payable to Medinet and our capital lease obligations. We paid a total of $23.1 million under the Loan Agreement in March 2017, which represented the principal balance and accrued interest outstanding under the Loan Agreement, and we terminated the capital lease obligations under the power generation agreements in November 2017.

Venture Loan and Security Agreement. In September 2014, we entered into the Loan Agreement with the Lenders under which we borrowed up to $25.0 million in two tranches of $12.5 million each. We borrowed the first tranche of $12.5 million upon the closing of the transaction in September 2014 and borrowed the second tranche of $12.5 million on August 7, 2015, following completion of enrollment of the ADAPT trial. The per annum interest rate for each tranche was a floating rate equal to 9.25% plus the amount by which the one-month London Interbank Offered Rate, or LIBOR, exceeds 0.50% (effectively a floating rate equal to 8.75% plus the one-month LIBOR Rate). The total per annum interest rate shall not exceed 10.75%. This loan was fully discharged on March 7, 2017 with the payment of $23.1 million and the issuance of five-year warrants to purchase an aggregate of 5,000 shares of common stock with a strike price of $26.00 per share.

Medinet. In December 2013, in connection with the license agreement with Medinet, as described in Note 12 to our consolidated financial statements, we borrowed $9.0 million pursuant to an unsecured promissory note that bears interest at a rate of 3.0% per annum. If we have not repaid the loan by December 31, 2018, then we have agreed to grant to Medinet a non-exclusive, royalty-bearing license to make and sell Arcelis products in Japan for the treatment of cancer. In such event, the amounts owing under the loan as of December 31, 2018 may constitute pre-paid royalties under the license or would be due and payable. Royalties under this license would be paid until the expiration of the licensed patent rights in Japan at a rate to be negotiated. If we and Medinet cannot agree on the royalty rate, Medinet has agreed to submit the matter to arbitration. Because the $9.0 million promissory note was issued at a below market interest rate, we allocated the proceeds of the loan between the license agreement and the debt at the time of issuance. Accordingly, as of the borrowing date, December 31, 2013, we recorded $6.9 million to notes payable, based upon an effective interest rate of 8.0%, and $2.1 million as a deferred liability.

During the year ended December 31, 2015, we recognized a $1.0 million milestone payment as deferred revenue under this license agreement and reduced the related note payable by $0.8 million and the deferred liability by $0.2 million. As of December 31, 2015, we recorded $7.5 million to notes payable, including $1.3 million of accrued interest. During the year ended December 31, 2016, we recorded $2.0 million milestone payment as deferred revenue under this license agreement and reduced the related note payable by $1.5 million and the deferred liability by $0.5 million. As of December 31, 2016, we recorded $6.4 million to notes payable, including $1.8 million of accrued interest. During the year ended December 31, 2017, we recognized a $2.0 million milestone payment as deferred revenue under the license agreement and reduced the related note payable by $1.5 million and the deferred liability by $0.5 million. As of December 31, 2017, we recorded $5.0 million to notes payable, including $1.9 million of accrued interest. On February 14, 2018, we notified Medinet that we agreed to have no further right under the license agreement to revoke the manufacturing and sale license, or the sale license only. In all other respects, the Medinet license agreement will remain in full force and effect. As a result of our decision to forego this revocation right, during the first quarter of 2018 we expect to recognize $5.8 million of revenue related to the achievement of milestones that had previously been recorded as deferred revenue.

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Results of Operations – Year-Over-Year Comparisons

The following table summarizes the results of our operations for each of the years ended December 31, 2015, 2016 and 2017, together with the changes in those items in dollars and as a percentage:

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>2016</th>
<th>2017</th>
<th>Change</th>
<th>% Change</th>
<th>Year Ended December 31,</th>
<th>2015</th>
<th>2016</th>
<th>Change</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>(in thousands)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revenue</td>
<td>$945</td>
<td>$1,899</td>
<td>$954</td>
<td>100.9%</td>
<td>$518</td>
<td>$945</td>
<td>$427</td>
<td>82.4%</td>
<td></td>
</tr>
<tr>
<td>Operating expenses:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>38,307</td>
<td>21,656</td>
<td>16,651</td>
<td>43.5%</td>
<td>62,055</td>
<td>38,307</td>
<td>23,748</td>
<td>38.3%</td>
<td></td>
</tr>
<tr>
<td>General and administrative</td>
<td>14,203</td>
<td>12,183</td>
<td>2,020</td>
<td>14.2%</td>
<td>11,011</td>
<td>14,203</td>
<td>3,192</td>
<td>29.0%</td>
<td></td>
</tr>
<tr>
<td>Impairment of property and equipment</td>
<td>741</td>
<td>27,254</td>
<td>26,513</td>
<td>*</td>
<td>—</td>
<td>741</td>
<td>741</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Restructuring costs</td>
<td>—</td>
<td>6,032</td>
<td>6,032</td>
<td>*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Gain on disposal of impaired property</td>
<td>—</td>
<td>(2,767)</td>
<td>(2,767)</td>
<td>*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total operating expenses</td>
<td>53,251</td>
<td>64,358</td>
<td>11,107</td>
<td>20.9%</td>
<td>73,066</td>
<td>53,251</td>
<td>19,815</td>
<td>27.1%</td>
<td></td>
</tr>
<tr>
<td>Loss from operations</td>
<td>(52,306)</td>
<td>(62,459)</td>
<td>10,153</td>
<td>(19.4%)</td>
<td>(72,548)</td>
<td>52,306</td>
<td>20,242</td>
<td>(27.9%)</td>
<td></td>
</tr>
<tr>
<td>Interest income</td>
<td>57</td>
<td>65</td>
<td>8</td>
<td>12.5%</td>
<td>25</td>
<td>57</td>
<td>32</td>
<td>128.0%</td>
<td></td>
</tr>
<tr>
<td>Interest expense</td>
<td>(1,775)</td>
<td>(1,308)</td>
<td>467</td>
<td>26.3%</td>
<td>(2,264)</td>
<td>(1,775)</td>
<td>489</td>
<td>21.6%</td>
<td></td>
</tr>
<tr>
<td>Gain on early extinguishment of debt</td>
<td>—</td>
<td>2,356</td>
<td>2,356</td>
<td>*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Change in fair value of warrant liability</td>
<td>1,007</td>
<td>20,758</td>
<td>19,751</td>
<td>*</td>
<td>—</td>
<td>1,007</td>
<td>1,007</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Other (loss) income</td>
<td>(11)</td>
<td>10</td>
<td>21</td>
<td>*</td>
<td>(2)</td>
<td>(11)</td>
<td>(9)</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td>$ (53,028)</td>
<td>$ (40,578)</td>
<td>$12,450</td>
<td>23.5%</td>
<td>$ (74,789)</td>
<td>$ (53,028)</td>
<td>$21,761</td>
<td>(29.1%)</td>
<td></td>
</tr>
</tbody>
</table>

* Not meaningful

Revenue

To date, we have not generated revenue from the sale of any products. During the years ended December 31, 2015, 2016 and 2017, substantially all of our revenue has been derived from our NIH and NIAID contract and our license agreement with Lummy HK. We may generate revenue in the future from government contracts and grants, payments from future license or collaboration agreements and product sales. We expect that any revenue we generate will fluctuate from quarter to quarter.
Revenue was $1.9 million for the year ended December 31, 2017, compared with $0.9 million for the year ended December 31, 2016, an increase of $0.9 million, or 100.9%. During the year ended December 31, 2017, we recognized revenue of $1.6 million under our license agreement with Lummy HK, consisting primarily of a $1.5 million milestone payment recognized as revenue, $0.2 million of reimbursed costs under our NIH and NIAID contract and $0.1 million from a sub-award reimbursed under the NIAID’s Division of AIDS grant provided directly to the University of North Carolina. This compares with revenue recognized during the year ended December 31, 2016 of $0.8 million from our NIH and NIAID contract and $0.1 million from our license agreement with Lummy HK for the reimbursement of technology transfer related costs. The decrease in revenue from our NIH and NIAID contract for the year ended December 31, 2017 compared with the year ended December 31, 2016 resulted from lower reimbursement under our NIH and NIAID contract primarily reflecting the achievement of certain specified development milestones during 2016.

Revenue was $0.9 million for the year ended December 31, 2016, compared with $0.5 million for the year ended December 31, 2015, an increase of $0.4 million or 82.4%. The $0.4 million increase for the year ended December 31, 2016 resulted from higher reimbursement under our NIH and NIAID contract and was primarily related to the achievement of certain specified development milestones during 2016.

### Research and Development Expenses

The table below summarizes our direct research and development expenses by program for the periods indicated. Our direct research and development expenses consist principally of external costs, such as fees paid to investigators, consultants, central laboratories and CROs, including in connection with our clinical trials, and related clinical trial fees. Research and development expenses also include commercial manufacturing development costs consisting primarily of costs incurred under our Invotech Development Agreement to develop and provide prototypes of the automated production system to be used for the manufacture of our Arcelis-based products and our Saint-Gobain Development Agreement to develop a range of disposables to be used in both our manual and automated manufacturing processes. We have been developing rocapuldenel-T and AGS-004 in parallel, and typically use our employee and infrastructure resources across multiple research and development programs. We do not allocate salaries, share-based compensation, employee benefit or other indirect costs related to our research and development function to specific product candidates. Those expenses are included in “Indirect research and development expense” in the table below.

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(in thousands)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct research and development expense by program:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rocapuldenel-T</td>
<td>$22,503</td>
<td>$11,031</td>
<td>$7,434</td>
</tr>
<tr>
<td>AGS-004</td>
<td>289</td>
<td>266</td>
<td>112</td>
</tr>
<tr>
<td>Other</td>
<td>40</td>
<td>12</td>
<td>—</td>
</tr>
<tr>
<td>Total direct research and development program expense</td>
<td>$22,832</td>
<td>$11,309</td>
<td>$7,546</td>
</tr>
<tr>
<td>Commercial manufacturing development</td>
<td>17,926</td>
<td>3,400</td>
<td>(373)</td>
</tr>
<tr>
<td>Total research and development expense</td>
<td>$62,055</td>
<td>$38,307</td>
<td>$21,656</td>
</tr>
</tbody>
</table>

Research and development expenses were $21.7 million for the year ended December 31, 2017, compared with $38.3 million for the year ended December 31, 2016, a decrease of $16.7 million, or 43.5%. The decrease in research and development expense reflects a $3.8 million decrease in direct research and development expense, a $3.8 million decrease in commercial manufacturing development expense, and a $9.1 million decrease in indirect research and development expense.
The decrease in direct research and development expenses resulted primarily from the following:

- Direct research and development expense for rocapuldencel-T decreased to $7.4 million for the year ended December 31, 2017 from $11.0 million for the year ended December 31, 2016. This decrease primarily reflects a reduction of costs related to the ongoing ADAPT trial of rocapuldencel-T.
- Direct research and development expense with respect to AGS-004 decreased to $0.1 million for the year ended December 31, 2017 from $0.3 million for the year ended December 31, 2016. This decrease primarily reflects decreased activity under the NIH and NIAID contract.

The decrease in commercial manufacturing development expense reflects our determination not to proceed with the development of commercial manufacturing capabilities following the recommendation of the IDMC to discontinue the ADAPT trial. During the year ended December 31, 2017, we recorded a credit of $0.4 million related to amounts owed to Saint-Gobain under the Saint-Gobain Development Agreement, which we recorded as a reduction of research and development expense.

The decrease in indirect research and development expense was primarily due to our decision following the IDMC recommendation to significantly reduce the size of our workforce engaged in research and development activities in March 2017. As of December 31, 2017, we had 29 employees engaged in such activities, compared with 99 employees engaged in such activities as of December 31, 2016.

Research and development expenses were $38.3 million for the year ended December 31, 2016, compared with $62.1 million for the year ended December 31, 2015, a decrease of $23.7 million, or 38.3%. The decrease in research and development expense reflects an $11.5 million decrease in direct research and development expense and a $14.5 million decrease in commercial manufacturing development expense, partially offset by a $2.3 million increase in indirect research and development expense. The decrease in direct research and development expenses resulted primarily from the following:

- Direct research and development expense for rocapuldencel-T decreased from $22.5 million for the year ended December 31, 2015 to $11.0 million in the year ended December 31, 2016 due primarily to the completion of patient enrollment in the ADAPT trial of rocapuldencel-T in July 2015.
- Direct research and development expense for AGS-004 was not significantly different in the year ended December 31, 2015 compared with the year ended December 31, 2016.

The $14.5 million decrease in research and development expense related to our commercial manufacturing development efforts reflects our determination during the fourth quarter of 2015 to significantly reduce our spending and activity related to the automated manufacturing process.

The $2.3 million increase in indirect research and development expense was primarily due to higher personnel costs of $1.1 million. In April 2016, we effected a reduction in force that resulted in termination costs related to severance and the partial acceleration of certain stock options totaling $1.2 million. Additionally, occupancy costs were $0.7 million higher during 2016 primarily due to rent incurred under the lease agreement for the Centerpoint facility and higher depreciation.

We had 118 employees engaged in research and development activities as of December 31, 2015 compared with 99 employees as of December 31, 2016.

The successful development of our clinical and preclinical product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of any of our clinical or preclinical product candidates or the period, if any, in which material net cash inflows from these product candidates may commence. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress, expense and results of our ongoing clinical trials;
- the scope, rate of progress, expense and results of additional clinical trials that we may conduct;
• the scope, rate of progress, expense and results of our commercial manufacturing development efforts;
• other research and development activities; and
• the timing of regulatory approvals.

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

General and Administrative Expenses

General and administrative expenses were $12.2 million for the year ended December 31, 2017, compared with $14.2 million for the year ended December 31, 2016, a decrease of $2.0 million or 14.2%. This decrease was primarily due to decreases of $0.7 million in personnel costs, $1.4 million in consulting costs and $0.3 million in marketing expenses, partially offset by an increase of $0.2 million in occupancy costs and $0.2 million in legal costs.

General and administrative expenses were $14.2 million for the year ended December 31, 2016 compared with $11.0 million for the year ended December 31, 2015, an increase of $3.2 million, or 29.0%. This increase was primarily due to an increase of $1.8 million in personnel costs, including salaries, bonuses, benefits and share-based compensation, and $1.3 million of additional outside services resulting primarily from the use of additional consultants, contracted services and legal fees for patents. Additionally, occupancy expenses increased $0.2 million and registration fees increased $0.1 million. These increases were partially offset by a $0.3 million decrease in software and computer supplies expense as our new enterprise resource planning system was implemented in 2015 and a $0.1 million decrease in marketing expenses.

Impairment Loss on Property and Equipment

We recognized an impairment loss on property and equipment of $27.3 million for the year ended December 31, 2017, compared with $0.7 million and $0 for the years ended December 31, 2016 and 2015, respectively. We review our property and equipment for impairment whenever events or changes indicate its carrying value may not be recoverable.

Impairment of Centerpoint and CTI Facilities and Construction-in-Progress

During March 2017, we determined that we no longer planned to develop our Centerpoint facility. In our statement of operations for the year ended December 31, 2017, we recorded an impairment loss of $18.3 million related to Construction-in-progress on the property. The property was sold during the fourth quarter of 2017.

Additionally, we determined during the three months ended March 31, 2017 that we would no longer need to develop various equipment included in Construction-in-progress under our current manufacturing plans. As such, we entered into agreements and understandings with various vendors to attempt to sell or dispose of this equipment at prices less than our carrying value. Accordingly, we determined that the fair value of this equipment held for sale was $0.6 million as of December 31, 2017 and recorded an impairment loss of $1.2 million during the year ended December 31, 2017. Additionally, during the year ended December 31, 2017 we recorded a $6.1 million impairment loss on other equipment included in Construction-in-progress that had to be abandoned or had no net realizable value at our Centerpoint facility.

We also recorded an impairment loss on Construction-in-progress on the property of $0.9 million at our CTI facility during the first quarter of the year ended December 31, 2017.
Impairment of Capital Leases

In August 2016, we entered into two power generation agreements with an electric utility company. We have accounted for the power generation agreements as capital leases for financial reporting purposes. Under the power generation agreements, the electric utility company agreed to design, procure, install, own and maintain electrical equipment at the Centerpoint facility to provide required electrical loads. Property, plant and equipment included $2.4 million as of December 31, 2016 under the power generation agreements in the Construction-in-progress account. In connection with the decision to no longer develop our Centerpoint facility, we recorded an impairment loss of $0.1 million during the year ended December 31, 2017. The property was sold during the fourth quarter of 2017.

Impairment of Property and Equipment

We recognized an impairment loss on property and equipment of $0.7 million for the year ended December 31, 2016. Prior to 2016, we planned to use a semi-automated manufacturing process for commercial supply. Under our new strategy, if we are able to successfully develop rocapuldec-T, we currently plan to use a fully manual manufacturing process to supply rocapuldec-T for product launch and then transition to a semi-automated manufacturing process following product launch and commercialization. As a result of this change in plans for manufacturing rocapuldec-T, we determined in the fourth quarter of 2016 that we will not require three isolator machines that were under construction and in various stages of completion by a vendor for the semi-automated manufacturing process. In March 2017, we sold the three isolator machines to third parties at prices less than our carrying value. Accordingly, we determined that the fair value of these three isolator machines was $1.5 million as of December 31, 2016 and an impairment loss of $0.7 million was recognized during the year ended December 31, 2016.

Restructuring Costs

We recognized restructuring costs of $6.0 million during the year ended December 31, 2017, compared with $0 during both the years ended December 31, 2016 and 2015. Following the February 2017 recommendation of the IDMC to discontinue the ADAPT trial for futility based on its planned interim data analysis, we implemented a restructuring of our operations and recorded impairments of property and equipment and leases, as discussed above.

Workforce Action Plan

On March 10, 2017, we enacted a workforce action plan designed to streamline operations and reduce our operating expenses. Under this plan, we reduced our workforce by 46 employees (or 38%) from 122 employees to 76 employees in March 2017. Through additional targeted reductions and attrition, the workforce was further reduced to 39 employees as of December 31, 2017. The principal objective of the reduction was to enable us to conserve our financial resources while we conducted a review of the preliminary ADAPT trial data set and discussed the data with the FDA. During the year ended December 31, 2017, we recognized $1.2 million in severance costs and $3.2 million in stock-based compensation expense from the acceleration of stock options and restricted stock for the employees associated with the workforce reduction.

CTI Lease Agreement

In January 2017, we entered into a ten-year lease agreement with two five-year renewal options for 40,000 square feet of manufacturing and office space at CTI on the Centennial Campus of North Carolina State University in Raleigh, North Carolina. We provided a security deposit in the amount of $2.4 million as security for obligations under the lease agreement, which was provided in the form of a letter of credit. We had intended to utilize this facility to prepare for a biologics license application, or BLA, to the U.S. Food & Drug Administration and to support initial commercialization of rocapuldec-T. We had expected to complete the initial build-out and equipping of the facility, including capacity qualification necessary for BLA filing, by the end of the first quarter of 2018. As a result of the IDMC recommendation in February 2017 to discontinue the ADAPT trial, we initiated discussions with the landlord of the CTI facility regarding the termination of this lease.
In March 2017 the landlord of our CTI facility notified us that it was terminating the lease due to nonpayment of invoices for up-fit costs, effective immediately. We never occupied the leased space. In the termination notice, the landlord asserted that we were in default under the lease due to nonpayment of invoices for up-fit costs. We did not dispute the occurrence of the event of default or the termination of the lease and did not seek to cure the default. In the termination notice, the landlord stated that we were liable for any and all costs incurred by the landlord in re-letting the premises, any deficiency between our scheduled rent for the remainder of the term of the lease and the rent charged to the new tenant, the unamortized portion of the funded up-fit costs, rent abatement, interest at the rate of 12% per annum on the sums noted and all attorneys’ fees incurred by the landlord in enforcing the lease. We had instructed the landlord to begin the process of re-letting the premises in order to mitigate damages. On March 31, 2017, we entered into the lease termination agreement with the landlord terminating the lease as of March 17, 2017. From the $2.4 million letter of credit, the landlord drew down $0.7 million to cover unpaid construction costs in March 2017 and $1.7 million in April 2017 for lease termination damages and agreed to return $0.1 million in consideration for being able to salvage some of the construction costs. Pursuant to the lease termination agreement, we have no further obligations under the lease. During the year ended December 31, 2017, we recorded a lease termination fee of $1.6 million, which is included in restructuring costs on the statement of operations. We also recorded an impairment loss on Construction-in-progress on the property of $0.9 million during the year ended December 31, 2017.

We believe that our current Technology Drive and Patriot Center facilities are sufficient for the manufacture of rocapuldencel-T and AGS-004 to support our ongoing clinical trials and any potential clinical trials that may be initiated in the near-term.

**Gain on Disposal of Impaired Property**

We recognized a gain on the disposal of impaired property of $2.8 million during the year ended December 31, 2017 compared with $0 during both the years ended December 31, 2016 and 2015. This gain resulted from the $1.8 million of proceeds that we received in connection with the sale of the Centerpoint facility and the $1.0 million gain from the disposal of certain property from the Saint-Gobain debt restructuring, both of which occurred during the fourth quarter of 2017 (see sections entitled Impairment of Centerpoint Facility and Construction-in-Progress above and Gain on Early Extinguishment of Debt below for further details).

**Interest Expense**

Interest expense was $1.3 million for the year ended December 31, 2017 compared with $1.8 million for the year ended December 31, 2016, a decrease of $0.5 million or 26.3%. The decrease resulted from our repayment of the Loan Agreement on March 6, 2017, which was partially offset by the interest expense we incurred following our decision to no longer capitalize the interest related to construction of our Centerpoint facility as we decided not to proceed with our plans to develop this facility.

Interest expense was $1.8 million for the year ended December 31, 2016, compared with $2.3 million for the year ended December 31, 2015, a decrease of $0.5 million or 21.6%. The decrease primarily resulted from the capitalization of interest payments on our debt related to Construction-in-progress during 2016.

Total interest cost during the year ended December 31, 2016 was $3.8 million, which included $2.0 million of capitalized interest related to Construction-in-progress. Total interest cost during the year ended December 31, 2015 was $3.1 million, which included $0.9 million of capitalized interest related to Construction-in-progress. Interest capitalized to Construction-in-progress is not included in interest expense. We did not capitalize interest related to Construction-in-progress during the year ended December 31, 2017.

**Gain on Early Extinguishment of Debt**

We recognized a gain on early extinguishment of debt of $2.4 million during the year ended December 31, 2017 compared with $0 for both the years ended December 31, 2016 and 2015. This gain resulted from three separate transactions during 2017.
On March 3, 2017, we entered into a payoff letter with the Lenders, pursuant to which we paid on March 6, 2017 a total of $23.1 million to the Lenders, representing the principal balance and accrued interest outstanding under the Loan Agreement in repayment of our outstanding obligations under the Loan Agreement. In addition, we issued to the Lenders five year warrants to purchase an aggregate of 5,000 shares of our common stock at an exercise price of $26.00 per share in consideration of the Lenders accepting the $23.1 million. We recognized a gain on this early extinguishment of debt of $0.2 million during the year ended December 31, 2017.

As of June 30, 2017, we had recorded a manufacturing research and development obligation payable to our vendor Invotech on our consolidated balance sheet at $8.3 million, representing $5.2 million in deferred fees, $2.3 million in estimated bonus payments and $0.7 million in accrued interest. On September 22, 2017, we entered into the Satisfaction and Release Agreement with Invotech. Under the Satisfaction and Release Agreement, we agreed to make, issue and deliver to Invotech (i) a cash payment of $0.5 million, (ii) 57,142 shares of our common stock and (iii) an unsecured convertible promissory note in the original principal amount of $5.2 million on account of and in full satisfaction and release of all of our payment obligations to Invotech arising under the Invotech Development Agreement prior to the date of the Satisfaction and Release Agreement including our obligation to pay Invotech up to a total of $8.3 million in deferred fees, bonus payments and accrued interest. As a result, we recognized a gain on the early extinguishment of debt of $1.5 million during the year ended December 31, 2017.

As of September 30, 2017, we had recorded accrued expenses of $4.8 million payable to our vendor Saint-Gobain. On November 22, 2017, we entered into the Saint-Gobain Satisfaction and Release Agreement with Saint-Gobain. Under the Saint-Gobain Satisfaction and Release Agreement, we agreed to make, issue and deliver to Saint-Gobain (i) a cash payment of $0.5 million, (ii) 34,499 shares of common stock, (iii) an unsecured convertible promissory note in the original principal amount of $2.4 million, and (iv) certain specified equipment originally provided to us by Saint-Gobain under the Saint-Gobain Development Agreement, on account of and in full satisfaction and release of all of our payment obligations to Saint-Gobain arising under the Saint-Gobain Development Agreement, prior to the date of the Saint-Gobain Satisfaction and Release Agreement, including the development fees and charges. As a result, we recognized a gain on the early extinguishment of debt of $0.6 million during the year ended December 31, 2017.

**Change in Fair Value of Warrant Liability**

The gain from the change in fair value of the warrant liability was $20.8 million and $1.0 million during the years ended December 31, 2017 and 2016, respectively. There were no warrants classified as a liability to purchase common stock outstanding during the year ended December 31, 2015.

The 2017 and 2016 gain amounts represent the change in the fair value of our liability for the warrants issued in August 2016, which contained provisions that could require cash settlement and were therefore recorded as a liability at fair value on the date of issuance and as of the end of each reporting period. The gain of $20.8 million from the warrant liability during the year ended December 31, 2017 was due to a significant decline in the price of our common stock and a shorter expected life of the August 2016 warrants. As of December 31, 2017, the fair value of the August 2016 warrants was $0.2 million.

The gain from the change in fair value of the warrant liability was $1.0 million for the year ended December 31, 2016, compared with $0 for the year ended December 31, 2015. This gain represented the decrease in the fair value of our warrant liability during the year ended December 31, 2016 for the August 2016 warrants. The fair value of the August 2016 warrants declined by $1.0 million from an initial valuation of $21.9 million to $20.9 million during the year ended December 31, 2016 primarily due to a slight decline in the price of our common stock and a shorter expected life of the August 2016 warrants.

**Liquidity and Capital Resources**

**Sources of Liquidity**

As of December 31, 2017, we had cash and cash equivalents of $15.2 million and working capital of $7.6 million.
Since our inception in May 1997 through December 31, 2017, we have funded our operations principally with $353.2 million from the sale of common stock, convertible debt, warrants and preferred stock, $32.9 million from the licensing of our technology, $107.3 million from government contracts, grants and license and collaboration agreements, and $25.0 million from the Loan Agreement.

**Troubled Debt Restructuring with Invetech.** As of June 30, 2017, we had recorded a manufacturing research and development obligation payable to Invetech on our consolidated balance sheet of $8.3 million, representing $5.2 million in deferred fees, $2.3 million in estimated bonus payments and $0.7 million in accrued interest. On September 22, 2017, we entered into the Invetech Satisfaction and Release Agreement. Under the Invetech Satisfaction and Release Agreement, we agreed to make, issue and deliver to Invetech (i) a cash payment of $0.5 million, (ii) 57,142 shares of our common stock and (iii) an unsecured convertible promissory note in the original principal amount of $5.2 million on account of and in full satisfaction and release of all of our payment obligations to Invetech arising under the Invetech Development Agreement prior to the date of the Invetech Satisfaction and Release Agreement, including our obligation to pay Invetech up to a total of $8.3 million in deferred fees, bonus payments and accrued interest.

The maturity date for the payment of principal and interest under the note is September 30, 2020. The note bears interest at a rate of 6.0% per annum, which interest will compound annually. For the quarterly period ended December 31, 2017, we paid Invetech $200,000 in cash under the note. We also are required to make a quarterly installment payment under the note for the fiscal quarter ending March 31, 2018 in an aggregate amount of up to $0.4 million, consisting of (i) cash in the amount of $0.2 million and (ii) if certain specified conditions are met as of the corresponding payment date, up to $0.2 million of shares of our stock. For the fiscal quarters ending June 30, 2018 through March 31, 2019, we are required to make quarterly installment payments under the note, each in an aggregate amount of up to $0.3 million, consisting of (i) cash in the amount of $150,000 and (ii) if certain specified conditions are met as of the corresponding payment date, up to $150,000 of shares of our common stock. For the fiscal quarters ending June 30, 2019 through June 30, 2020, we are required to make quarterly installment payments under the note, each in an amount of $150,000, payable in cash. Subject to Invetech’s conversion rights, we may prepay the note in full or in part at any time without penalty or premium.

The note also provides that on the anniversary of the issue date of the note for each of the first three years following the issue date, the outstanding principal amount of the note, if any, plus accrued and unpaid interest thereon shall automatically be deemed to be reduced by $250,000, if and only if we have paid all debt service payments due under the note on or prior to the relevant anniversary date and no event of default, fundamental transaction or change of control, each as defined in the note, has occurred on or prior to such anniversary date.

Upon maturity of the note or at any time within 75 days of such maturity, or upon the occurrence of certain events of default, Invetech may, at its option, elect to convert any amount of the outstanding principal and accrued interest into shares of our common stock. Upon a change of control pursuant to which Invetech has a redemption right, Invetech may, at its option, elect to convert any amount of the outstanding principal and accrued interest, less any remaining installment payments required to be made in cash, into shares of our common stock. In each case, the number of shares of common stock issuable upon such complete or partial conversion of the note is determined by dividing the portion of the principal and accrued or unpaid interest to be converted by $10.00 per share (as adjusted for any stock dividend, stock split, stock combination, reclassification or similar transaction). We will be required to pay any amount not so converted in cash.

**Troubled Debt Restructuring with Saint-Gobain.** As of September 30, 2017, we had recorded accrued expenses of $4.8 million payable to Saint-Gobain. On November 22, 2017, we entered into the Saint-Gobain Satisfaction and Release Agreement. Under the Saint Gobain Satisfaction and Release Agreement, we agreed to make, issue and deliver to Saint-Gobain (i) a cash payment of $0.5 million, (ii) 34,499 shares of common stock, (iii) an unsecured convertible promissory note in the original principal amount of $2.4 million, and (iv) certain specified equipment originally provided to us by Saint-Gobain under the Saint-Gobain Development Agreement, on account of and in full satisfaction and release of all of our payment obligations to Saint-Gobain arising under the Saint-Gobain Development Agreement, prior to the date of the Saint-Gobain Satisfaction and Release Agreement, including the development fees and charges. As a result, we recognized a gain on the early extinguishment of debt of $0.6 million during the year ended December 31, 2017.
The maturity date for the payment of principal and interest under the note is September 30, 2020. The note bears interest at a rate of 6.0% per annum, which interest will compound quarterly. For the quarterly period ended December 31, 2017, we paid Saint-Gobain $270,000 in cash under the note. We are required to make a quarterly installment payment under the note for the fiscal quarter ending March 31, 2018, in an aggregate amount of up to $340,000, consisting of (i) cash in the amount of $200,000 and (ii) if certain specified conditions are met as of the corresponding payment date, up to $140,000 of shares of our common stock. For the fiscal quarters ending June 30, 2018 and September 30, 2018, we are required to make quarterly installment payments under the note, each in an aggregate amount of up to $245,000, consisting of (i) cash in the amount of $125,000 and (ii) if certain specified conditions are met as of the corresponding payment date, up to $120,000 of shares of our common stock. For the fiscal quarters ending December 31, 2018 and March 31, 2019, we are required to make quarterly installment payments under the note, each in an aggregate amount of up to $220,000, consisting of (i) cash in the amount of $100,000 and (ii) if certain specified conditions are met as of the corresponding payment date, up to $120,000 of shares of our common stock. For the fiscal quarter ending December 31, 2017, March 31, 2018, June 30, 2018, September 30, 2018, December 31, 2018 and March 31, 2019, if the conditions required for the issuance of common stock are not met solely because the stock price of the common stock at the time is less than $4.058 per share (as adjusted for any stock dividend, stock split, stock combination, reclassification or similar transaction), then we will be required to pay in each such quarter cash equal to 50% of the value of the common stock that would otherwise have been issued. For the fiscal quarters ending June 30, 2019 through June 30, 2020, we are required to make quarterly installment payments under the note, each in an amount of $100,000, payable in cash. For the year ended December 31, 2017, we made an installment payment of $270,000 under the note.

Upon maturity of the note or at any time during the 75-day period prior to the maturity date of the note, Saint-Gobain may, at its option, elect to convert any amount of the outstanding principal and accrued interest into shares of our common stock. We will be required to pay any amount not so converted in cash. Upon a change of control pursuant to which Saint-Gobain has a redemption right, Saint-Gobain may, at its option, elect to convert any amount of the outstanding principal and accrued interest, less any remaining installment payments required to be made in cash, into shares of our common stock. We will be required to pay any amount not so converted in cash. Upon the occurrence of certain events of default, Saint-Gobain may, at its option, elect to convert any amount of the outstanding principal and accrued interest into shares of our common stock. We will be required to pay any amount not so converted in cash. Upon the occurrence of certain events of default, Saint-Gobain may, at its option, elect to convert any amount of the outstanding principal and accrued interest into shares of our common stock. Unless Saint-Gobain has elected to exercise these conversion rights, we, subject to specified exceptions, may prepay the note in whole or in part, in cash, at any time without penalty or premium.

**Venture Loan and Security Agreement**. In September 2014, we entered into the Loan Agreement with the Lenders, under which we borrowed $25.0 million in two tranches of $12.5 million each.

The per annum interest rate for each tranche was a floating rate equal to 9.25% plus the amount by which the one-month LIBOR exceeds 0.50% (effectively a floating rate equal to 8.75% plus the one-month LIBOR Rate). The total per annum interest rate could not exceed 10.75%.

On March 3, 2017, we entered into a payoff letter with the Lenders, pursuant to which we paid, on March 6, 2017, a total of $23.1 million to the Lenders, representing the principal balance and accrued interest outstanding under the Loan Agreement in repayment of our outstanding obligations under the Loan Agreement. In addition, we issued to the Lenders five year warrants to purchase an aggregate of 5,000 shares of common stock at an exercise price of $26.00 per share in consideration of the Lenders acceptance of $23.1 million as payment in full. Upon the payment of the $23.1 million and the issuance of the warrants pursuant to the payoff letter, all of our outstanding indebtedness and obligations to the Lenders under the Loan Agreement were deemed paid in full, and the Loan Agreement and the notes thereunder were terminated.

**At-the-Market Offering**. On May 8, 2015, we filed a shelf registration statement on Form S-3, or the 2015 Shelf, with the SEC, which covers the offering, issuance and sale of up to $125.0 million of our common stock, preferred stock, debt securities, depositary shares, purchase contracts, purchase units and warrants. We simultaneously entered into a sales agreement, or the Original Sales Agreement, with Cowen and Company LLC, or Cowen, to provide for the offering, issuance and sale of up to $30.0 million of our common stock from time to time in “at-the-market” offerings under the 2015 Shelf. The 2015 Shelf was declared effective by the SEC on May 14, 2015.
On January 9, 2017, we filed a shelf registration statement on Form S-3, or the 2017 Shelf, with the SEC, which covers the offering, issuance and sale of up to $200.0 million of our common stock, preferred stock, debt securities, depositary shares, purchase contracts, purchase units and warrants and which became effective on January 24, 2017. On February 2, 2018, we amended and restated the Original Sales Agreement with Cowen, or the Amended and Restated Sales Agreement, in order to increase the maximum aggregate offering price of our shares of common stock that may be offered from time to time in “at-the-market offerings” by $15.0 million from $30.0 million to $45.0 million. On February 2, 2018, we filed a prospectus supplement with the SEC in connection with the issuance and sale of the additional shares available under the 2017 Shelf. We refer to the Original Sales Agreement and the Amended and Restated Sales Agreement collectively as the Sales Agreement.

Under the Sales Agreement, we pay Cowen a commission of up to 3% of the gross proceeds. During the year ended December 31, 2016, we sold 43,634 shares of common stock pursuant to the Original Sales Agreement, resulting in proceeds of $5.5 million, net of commissions and issuance costs. During the year ended December 31, 2017, we sold 3,373,967 shares of common stock pursuant to the Sales Agreement, resulting in proceeds of $15.5 million, net of commissions and issuance costs. As of March 16, 2018, we had raised an additional $7.3 million of proceeds through the sale of our common stock subsequent to December 31, 2017 under the Sales Agreement and $15.8 million remained available for sale under the Sales Agreement.

**Follow-On Public Offering.** On August 2, 2016, we issued and sold 454,545 shares of common stock and warrants to purchase an aggregate of 340,909 shares of common stock, in an underwritten public offering at a price to the public of $110.00 per share and accompanying warrant. The shares of common stock and warrants were sold in combination, with one warrant to purchase up to 0.75 of a share of common stock accompanying each share of common stock sold. The warrants have an exercise price of $110.00 per share, became immediately exercisable upon issuance and will expire on August 2, 2021. The aggregate net proceeds to us of the offering were approximately $48.2 million after deducting underwriting discounts and commissions and offering expenses.

**Convertible Note Issued to Pharmstandard.** On June 15, 2017, we entered into a convertible note purchase agreement with Pharmstandard, pursuant to which we agreed to issue and sell to Pharmstandard a convertible secured promissory note in the original principal amount of $6.0 million in a private placement. We issued the note to Pharmstandard on June 21, 2017, the closing date of the financing. Under the note, the maturity date for the payment of principal and interest is the fifth anniversary of the issue date. The note bears interest at a rate of 9.5% per annum, which interest compounds annually. The note is secured by a lien on and security interest in all of our intellectual property. We may prepay the note in whole or in part at any time without penalty or premium. Upon the occurrence of certain events of default, Pharmstandard will have the option to require us to repay the unpaid principal amount of the note and any unpaid accrued interest.

In addition, at Pharmstandard’s election, Pharmstandard may convert the entire principal and interest of the note into shares of our common stock at a price per share equal to $10.00. However, Pharmstandard will not be permitted to convert the entire note if such conversion would result in Pharmstandard and its affiliates holding shares that exceed 39.9% of the total number of outstanding shares of our common stock or 39.9% of the combined voting power of all of our outstanding securities. To the extent that conversion of the entire note would cause Pharmstandard and its affiliates to exceed these thresholds, Pharmstandard may convert a portion of the note to the extent these thresholds are not exceeded by such partial conversion.

Pharmstandard is our largest stockholder, and beneficially owned, in the aggregate, shares representing approximately 18.83% of our outstanding common stock as of February 28, 2018. In addition, two members of our board of directors are closely associated with Pharmstandard.

We paid $23,000 in legal expenses of Pharmstandard, including legal expenses incurred in connection with our resale registration obligations set forth in a registration rights agreement that we entered into with Pharmstandard. We have granted Pharmstandard, and Pharmstandard has granted us, indemnification rights with respect to each parties’ respective representations, warranties, covenants and agreements under the note purchase agreement.
Cash Flows

The following table sets forth the major sources and uses of cash for the periods set forth below:

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>(in thousands)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net cash (used in) provided by:</td>
<td>$ (61,021)</td>
<td>$ (40,677)</td>
<td>$ (35,425)</td>
</tr>
<tr>
<td>Operating activities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Investing activities</td>
<td>8,923</td>
<td>(14,327)</td>
<td>316</td>
</tr>
<tr>
<td>Financing activities</td>
<td>21,062</td>
<td>101,810</td>
<td>(2,684)</td>
</tr>
<tr>
<td>Effect of exchange rate changes on cash</td>
<td>(24)</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Net increase (decrease) in cash and cash equivalents</td>
<td>$ (31,060)</td>
<td>$ 46,810</td>
<td>$ (37,785)</td>
</tr>
</tbody>
</table>

Operating Activities. Net cash used in operating activities of $61.0 million during the year ended December 31, 2015 was primarily a result of our $74.8 million net loss, partially offset by non-cash items of $7.2 million and changes in operating assets and liabilities of $6.6 million. These non-cash items primarily consisted of depreciation and amortization expense of $0.7 million, share-based compensation expense of $4.0 million, payment of $2.1 million for research and development services through the issuance of shares of common stock and amortization of debt issuance costs and debt discounts of $0.3 million. In addition, accrued expenses increased by $0.8 million, prepaid expenses and other receivables decreased by $0.2 million, long-term deferred liabilities increased by $1.5 million and the long-term portion of our manufacturing research and development obligation increased by $4.3 million, which were partially offset by a decrease in accounts payable of $0.1 million.

Net cash used in operating activities of $40.7 million during the year ended December 31, 2016 was primarily a result of our $53.0 million net loss, partially offset by non-cash items of $6.2 million and changes in operating assets and liabilities of $6.1 million. The non-cash items primarily reflect depreciation and amortization expense of $1.0 million, share-based compensation expense of $5.1 million, common stock issued as payment for services of $0.3 million, an impairment loss on property and equipment of $0.7 million and amortization of debt discount of $0.1 million, partially offset by the non-cash gain on the fair value of the warrant liability of $1.0 million. Accrued expenses increased by $4.9 million, accounts payable increased by $1.2 million and the manufacturing research and development obligation increased by $0.4 million, which increases were partially offset by an increase in prepaid expenses and other receivables of $0.3 million and a decrease in deferred liabilities of $0.1 million.

Net cash used in operating activities of $35.4 million during the year ended December 31, 2017 was primarily a result of our $40.6 million net loss and an increase in net operating assets of $6.7 million, partially offset by non-cash items of $11.9 million. The increase in net operating assets reflects a decrease in accrued expenses of $3.6 million, a decrease in accounts payable of $2.2 million, a decrease in manufacturing research and development obligation of $0.4 million, an increase in prepaid expenses and other receivables of $0.4 million and a decrease in deferred liabilities of $0.1 million. The non-cash items primarily reflect an impairment loss on property and equipment of $27.3 million, compensation expense related to stock options of $8.9 million, depreciation and amortization expense of $1.0 million and interest accrued on long term debt of $0.7 million, partially offset by a decrease in the fair value of the warrant liability of $20.7 million, a gain on the early extinguishment of debt of $2.4 million and a gain on the disposal of assets held for sale of $2.8 million.

Investing Activities. Net cash provided by (used in) investing activities was $8.9 million, ($14.3) million and $0.3 million for the years ended December 31, 2015, 2016 and 2017, respectively. Cash provided by and used in investing activities during each of these periods primarily reflected our purchases of property and equipment and purchases and maturities of short-term investments.

Cash provided by investing activities during the year ended December 31, 2015 included $20.7 million in proceeds from maturities of short-term investments and the receipt of $0.6 million from a restricted cash account securing a letter of credit, partially offset by purchases of property and equipment of $9.7 million and purchases of short-term investments of $2.7 million. Cash used in investment activities during the year ended December 31, 2016 consisted of $15.3 million of purchases of property and equipment, partially offset by proceeds of $1.0 million from maturities of short-term investments. Cash provided by investing activities during the year ended December 31, 2017 consisted of $3.7 million of purchases of property and equipment, offset by proceeds of $3.3 million from the sale of property and equipment and the receipt of $0.7 million from a restricted cash account securing a letter of credit.
Financing Activities. Net cash provided by financing activities was $21.1 million and $101.8 million for the years ended December 31, 2015 and 2016, respectively. Net cash used in financing activities was $2.7 million for the year ended December 31, 2017.

Cash provided by financing activities for the year ended December 31, 2015 consisted of $12.5 million of loan proceeds from our Loan Agreement, $8.6 million of proceeds from the sale of common stock and $0.4 million of proceeds from the exercise of stock options and from our employee stock purchase plan, partially offset by $35,480 of payments on notes payable. Cash provided by financing activities for the year ended December 31, 2016 consisted primarily of proceeds of $105.2 million from the issuance and sale of common stock and warrants under a private placement financing and a follow-on public offering and from the issuance and sale of common stock pursuant to the Sales Agreement. Additionally, cash provided by financing activities during the year ended December 31, 2016 also included $0.3 million of proceeds from the exercise of common stock warrants and $0.4 million of proceeds from the exercise of stock options and from our employee stock purchase plan, partially offset by $2.4 million from the payment of stock issuance costs, $1.6 million in payments on notes payable and $0.2 million in payments on our facility lease obligation and capital lease obligations. Cash used in financing activities for the year ended December 31, 2017 consisted of $23.6 million for repayment of the Loan Agreement and $0.5 million of payments on convertible notes payable, partially offset by $6.0 million of proceeds from the issuance of the convertible note issued to Pharmstandard and $15.5 million of proceeds from the issuance of common stock through our at-the-market offering.

Other Significant Changes in the Consolidated Balance Sheet as of December 31, 2017 Compared with December 31, 2016

Property and equipment, net, decreased by $37.4 million from $41.0 million to $3.6 million from December 31, 2016 to December 31, 2017 primarily due to impairment charges of $27.3 million and the reclassification of $10.3 million of property to current Assets held for sale, of which $0.6 million remained as of December 31, 2017.

Notes payable decreased by $25.1 million from $30.1 million to $5.0 million from December 31, 2016 to December 31, 2017, primarily due to the early pay-off of our Loan Agreement in March 2017.

Convertible notes payable increased to $14.5 million from $0 from December 31, 2016 to December 31, 2017, primarily due to the issuance of a $6.0 million convertible note plus accrued interest to Pharmstandard in June 2017, the issuance of a $5.2 million convertible note plus accrued interest to Invetech in August 2017 pursuant to a troubled debt restructuring transaction and the issuance of a $2.4 million convertible note plus accrued interest to Saint-Gobain in November 2017 pursuant to a troubled debt restructuring transaction.

Manufacturing research and development obligation decreased to $0 from $8.2 million from December 31, 2016 to December 31, 2017 as a result of the Invetech troubled debt restructuring transaction.

The fair value of our warrant liability decreased by $20.7 million from December 31, 2016 to December 31, 2017 from $20.9 million to $0.2 million primarily as a result of the decline in the market price of our common stock relative to the exercise price of the warrants.

Funding Requirements

To date, we have not generated any product revenue from our development stage product candidates. We do not know when, or if, we will generate any product revenue. We do not expect to generate significant product revenue unless or until we obtain marketing approval of, and commercialize, rocapuldencel-T or AGS-004. Despite our cost containment measures, including the March 2017 workforce reduction, we expect that our ongoing expenses will be substantial and may increase in connection with our ongoing activities, particularly as we continue our ADAPT trial of rocapuldencel-T, if we initiate additional clinical trials of rocapuldencel-T and AGS-004, and, provided that we continue the development of our programs, seek regulatory approval for our product candidates and to establish a commercial manufacturing facility or otherwise arrange for commercial manufacturing. In addition, if we obtain regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. We will need substantial additional funding in connection with our continuing operations.
As of December 31, 2017, we had cash and cash equivalents of $15.2 million and working capital of $7.6 million. We do not currently have sufficient cash resources to pay all of our accrued obligations in full or to continue our business operations beyond the end of 2018. This raises substantial doubt about our ability to continue as a going concern. Therefore, we will need to raise additional capital prior to such time in order to continue to operate our business beyond that time. Alternatively, we may seek to engage in one or more potential transactions, such as the sale of our company, a strategic partnership with one or more parties or the licensing, sale or divestiture of some of our assets or proprietary technologies, but there can be no assurance that we will be able to enter into such a transaction or transactions on a timely basis or on terms that are favorable to us, or at all. Under these circumstances, we may instead determine to dissolve and liquidate our assets or seek protection under the bankruptcy laws. If we decide to dissolve and liquidate our assets or to seek protection under the bankruptcy laws, it is unclear to what extent we will be able to pay our obligations, and, accordingly, it is further unclear whether and to what extent any resources will be available for distributions to stockholders.

We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development of our product candidates.

Our future capital requirements will depend on many factors, including:

• our decision to continue development of rocapuldencel-T and our pivotal Phase 3 ADAPT clinical trial;
• the progress and results of any investigator initiated clinical trials of rocapuldencel-T that we may support;
• the progress and results of the ongoing investigator-initiated clinical trial of AGS-004 in combination with vorinostat for HIV eradication and the planned investigator-initiated clinical trial of AGS-004 that we support and our ability to obtain additional funding under our NIH and NIAID contract for our AGS-004 program;
• the development, initiation and support of additional clinical trials of rocapuldencel-T in mRCC or other indications and AGS-004 in HIV;
• the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates or for the PD1 monoclonal antibodies which we have an option to in-license, should we decide to exercise our option;
• the costs and timing of establishing a commercial manufacturing facility or of alternative arrangements for commercial manufacturing and any costs and liabilities associated with financing arrangements entered into to fund the costs of these activities;
• the costs, timing and outcome of regulatory submissions and review of our product candidates;
• the costs of commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive regulatory approval;
• the potential need to repay the $4.0 million in principal remaining outstanding under the loan under our license agreement with Medinet;
• payments due under our agreement with Medpace for the conduct of the ADAPT clinical trial;
• revenue, if any, received from commercial sales of our product candidates, should any of our product candidates be approved by the FDA or a similar regulatory authority outside the United States;
• the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;

• the extent to which we acquire or invest in other businesses, products and technologies;

• our ability to obtain government or other third party funding for the development of our product candidates; and

• our ability to establish collaborations on favorable terms, if at all, particularly arrangements to develop, market and distribute rocapuldencel-T outside North America and arrangements for the development and commercialization of our non-oncology product candidates, including AGS-004.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, government contracts, government and other third party grants or other third party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, stockholder ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect stockholder rights. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

In 2017, we received several deficiency letters from the Listing Qualifications Department of The Nasdaq Stock Market notifying us that we were not in compliance with various requirements for continued listing on The Nasdaq Global Market, including the $50 million minimum market value of listed securities requirement, the $1.00 minimum bid price, the $15 million minimum market value of publicly held shares requirement. In October 2017, we received two letters from The Nasdaq Global Market with respect to these deficiencies providing that, unless we requested a hearing before a Nasdaq Hearing Panel, our common stock would be delisted. In January 2018, we had a hearing before the Nasdaq Qualifications Listing Panel, or the Panel, at which we requested continued listing pending our return to compliance with such requirements. On January 17, 2018, we received a determination from Nasdaq indicating that our listing would be transferred from The Nasdaq Global Market to The Nasdaq Capital Market, provided that we demonstrated, on or before February 2, 2018, a closing bid price of $1.00 or more for a minimum of ten prior consecutive trading days, that, on or before April 24, 2018, we satisfied the $2.5 million stockholders’ equity requirement and demonstrated our ability to maintain compliance with the minimum stockholders’ equity requirement through the end of fiscal 2018, among other actions, and that we continued to meet the requirements for continued listing on The Nasdaq Capital Market. On February 15, 2018 we received formal notice from Nasdaq that we have evidenced full compliance with the minimum $1.00 bid price requirement for continued listing on The Nasdaq Capital Market. We are not currently in compliance with the stockholders’ equity requirement. If we are unable to regain compliance to the satisfaction of the Panel and our common stock is delisted from trading, our ability to raise capital to continue to fund our operations by selling shares and our ability to acquire other companies or technologies by using our shares as consideration will be impaired.

If we raise additional funds through government or other third party funding, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. We are seeking government or other third party funding for the continued development of AGS-004. In January 2014, CARE agreed that it would fund all patient clinical costs of Stage 1 of our adult eradication clinical trial of AGS-004, except for the associated manufacturing costs for which we were responsible. NIAID’s Division of AIDS has approved $6.6 million in funding for Stage 2 of this Phase 2 clinical trial to be provided directly to the University of North Carolina. If we are unable to raise additional government or other third party funding when needed, we may be required to delay, limit, reduce or terminate our development of AGS-004 or to grant rights to develop and market AGS-004 that we would otherwise prefer to keep for ourselves.

Critical Accounting Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States, or U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. We evaluate these estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Our actual results may differ from these estimates under different assumptions or conditions.
While our significant accounting policies are more fully described in Note 1 to our consolidated financial statements appearing in “Item 8. Financial Statements and Supplementary Data,” we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Revenue Recognition

We recognize revenue in accordance with the Financial Accounting Standards Board, or FASB, Accounting Standards Codification 605, Revenue Recognition, or ASC 605. We recognize revenue when the following criteria are met: persuasive evidence of an arrangement exists, services have been rendered, the price is fixed or determinable, and collectability is reasonably assured.

We have previously entered into license agreements with collaborators. The terms of these agreements have included nonrefundable signing and licensing fees, as well as milestone payments and royalties on any future product sales developed by the collaborators under these licenses. We assess these multiple elements in accordance with ASC 605, in order to determine whether particular components of the arrangement represent separate units of accounting.

These collaboration agreements are accounted for in accordance with Accounting Standards Update, or ASU, No. 2009-13, Topic 605—Multiple-Deliverable Revenue Arrangements, or ASU 2009-13. This guidance requires the application of the “relative selling price” method when allocating revenue in a multiple deliverable arrangement. The selling price for each deliverable shall be determined using vendor specific objective evidence of selling price, if it exists; otherwise, third-party evidence of selling price shall be used. If neither exists for a deliverable, the vendor shall use its best estimate of the selling price for that deliverable.

We recognize upfront license payments as revenue upon delivery of the license only if the license has standalone value and the fair value of the undelivered performance obligations can be determined. If the fair value of the undelivered performance obligations cannot be determined, such obligations are accounted for separately as the obligations are fulfilled. If the license is considered to either not have stand-alone value or have stand-alone value but the fair value of any of the undelivered performance obligations cannot be determined, the arrangement is accounted for as a single unit of accounting and the license payments and payments for performance obligations are recognized as revenue over the estimated period of when the performance obligations are performed.

Whenever we determine that an arrangement should be accounted for as a single unit of accounting, we must determine the period over which the performance obligations will be performed and revenue will be recognized. If we cannot reasonably estimate the timing and the level of effort to complete our performance obligations under the arrangement, then we recognize revenue under the arrangement on a straight-line basis over the period that we expect to complete our performance obligations.

Our license agreements with Pharmstandard, Green Cross, Medinet and Lummy HK provide for, and any future license agreements we may enter into may provide for, milestone payments. Revenues from milestones, if they are non-refundable and considered substantive, are recognized upon successful accomplishment of the milestones. If not considered substantive, milestones are initially deferred and recognized over the remaining performance obligation. If no performance obligation exists, milestones are recognized when earned. Pharmstandard is considered a related party based on Pharmstandard’s ownership of our stock.

Our current license agreements with Pharmstandard, Green Cross, Medinet and Lummy HK provide for, and any future license agreements we may enter into may provide for, royalty payments. To date, we have not received any royalty payments and accordingly have not recognized any related revenue. We will recognize royalty revenue upon the sale of the related products, provided we have no remaining performance obligations under the arrangements.
We record deferred revenue when payments are received in advance of the culmination of the earnings process. This revenue is recognized in future periods when the applicable revenue recognition criteria have been met.

In September 2006, we entered into a multi-year research contract with the NIH and NIAID to design, develop and clinically test an autologous HIV immunotherapy capable of eliciting therapeutic immune responses. We are using funds from this contract to develop AGS-004. Under this contract, as amended, the NIH and NIAID have committed to fund up to a total of $39.8 million, including reimbursement of direct expenses and allocated overhead and general and administrative expenses of up to $38.4 million and payment of other specified amounts totaling up to $1.4 million upon our achievement of specified development milestones. Since September 2010, we have received reimbursement of our allocated overhead and general and administrative expenses at provisional indirect cost rates equal to negotiated provisional indirect cost rates agreed to with the NIH and NIAID in September 2010. These provisional indirect cost rates are subject to adjustment based on our actual costs pursuant to the agreement with the NIH and NIAID. This commitment originally extended until May 2013. We agreed to an additional modification of our contract with the NIH and NIAID under which the NIH and NIAID agreed to increase their funding commitment to us by an additional $5.4 million in connection with the extension of the contract from May 2013 to September 2015. Additionally, a contract modification for a $0.5 million increase was agreed to by the NIH on September 18, 2014 to cover a portion of the manufacturing costs of the planned Phase 2 clinical trial of AGS-004 for long-term viral control in pediatric patients. On June 29, 2016, a contract modification was agreed to that extended the NIH and NIAID’s commitment under the contract to July 31, 2018. We have agreed to a statement of work under the contract, and are obligated to furnish all the services, qualified personnel, material, equipment, and facilities, not otherwise provided by the U.S. government, needed to perform the statement of work.

We recognize revenue from reimbursements earned in connection with the NIH and NIAID contract as reimbursable costs are incurred. We recognize revenues from the achievement of milestones under the NIH and NIAID contract upon the accomplishment of any such milestone.

For the years ended December 31, 2015, 2016 and 2017, we recorded revenue under the NIH and NIAID agreement of $448,273, $807,968 and $177,926, respectively. We have recorded total revenue of $38.3 million through December 31, 2017 under the NIH and NIAID agreement. As of December 31, 2017, there was up to $1.5 million of potential revenue remaining to be earned under the agreement with the NIH and NIAID. As of December 31, 2016 and 2017, we recorded a receivable from the NIH and NIAID of $136,140 and $31,977, respectively. The concentration of credit risk is equal to the outstanding accounts receivable and such risk is subject to the credit worthiness of the NIH and NIAID. There have been no credit losses under this arrangement. Any of the funding sources may request reimbursement for expenses or return of funds, or both, as a result of noncompliance by us with the terms of the grants. No reimbursement of expenses or return of funds for noncompliance has been requested or made since inception of the contract and grants.
On August 2, 2016, we issued warrants to purchase 454,545 shares of common stock at an exercise price of $110.00 expiring on August 2, 2021, in connection with the Company’s follow-on offering. The warrants had an original life of five years and remain outstanding as of December 31, 2017. The warrants include provisions that could require cash settlement and are therefore recorded as a liability on our balance sheet at their estimated fair value on the date of issuance and at each reporting period. As of the end of each subsequent reporting period, the warrants are required to be remeasured at fair value. Changes in fair value from the previous reporting period are recorded as a gain or loss in other income or expense in our statement of operations. If the warrants increase in fair value from the previous reporting period, the liability increases and a loss is recorded. Conversely, if the warrants decrease in fair value, the liability decreases and a gain is recorded.

The fair value of the warrants is measured using the Black-Scholes valuation model. Inherent in the Black-Scholes valuation model are estimates and assumptions related to expected stock price volatility, expected life, risk-free interest rate and dividend yield. Our estimates underlying the assumptions used in the Black-Scholes valuation model are subject to risks and uncertainties. These estimates and assumptions may change over time and such changes will affect the fair value of the warrants.

The risk-free interest rate is based on the U.S. Treasury yield curve in effect on the date of valuation equal to the expected life of the August 2016 Warrants. An increase in the risk-free interest rate will increase the value of the warrants. The dividend yield percentage is zero because we neither currently pay dividends nor do we intend to do so during the expected term of the warrants. Expected stock price volatility is based on the weighted average of the Company’s historical common stock volatility and the volatility of several peer public companies. An increase in the expected stock price volatility will increase the value of the warrants. The expected life of the warrants is assumed to be equivalent to their remaining contractual term. As the expected life of the warrants decreases, so will the fair value. The assumptions used to value the warrants as of December 31, 2016 and 2017 were as follows:

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2016</th>
<th>December 31, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise price of warrants</td>
<td>$110.00</td>
<td>$110.00</td>
</tr>
<tr>
<td>Closing underlying stock price</td>
<td>$98.00</td>
<td>$3.00</td>
</tr>
<tr>
<td>Expected stock price volatility</td>
<td>84%</td>
<td>112%</td>
</tr>
<tr>
<td>Expected life (in years)</td>
<td>4.58</td>
<td>3.58</td>
</tr>
<tr>
<td>Risk-free interest rate</td>
<td>1.93%</td>
<td>2.04%</td>
</tr>
<tr>
<td>Expected dividend yield</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Valuation per common share underlying each warrant</td>
<td>$61.38</td>
<td>$0.49</td>
</tr>
<tr>
<td>Total liability for warrants on the balance sheet</td>
<td>$20,926,061</td>
<td>$167,636</td>
</tr>
<tr>
<td>Decrease in fair value during the year ended</td>
<td>$1,007,352</td>
<td>$20,758,425</td>
</tr>
</tbody>
</table>
Share-Based Compensation

In accordance with ASC 718, *Stock Compensation*, we record the fair value of stock options, restricted stock awards and other share-based compensation issued to employees as of the grant date as compensation expense. We recognize expense over the requisite service period, which is typically the vesting period. For non-employees, we also record stock options, restricted stock awards and other share-based compensation issued to these non-employees at their fair value as of the grant date. We then periodically remeasure the awards to reflect the current fair value at each reporting period and recognize expense over the related service period.

We calculate the fair value of share-based compensation awards using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of subjective assumptions, including stock price volatility, the expected life of stock options, risk free interest rate and the fair value of the underlying common stock on the date of grant.

- We do not have sufficient history to estimate the volatility of our common stock price. We calculate expected volatility based on reported data for selected reasonably similar publicly traded companies for which the historical information is available. For the purpose of identifying peer companies, we consider characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status. We plan to continue to use the guideline peer group volatility information until the historical volatility of our common stock is relevant to measure expected volatility for future option grants.
- The assumed dividend yield is based on our expectation of not paying dividends in the foreseeable future.
- The expected term represents the period that the share-based awards are expected to be outstanding. Our historical share option exercise experience does not provide a reasonable basis upon which to estimate an expected term because of a lack of sufficient data. Therefore, we estimate the expected term by using the simplified method provided by the SEC. The simplified method calculates the expected term as the average of the time-to-vesting and the contractual life of the options.
- We determine the risk-free interest rate by reference to implied yields available from U.S. Treasury securities with a remaining term equal to the expected life assumed at the date of grant.
- We estimate forfeitures based on our historical analysis of actual stock option forfeitures.

The assumptions that we used in the Black-Scholes option-pricing model for the years ended December 31, 2015, 2016 and 2017, are set forth below:

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-free interest rate</td>
<td>2.05%</td>
<td>1.50%</td>
<td>2.26%</td>
</tr>
<tr>
<td>Dividend yield</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Expected option term (in years)</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Volatility</td>
<td>87%</td>
<td>82%</td>
<td>86%</td>
</tr>
</tbody>
</table>

Contractual Obligations and Commitments

The following table summarizes our significant contractual obligations and commercial commitments as of December 31, 2017 and the effects such obligations are expected to have on our liquidity and cash flows in future periods (in thousands):

<table>
<thead>
<tr>
<th>Payments Due by Period</th>
<th>Total</th>
<th>Less Than 1 Year</th>
<th>1-3 Years</th>
<th>3-5 Years</th>
<th>More Than 5 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating leases for existing facilities and equipment</td>
<td>$2,955</td>
<td>$602</td>
<td>$1,297</td>
<td>$1,027</td>
<td>$29</td>
</tr>
<tr>
<td>Convertible note payable to Pharmstandard, including interest</td>
<td>9,448</td>
<td>—</td>
<td>—</td>
<td>9,448</td>
<td>—</td>
</tr>
<tr>
<td>Convertible note payable to Invitech, including interest</td>
<td>5,846</td>
<td>1,300</td>
<td>4,546</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Convertible note payable to Saint-Gobain, including interest</td>
<td>2,335</td>
<td>1,050</td>
<td>1,285</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Note payable to Medinet, including interest</td>
<td>4,992</td>
<td>4,992</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Other notes payable, including interest</td>
<td>14</td>
<td>14</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td>$25,590</td>
<td>$7,958</td>
<td>$7,128</td>
<td>$10,475</td>
<td>$29</td>
</tr>
</tbody>
</table>
We are a party to license agreements with universities and other third parties, as well as patent assignment agreements, under which we have obtained rights to patents, patent applications and know-how. Under these agreements, we have agreed to pay the other parties milestone payments upon the achievement of specified clinical, regulatory and commercialization events and royalties based on future sales of products. We have not included these payments in the table as we cannot estimate if, when or in what amounts such payments will become due under these agreements.

For more information, see Note 6 of the consolidated financial statements for a description of the convertible notes payable to Pharmstandard, Invetech and Saint-Gobain, and the note payable to Medinet.

Net Operating Losses

As of December 31, 2017, we had U.S. federal and state, and Canadian federal and provincial net operating loss carryforwards of $300.8 million, $338.5 million, $6.1 million, and $6.1 million, respectively. These net operating loss carryforwards begin to expire in 2018, 2017, 2026 and 2026, respectively. As of December 31, 2017, we also had unlimited Luxembourg net operating loss carryforwards of $217,000. As of December 31, 2017, we had U.S. federal and state tax credit carryforwards of $8.2 million and $0.3 million, respectively. These credit carryforwards begin to expire in 2020 and 2024, respectively. As of December 31, 2017, we had Canadian investment tax credit carryforwards of $0.03 million that begin to expire in 2024. The utilization of the net operating loss and tax credit carryforwards may be subject to limitation under the rules regarding a change in stock ownership as determined by the Internal Revenue Code, and state and foreign tax laws. Section 382 of the Internal Revenue Code of 1986, as amended, imposes annual limitations on the utilization of net operating loss carryforwards, other tax carryforwards, and certain built-in losses upon an ownership change as defined under that section. In general terms, an ownership change may result from transactions that increase the aggregate ownership of certain of our stockholders by more than 50 percentage points over a three-year testing period. We believe that we experienced an ownership change during 2014 under Section 382. Due to the Section 382 limitation resulting from the ownership change, $28.2 million of our U.S. federal net operating losses are expected to expire unused. Additionally, our U.S. federal tax credits and state net operating losses may be limited. The amount of U.S. federal net operating losses expected to expire due to the Section 382 limitation has not been recognized in our consolidated financial statements as of December 31, 2017. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carry-forwards and other tax credit carryforwards to offset U.S. federal taxable income may be subject to limitations, which potentially could result in increased future tax liability to us. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited.

As of December 31, 2017, we have received $2.9 million in refunds through scientific research and experimental development tax credits through our consolidated subsidiary in Canada.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements as defined under Securities and Exchange Commission, or SEC, rules.
Our primary exposure to market risk is limited to our cash and cash equivalents, all of which have maturities of three months or less. The related interest income sensitivity is affected by changes in the general level of short-term U.S. interest rates. We primarily invest in high quality, short-term marketable debt securities issued by high quality financial and industrial companies.

Due to the short-term duration and low risk profile of our cash, cash equivalents and short-term investments, an immediate 10.0% change in interest rates would not have a material effect on the fair value of our portfolio. Accordingly, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a sudden change in market interest rates on our cash, cash equivalents and short-term investments.

We do not believe that our cash and cash equivalents have significant risk of default or illiquidity. While we believe our cash and cash equivalents do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in fair value. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits.

All of our other debt instruments and liabilities that incur interest charges do so at fixed rates. We incur interest expense at fixed rates under the promissory note payable to Medinet (3% per annum), the convertible note payable to Pharmstandard (9.5% per annum), the convertible note payable to Invetech (6% per annum), the convertible note payable to Saint-Gobain (6% per annum) and other notes payable (8.31% per annum).
Item 8. Financial Statements and Supplementary Data.

Our financial statements and the financial statement schedule required by this item, together with the report of our independent registered public accounting firm and the notes to our financial statements, appear on pages F-1 through F-43 of this Annual Report on Form 10-K and are incorporated herein by reference.


There has been no change of accountants nor any disagreements with accountants on any matter of accounting principles or practices or financial disclosure required to be reported under this Item.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Under the supervision of and with the participation of our management, including our chief executive officer, who is our principal executive officer, and our chief financial officer, who is our principal financial officer, we conducted an evaluation of the effectiveness of our disclosure controls and procedures as of December 31, 2017, the end of the period covered by this Annual Report. The term “disclosure controls and procedures,” as set forth in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to provide reasonable assurance 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 rules and forms promulgated by the Securities and Exchange Commission, or the SEC.

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, 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, 2017, 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.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.


Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our management, under the supervision and with the participation of our principal executive officer and principal financial officer, conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under this framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2017.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to a transition period established by the rules of the SEC for newly public companies.

Item 9B. Other Information

On March 28, 2018, our compensation committee approved restricted stock awards for 27,150 shares of common stock for Mr. Abbey, 67,887 shares of common stock for Dr. Nicolette and 22,629 shares of common stock for Dr. Katz. The restricted stock awards are subject to a lapsing right of repurchase, which will lapse with respect to 50% of the shares on June 15, 2018 and with respect to the remaining 50% of the shares on December 14, 2018.
PART III

Item 10. Directors, Executive Officers and Corporate Governance

The following table sets forth the name, age and position of each of our executive officers and directors as of February 28, 2018.

<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeffrey D. Abbey</td>
<td>56</td>
<td>President, Chief Executive Officer and Director</td>
</tr>
<tr>
<td>Charles A. Nicolette, Ph.D.</td>
<td>55</td>
<td>Chief Scientific Officer and Vice President of Research and Development</td>
</tr>
<tr>
<td>Richard D. Katz, M.D.</td>
<td>54</td>
<td>Vice President and Chief Financial Officer</td>
</tr>
<tr>
<td>Lori R. Harrelson</td>
<td>48</td>
<td>Vice President of Finance</td>
</tr>
<tr>
<td>Hubert Birner, Ph.D.(1)(3)</td>
<td>52</td>
<td>Chairman of the Board of Directors</td>
</tr>
<tr>
<td>Robert F. Carey(1)(2)</td>
<td>60</td>
<td>Director</td>
</tr>
<tr>
<td>Igor Krol</td>
<td>45</td>
<td>Director</td>
</tr>
<tr>
<td>Richard G. Morrison(1)(2)</td>
<td>82</td>
<td>Director</td>
</tr>
<tr>
<td>Irackly Mtibelishvily (3)</td>
<td>46</td>
<td>Director</td>
</tr>
<tr>
<td>Sander van Deventer M.D., Ph.D.</td>
<td>63</td>
<td>Director</td>
</tr>
</tbody>
</table>

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

Jeffrey D. Abbey has served as our president and chief executive officer and a member of our board of directors since February 2010. Mr. Abbey served in various other positions at our company from September 2002 to February 2010, including as our vice president of business development from February 2004 to January 2009 and as our chief business officer from January 2009 to February 2010. Prior to joining us, Mr. Abbey served as vice president of business development and finance at Internet Appliance Network, an information technology company, from 1999 to 2001. Mr. Abbey was a partner at Eilenberg and Krause, LLP, a corporate law firm, from 1994 to 1999. Mr. Abbey received an A.B. in mathematical economics from Brown University and an M.B.A. and J.D. from the University of Virginia. We believe that Mr. Abbey is qualified to serve on our board of directors due to his extensive knowledge of our company and our industry.

Charles A. Nicolette, Ph.D. has served as our chief scientific officer since December 2007 and as our vice president of research and development since December 2004. Dr. Nicolette served as our vice president of research from July 2003 to December 2004. Prior to joining us, Dr. Nicolette served in various positions at Genzyme Molecular Oncology, Inc., a biotechnology company, from 1997 to 2003, most recently as director of Antigen Discovery. Dr. Nicolette received a B.S. from the State University of New York at Stony Brook and a Ph.D. in biochemistry and cellular and developmental biology from the State University of New York at Stony Brook, completing his doctoral dissertation and post-doctoral fellowship at Cold Spring Harbor Laboratory.

Richard D. Katz, M.D. has served as our vice president and chief financial officer since July 2016. Prior to joining us, Dr. Katz served as chief financial officer for Viamet Pharmaceuticals, Inc., a biotechnology company, from February 2011 to May 2016. Dr. Katz also served as chief financial officer at Icagen, Inc., a biotechnology company, from April 2001 to November 2011. Prior to Icagen, Dr. Katz served as a vice president in the healthcare group at Goldman, Sachs & Company. Dr. Katz received an A.B. magna cum laude from Harvard University, an M.D. from the Stanford University School of Medicine and an M.B.A. from Harvard Business School.

Lori R. Harrelson has served as our vice president of finance since July 2011. Ms. Harrelson served as our director of finance and accounting from January 2007 to July 2011 and as our director of accounting and financial reporting from September 2004 to January 2007. Prior to joining us, Ms. Harrelson served as manager at LipoScience, Inc., a diagnostic company, from 2001 to 2004 and a senior auditor at Ernst & Young, from 1997 to 2001. Ms. Harrelson received a B.S. in finance from East Carolina University and is a certified public accountant.
Hubert Birner, Ph.D. has served as chairman of our board of directors since 2005 and a member of our board of directors since 2001. Dr. Birner joined the Munich office of TVM Capital, a venture capital firm and an affiliate of ours, as an investment manager in 2000 and currently serves as the managing partner of the firm. From 1998 to 2000, Dr. Birner served as head of European business development and director of marketing for Germany at Zeneca Agrochemicals, a biopharmaceutical company. Prior to joining Zeneca Agrochemicals, Dr. Birner served as a management consultant in McKinsey & Company’s European healthcare and pharmaceutical practice. Dr. Birner currently serves on the board of directors of Proteon Therapeutics, Inc., Acer Therapeutics Inc., which are publicly traded companies, and Noxxon Pharma BV, AL-S Pharma AG, Centogene AG and SpeP harm Holdings BV, which are privately traded companies. Dr. Birner previously served on the board of directors of Horizon Pharma, Inc., Bioxell SA, Evotec AG, Probiodrug AG and Jerini AG. Dr. Birner received an M.B.A. from Harvard Business School and a doctorate in biochemistry from Ludwig-Maximilians University in Munich, Germany. His doctoral thesis was honored with the Hoffmann-La Roche prize for outstanding basic research in metabolic diseases. We believe that Dr. Birner is qualified to serve as chairman of our board of directors due to his extensive experience with biopharmaceutical companies and his years of experience providing strategic and advisory services to pharmaceutical and biotechnology companies as a lead director and investor.

Robert F. Carey has served as a member of our board of directors since September 2015. Mr. Carey has been executive vice president, chief business officer for Horizon Pharma plc since March 2014. Prior to that, Mr. Carey served as managing director and head of the healthcare investment banking group at JMP Securities LLC, or JMP, a full-service investment bank, from March 2003 to March 2014. Prior to joining JMP, Mr. Carey was a managing director in the healthcare groups at Dresdner Kleinwort Wasserstein and Vector Securities International, Inc. Mr. Carey also has held roles at Shearson Lehman Hutton and Ernst & Whinney. Mr. Carey received his B.A. in accounting from the University of Notre Dame. We believe that Mr. Carey is qualified to serve on our board of directors due to his valuable and relevant healthcare investment banking experience with financings, mergers, acquisitions and global expansion and other strategic transactions as well as his role as a CPA supporting the audits of public and private corporations, which we expect will assist Mr. Carey in fulfilling his duties as chair of our audit committee.

Igor Krol has served as a member of the board of directors since June 2016. Mr. Krol has been chief executive officer of Veset International Ltd., or Veset, a software company since June 2015. Prior to that, Mr. Krol served as chief operating officer of Veset from November 2013 to May 2015. Prior to joining Veset, Mr. Krol spent 12 years in investment banking at Sberbank CIB as senior director from March 2012 to June 2013 and Citigroup Investment Banking, or Citigroup as director from March 2001 to January 2012. Mr. Krol still maintains an advisory role with Pharmstandard, one of our principal stockholders. Prior to that, Mr. Krol worked at Nestle, a global consumer company in varying roles including finance and purchasing between 1996 and 1999. Mr. Krol holds an M.B.A. degree from INSEAD, Fontainebleau, France, and B.A. in Systems Engineering from MIREA Technical University, Moscow, Russia. We believe that Mr. Krol is qualified to serve on our board of directors due to his relevant corporate finance and investment banking experience with mergers, acquisitions and financings, as well experience in operational, financial and information technology matters.

Richard G. Morrison has served as a member of the board of directors since September 2017. Dr. Morrison served on the faculty of the Cameron School of Business at the University of North Carolina Wilmington from January 1995 until December 2015 when he retired. Prior to joining the Cameron School of Business, Mr. Morrison spent the majority of his career at Eli Lilly and Company where he served for thirty years in a variety of international leadership roles, including most recently as president and general manager of Lilly’s operations in Latin America. Prior to serving as president and general manager of Lilly’s operations in Latin America, Dr. Morrison held several marketing and executive management positions in Europe, Africa and the Middle East, in both the pharmaceutical and agricultural divisions of the company. Dr. Morrison has also served on a number of boards of directors of companies in the medical industry, including aaiPharma, Inc. (now Alcami Corporation), a public pharmaceutical company, BeaconMedaes LLC (now Atlas Copco North America LLC), a private medical device company, Icagen, Inc., a public biotechnology company and the Diatron Group, a private medical instruments company. Dr. Morrison holds Masters and Ph.D. degrees from Louisiana State University and a B.S. degree from Stephen F. Austin University in East Texas, and served in the United States Navy. Over the years he has served on the boards of numerous charitable organizations, including the Raleigh North Carolina Chapter of the Juvenile Diabetes Research Foundation and the North Carolina Methodist Home for Children, and is co-Chair of the Mission of Hope for Sierra Leone, an organization dedicated to improving healthcare in Africa. We believe that Mr. Morrison is qualified to serve on our board of directors due to his variety of international leadership roles and experience in executive management positions in the pharmaceutical industry.
Irackly Mtibelishvily has served as a member of our board of directors since 2016. Since 1998, Mr. Mtibelishvily has served in several capacities for Citigroup. Since 2012, Mr. Mtibelishvily has held the position of managing director and chairman of corporate and investment banking for Russia and CIS at Citigroup and in December 2015 was appointed chairman of corporate and investment banking for Central and Eastern Europe Middle East and Africa. Mr. Mtibelishvily is a specialist in corporate finance, capital markets, securities, and mergers and acquisitions. Prior to joining Citigroup, Mr. Mtibelishvily was with the multinational law firm Clifford Chance LLP from 1994 to 1998. Mr. Mtibelishvily earned a master of international legal studies degree from the Moscow State Institute of International Relations and a master of laws degree from the University of Virginia Law School. We believe that Mr. Mtibelishvily is qualified to serve on our board of directors due to his 25 years of transactional and management experience in the field of investment banking and corporate finance.

Sander van Deventer, M.D., Ph.D. has served as a member of our board of directors since 2001. Dr. van Deventer has been a general partner of Forbion Capital Partners (formerly ABN AMRO Capital), an affiliate of ours, since 2006. From 2008 to 2009, he served as the chief executive officer of Amsterdam Molecular Therapeutics, or AMT, a gene therapy company that he co-founded in 1998. He has also served as a member of AMT’s board of directors since 2007 and as a member of the board of directors of UniQure N.V. (formerly UniQure B.V.) since February 2014. Dr. van Deventer has also served as a professor of translational gastroenterology at Leiden University since 2008. He received an M.D. and Ph.D. from the University of Amsterdam. We believe that Dr. van Deventer is qualified to serve on our board of directors due to his experience as a founder of a biopharmaceutical company and his expertise in clinical development.

**Board Composition and Election of Directors**

Our board of directors is currently authorized to have up to eight members. In accordance with the terms of our certificate of incorporation and bylaws, our board of directors is divided into three classes, class I, class II and class III, with members of each class serving staggered three-year terms. The members of the classes are divided as follows:

- the class I directors are Sander van Deventer, M.D., Ph.D. and Igor Krol, and their term expires at our annual meeting of stockholders to be held in 2018;
- the class II directors are Hubert Birner, Ph.D. and Robert F. Carey, and their term expires at our annual meeting of stockholders to be held in 2019; and
- the class III directors are Jeffrey D. Abbey, Irackly Mtibelishvily and Richard G. Morrison, and their term expires at our annual meeting of stockholders to be held in 2020.

Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires. In accordance with the terms of our certificate of incorporation and bylaws, our directors are only able to be removed for cause by the affirmative vote of the holders of 75% or more of our voting stock.

There are no family relationships among any of our directors or executive officers.

**Audit Committee**

The current members of our audit committee are Robert F. Carey, Hubert Birner, Ph.D. and Richard G. Morrison. Mr. Carey chairs our audit committee. Ralph Snyderman, M.D. served as a member of our audit committee from December 2016 to March 2017 at which time he resigned as a member of our board of directors. Our audit committee’s responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from such firm;

- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;

- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;

- overseeing our internal audit function, if any;

- overseeing our risk assessment and risk management policies;

- establishing policies regarding hiring employees from our independent registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;

- meeting independently with our internal auditing staff, our independent registered public accounting firm and management;

- reviewing and approving or ratifying any related person transactions; and

- preparing the audit committee report required by SEC rules.

All audit and non-audit services, other than de minimis non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our board of directors has determined that Mr. Carey is an “audit committee financial expert” as defined in applicable SEC rules and qualifies as independent as defined under applicable Nasdaq rules.

**Code of Ethics and Code of Conduct**

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or persons performing similar functions. We have posted a current copy of the code on our website, www.argotherapeutics.com. In addition, we have posted on our website all disclosures that are required by law or Nasdaq stock market listing standards concerning any amendments to, or waivers from, any provision of the code.

**Section 16(a) Beneficial Ownership Reporting Compliance**

Section 16(a) of the Exchange Act requires our directors, executive officers and holders of more than 10% of a registered class of our equity securities to file with the SEC initial reports of ownership of our equity securities on a Form 3 and reports of changes in such ownership on a Form 4 or Form 5. Based solely on our review of copies of such filings by our directors, executive officers, and 10% shareholders, or written representations from certain of those persons, we believe that all filings required to be made by those persons during fiscal 2017 were timely made.
Item 11. Executive Compensation

This section describes the material elements of compensation awarded to, earned by or paid to each of our named executive officers in 2017. This section also provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our named executive officers and is intended to place into perspective the data presented in the tables and narrative that follow. Our “named executive officers” for 2017 were:

- Jeffrey D. Abbey, our president and chief executive officer;
- Charles A. Nicolette, Ph.D., our vice president of research and development and chief scientific officer; and
- Richard D. Katz, our vice president and chief financial officer.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to our named executive officers during the years ended December 31, 2017 and 2016.

<table>
<thead>
<tr>
<th>Name and Principal Position</th>
<th>Year</th>
<th>Salary ($)</th>
<th>Bonus ($) (1)(2)</th>
<th>Option Awards ($) (3)</th>
<th>Stock Awards ($) (4)</th>
<th>All Other Compensation ($) (5)</th>
<th>Total ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeffrey D. Abbey (6)</td>
<td>2017</td>
<td>480,000</td>
<td>119,556</td>
<td>1,432,081</td>
<td>__</td>
<td>13,911</td>
<td>2,045,548</td>
</tr>
<tr>
<td>President and Chief Executive Officer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charles A. Nicolette, Ph.D. (4)</td>
<td>2016</td>
<td>450,000</td>
<td>349,969</td>
<td>1,029,892</td>
<td>91,940</td>
<td>26,477</td>
<td>1,948,278</td>
</tr>
<tr>
<td>Vice President of Research and Development and Chief Scientific Officer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Richard D. Katz (7)</td>
<td>2017</td>
<td>305,000</td>
<td>75,967</td>
<td>389,342</td>
<td>__</td>
<td>12,555</td>
<td>782,864</td>
</tr>
<tr>
<td>Vice President and Chief Financial Officer</td>
<td></td>
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<td></td>
<td></td>
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</tr>
</tbody>
</table>

(1) In lieu of paying annual cash bonuses for 2017, in August 2017 we granted restricted stock awards to each of our executive officers, including 31,134 shares of our common stock to Mr. Abbey, 24,972 shares to Dr. Nicolette and 19,783 shares to Dr. Katz. The number of shares of common stock granted to each named executive officer was determined by dividing 25% of their annual base salary by the closing price of our common stock on the date of grant. Each of the restricted stock awards was subject to a lapsing right of repurchase in our favor, which right lapsed with respect to 50% of the underlying shares on January 2, 2018 and the remaining 50% on January 9, 2018.

(2) In lieu of paying an annual bonus to each of our named executive officers entirely in cash for 2016, in January 2017 we paid 75% of the annual bonus in cash and paid the balance of the annual bonus through the grant of restricted stock awards having a value equal to 25% of the annual bonus, including 593 shares of common stock to Mr. Abbey, 282 shares to Dr. Nicolette and 197 shares to Dr. Katz. The number of shares of common stock granted to each named executive officer was calculated by dividing 25% of the amount of such officer’s 2016 annual bonus that would otherwise have been paid by the closing price of our common stock on January 13, 2017. Each of the restricted stock awards was subject to a lapsing right of repurchase in our favor, which right lapsed with respect to 100% of the underlying shares of each award on April 19, 2017. In addition to the cash and non-cash bonuses mentioned above, Mr. Abbey also received an additional cash bonus of $100,000 for 2016.

(3) The amounts reported in the “Option Awards” column reflect the aggregate grant date fair value of share-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board Accounting Standard Codification Topic 718, or FASB ASC Topic 718. See Note 11 to our consolidated financial statements appearing in this Annual Report on Form 10-K.

(4) The amounts reported in the “Stock Awards” column reflect the aggregate fair value of share-based compensation awarded during the year ended December 31, 2016 computed in accordance with the provisions of FASB ASC Topic 718. The amounts reported in the “Stock Awards” column reflect restricted stock awards and restricted stock units awarded to our named executive officers. In December 2016, Mr. Abbey and Dr. Nicolette were granted restricted stock awards of 277 shares and 555 shares of common stock, respectively. Each of the restricted stock awards was subject to a lapsing right of repurchase in our favor, which right lapsed with respect to 100% of the underlying shares of each award on December 9, 2017. In June 2016, Mr. Abbey and Dr. Nicolette were each awarded restricted stock units for 546 shares of common stock, which vested over a twelve month period in connection with their ongoing employment. See Note 9 to our consolidated financial statements appearing in this Annual Report on Form 10-K.

(5) The amounts reported in the “All Other Compensation” column reflect, for each named executive officer, 401(k) matching contributions, the sum of the incremental cost to us of all perquisites and other personal benefits and includes post-tax insurance earnings.

(6) Mr. Abbey serves as a member of our board of directors but does not receive any additional compensation for his service as a director.

(7) Mr. Katz was hired in July 2016.
The primary elements of our executive compensation program are:

- base salary;
- annual cash bonuses; and
- equity incentive awards.

We strive to achieve an appropriate mix between the various elements of our compensation program to meet our compensation objectives and philosophy; however, we have not adopted any formal policies or guidelines for allocating compensation among these elements.

**Base Salary.** We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary. In 2017, we paid an annual base salary of $480,000 to Mr. Abbey, $385,000 to Dr. Nicolette and $305,000 to Dr. Katz. In 2018, the annual salary for each of Mr. Abbey, Dr. Nicolette and Dr. Katz will be $480,000, $385,000 and $305,000, respectively.

**Annual Bonus.** In addition to base salaries, our executive officers are eligible to receive annual discretionary cash bonuses based on the achievement of corporate objectives and individual performance. Bonuses are typically prorated on a monthly basis, as applicable, for executive officers who commence employment after the beginning of the year. Our executive officers’ annual bonus opportunities are generally set as a specified percentage of annual base salary. The 2017 annual target bonus amount was 60% of base salary for Mr. Abbey, 40% of base salary for Dr. Nicolette and 40% of base salary for Dr. Katz. In determining Mr. Abbey’s annual bonus for 2017, we attributed 100% of the target bonus to the achievement of specified corporate objectives and in determining Dr. Nicolette and Dr. Katz’s annual bonuses for 2017, we attributed 75% of the target bonus to the achievement of specified corporate objectives and 25% to the individual’s effectiveness in helping us achieve our corporate objectives or other individual performance criteria. The annual corporate objectives are recommended by our chief executive officer and approved by the compensation committee and the board of directors. In lieu of paying annual cash bonuses for 2017, in August 2017 we granted restricted stock awards to each of our executive officers, including 31,134 shares to Mr. Abbey, 24,972 shares to Dr. Nicolette and 19,783 shares to Dr. Katz. The number of shares of common stock granted to each named executive officer was determined by dividing 25% of their annual base salary by the closing price of our common stock on the date of grant. Each of the restricted stock awards was subject to a lapsing right of repurchase in our favor, which right lapsed with respect to 50% of the underlying shares on January 2, 2018 and the remaining 50% on January 9, 2018. In lieu of paying annual cash bonuses entirely in cash for 2016, in January 2017 we paid 75% of the annual bonus in cash and paid the balance of the annual bonus through the grant of restricted stock awards under our 2014 stock incentive plan, having a value equal to 25% of the annual bonus, including 593 shares of common stock to Mr. Abbey, 282 shares to Dr. Nicolette and 197 shares to Dr. Katz. The number of shares of common stock granted to each named executive officer was calculated by dividing 25% of the amount of such officer’s 2016 annual bonus that would otherwise have been paid by the closing price of our common stock on January 13, 2017. Each of the restricted stock awards was subject to a lapsing right of repurchase in our favor, which right lapsed with respect to 100% of the underlying shares of each award on April 19, 2017. In addition to the above mentioned bonuses, Mr. Abbey received an additional cash bonus of $100,000 for 2016.
In 2018, the target annual bonus for each of Mr. Abbey, Dr. Nicolette and Dr. Katz will be 60%, 40% and 40%, respectively.

**Equity Incentive Awards.** Our equity award program is the primary vehicle for offering long-term incentives to our executives. We believe that equity awards provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. To date, we have used stock option grants for this purpose because we believe they are an effective means by which to align the long-term interests of our executive officers with those of our stockholders. The use of options also can provide tax and other advantages to our executive officers relative to other forms of equity compensation. We believe that our equity awards are an important retention tool for our executive officers, as well as for our other employees.

We award stock options and restricted stock awards broadly to our employees, including to our non-executive employees. Grants to our executives and other employees are made at the discretion of our board of directors and are not made at any specific time period during a fiscal year. All of our named executive officers have received stock option grants under our 2008 stock incentive plan or our 2014 stock incentive plan, each of which is described below. No further options may be granted under the 2008 stock incentive plan. In 2016, the Company granted to Mr. Abbey and Mr. Nicolette restricted stock awards and restricted stock units to better align the officers’ total compensation with the compensation of chief executive officers and chief scientific officers at peer companies.

Initial option grants to our executive officers are generally set forth in their employment agreements. These initial grants are the product of negotiation with the executive officer, but we generally seek to establish equity ownership levels that we believe are commensurate with the equity stakes held by executive officers serving in similar roles at comparable biopharmaceutical companies. In addition, from time to time in connection with corporate finance transactions and at other times as our compensation committee and board of directors deem appropriate, we provide subsequent option grants to those executive officers determined to be performing well.

The majority of the stock option grants we have made to our executive officers vest over four years. However, from time to time, our board of directors has approved grants with different and sometimes shorter vesting provisions.

On March 28, 2018, we granted restricted stock awards for 67,887 shares of common stock to Mr. Abbey, 27,150 shares of common stock to Dr. Nicolette and 22,629 shares of common stock to Dr. Katz. The restricted stock awards are subject to a lapsing right of repurchase, which will lapse with respect to 50% of the shares on June 15, 2018 and with respect to the remaining 50% of the shares on December 14, 2018.

**Outstanding Equity Awards as of December 31, 2017**

The following table provides information about outstanding stock options held by each of our named executive officers as of December 31, 2017. All of the listed options were granted under our 2014 stock incentive plan and 2008 stock incentive plan.
<table>
<thead>
<tr>
<th>Name</th>
<th>Number of Securities Underlying Unexercised Options (#)</th>
<th>Number of Securities Underlying Unexercised Options (#)</th>
<th>Option Exercise Price ($)</th>
<th>Option Expiration Date</th>
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</thead>
<tbody>
<tr>
<td>Jeffrey D. Abbey</td>
<td>708</td>
<td>—</td>
<td>84.00(1)</td>
<td>7/2/18</td>
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<td></td>
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<td>19,305</td>
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<td>116.40</td>
<td>11/11/23</td>
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<td>116.40</td>
<td>11/11/23</td>
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<td>2,494</td>
<td>426(2)</td>
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<td>7/27/24</td>
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<td>2,190</td>
<td>—</td>
<td>121.80</td>
<td>7/27/24</td>
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<td>2,190</td>
<td>—</td>
<td>121.80</td>
<td>7/27/24</td>
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<td></td>
<td>3,750</td>
<td>2,250(3)</td>
<td>156.00</td>
<td>6/16/25</td>
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<td>4,687</td>
<td>7,813(4)</td>
<td>148.20</td>
<td>6/12/26</td>
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<td></td>
<td>—</td>
<td>19,310(5)</td>
<td>97.00</td>
<td>1/18/27</td>
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<td>Charles A. Nicolette, Ph.D.</td>
<td>732</td>
<td>—</td>
<td>84.00(1)</td>
<td>7/2/18</td>
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<tr>
<td></td>
<td>294</td>
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<td></td>
<td>1,586</td>
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<td></td>
<td>768</td>
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<td>7/27/24</td>
</tr>
<tr>
<td></td>
<td>—</td>
<td>—</td>
<td>121.80</td>
<td>7/27/24</td>
</tr>
<tr>
<td></td>
<td>2,343</td>
<td>1,407(3)</td>
<td>156.00</td>
<td>6/16/25</td>
</tr>
<tr>
<td></td>
<td>3,281</td>
<td>5,469(4)</td>
<td>148.20</td>
<td>6/12/26</td>
</tr>
<tr>
<td></td>
<td>—</td>
<td>9,250(5)</td>
<td>97.00</td>
<td>1/18/27</td>
</tr>
<tr>
<td>Richard D. Katz</td>
<td>5,625</td>
<td>9,375(6)</td>
<td>126.00</td>
<td>7/10/26</td>
</tr>
<tr>
<td></td>
<td>—</td>
<td>5,250(5)</td>
<td>97.00</td>
<td>1/18/27</td>
</tr>
</tbody>
</table>

(1) In April 2012, our board of directors approved the repricing of stock options that had exercise prices between $217.20 and $733.20 per share, including this option, to the then estimated fair value of our common stock, determined to be an exercise price of $84.00 per share.

(2) These options were granted on July 28, 2014 and vested as to 25% of the shares on July 1, 2015, with the remaining 75% of the shares vesting in equal amounts monthly over the three year period commencing on July 1, 2015, provided that the recipient continues to provide services to us over such period.

(3) These options were granted on June 17, 2015 and will vest as to 25% of the shares on June 1, 2016, with the remaining 75% of the shares vesting in equal amounts monthly over the three year period commencing on June 1, 2016, provided that the recipient continues to provide services to us over such period.
These options were granted on June 13, 2016 and vested as to 25% of the shares on June 1, 2017, with the remaining 75% of the shares vesting in equal amounts monthly over the three year period commencing on June 1, 2017, provided that the recipient continues to provide services to us over such period.

These options were granted on January 19, 2017 and vested as to 25% of the shares on January 1, 2018, with the remaining 75% of the shares vesting in equal amounts monthly over the three year period commencing on January 1, 2018, provided that the recipient continues to provide services to us over such period.

These options were granted on July 11, 2016 and vested as to 25% of the shares on July 1, 2017, with the remaining 75% of the shares vesting in equal amounts monthly over the three year period commencing on July 1, 2017, provided that the recipient continues to provide services to us over such period.

Agreements with our Named Executive Officers

We have entered into written employment agreements with each of our named executive officers. The agreements set forth the terms of the named executive officer’s compensation, including base salary, severance and an annual cash bonus opportunity. In addition, the agreements provide that the named executive officers are eligible to participate in company-sponsored benefit programs that are available generally to all of our employees. The agreements also subject our named executive officers to certain non-competition and non-solicitation restrictions. In connection with the commencement of their employment with us, our named executive officers executed our standard confidential information and invention assignment agreements.

Each named executive officer is eligible to receive an annual performance cash bonus under his employment agreement based on the achievement of corporate objectives and the named executive officer’s individual performance, which is determined by our board of directors in its sole discretion. The bonus opportunity is calculated as a percentage of the named executive officer’s then annual base salary. For the year ended December 31, 2017, the target annual bonus for each named executive officer was 60% for Mr. Abbey, 40% for Dr. Nicolette and 40% for Dr. Katz. Each named executive officer must be employed on the date the bonus is paid in order to be eligible for and receive his annual bonus.

Potential Payments upon Termination or Change in Control

Upon execution and effectiveness of a separation agreement and release of all claims, each named executive officer is entitled to severance payments if his employment is terminated under specified circumstances pursuant to the terms of his employment agreement.

If we terminate Mr. Abbey’s, Dr. Nicolette’s or Dr. Katz’s employment without cause or if each such named executive officer terminates his employment with us for good reason in accordance with the terms of his employment agreement, the named executive officer is entitled to receive from us an amount equal to nine months of his then annual base salary, payable in nine equal monthly installments in accordance with our payroll practices, and standard health insurance coverage for a period of nine months, subject to such benefits being available to non-employees. If the named executive officer’s standard health insurance coverage is not available to non-employees under our company sponsored plan, we will reimburse the named executive officer in an amount equal to the cost of the premium for coverage under a medical plan at the same level and on the same terms and conditions in place immediately before his termination.

If we terminate Mr. Abbey or Mr. Nicolette’s employment without cause or if such executive officer terminates his employment with us for good reason in accordance with the terms of his employment agreement, in either case within 90 days before or six months after a “change in control event” as defined in our 2008 stock incentive plan, and such event also constitutes a “change in control event” within the meaning of the regulations promulgated under Section 409A of the Internal Revenue Code, as amended, or the Code, Mr. Abbey and Dr. Nicolette will be entitled to receive the payments and benefits specified above for a period of 15 months rather than nine months. Additionally, in such circumstances, Mr. Abbey and Dr. Nicolette will each be entitled to receive an amount equal to 15 months of his target bonus for the year in which his employment terminates, payable in 15 equal monthly installments in accordance with our payroll practices.
If we terminate Dr. Katz’s employment without cause or if Dr. Katz terminates his employment with us for good reason in accordance with the terms of his employment agreement, in either case within 90 days before or six months after a change in control as defined in the 2014 stock incentive plan and such event also constitutes a “change in control event” within the meaning of the regulations promulgated under Section 409A of the Code, Dr. Katz will be entitled to receive the payments and benefits specified above for a period of nine months and additionally, Dr. Katz will be entitled to receive an amount equal to nine months of his target bonus for the year in which his employment terminates, payable in nine equal monthly installments in accordance with our payroll practices.

2014 Stock Incentive Plan

In January 2014, our board of directors adopted and our stockholders approved the 2014 stock incentive plan, which became effective immediately prior to the closing of our initial public offering, or IPO, in February 2014. The 2014 stock incentive plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. As of February 28, 2018, the total number of shares of common stock authorized for issuance under the 2014 stock incentive plan is equal to the sum of 807,011 shares, plus an annual increase to be added on the first day of each of the fiscal year, beginning with the fiscal year ending December 31, 2019 and continuing each fiscal year until, and including, the fiscal year ending December 31, 2024, equal to the lowest of (i) 250,000 shares of Common Stock, (ii) four percent (4%) of the outstanding shares of common stock on such date or (iii) an amount determined by our board of directors.

Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2014 stock incentive plan. However, incentive stock options may only be granted to our employees.

Pursuant to the terms of the 2014 stock incentive plan, our board of directors administers the plan and, subject to any limitations in the plan, selects the recipients of awards and determines:

- the number of shares of our common stock covered by options and the dates upon which the options become exercisable;
- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- the exercise price of options, which may not be less than the fair market value of our common stock on the date of grant of the options; and
- the number of shares of our common stock subject to any stock appreciation rights, restricted stock awards, restricted stock units or other stock-based awards and the terms and conditions of such awards, including conditions for repurchase, issue price and repurchase price.

As of February 28, 2018, options to purchase 188,499 shares of our common stock, at a weighted average exercise price per share of $113.36 were outstanding under the 2014 stock incentive plan. As of February 28, 2018, 254,706 shares of our common stock remained available for future issuance under the 2014 stock incentive plan.

Our board of directors has delegated authority to an executive officer to grant awards under the 2014 stock incentive plan to all of our employees, except employees at or above the director level. Our board of directors has fixed the terms of the awards to be granted by such executive officer, including the exercise price of such awards, and the maximum number of shares subject to awards that such executive officer may make.
Upon a merger or other reorganization event, our board of directors may, in its sole discretion, take any one or more of the following actions pursuant to the 2014 stock incentive plan as to some or all outstanding awards other than restricted stock:

- provide that all outstanding awards shall be assumed, or substantially equivalent awards shall be substituted, by the acquiring or successor corporation (or an affiliate thereof);

- upon written notice to a participant, provide that all of the participant’s unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised by the participant;

- provide that outstanding awards shall become exercisable, realizable or deliverable, or restrictions applicable to an award shall lapse, in whole or in part, prior to or upon such reorganization event;

- in the event of a reorganization event pursuant to which holders of shares of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to the participants with respect to each award held by a participant equal to (1) the number of shares of common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award; and

- provide that, in connection with a liquidation or dissolution, awards shall convert into the right to receive liquidation proceeds.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than a liquidation or dissolution, the repurchase and other rights with respect to outstanding restricted stock will continue for the benefit of the successor company and will, unless the board of directors may otherwise determine, apply to the cash, securities or other property into which shares of our common stock are converted or exchanged pursuant to the reorganization event. Upon the occurrence of a reorganization event involving a liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied, unless otherwise provided in the agreement evidencing the restricted stock award.

At any time, our board of directors may, in its sole discretion, provide that any award under the 2014 stock incentive plan will become immediately exercisable in full or in part, free of some or all restrictions or conditions, or otherwise realizable in full or in part.

No award may be granted under the 2014 stock incentive plan on or after January 17, 2024. Our board of directors may amend, suspend or terminate the 2014 stock incentive plan at any time, except that stockholder approval will be required to comply with applicable law or stock market requirements.

2008 Stock Incentive Plan

In February 2008, our board of directors adopted our 2008 stock incentive plan. Our stockholders approved our 2008 stock incentive plan in March 2008. Upon the completion of our IPO in February 2014, our board of directors determined not to grant any further awards under the 2008 stock incentive plan but all outstanding awards continue to be governed by their existing terms.

Types of Awards. The 2008 stock incentive plan provided for the grant of incentive stock options within the meaning of Section 422 of the Internal Revenue Code, nonstatutory stock options, restricted stock awards, consisting of restricted stock and restricted stock units, and other forms of stock-based awards. Awards under the plan were granted to our employees, directors and individual consultants and advisors. Only our employees were eligible to receive incentive stock options.
When initially adopted, an aggregate of 10,063 shares were reserved for issuance under the 2008 stock incentive plan. The 2008 stock incentive plan was subsequently amended to increase the total number of shares which were available for issuance under the plan prior to our initial public offering to 116,294.

As of February 28, 2018, options to purchase 79,757 shares of our common stock, at a weighted average exercise price per share of $109.20, were outstanding under the 2008 stock incentive plan.

Administration. Our board of directors, or a duly authorized committee thereof, is authorized to administer our 2008 stock incentive plan. Our board of directors has delegated certain authority to administer the 2008 stock incentive plan to our compensation committee; however, our general practice was that awards were approved by the board of directors. Our board of directors or its authorized committee has the authority under the plan to interpret and adopt rules and procedures relating to the 2008 stock incentive plan, as well as to determine the terms of any award or amend the terms of any award made under the plan. No amendment to any award made under the plan may materially and adversely affect the rights of a participant under any outstanding award without the participant’s consent.

Stock Options. Each stock option awarded under the 2008 stock incentive plan was granted pursuant to a notice of stock option and stock option agreement. The board of directors determined the exercise price for a stock option, within the terms and conditions of the 2008 stock incentive plan, provided that the exercise price of a stock option generally could not be less than 100% of the fair market value of our common stock on the date of grant. The vesting and other terms of each grant under the 2008 stock incentive plan were determined by the board of directors in its discretion; however, shares subject to stock options granted under the 2008 stock incentive plan generally vest in installments over a specified period of service, typically four years.

The board of directors determined the term of stock options granted under the 2008 stock incentive plan, subject to limitations in the case of some incentive stock options, as described below. In general, if an optionee’s service relationship with us, or any of our affiliates, ceases for any reason other than disability, death or cause, the optionee may generally exercise the vested portion of any option for a period of three months following the cessation of service. If an optionee’s service relationship with us, or any of our affiliates, ceases due to disability or death or if an optionee dies within a specified period following cessation of service, the optionee or a beneficiary generally may exercise the vested portion of any option for a period of 12 months following the death or disability. If an optionee’s services are terminated for cause, options generally terminate immediately upon such termination. In no event may an option be exercised beyond the expiration of its term.

Stock purchased upon the exercise of a stock option may, depending on the terms of the particular option agreement, be paid for using any of the following: (1) cash or check, (2) a broker-assisted cashless exercise, (3) so long as our common stock is registered under the Securities Exchange Act of 1934, the tender of common stock previously owned by the optionee, (4) delivery of a promissory note, (5) payment of other lawful consideration as determined by the plan administrator, or (6) any combination of the above.

Tax Limitations on Incentive Stock Options. Incentive stock options are subject to certain restrictions contained in the Internal Revenue Code. Among such restrictions, incentive stock under the 2008 stock incentive plan could only be granted only to our employees. The maximum term of an incentive stock option is ten years from the date of grant. Any incentive stock option granted to any person who, at the time of the grant, owned or was deemed to own stock possessing more than 10% of our total combined voting power or that of any of our affiliates had to have an exercise price equal at least to 110% of the fair market value of the stock subject to the option on the date of grant, and the term of the incentive stock option may not exceed five years from the date of grant. The aggregate fair market value, determined at the time of grant, of shares of our common stock with respect to incentive stock options that are exercisable for the first time by an optionee during any calendar year under all of our stock plans may not exceed $100,000.

Restricted Stock Awards. Each restricted stock award granted under the 2008 stock incentive plan was granted pursuant to a summary of restricted stock purchase and a restricted stock purchase agreement. An award of restricted stock entitles a participant to acquire shares of our common stock that are subject to specified restrictions, which may include a repurchase right or forfeiture right, if the shares are issued at no cost, in our favor that lapses in accordance with a vesting schedule or as conditions specified in the award are satisfied. The board of directors determined the terms and conditions of restricted stock awards, including the conditions for repurchase or forfeiture and the purchase price, if any. Unless the board of directors determined otherwise, participants holding shares of restricted stock are entitled to all ordinary cash dividends paid with respect to such shares.
Amendment. The board of directors may amend, suspend or terminate the plan at any time, subject to approval of the stockholders in certain circumstances if required by the Internal Revenue Code to ensure that incentive stock options are tax-qualified and to a participant’s consent to the extent that any amendment to the plan may materially and adversely affect the rights of a participant under any outstanding award.

Effect of Certain Corporate Transactions. Unless otherwise provided in an individual award document, in the event of specified changes of control of our company, our board of directors may take any one or more actions as to any outstanding equity award, or as to a portion of any outstanding equity award, including:

• providing that such awards will be assumed, or substantially equivalent awards substituted, by the acquiring or succeeding corporation or an affiliate thereof;
• providing, upon notice to the participant, that all unexercised awards will terminate immediately prior to the consummation of such transaction unless exercised within a specified period of time;
• providing that all or any outstanding awards will become vested or exercisable, or restrictions applicable to such awards will lapse, in full or in part, at or immediately prior to such event;
• in the event of a consolidation, merger, combination, reorganization or similar transaction under the terms of which holders of our common stock will receive a cash payment per share surrendered in the transaction, making or providing for an equivalent cash payment in exchange for the termination of such equity awards; or
• providing that in the event of a liquidation or dissolution awards will convert into the right to receive liquidation proceeds.
• The majority of the awards granted under the 2008 stock incentive plan provide that the unvested portion of such award would become fully vested upon specified changes of control of our company.

Transferability. Awards made under the 2008 stock incentive plan are not transferable except by will or by the laws of descent or distribution or, other than in the case of an incentive stock option, pursuant to a domestic relations order.

2014 Employee Stock Purchase Plan

In January 2014, our board of directors adopted and our stockholders approved the 2014 Employee Stock Purchase Plan, or the 2014 ESPP, which became effective immediately prior to the closing of our IPO. Under the 2014 ESPP, as of February 28, 2018, an aggregate of 10,899 shares of the Company’s common stock are reserved for issuance. Our compensation committee administers the 2014 ESPP.

The 2014 ESPP provides for six month purchase plan periods during which eligible employees can elect to have wages or salary withheld through payroll deductions for the purpose of purchasing shares at the end of the period. All of our employees or employees of any designated subsidiary, as defined in the 2014 ESPP, are eligible to participate in the 2014 ESPP, provided that:

• such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year;
• such person has been employed by us or a designated subsidiary for at least three months prior to enrolling in the 2014 ESPP; and
• such person was our employee or an employee of a designated subsidiary on the first day of the applicable purchase plan period under the 2014 ESPP.
No employee is eligible to receive an option to purchase shares of our common stock that would result in the employee owning 5% or more of the total combined voting power or value of our stock immediately after the grant of such option.

Purchase plan periods under the 2014 ESPP will commence at such time or times as our board of directors determines. The last purchase plan period under the 2014 ESPP was from March 1, 2017 through August 31, 2017. Payroll deductions made during each purchase plan period will be held for the purchase of our common stock at the end of each purchase plan period.

On the offering commencement date of each purchase plan period, we will grant to each eligible employee who is then a participant in the 2014 ESPP an option to purchase shares of our common stock. The employee may authorize up to a maximum of 10% of his or her base pay to be deducted by us during the purchase plan period. Each employee who continues to be a participant in the 2014 ESPP on the last business day of the purchase plan period is deemed to have exercised the option, to the extent of accumulated payroll deductions within the 2014 ESPP ownership limits. Under the terms of the 2014 ESPP, the option exercise price shall be determined by our board of directors for each purchase plan period and the option exercise price will be at least 85% of the applicable closing price. If our board of directors does not make a determination of the option exercise price, the option exercise price will be 85% of the lesser of the closing price of our common stock on either the first business day of the purchase plan period or the last business day of the purchase plan period. In no event may an employee purchase in any one purchase plan period a number of shares that exceeds the number of shares determined by dividing (1) the product of $2,083 and the number of full months in the purchase plan period by (2) the closing price of a share of our common stock on the commencement date of the purchase plan period.

Our board of directors may, in its discretion, choose a different purchase plan period of twelve months or less for each offering.

An employee who is not a participant on the last day of the purchase plan period is not entitled to exercise any option, and the employee’s accumulated payroll deductions will be refunded. An employee’s rights under the purchase plan terminate upon voluntary withdrawal from the purchase plan at any time, or when the employee ceases employment for any reason.

We are required to make equitable adjustments in connection with the 2014 ESPP and any outstanding awards to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combination of shares, reclassification of shares, spin-offs and other similar changes in capitalization.

Upon the occurrence of a reorganization event, as defined in the 2014 ESPP, our board of directors is authorized to take any one or more of the following actions as to outstanding options under the 2014 ESPP:

• provide that options will be assumed, or substantially equivalent options will be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);

• upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by our board of directors;

• upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;

• upon the occurrence of a reorganization event in which holders of our common stock will receive a cash payment for each share surrendered in the reorganization event, change the last day of the purchase plan period to be the date of the consummation of the reorganization event and provide that participants will receive a cash payment equal to the acquisition price times the number of shares of common stock that the participant’s accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the option price minus the result of multiplying such number of shares by such option price; and

• provide that, in connection with a liquidation or dissolution of our company, options will convert into the right to receive liquidation proceeds (net of the option price).
Our board of directors may at any time, and from time to time, amend or suspend the 2014 ESPP. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Code. Further, our board of directors may not make any amendment that would cause the 2014 ESPP to fail to comply with Section 423 of the Code. Our board of directors may terminate the 2014 ESPP at any time. Upon termination, we will refund all amounts in the accounts of participating employees.

**Director Compensation**

Our non-employee director compensation program is designed to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors’ interests with those of our stockholders. The form and amount of director compensation paid under our program is reviewed and assessed from time to time by the compensation committee with changes, if any, recommended to the board for action. Director compensation may take the form of cash, equity, and other benefits ordinarily available to directors.

Our non-employee director compensation program provides that non-employee directors receive a grant of stock options to purchase 1,500 shares upon election to the board, which option vests in equal quarterly installments over a term of three years so long as such person continues to serve as a director and an annual grant of options to purchase 750 shares upon the annual meeting of stockholders, which option vests in equal quarterly installments over a term of one year so long as such person continues to serve as a director. These grants are made under our 2014 stock incentive plan. The non-employee director compensation program also provides for our non-employee directors to receive an annual retainer of $40,000, and an additional retainer of $25,000 in the event such director is the chairman or lead director. If the non-employee director is a member of our audit or compensation committee, he or she would receive an additional $7,500 retainer, which is increased to $15,000 if such director is serving as the chair of such committee. If the non-employee director is a member of our nominating and corporate governance committee, he or she would receive an additional $5,000 retainer, which is increased to $10,000 if such director is serving as the chair of such committee. These retainers are paid to each non-employee director quarterly in arrears.

We reimburse each non-employee director for reasonable travel expenses and fees incurred in connection with attendance at board and committee meetings on our behalf, and for expenses such as supplies.

**2017 Compensation of Non-Employee Directors**

Our non-employee directors received the following aggregate amounts of compensation in respect of the year ended December 31, 2017:

<table>
<thead>
<tr>
<th>Name</th>
<th>Fees Earned or Paid in Cash ($)</th>
<th>Option Awards (1) ($)</th>
<th>Total ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hubert Birner, Ph.D.</td>
<td>82,500</td>
<td>35,226</td>
<td>117,726</td>
</tr>
<tr>
<td>Robert F. Carey</td>
<td>87,500</td>
<td>35,226</td>
<td>122,726</td>
</tr>
<tr>
<td>Igor Krol</td>
<td>40,000</td>
<td>35,226</td>
<td>75,226</td>
</tr>
<tr>
<td>Irackly Mtibelishvily</td>
<td>45,000</td>
<td>—</td>
<td>45,000</td>
</tr>
<tr>
<td>Richard G. Morrison (2)</td>
<td>11,875</td>
<td>3,754</td>
<td>15,629</td>
</tr>
<tr>
<td>Ralph Snyderman, M.D. (3)</td>
<td>13,750</td>
<td>—</td>
<td>13,750</td>
</tr>
<tr>
<td>Sander van Deventer, M.D., Ph.D.</td>
<td>55,000</td>
<td>35,226</td>
<td>90,226</td>
</tr>
</tbody>
</table>

(1) The amounts shown in this column reflect the aggregate grant date fair value of the option awards granted to our non-employee directors computed in accordance with the FASB ASC Topic 718. The assumptions made in determining the fair values of our option awards are set forth in Note 11 of the notes to our financial statements presented elsewhere in this Annual Report on Form 10-K. As of December 31, 2017, the aggregate number of unexercised options to purchase shares of our common stock outstanding for each director listed above, including both vested and unvested shares, was as follows: Dr. Birner, 1,575 shares; Mr. Carey, 1,300 shares; Mr. Krol, 1,025 shares; Mr. Mtibelishvily, 1,500 shares; Mr. Morrison, 1,500 shares; and Dr. van Deventer, 1,575 shares.

(2) Richard G. Morrison joined our board of directors in September 2017.

(3) Ralph Snyderman resigned from our board of directors in March 2017.
None of our executive officers serves as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee. None of the members of our compensation committee is, or has ever been, an officer or employee of our company. The current members of our compensation committee are Richard G. Morrison and Robert F. Carey. Mr. Morrison chairs our compensation committee. Ralph Snyderman, M.D. served as a member of our compensation committee from December 2016 to March 2017 at which time he ceased to serve as a member of our board of directors. Sander van Deventer served as a member and chairman of our compensation committee during the fiscal year ended December 31, 2017 until January 2018.
Equity Compensation Plan Information

The following table shows information relating to our equity compensation plans as of December 31, 2017.

<table>
<thead>
<tr>
<th>Plan Category</th>
<th>Number of securities to be issued upon exercise of outstanding options, warrants and rights</th>
<th>Weighted average exercise price of outstanding options, warrants and rights</th>
<th>Number of securities remaining available for future issuance under equity compensation plans (excluding securities in first column) (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equity compensation plans approved by security holders</td>
<td>269,514</td>
<td>$111.91</td>
<td>16,634</td>
</tr>
<tr>
<td>Equity compensation plans not approved by security holders</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td>269,514</td>
<td>$111.91</td>
<td>16,634</td>
</tr>
</tbody>
</table>

(1) Reflects the total number of shares of our common stock available for issuance under the 2014 stock incentive plan and the 2014 ESPP as of December 31, 2017. Our 2014 stock incentive plan contains an “evergreen” provision that currently provides for an annual increase in the number of shares of our common stock available for issuance under the plan on the first day of each fiscal year beginning with the fiscal year ending December 31, 2018 and continuing each fiscal year until, and including, the fiscal year ending December 31, 2024, equal to the lowest of 250,000 shares of common stock, four percent (4%) of the outstanding shares of common stock on such date or an amount determined by our board of directors. On January 1, 2018, 236,264 additional shares of our common stock were authorized for issuance under the 2014 stock incentive plan.
The following table sets forth information with respect to the beneficial ownership of our common stock, as of February 28, 2018 by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options or warrants that are currently exercisable or exercisable within 60 days of February 28, 2018 are considered outstanding and beneficially owned by the person holding the options or warrants for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable.

Except as otherwise set forth in the footnotes below, the address of the beneficial owner is c/o Argos Therapeutics, Inc., 4233 Technology Drive, Durham, North Carolina 27704. Beneficial ownership representing less than one percent of our outstanding common stock is denoted with an “*.”

<table>
<thead>
<tr>
<th>Name and Address of Beneficial Owner</th>
<th>Number of Shares Beneficially Owned</th>
<th>Percentage of Shares Beneficially Owned</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>5% Stockholders:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmstandard International S.A. (1)</td>
<td>1,682,183</td>
<td>18.83%</td>
</tr>
<tr>
<td>ForArgos B.V. (2)</td>
<td>450,616</td>
<td>5.60</td>
</tr>
<tr>
<td><strong>Directors and Named Executive Officers:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sander van Deventer, M.D., Ph.D. (3)</td>
<td>452,443</td>
<td>5.62</td>
</tr>
<tr>
<td>Hubert Birner, Ph.D. (4)</td>
<td>115,946</td>
<td>1.46</td>
</tr>
<tr>
<td>Robert Carey (5)</td>
<td>1,610</td>
<td>*</td>
</tr>
<tr>
<td>Irackly Mtibelishvily (6)</td>
<td>1,369</td>
<td>*</td>
</tr>
<tr>
<td>Igor Krol (7)</td>
<td>983</td>
<td>*</td>
</tr>
<tr>
<td>Richard G. Morrison (8)</td>
<td>250</td>
<td>*</td>
</tr>
<tr>
<td>Jeffrey D. Abbey (9)</td>
<td>77,863</td>
<td>*</td>
</tr>
<tr>
<td>Charles A. Nicolette, Ph.D. (10)</td>
<td>44,441</td>
<td>*</td>
</tr>
<tr>
<td>Richard D. Katz (11)</td>
<td>17,899</td>
<td>*</td>
</tr>
<tr>
<td>All executive officers and directors as a group (10 persons) (12)</td>
<td>733,361</td>
<td>8.98%</td>
</tr>
</tbody>
</table>

(1) The address of Pharmstandard International S.A. is 65, Boulevard Grande Duchesse Charlotte, L-1331 Luxembourg, Grand Duchy of Luxembourg. Consists of (i) 657,139 shares of common stock (ii) warrants to purchase 256,030 shares of common stock (iii) 600,000 shares of common stock issuable upon conversion of the principal under the convertible note and (iv) 169,014 shares of common stock issuable within 60 days of February 28, 2018 in consideration for the rights granted under the Option Agreement (as defined below). This number does not include shares of common issuable upon conversion of the accrued interest under the convertible note. Pharmstandard International S.A. is a wholly owned subsidiary of Joint Stock Company “Pharmstandard.” As the parent entity, Joint Stock Company “Pharmstandard” has voting and investment control over the shares of the Company held by Pharmstandard International S.A.
The address of ForArgos B.V. is Gooimeer 2-35 1411 DC Naarden, the Netherlands. Consists of (i) 309,998 shares of common stock held by ForArgos B.V. and (ii) warrants to purchase 140,618 shares of common stock. Forbion 1 Management B.V., the director of ForArgos B.V., has voting and investment power over the shares and warrants held by ForArgos B.V., which are exercised through Forbion 1 Management B.V.’s investment committee, consisting of L.P.A. Bergstein, H. A. Slootweg, M. A. van Osch, G. J. Mulder and Sander van Deventer. None of the members of the investment committee has individual voting and investment power with respect to such shares, and the members disclaim beneficial ownership of such shares except to the extent of their pecuniary interests therein.

Consists of (i) 450,616 shares of common stock beneficially owned by ForArgos B.V. as described in footnote (2) above, (ii) 252 shares of common stock owned directly and (iii) 1,575 shares of common stock issuable upon exercise of options that are exercisable as of February 28, 2018 or will become exercisable within 60 days after such date.

Consists of (i) 113,737 shares of common stock beneficially owned by TVM V Life Science Ventures GmbH & Co. KG, for which Hubert Birner has shared voting and shared investment authority (ii) 634 shares of common stock owned directly and (iii) 1,575 shares of common stock issuable upon exercise of options that are exercisable as of February 28, 2018 or will become exercisable within 60 days after such date. Hubert Birner disclaims beneficial ownership of these shares, except to the extent of their pecuniary interest therein, if any.

Consists of (i) 410 shares of common stock and (ii) 1,200 shares of common stock issuable upon exercise of options that are exercisable as of February 28, 2018 or will become exercisable within 60 days after such date.

Consists of (i) 744 shares of common stock and (ii) 625 shares of common stock issuable upon exercise of options that are exercisable as of February 28, 2018 or will become exercisable within 60 days after such date.

Consists of (i) 193 shares of common stock and (ii) 790 shares of common stock issuable upon exercise of options that are exercisable as of February 28, 2018 or will become exercisable within 60 days after such date.

Consists of 250 shares of common stock issuable upon exercise of options that are exercisable as of February 28, 2018 or will become exercisable within 60 days after such date.

Consists of (i) 25,450 shares of common stock and (ii) 52,413 shares of common stock issuable upon exercise of options that are exercisable as of February 28, 2018 or will become exercisable within 60 days after such date.

Consists of (i) 20,056 shares of common stock and (ii) 24,385 shares of common stock issuable upon exercise of options that are exercisable as of February 28, 2018 or will become exercisable within 60 days after such date.

Consists of (i) 9,697 shares of common stock and (ii) 8,202 shares of common stock issuable upon exercise of options that are exercisable as of February 28, 2018 or will become exercisable within 60 days after such date.

Consists of (i) 475,726 shares of common stock, (ii) warrants to purchase 157,839 shares of common stock and (iii) 99,796 shares of common stock issuable upon exercise of options that are exercisable as of February 28, 2018 or will become exercisable within 60 days after such date.
Item 13. Certain Relationships and Related Transactions, and Director Independence

Since January 1, 2017, we have engaged in the following transactions, in which the amount involved in the transaction exceeds $120,000 with our directors, executive officers and holders of more than 5% of our voting securities, and affiliates or immediate family members of our directors, executive officers and holders of more than 5% of our voting securities. We believe that all of these transactions were on terms as favorable as we could have obtained from unrelated third parties. Compensation arrangements for our directors and named executive officers are described in “Item 11. Executive Compensation.”

Participation in our 2017 Note Financing

On June 15, 2017, we entered into a note purchase agreement with Pharmstandard International S.A., or Pharmstandard, our principal stockholder, pursuant to which we agreed to issue and sell to Pharmstandard a convertible secured promissory note in the original principal amount of $6,000,000 in a private placement. The financing closed on June 21, 2017. Igor Krol and Irakly Mtibelishvily, both members of our board of directors, are closely associated with Pharmstandard.

On June 21, 2017, we issued the note to Pharmstandard. Under the note, the maturity date for the payment of principal and interest is the fifth anniversary of the issue date. The note bears interest at a rate of 9.5% per annum, which interest will compound annually. As of February 28, 2018, the amount of principal and accrued interest owed under the note was $6,395,096. The note is secured by a lien on and security interest in all of our intellectual property. We may prepay the note in whole or in part at any time without penalty or premium. Upon the occurrence of certain events of default, Pharmstandard has the option to require us to repay the unpaid principal amount of the note and any unpaid accrued interest. In addition, at Pharmstandard’s election, Pharmstandard may elect to convert the principal and interest on the note into shares of our common stock at a price per share equal to $10.00, which is the product of 1.225 and the closing price of our common stock on The Nasdaq Global Market on June 14, 2017. However, Pharmstandard is not permitted to convert the note if such conversion would result in Pharmstandard and its affiliates holding shares that exceed 39.9% of the total number of outstanding shares of our common stock or 39.9% of the combined voting power of all our outstanding securities.

Option Agreement

On February 1, 2018, we entered into an option agreement with Pharmstandard and Actigen Limited, or Actigen, to evaluate, with an option to license, certain patent rights and know-how related to a group of fully human PD1 monoclonal antibodies and related technology held by Actigen.

Actigen previously granted Pharmstandard an option to exclusively license the patent rights. Under the option agreement, Pharmstandard granted to us (i) an exclusive license for evaluation purposes only to make, have made, use and import the PD1 monoclonal antibodies covered by the patent rights (but not offer to sell or sell products and processes covered by or incorporating the patent rights) for a period of one year from the date of the agreement, and (ii) an option exercisable during the one-year exercise period to obtain an exclusive license (with the right to sublicense) under the patent rights to make, have made, use, offer for sale, sell and import (with a right to grant sublicenses) the PD1 monoclonal antibodies for all prophylactic, therapeutic and diagnostic uses and for all human diseases and conditions in the United States and Canada. The parties have agreed that, if we exercise the option during the one-year exercise period, the parties will negotiate in good faith a license agreement on or before April 2, 2018, on the terms and conditions outlined in the option agreement, including payments by us to Pharmstandard of (i) an upfront license fee of $3.6 million, payable upon execution of the license agreement in our common stock, (ii) various development and regulatory milestone payments totaling $8.5 million, and (iii) upper single digit percentage royalties on net sales of any pharmaceutical product or therapeutic regimen incorporating the licensed PD1 monoclonal antibodies that will apply on a country-by-country basis until the later of the last to expire patent or ten years from the date of first commercial sale, against which the first $5.0 million of our development expenditures will be credited as prepaid royalties.
In consideration for the rights granted under the option agreement, we will issue to Pharmstandard, on or before April 2, 2018 169,014 shares of our common stock, the value of which will be creditable against the upfront license fee. Unless earlier terminated by any party for uncured material breach or by us without cause upon thirty days prior written notice, the option agreement will terminate upon the later of the end of the one year exercise period if we decide not to exercise the option or sixty days after we exercise the option.

Indemnification Agreements

Our certificate of incorporation provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered into indemnification agreements with all of our directors and executive officers. These agreements may require us, among other things, to indemnify each such director for some expenses, including attorneys’ fees, judgments, fines and settlement amounts incurred by him in any action or proceeding arising out of his service as one of our directors.

401(k) Retirement Plan

We maintain a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code. In general, all of our employees are eligible to participate, beginning on the first day of the month following commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to $18,000 in 2017, and have the amount of the reduction contributed to the 401(k) plan. For the years ended December 31, 2017 and 2016, we matched 50% of an employee’s contribution up to a maximum of 6% of the participant’s compensation. Matching contributions made to each of our named executive officers are included in the “All Other Compensation” column in the summary compensation table in the section “Executive Compensation – Summary Compensation Table” above.

Policies and Procedures for Related Person Transactions

Our board of directors has adopted written policies and procedures for the review of any transaction, arrangement or relationship in which we are a participant, the amount involved exceeds $120,000, and one of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, each of whom we refer to as a “related person,” has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a “related person transaction,” the related person must report the proposed related person transaction to our chief executive officer. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the committee after full disclosure of the related person’s interest in the transaction. As appropriate for the circumstances, the committee will review and consider:

- the related person’s interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person’s interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
• the purpose of, and the potential benefits to us of, the transaction; and

• any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

The committee may approve or ratify the transaction only if the committee determines that, under all of the circumstances, the transaction is in, or is not inconsistent with, our best interests. The committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC’s related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

• interests arising solely from the related person’s position as an executive officer of another entity (whether or not the person is also a director of such entity), that is a participant in the transaction, where (a) the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, (b) the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction, and (c) the amount involved in the transaction equals less than the greater of $200,000 dollars or 5% of the annual gross revenues of the other entity that is a party to the transaction; and

• a transaction that is specifically contemplated by provisions of our charter or bylaws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by the compensation committee in the manner specified in its charter.
Director Independence

Applicable Nasdaq rules require a majority of a listed company’s board of directors to be comprised of independent directors. In addition, Nasdaq rules require that, subject to specified exceptions, each member of a listed company’s audit, compensation and nominating and corporate governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and that compensation committee members satisfy independence criteria set forth in Rule 10C-1 under the Exchange Act. Under applicable Nasdaq rules, a director only qualifies as an “independent director” if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In addition, in affirmatively determining the independence of any director who will serve on a listed company’s compensation committee, Rule 10C-1 under the Exchange Act requires that a company’s board of directors must consider all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director’s ability to be independent from management in connection with the duties of a compensation committee member, including: the source of compensation to the director, including any consulting, advisory or other compensatory fee paid by such company to the director, and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

Our board of directors has determined that all of our directors who served during the fiscal year ended December 31, 2017, other than Mr. Abbey, are independent directors, in each case as defined by applicable Nasdaq rules, including, in the case of all directors who served on our audit committee during the fiscal year ended December 31, 2017, the independence criteria set forth in Rule 10A-3 under the Exchange Act, and in the case of all directors who served on our compensation committee during the fiscal year ended December 31, 2017, the independence criteria set forth in Rule 10C-1 under the Exchange Act. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deems relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director.
Item 14. Principal Accountant Fees and Services

PricewaterhouseCoopers LLP has been approved by our audit committee to act as our independent registered public accounting firm for the year ending December 31, 2017.

Audit and other fees billed to us by PricewaterhouseCoopers, LLP for the years ended December 31, 2017 and 2016 are as follows:

<table>
<thead>
<tr>
<th>Service Type</th>
<th>2017</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Audit Fees (1)</td>
<td>$398,100</td>
<td>$403,564</td>
</tr>
<tr>
<td>Audit-Related Fees (2)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Tax Fees (3)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>All Other Fees (4)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total Fees for Services Provided</td>
<td>$398,100</td>
<td>$403,564</td>
</tr>
</tbody>
</table>

(1) Audit fees include fees associated with the annual audit, reviews of interim financial statements included in our quarterly reports on Form 10-Q and SEC registration statements, accounting and reporting consultations.

(2) There were no audit-related fees for the years ended December 31, 2017 or 2016.

(3) There were no tax fees for the years ended December 31, 2017 or 2016.

(4) Other fees include fees billed for other services rendered not included within Audit Fees, Audit Related Fees or Tax Fees. There were no other fees for the years ended December 31, 2017 or 2016. PricewaterhouseCoopers LLP did not perform any professional services related to financial information systems design and implementation for us in the year ended December 31, 2017 or 2016.

The audit committee has determined in its business judgment that the provision of non-audit services described above is compatible with maintaining PricewaterhouseCoopers LLP’s independence.

In 2014, the audit committee adopted a formal policy concerning approval of audit and non-audit services to be provided to the Company by its independent registered public accounting firm, PricewaterhouseCoopers LLP. The policy requires that all services to be provided by PricewaterhouseCoopers LLP, including audit services and permitted audit-related and non-audit services, must be preapproved by the audit committee, provided that de minimis non-audit services may instead be approved in accordance with applicable SEC rules. The board of directors preapproved all audit and non-audit services provided by PricewaterhouseCoopers LLP during years ended December 31, 2017 and 2016.
PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are included in this Annual Report on Form 10-K:

1. The following Report and Consolidated Financial Statements of the Company are included in this Annual Report:

   Report of Independent Registered Public Accounting Firm
   Consolidated Balance Sheets
   Consolidated Statements of Operations
   Consolidated Statements of Comprehensive Loss
   Consolidated Statements of Changes in Stockholders’ (Deficit) Equity
   Consolidated Statements of Cash Flows
   Notes to Consolidated Financial Statements
   Financial Statement Schedule:
   Schedule II – Valuation and Qualifying Accounts

2. All other schedules are omitted as they are inapplicable or the required information is furnished in the Consolidated Financial Statements or notes thereto.

3. Exhibits:

<table>
<thead>
<tr>
<th>Exhibit Number</th>
<th>Description of Exhibit</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 *</td>
<td>Restated Certificate of Incorporation of the Registrant, as amended</td>
</tr>
<tr>
<td>3.2</td>
<td>Amended and Restated Bylaws of the Registrant (filed as Exhibit 3.2 to the Registrant’s Current Report on Form 8-K (File No. 001-35443) on February 18, 2014 and incorporated herein by reference)</td>
</tr>
<tr>
<td>4.1</td>
<td>Specimen Stock Certificate evidencing the shares of common stock (filed as Exhibit 4.1 to Amendment No. 1 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on January 21, 2014 and incorporated herein by reference)</td>
</tr>
<tr>
<td>4.2</td>
<td>Fifth Amended and Restated Registration Rights Agreement, dated as of August 9, 2013 (filed as Exhibit 4.2 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)</td>
</tr>
<tr>
<td>4.3</td>
<td>Amendment No. 1 to Fifth Amended and Restated Registration Rights Agreement, dated September 29, 2014 (amending the Registrant’s Fifth Amended and Restated Registration Rights Agreement, dated August 9, 2013) (filed as Exhibit 4.3 to the Registrant’s Annual Report on Form 10-K on March 16, 2017 and incorporated herein by reference)</td>
</tr>
<tr>
<td>4.4</td>
<td>Amendment No. 2 to Fifth Amended and Restated Registration Rights Agreement, dated July 14, 2016 (amending the Registrant’s Fifth Amended and Restated Registration Rights Agreement, dated August 9, 2013) (filed as Exhibit 4.2 to the Registrant’s Quarterly Report on Form 10-Q (File No. 001-35443) on August 15, 2016 and incorporated herein by reference)</td>
</tr>
<tr>
<td>4.5</td>
<td>Amendment No. 3 to Fifth Amended and Restated Registration Rights Agreement, dated March 6, 2017 (amending the Registrant’s Fifth Amended and Restated Registration Rights Agreement, dated August 9, 2013) (filed as Exhibit 4.5 to the Registrant’s Annual Report on Form 10-K on March 16, 2017 and incorporated herein by reference)</td>
</tr>
<tr>
<td>4.6</td>
<td>Form of Warrant Agreement by and among the Company and Computershare Inc. and Computershare Trust Company, N.A. (filed as Exhibit 4.1 to the Registrant’s Current Report on Form 8-K on July 29, 2016 and incorporated herein by reference)</td>
</tr>
</tbody>
</table>

4.8 Registration Rights Agreement, dated September 22, 2017, by and between the Company and Invtech Pty Ltd (filed as Exhibit 10.2 to the Registrant’s Current Report on Form 8-K filed on September 25, 2017 and incorporated herein by reference)

4.9 Registration Rights Agreement, dated November 22, 2017, by and between the Company and Saint-Gobain Performance Plastics Corporation (filed as exhibit 10.2 to Registrant’s Current Report on Form 8-K filed on November 28, 2017 and incorporated herein by reference)

10.1+ 2008 Stock Incentive Plan, as amended (filed as Exhibit 10.2 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

10.2+ Form of Incentive Stock Option Agreement under 2008 Stock Incentive Plan (filed as Exhibit 10.3 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

10.3+ Form of Nonstatutory Stock Option Agreement under 2008 Stock Incentive Plan (filed as Exhibit 10.4 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

10.4+ 2014 Stock Incentive Plan, as amended (filed as Exhibit 10.1 to the Registrant’s Current Report on Form 8-K filed on August 2, 2017 and incorporated herein by reference)

10.5+ Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan (filed as Exhibit 10.6 to Amendment No. 1 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on January 21, 2014 and incorporated herein by reference)

10.6+ Form of Nonstatutory Stock Option Agreement under 2014 Stock Incentive Plan (filed as Exhibit 10.7 to Amendment No. 1 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on January 21, 2014 and incorporated herein by reference)

10.7 Lease Agreement, dated as of January 16, 2001, between the Registrant and HCP MOP, as amended (filed as Exhibit 10.8 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

10.8+ Employment Agreement between the Registrant and Jeffrey D. Abbey, dated December 9, 2013 (filed as Exhibit 10.9 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

10.9+ Employment Agreement between the Registrant and Charles A. Nicolette, dated December 9, 2013 (filed as Exhibit 10.10 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

10.10+ Employment Agreement between the Registrant and Lori R. Harrelson, dated December 9, 2013 (filed as Exhibit 10.12 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

10.11+ Employment Agreement between the Registrant and Richard D. Katz, dated July 1, 2016 (filed as Exhibit 10.1 to the Registrant’s Current Report on Form 8-K (File No. 001-35443) on July 11, 2016 and incorporated herein by reference)
Form of Indemnification Agreement between the Registrant and each director and executive officer (filed as Exhibit 10.14 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

Contract No. HHSN266200600019C, dated September 30, 2006, by and among the Registrant, the National Institutes of Health and the National Institutes of Allergy and Infectious Diseases, as amended (filed as Exhibit 10.15 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

License Agreement, dated August 9, 2013, by and between the Registrant and Pharmstandard S.A. (filed as Exhibit 10.16 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

License Agreement, dated July 31, 2013, by and between the Registrant and Green Cross Corp. (filed as Exhibit 10.17 to Amendment No. 1 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on January 21, 2014 and incorporated herein by reference)

License Agreement, dated July 28, 2011, by and between the Registrant and Celldex Therapeutics, Inc. (filed as Exhibit 10.18 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

License Agreement, dated January 10, 2000, by and between the Registrant and Duke University, as amended (filed as Exhibit 10.19 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on December 30, 2013 and incorporated herein by reference)

Acknowledgement Agreement, dated November 4, 2013, by and between the Registrant and Pharmstandard International S.A. (filed as Exhibit 10.20 to Amendment No. 1 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on January 21, 2014 and incorporated herein by reference)

2014 Employee Stock Purchase Plan (filed as Exhibit 10.21 to Amendment No. 1 to the Registrant’s Registration Statement on Form S-1 (File No. 333-193137) on January 21, 2014 and incorporated herein by reference)

Lease Agreement, dated August 18, 2014, by and between by and between the Registrant and TKC LXXII, LLC (filed as Exhibit 10.1 to the Registrant’s Current Report on Form 8-K on August 22, 2014 and incorporated herein by reference)

Venture Loan and Security Agreement, dated September 29, 2014, by and between the Registrant and Horizon Technology Finance Corporation and Fortress Credit Co LLC (filed as Exhibit 10.1 to the Registrant’s Current Report on Form 8-K on September 30, 2014 and incorporated herein by reference)

Form of Warrant to Purchase Common Stock, issued to Horizon Technology Finance Corporation on September 29, 2014 (filed as Exhibit 10.2 to the Registrant’s Current Report on Form 8-K on September 30, 2014 and incorporated herein by reference)

Form of Warrant to Purchase Common Stock, issued to Drawbridge Special Opportunities Fund LP on September 29, 2014 (filed as Exhibit 10.3 to the Registrant’s Current Report on Form 8-K on September 30, 2014 and incorporated herein by reference)

Development Agreement, dated October 29, 2014, by and between the Registrant and Invetech Lty Ltd (filed as Exhibit 10.5 to the Registrant’s Quarterly Report on Form 10-Q on November 14, 2014 and incorporated herein by reference)

Development Agreement, dated January 5, 2015, by and between the Registrant and Saint-Gobain Performance Plastics Corporation (filed as Exhibit 10.27 to the Registrant’s Annual Report on Form 10-K on March 31, 2015 and incorporated herein by reference)
Second Amendment to Development Agreement, dated as of December 23, 2016 amending that certain Development Agreement dated January 5, 2015 entered into by and between the Registrant and Saint-Gobain Performance Plastics Corporation (filed as Exhibit 10.28 to the Registrant’s Annual Report on Form 10-K on March 16, 2017 and incorporated herein by reference)

Purchase and Sale Agreement, dated February 16, 2015, by and between the Registrant and TKC LXXII, LLC (filed as Exhibit 10.1 to the Registrant’s Current Report on Form 8-K on February 20, 2015 and incorporated by reference)

Novated, Amended and Restated License Agreement effective as of October 1, 2014, by and between the Registrant and MEDcell Co., Ltd., as amended on December 28, 2015 and January 28, 2016 (filed as Exhibit 10.29 to the Registrant’s Annual Report on Form 10-K on March 31, 2015 and incorporated herein by reference)

Modification No. 11, effective September 18, 2014, to Contract No. HHSN266200600019C dated September 30, 2006, by and among the Registrant, the National Institutes of Health and the National Institutes of Allergy and Infectious Diseases, as amended (filed as Exhibit 10.1 to the Registrant’s Quarterly Report on Form 10-Q on November 16, 2015 and incorporated herein by reference)

License Agreement, dated April 7, 2015, by and between the Registrant and Lummy (Hong Kong) Co., Ltd. (filed as Exhibit 10.2 to the Registrant’s Quarterly Report on Form 10-Q on May 15, 2015 and incorporated herein by reference)

Master Process Development and Supply Agreement, dated December 22, 2015, by and between the Registrant and Cellscript, LLC (filed as Exhibit 10.30 to the Registrant’s Annual Report on Form 10-K on March 30, 2016 and incorporated herein by reference)

Securities Purchase Agreement, dated March 4, 2016, by and between the Registrant and the investors named therein (filed as Exhibit 10.1 to the Registrant’s Current Report on Form 8-K on March 7, 2016 and incorporated herein by reference)

Form of Common Stock Warrant (filed as Exhibit 10.2 to the Registrant’s Current Report on Form 8-K on March 7, 2016 and incorporated herein by reference)

Registration Rights Agreement, dated March 4, 2016, by and between the Registrant and the investors named therein (filed as Exhibit 10.3 to the Registrant’s Current Report on Form 8-K on March 7, 2016 and incorporated herein by reference)

Amended and Restated Sales Agreement, dated February 2, 2018, by and between the Registrant and Cowen and Company, LLC (filed as Exhibit 1.1 to the Registrant’s Current Report on Form 8-K on February 5, 2018 and incorporated herein by reference)

Fifth Amendment to Lease Agreement and Third Amendment to Purchase and Sale Agreement, dated as of July 1, 2016 amending that certain Lease Agreement, dated August 18, 2014, by and between the Registrant and TKC LXXII, LLC and that certain Purchase and Sale Agreement, dated February 16, 2015, by and between the Registrant and TKC LXXII, LLC (filed as Exhibit 10.3 to the Registrant’s Quarterly Report on Form 10-Q (File No. 001-35443 on August 15, 2016 and incorporated herein by reference)

Sixth Amendment to Lease Agreement and Fourth Amendment to Purchase and Sale Agreement, dated as of September 30, 2016 amending that certain Lease Agreement, dated August 18, 2014, by and between the Registrant and TKC LXXII, LLC and that certain Purchase and Sale Agreement, dated February 16, 2015, by and between the Registrant and TKC LXXII, LLC (filed as Exhibit 10.4 to the Registrant’s Quarterly Report on Form 10-Q (File No. 001-35443) on November 14, 2016 and incorporated herein by reference)

Payoff Letter, entered into as of March 3, 2017, among Argos Therapeutics, Inc. and the lenders under the Venture Loan and Security Agreement, dated as of September 29, 2014 (filed as Exhibit 10.1 to the Registrant’s Current Report on Form 8-K on March 6, 2017 and incorporated herein by reference)

Warrant issued to Horizon Technology Finance Corporation, dated March 3, 2017 (filed as Exhibit 10.2 to the Registrant’s Current Report on Form 8-K on March 6, 2017 and incorporated herein by reference)

Warrant issued to Fortress Credit Opportunities V CLO Limited, dated March 3, 2017 (filed as Exhibit 10.3 to the Registrant’s Current Report on Form 8-K on March 6, 2017 and incorporated herein by reference)

Modification No. 13, effective June 29, 2016, to Contract No. HHSN266200600019C dated September 30, 2006, by and among the Registrant, the National Institutes of Health and the National Institutes of Allergy and Infectious Diseases, as amended (filed as Exhibit 10.44 to the Registrant’s Annual Report on Form 10-K on March 16, 2017 and incorporated herein by reference)

First Amendment to License Agreement, dated December 5, 2016, by and between Registrant and Lummy (Hong Kong) Co., Ltd. (filed as Exhibit 10.6 to the Registrant’s Quarterly Report on Form 10-Q on May 10, 2017 and incorporated herein by reference)

Lease Termination Agreement, dated March 31, 2017, by and between Registrant and Keystone-Centennial II, LLC (filed as Exhibit 10.7 to the Registrant’s Quarterly Report on Form 10-Q on May 10, 2017 and incorporated herein by reference)

Note Purchase Agreement, dated June 15, 2017, by and between the Company and Pharmstandard International S.A., including a form of the Convertible Secured Promissory Note to be issued by the Company and the Security Agreement to be entered into by the Company and Pharmstandard International S.A. (filed as Exhibit 10.1 to the Registrant’s Current Report on Form 8-K filed on June 16, 2017 and incorporated herein by reference)

Satisfaction and Release Agreement, dated September 22, 2017, by and between the Company and Invetech Pty Ltd, including a form of Convertible Unsecured Promissory Note to be issued by the Company (filed as Exhibit 10.1 to the Registrant’s Current Report on Form 8-K filed on September 25, 2017 and incorporated herein by reference)

Form of Restricted Stock Agreement under the 2014 Stock Incentive Plan (filed as Exhibit 10.4 to the Registrant’s Quarterly Report on Form 10-Q filed on November 9, 2017 and incorporated herein by reference)

Satisfaction and Release Agreement, dated November 22, 2017, by and between the Company and Saint-Gobain Performance Plastics Corporation, including a form of the Convertible Unsecured Promissory Note to be issued by the Company (filed as exhibit 10.1 to Registrant’s Current Report on Form 8-K filed on November 28, 2017 and incorporated herein by reference)

Option Agreement, dated February 1, 2018, by and between the Registrant, Pharmstandard International S.A. and Actigen Limited

Second Amendment to License Agreement, dated October 18, 2017, between Registrant and Lummy (Hong Kong) Co., Ltd.

Third Amendment to License Agreement, dated March 23, 2018, between Registrant and Lummy (Hong Kong) Co., Ltd.
Subsidiaries of the Registrant (filed as Exhibit 21.1 to the Registrant’s Registration Statement on Form S-1 on December 30, 2013 and incorporated herein by reference)

Consent of PricewaterhouseCoopers LLP, an independent registered public accounting firm

Certification of principal executive officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

Certification of principal financial officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

Certifications pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002, by the Registrant’s principal executive officer and principal financial officer

101.INS XBRL Instance Document

101.SCH XBRL Taxonomy Extension Schema Document

101.CAL XBRL Taxonomy Extension Calculation Linkbase Document

101.DEF XBRL Taxonomy Extension Definition Linkbase Document

101.LAB XBRL Taxonomy Extension Label Linkbase Document

101.PRE XBRL Taxonomy Extension Presentation Linkbase Document

†Confidential treatment granted as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission

# Confidential treatment requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

+ Management contract or compensatory plan or arrangement required to be filed as exhibits hereto pursuant to Item 15(a) of Form 10-K.

* Filed herewith.

**Item 16. Form 10-K Summary**

Not Applicable.
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.

ARGOS THERAPEUTICS, INC.

By: /s/ Jeffrey D. Abbey  
Name: Jeffrey D. Abbey  
Title: President and Chief Executive Officer  
Date: April 2, 2018

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant on April 2, 2018 in the capacities indicated.

<table>
<thead>
<tr>
<th>Signature</th>
<th>Title</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>/s/ Jeffrey D. Abbey</td>
<td>President, Chief Executive Officer and Director (Principal Executive Officer)</td>
<td>April 2, 2018</td>
</tr>
<tr>
<td>Jeffrey D. Abbey</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Richard D. Katz</td>
<td>Vice President and Chief Financial Officer (Principal Financial Officer)</td>
<td>April 2, 2018</td>
</tr>
<tr>
<td>Richard D. Katz, M.D.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Lori R. Harrelson</td>
<td>Vice President of Finance (Principal Accounting Officer)</td>
<td>April 2, 2018</td>
</tr>
<tr>
<td>Lori R. Harrelson</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Hubert Birner</td>
<td>Director</td>
<td>April 2, 2018</td>
</tr>
<tr>
<td>Hubert Birner, Ph.D.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Robert F. Carey</td>
<td>Director</td>
<td>April 2, 2018</td>
</tr>
<tr>
<td>Robert F. Carey</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Igor Krol</td>
<td>Director</td>
<td>April 2, 2018</td>
</tr>
<tr>
<td>Igor Krol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Richard G. Morrison</td>
<td>Director</td>
<td>April 2, 2018</td>
</tr>
<tr>
<td>Richard G. Morrison</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Irackly Mtibelishvily</td>
<td>Director</td>
<td>April 2, 2018</td>
</tr>
<tr>
<td>Irackly Mtibelishvily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Sander van Deventer</td>
<td>Director</td>
<td>April 2, 2018</td>
</tr>
<tr>
<td>Sander van Deventer, M.D., Ph.D.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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<td></td>
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<td>Consolidated Statements of Operations</td>
<td>F-4</td>
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<td>Consolidated Statements of Comprehensive Loss</td>
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<td>Consolidated Statements of Changes in Stockholders' Equity (Deficit)</td>
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<td>Consolidated Statements of Cash Flows</td>
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<td>Financial Statement Schedule:</td>
<td></td>
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<tr>
<td>Schedule II – Valuation and Qualifying Accounts</td>
<td>F-43</td>
</tr>
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F-1
Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Argos Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Argos Therapeutics, Inc. and its subsidiaries as of December 31, 2017 and 2016, and the related consolidated statements of operations, comprehensive loss, changes in stockholders’ equity (deficit), and cash flows for each of the three years in the period ended December 31, 2017, including the related notes and financial statement schedule of valuation and qualifying accounts for each of the three years in the period ended December 31, 2017 listed in the accompanying index (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, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017 in conformity with accounting principles generally accepted in the United States of America.

Substantial Doubt About the Company’s Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has suffered recurring losses from operations and has an accumulated deficit that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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

/s/PricewaterhouseCoopers LLP

Raleigh, North Carolina
April 2, 2018

We have served as the Company's auditor since 2001.
ARGOS THERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS

December 31, 2016 2017

<table>
<thead>
<tr>
<th>Assets</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>$52,973,376</td>
<td>$15,188,838</td>
</tr>
<tr>
<td>Assets held for sale</td>
<td>1,452,172</td>
<td>600,000</td>
</tr>
<tr>
<td>Prepaid expenses</td>
<td>940,106</td>
<td>1,252,134</td>
</tr>
<tr>
<td>Other receivables</td>
<td>136,140</td>
<td>143,449</td>
</tr>
<tr>
<td><strong>Total current assets</strong></td>
<td>$55,501,794</td>
<td>$17,184,421</td>
</tr>
<tr>
<td>Property and equipment, net</td>
<td>40,951,577</td>
<td>3,582,323</td>
</tr>
<tr>
<td>Restricted cash</td>
<td>740,000</td>
<td>—</td>
</tr>
<tr>
<td>Other assets</td>
<td>11,020</td>
<td>11,020</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td>$97,204,391</td>
<td>$20,777,764</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Liabilities and Stockholders’ Equity (Deficit)</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current liabilities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accounts payable</td>
<td>$5,377,377</td>
<td>$970,650</td>
</tr>
<tr>
<td>Accrued expenses</td>
<td>9,980,891</td>
<td>1,263,867</td>
</tr>
<tr>
<td>Current portion of notes payable</td>
<td>11,475,480</td>
<td>4,972,649</td>
</tr>
<tr>
<td>Current portion of other convertible notes</td>
<td>—</td>
<td>2,350,000</td>
</tr>
<tr>
<td>Current portion of manufacturing research and development obligation</td>
<td>3,653,203</td>
<td>—</td>
</tr>
<tr>
<td>Current portion of capital lease obligations</td>
<td>122,887</td>
<td>—</td>
</tr>
<tr>
<td><strong>Total current liabilities</strong></td>
<td>$30,609,838</td>
<td>9,557,166</td>
</tr>
<tr>
<td>Convertible note payable to related party</td>
<td>—</td>
<td>6,302,959</td>
</tr>
<tr>
<td>Long-term portion of other convertible notes</td>
<td>—</td>
<td>5,830,583</td>
</tr>
<tr>
<td>Long-term portion of notes payable</td>
<td>18,673,298</td>
<td>—</td>
</tr>
<tr>
<td>Long-term portion of manufacturing research and development obligation</td>
<td>4,509,033</td>
<td>—</td>
</tr>
<tr>
<td>Long-term portion of facility lease obligation</td>
<td>7,390,000</td>
<td>—</td>
</tr>
<tr>
<td>Long-term portion of capital lease obligations</td>
<td>2,202,966</td>
<td>—</td>
</tr>
<tr>
<td>Deferred liabilities</td>
<td>6,723,500</td>
<td>8,153,500</td>
</tr>
<tr>
<td>Warrants</td>
<td>20,926,061</td>
<td>167,636</td>
</tr>
<tr>
<td><strong>Stockholders’ equity (deficit)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preferred stock $0.001 par value; 5,000,000 shares authorized as of December 31, 2016 and 2017; 0 shares issued and outstanding as of December 31, 2016 and 2017</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Common stock $0.001 par value; 200,000,000 shares authorized as of December 31, 2016 and 2017; 2,063,158 and 5,906,620 shares issued and outstanding as of December 31, 2016 and 2017</td>
<td>2,063</td>
<td>5,907</td>
</tr>
<tr>
<td>Accumulated other comprehensive loss</td>
<td>(134,208)</td>
<td>(125,864)</td>
</tr>
<tr>
<td>Additional paid-in capital</td>
<td>338,288,657</td>
<td>363,450,204</td>
</tr>
<tr>
<td>Accumulated deficit</td>
<td>(331,986,817)</td>
<td>(372,564,327)</td>
</tr>
<tr>
<td><strong>Total stockholders’ equity (deficit)</strong></td>
<td>$6,169,695</td>
<td>(9,234,080)</td>
</tr>
<tr>
<td><strong>Total liabilities and stockholders’ equity (deficit)</strong></td>
<td>$97,204,391</td>
<td>$20,777,764</td>
</tr>
</tbody>
</table>

The accompanying notes are an integral part of these consolidated financial statements.
# ARGOS THERAPEUTICS, INC.

## CONSOLIDATED STATEMENTS OF OPERATIONS

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Revenue</strong></td>
<td>$518,329</td>
<td>$945,468</td>
<td>$1,899,398</td>
</tr>
<tr>
<td><strong>Operating expenses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>62,054,823</td>
<td>38,307,236</td>
<td>21,656,096</td>
</tr>
<tr>
<td>General and administrative</td>
<td>11,011,011</td>
<td>14,203,301</td>
<td>12,183,235</td>
</tr>
<tr>
<td>Impairment of property and equipment</td>
<td>—</td>
<td>741,114</td>
<td>27,254,385</td>
</tr>
<tr>
<td>Restructuring costs</td>
<td>—</td>
<td>—</td>
<td>6,031,779</td>
</tr>
<tr>
<td>Gain on disposal of impaired property</td>
<td>—</td>
<td>—</td>
<td>(2,767,540)</td>
</tr>
<tr>
<td><strong>Total operating expenses</strong></td>
<td>73,065,834</td>
<td>53,251,651</td>
<td>64,357,955</td>
</tr>
<tr>
<td><strong>Operating loss</strong></td>
<td>(72,547,505)</td>
<td>(52,306,183)</td>
<td>(62,458,557)</td>
</tr>
<tr>
<td><strong>Other income (expense)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interest income</td>
<td>25,382</td>
<td>57,326</td>
<td>64,485</td>
</tr>
<tr>
<td>Interest expense</td>
<td>(2,263,599)</td>
<td>(1,774,740)</td>
<td>(1,308,201)</td>
</tr>
<tr>
<td>Gain on early extinguishment of debt</td>
<td>—</td>
<td>—</td>
<td>2,356,478</td>
</tr>
<tr>
<td>Change in fair value of warrant liability</td>
<td>—</td>
<td>1,007,352</td>
<td>20,758,425</td>
</tr>
<tr>
<td><strong>Other (loss) income</strong></td>
<td>(2,799)</td>
<td>(11,865)</td>
<td>9,860</td>
</tr>
<tr>
<td><strong>Other income (expense), net</strong></td>
<td>(2,241,016)</td>
<td>(721,927)</td>
<td>21,881,047</td>
</tr>
<tr>
<td><strong>Net loss</strong></td>
<td>$ (74,788,521)</td>
<td>$ (53,028,110)</td>
<td>$ (40,577,510)</td>
</tr>
<tr>
<td>Net loss attributable to common stockholders per share, basic and diluted</td>
<td>$ (73.12)</td>
<td>$ (33.14)</td>
<td>$ (13.45)</td>
</tr>
<tr>
<td>Weighted average shares outstanding, basic and diluted</td>
<td>1,022,862</td>
<td>1,600,286</td>
<td>3,017,409</td>
</tr>
</tbody>
</table>

The accompanying notes are an integral part of these consolidated financial statements.
ARGOS THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

<table>
<thead>
<tr>
<th></th>
<th>Year Ended December 31,</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2015</td>
<td>2016</td>
<td>2017</td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td>$(74,788,521)</td>
<td>$(53,028,110)</td>
<td>$(40,577,510)</td>
<td></td>
</tr>
<tr>
<td>Other comprehensive loss:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foreign currency translation (loss) gain</td>
<td>(25,061)</td>
<td>3,766</td>
<td>8,344</td>
<td></td>
</tr>
<tr>
<td>Unrealized (loss) gain on short-term investments</td>
<td>11,657</td>
<td>271</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Total comprehensive loss</td>
<td>$(74,801,925)</td>
<td>$(53,024,073)</td>
<td>$(40,569,166)</td>
<td></td>
</tr>
</tbody>
</table>

The accompanying notes are an integral part of these consolidated financial statements.
## CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS’ EQUITY (DEFICIT)

<table>
<thead>
<tr>
<th>Shares</th>
<th>Common Stock</th>
<th>Additional Paid-in Capital</th>
<th>Accumulated Other Comprehensive Income (Loss)</th>
<th>Accumulated Deficit</th>
<th>Total Stockholders’ Equity (Deficit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>982,870</td>
<td>$ 983</td>
<td>$ 235,645,848</td>
<td>$(124,841)</td>
<td>$(204,170,186)</td>
<td>$ 31,351,804</td>
</tr>
<tr>
<td>95,309</td>
<td>95</td>
<td>10,681,337</td>
<td>—</td>
<td>—</td>
<td>10,681,432</td>
</tr>
<tr>
<td>2,227</td>
<td>2</td>
<td>201,086</td>
<td>—</td>
<td>—</td>
<td>201,088</td>
</tr>
<tr>
<td>—</td>
<td>—</td>
<td>4,014,938</td>
<td>—</td>
<td>—</td>
<td>4,014,938</td>
</tr>
<tr>
<td>1,669</td>
<td>2</td>
<td>207,214</td>
<td>—</td>
<td>—</td>
<td>207,216</td>
</tr>
<tr>
<td>—</td>
<td>—</td>
<td>11,657</td>
<td>—</td>
<td>—</td>
<td>11,657</td>
</tr>
<tr>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1,082,075</td>
<td>1,082</td>
<td>$ 250,894,435</td>
<td>$(138,245)</td>
<td>$(278,958,707)</td>
<td>$ 28,201,435</td>
</tr>
<tr>
<td>954,735</td>
<td>955</td>
<td>83,279,673</td>
<td>—</td>
<td>—</td>
<td>83,297,673</td>
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<tr>
<td>16,556</td>
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<td>836,618</td>
<td>—</td>
<td>—</td>
<td>836,634</td>
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<tr>
<td>2,608</td>
<td>3</td>
<td>288,998</td>
<td>—</td>
<td>—</td>
<td>289,001</td>
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<td>—</td>
<td>—</td>
<td>4,933,988</td>
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<td>4,933,988</td>
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<tr>
<td>3,322</td>
<td>3</td>
<td>262,816</td>
<td>—</td>
<td>—</td>
<td>262,819</td>
</tr>
<tr>
<td>1,059</td>
<td>1</td>
<td>133,569</td>
<td>—</td>
<td>—</td>
<td>133,570</td>
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<tr>
<td>2,803</td>
<td>3</td>
<td>299,292</td>
<td>—</td>
<td>—</td>
<td>299,992</td>
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<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2,063,158</td>
<td>2,063</td>
<td>$ 338,288,657</td>
<td>$(134,208)</td>
<td>$(331,986,817)</td>
<td>$ 6,169,695</td>
</tr>
<tr>
<td>3,373,967</td>
<td>3,374</td>
<td>15,461,009</td>
<td>—</td>
<td>—</td>
<td>15,464,383</td>
</tr>
<tr>
<td>91,643</td>
<td>92</td>
<td>339,908</td>
<td>—</td>
<td>—</td>
<td>340,000</td>
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<tr>
<td>376,424</td>
<td>377</td>
<td>1,920,955</td>
<td>—</td>
<td>—</td>
<td>1,921,332</td>
</tr>
<tr>
<td>—</td>
<td>—</td>
<td>7,340,820</td>
<td>—</td>
<td>—</td>
<td>7,340,820</td>
</tr>
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<td>1,428</td>
<td>1</td>
<td>11,755</td>
<td>—</td>
<td>—</td>
<td>11,756</td>
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<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5,906,620</td>
<td>5,907</td>
<td>$ 363,450,204</td>
<td>$(125,864)</td>
<td>$(372,564,327)</td>
<td>$ (9,234,080)</td>
</tr>
</tbody>
</table>

The accompanying notes are an integral part of these consolidated financial statements.
ARGOS THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash flows from operating activities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td>$(74,788,521)</td>
<td>$(53,028,110)</td>
<td>$(40,577,510)</td>
</tr>
<tr>
<td>Adjustments to reconcile net loss to net cash used in operating activities:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depreciation and amortization</td>
<td>680,444</td>
<td>952,341</td>
<td>967,891</td>
</tr>
<tr>
<td>Share-based compensation expense</td>
<td>4,014,938</td>
<td>5,103,494</td>
<td>8,867,616</td>
</tr>
<tr>
<td>Common stock issued as payment for research and development services</td>
<td>2,111,432</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Common stock issued as payment for other services</td>
<td>—</td>
<td>290,998</td>
<td>—</td>
</tr>
<tr>
<td>Amortization of debt issuance costs</td>
<td>216,424</td>
<td>34,004</td>
<td>—</td>
</tr>
<tr>
<td>Amortization of debt discount</td>
<td>116,042</td>
<td>140,816</td>
<td>—</td>
</tr>
<tr>
<td>Interest accrued on long-term debt</td>
<td>25,732</td>
<td>—</td>
<td>664,321</td>
</tr>
<tr>
<td>Impairment loss on property and equipment</td>
<td>—</td>
<td>741,114</td>
<td>27,254,385</td>
</tr>
<tr>
<td>Gain on early extinguishment of debt</td>
<td>—</td>
<td>—</td>
<td>(2,356,478)</td>
</tr>
<tr>
<td>Decrease in fair value of warrant liability</td>
<td>—</td>
<td>(1,007,352)</td>
<td>(20,758,425)</td>
</tr>
<tr>
<td>Gain on disposal of impaired property</td>
<td>—</td>
<td>—</td>
<td>(2,767,540)</td>
</tr>
<tr>
<td>Other</td>
<td>2,799</td>
<td>11,865</td>
<td>—</td>
</tr>
<tr>
<td>Net cash used in operating activities</td>
<td>(61,020,674)</td>
<td>(40,676,965)</td>
<td>(35,424,886)</td>
</tr>
<tr>
<td>Cash flows from investing activities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Purchase of property and equipment</td>
<td>(9,686,643)</td>
<td>(15,329,980)</td>
<td>(3,674,358)</td>
</tr>
<tr>
<td>Proceeds from sale of property and equipment</td>
<td>—</td>
<td>3,250,631</td>
<td>—</td>
</tr>
<tr>
<td>Purchases of short-term investments</td>
<td>(2,677,155)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>(Payment to) receipt from restricted cash account securing letter of credit</td>
<td>585,000</td>
<td>—</td>
<td>740,000</td>
</tr>
<tr>
<td>Proceeds from maturity of short-term investments</td>
<td>20,702,000</td>
<td>1,003,431</td>
<td>—</td>
</tr>
<tr>
<td>Net cash provided by (used in) investing activities</td>
<td>8,923,202</td>
<td>(14,326,549)</td>
<td>316,273</td>
</tr>
<tr>
<td>Cash flows from financing activities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proceeds from sale of common stock and warrants</td>
<td>8,570,000</td>
<td>105,213,087</td>
<td>15,464,383</td>
</tr>
<tr>
<td>Stock issuance costs</td>
<td>—</td>
<td>(2,374,072)</td>
<td>—</td>
</tr>
<tr>
<td>Proceeds from issuance of notes payable with detachable common stock warrants</td>
<td>12,500,000</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Proceeds from issuance of convertible note payable to related party</td>
<td>—</td>
<td>—</td>
<td>6,000,000</td>
</tr>
<tr>
<td>Payment on facility lease obligation</td>
<td>(381,033)</td>
<td>(100,000)</td>
<td>—</td>
</tr>
<tr>
<td>Payments on notes payable</td>
<td>(35,480)</td>
<td>(1,562,500)</td>
<td>(24,113,786)</td>
</tr>
<tr>
<td>Payments on capital lease obligations</td>
<td>—</td>
<td>(62,811)</td>
<td>(46,506)</td>
</tr>
<tr>
<td>Proceeds from exercise of common stock warrants</td>
<td>299,932</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Proceeds from exercise of employee stock purchase plan rights</td>
<td>207,233</td>
<td>262,819</td>
<td>11,756</td>
</tr>
<tr>
<td>Proceeds from exercise of common stock options</td>
<td>201,067</td>
<td>133,571</td>
<td>—</td>
</tr>
<tr>
<td>Net cash provided by (used in) financing activities</td>
<td>21,061,787</td>
<td>101,810,026</td>
<td>(2,684,153)</td>
</tr>
<tr>
<td>Effect of exchange rates changes on cash</td>
<td>(24,761)</td>
<td>3,720</td>
<td>8,228</td>
</tr>
<tr>
<td>Net (decrease) increase in cash and cash equivalents</td>
<td>(31,060,446)</td>
<td>46,810,237</td>
<td>(37,784,538)</td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beginning of period</td>
<td>37,223,590</td>
<td>6,163,144</td>
<td>52,973,376</td>
</tr>
<tr>
<td>End of period</td>
<td>6,163,144</td>
<td>52,973,376</td>
<td>$15,188,838</td>
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</tbody>
</table>

Supplemental disclosure of cash flow information

Supplemental disclosure of noncash investing and financing activities

<table>
<thead>
<tr>
<th>Description</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Issuance of common stock for research and development and other services</td>
<td>2,111,432</td>
<td>290,998</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of warrants in exchange for early extinguishment of debt</td>
<td>2,111,432</td>
<td>290,998</td>
<td>—</td>
</tr>
<tr>
<td>Issuance of convertible notes in exchange for early extinguishment of debt</td>
<td>—</td>
<td>—</td>
<td>87,100</td>
</tr>
<tr>
<td>Issuance of common stock in exchange for early extinguishment of debt</td>
<td>—</td>
<td>—</td>
<td>87,100</td>
</tr>
<tr>
<td>Interest capitalized on construction-in-progress</td>
<td>2,111,432</td>
<td>290,998</td>
<td>—</td>
</tr>
<tr>
<td>Purchases of property and equipment included in accounts payable and accrued expenses</td>
<td>2,658,958</td>
<td>3,073,708</td>
<td>2,470,118</td>
</tr>
<tr>
<td>Recognition of asset and facility lease obligation related to construction of new property</td>
<td>2,658,958</td>
<td>3,073,708</td>
<td>2,470,118</td>
</tr>
<tr>
<td>Stock issuance costs included in accounts payable and accrued expenses</td>
<td>—</td>
<td>266,348</td>
<td>—</td>
</tr>
<tr>
<td>Property recognized under capital lease obligations</td>
<td>—</td>
<td>2,372,880</td>
<td>—</td>
</tr>
</tbody>
</table>

The accompanying notes are an integral part of these consolidated financial statements.
1. Organization and Accounting Policies

Argos Therapeutics, Inc. (the “Company”), was incorporated in the State of Delaware on May 8, 1997. The Company is an immuno-oncology company focused on the development and commercialization of individualized immunotherapies for the treatment of cancer and infectious diseases based on its proprietary precision immunotherapy technology platform called Arcelis.

The Company’s most advanced product candidate is rocapuldencel-T, which it is developing for the treatment of metastatic renal cell carcinoma (“mRCC”) and other cancers. The Company is currently conducting a pivotal Phase 3 clinical trial of rocapuldencel-T plus sunitinib or another therapy for the treatment of newly diagnosed mRCC. This trial is referred to as the ADAPT trial. In February 2017, the independent data monitoring committee (the “IDMC”), for the ADAPT trial recommended that the trial be discontinued for futility based on its planned interim data analysis. Notwithstanding the IDMC’s recommendation, the Company determined to continue to conduct the trial while it analyzed interim data from the trial. The Company is currently finalizing the amendment and plans to file it prior to a new interim data analysis planned for the second quarter of 2018. In connection with the Company’s determination to amend the ADAPT protocol, the special protocol assessment (the “SPA”) for the ADAPT trial ceased to be in effect. Additionally, the Company is developing a protocol for a Phase 2 clinical trial of rocapuldencel-T in combination with a checkpoint inhibitor for the treatment of patients with mRCC, but does not intend to initiate this trial unless and until the Company obtains financing to fund the trial.

The Company is developing AGS-004, its second Arcelis-based product candidate, for the treatment of HIV. The Company has completed Phase 1 and Phase 2 trials funded by government grants and a Phase 2b trial that was funded in full by the National Institutes of Health (“NIH”) and the National Institute of Allergy and Infectious Diseases (“NIAID”). The Company is currently supporting an ongoing investigator-initiated clinical trial of AGS-004 in adult HIV patients evaluating the use of AGS-004 in combination with vorinostat, a latency reversing drug, for HIV eradication, and plans to support an investigator-initiated Phase 2 clinical trial of AGS-004 evaluating AGS-004 for long-term viral control in pediatric patients provided that results from its ongoing trial in adult HIV patients are favorable and government funding is available.

Basis of Presentation and Going Concern

The Company’s consolidated financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and the settlement of liabilities and commitments in the normal course of business. The Company has evaluated principal conditions and events that may raise substantial doubt about its ability to continue as a going concern within one year from the date that these financial statements are issued. The Company has incurred losses in each year since inception and as of December 31, 2017, had an accumulated deficit of $372.6 million. Also, as of December 31, 2017, the Company’s current assets totaled $17.2 million compared with current liabilities of $9.6 million, and the Company had cash and cash equivalents of $15.2 million. The Company’s primary use of cash is to fund its operating expenses, which consist principally of research and development expenditures necessary to advance its product candidates. The Company has evaluated its expected, probable future cash flow needs and has determined that it expects to incur substantial losses in the future as it conducts planned operating activities. Based upon its current and projected cash flow, the Company concluded there is substantial doubt about its ability to continue as a going concern. The financial statements for the year ended December 31, 2017 do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from uncertainty related to the Company’s ability to continue as a going concern.
On March 3, 2017, the Company entered into a payoff letter with Horizon Technology Finance Corporation and Fortress Credit Co LLC (the “Lenders”) under a venture loan and security agreement (the “Loan Agreement”) pursuant to which the Company paid, on March 6, 2017, a total of $23.1 million to the Lenders, representing the principal balance and accrued interest outstanding under the Loan Agreement in repayment of the Company’s outstanding obligations under the Loan Agreement. In addition, the Company issued to the Lenders five year warrants to purchase an aggregate of 5,000 shares of common stock at an exercise price of $26.00 per share in consideration of the Lenders acceptance of $23.1 million as payment in full. Upon the payment of the $23.1 million and the issuance of the warrants pursuant to the payoff letter, all of the Company’s outstanding indebtedness and obligations to the Lenders under the Loan Agreement were paid in full, and the Loan Agreement and the notes thereunder were terminated.

In March 2017, the Company announced that its board of directors approved a workforce action plan designed to streamline operations and reduce operating expenses. The Company recognized $1.2 million in severance costs, all of which was paid as of December 31, 2017. The Company also recognized $3.2 million in stock-based compensation expense from the acceleration of vesting of stock options and restricted held by the terminated employees during the year ended December 31, 2017.

In June 2017, the Company raised net proceeds of $6.0 million through the issuance of a secured convertible note to Pharmstandard International S.A. (“Pharmstandard”), a collaborator and the Company’s largest stockholder, in the aggregate principal amount of $6.0 million.

In August 2017, the Company also entered into an agreement with Medpace, Inc. (“Medpace”), regarding $1.5 million in deferred fees that the Company owes Medpace for contract research and development services. Under the agreement, the Company paid $0.85 million of the amount during the third quarter 2017 and agreed to pay the balance by April 2018.

In September 2017, the Company entered into a satisfaction and release agreement (the “Satisfaction and Release Agreement”) with Invetech Pty Ltd (“Invetech”). Under the Invetech Satisfaction and Release Agreement, the Company agreed to make, issue and deliver to Invetech (i) a cash payment of $0.5 million, (ii) 57,142 shares of common stock and (iii) an unsecured convertible promissory note in the original principal amount of $5.2 million, on account of and in full satisfaction and release of all of the Company’s payment obligations to Invetech arising under the Company’s development agreement with Invetech (the “Invetech Development Agreement”) prior to the date of the Invetech Satisfaction and Release Agreement, including the Company’s obligation to pay Invetech up to a total of $8.3 million in deferred fees, bonus payments and accrued interest.

In November 2017, the Company entered into a satisfaction and release agreement (the “Saint-Gobain Satisfaction and Release Agreement”) with Saint-Gobain Performance Plastics Corporation (“Saint-Gobain”). Under the Saint-Gobain Satisfaction and Release Agreement, the Company agreed to make, issue and deliver to Saint-Gobain (i) a cash payment of $0.5 million, (ii) 34,499 shares of common stock, (iii) an unsecured convertible promissory note in the original principal amount of $2.4 million, and (iv) certain specified equipment originally provided to the Company by Saint-Gobain under the development agreement with Saint-Gobain, or the (“Saint-Gobain Development Agreement”), on account of and in full satisfaction and release of all of the Company’s payment obligations to Saint-Gobain arising under the Saint-Gobain Development Agreement, prior to the date of the Saint-Gobain Satisfaction and Release Agreement, including the development fees and charges. In connection with entering into the Saint-Gobain Satisfaction and Release Agreement, the Company and Saint-Gobain entered into an amendment to the Saint-Gobain Development Agreement to extend the term to December 31, 2019.

From June 2017 through December 31, 2017, the Company raised proceeds of $15.5 million through the issuance of common stock in an at-the-market offering under its sales agreement with Cowen & Company, LLC (“Cowen”). As of March 16, 2018, an additional $7.3 million of proceeds was raised subsequent to December 31, 2017.
As of December 31, 2017, the Company had cash and cash equivalents of $15.2 million and working capital of $7.6 million. The Company does not currently have sufficient cash resources to pay all of its accrued obligations in full or to continue its business operations beyond the end of 2018. Therefore, the Company will need to raise additional capital prior to such time in order to continue to operate its business beyond that time. Alternatively, the Company may seek to engage in one or more potential transactions, such as the sale of the company, a strategic partnership with one or more parties or the licensing, sale or divestiture of some of its assets or proprietary technologies, but there can be no assurance that the Company will be able to enter into such a transaction or transactions on a timely basis or on terms that are favorable to the Company. Under these circumstances, the Company may instead determine to dissolve and liquidate its assets or seek protection under the bankruptcy laws. If the Company decides to dissolve and liquidate its assets or to seek protection under the bankruptcy laws, it is unclear to what extent the Company will be able to pay its obligations, and, accordingly, it is further unclear whether and to what extent any resources will be available for distributions to stockholders.

Until such time, if ever, as the Company can generate substantial product revenues, it expects to seek to raise additional funds through a combination of equity offerings, debt financings, government contracts, government and other third party grants or other third party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. There can be no assurance that the Company will be able to generate funds in these manners, on terms acceptable to the Company, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company’s business, results of operations and financial condition and the Company could be forced to delay, reduce, terminate or eliminate its product development programs, wind up its operations, liquidate or seek bankruptcy protection.

The consolidated financial statements include the accounts of the Company and DC Bio Corp., the Company’s Canadian wholly-owned subsidiary, an unlimited liability corporation incorporated in the Province of Nova Scotia. Significant intercompany transactions and accounts have been eliminated.

On January 18, 2018, the Company effected a one-for-twenty reverse split of its common stock. All references to shares of common stock outstanding, average number of shares outstanding and per share amounts in these consolidated financial statements and notes to consolidated financial statements have been restated to reflect the reverse split on a retroactive basis.

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 and disclosure of contingent assets and liabilities as of the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and DC Bio Corp., the Company’s Canadian wholly-owned subsidiary, an unlimited liability corporation incorporated in the Province of Nova Scotia and Argos Therapeutics (Europe)S.à.r.l., the Company’s wholly-owned subsidiary, a société anonyme à responsabilité limitée incorporated in Luxembourg. Significant intercompany transactions and accounts have been eliminated.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration of common stock equivalents. Diluted net loss per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the diluted net loss per share calculation, preferred stock, stock options and warrants are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive and, therefore, basic and diluted net loss per share were the same for all periods presented.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less as of the date of purchase to be cash equivalents. Cash deposits are all in financial institutions in the United States of America, Canada and the European Union. The Company maintains cash in accounts which are in excess of federally insured limits. As of December 31, 2016 and 2017, $52,723,376 and $14,688,838, respectively, in cash and cash equivalents was uninsured.
Credit Risk

Financial instruments which potentially subject the Company to concentrations of credit risk consist principally of cash and cash equivalents and short-term investments.

Property and Equipment

Property and equipment are recorded at cost and depreciated over their estimated useful lives using the straight-line method. Property and equipment held under capital leases and leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the related asset. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is credited or charged to income. Repairs and maintenance costs are expensed as incurred.

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets whenever significant events or changes in circumstances occur that indicate that the carrying amount of an asset may be impaired. Recoverability of these assets is determined by comparing the forecasted undiscounted future cash flows from the operations to which the assets relate, based on the Company’s best estimates using appropriate assumptions and projections at the time, to the carrying amount of the assets. If the carrying value is determined not to be recoverable from future operating cash flows, the asset is deemed impaired and an impairment loss is recognized equal to the amount by which the carrying amount exceeds the estimated fair value of the asset or assets. The Company recognized $0.7 million and $27.3 million of impairment losses during the years ended December 31, 2016 and 2017, respectively (see Note 3). No such impairments were recognized during the year ended December 31, 2015.

Accounting for Outstanding Warrants as Liabilities

The Company has outstanding warrants issued in August 2016 and that remain outstanding as of December 31, 2017 that include provisions that could require cash settlement. Accordingly, these warrants were recorded as liabilities at the estimated fair value as of the date of issuance. These warrants are then required to be recorded at fair value as of the end of each subsequent reporting period, with changes in fair value recorded as other income or expense in the Company’s consolidated statement of operations in each subsequent period.

The fair value of warrants recorded as liabilities is measured using the Black-Scholes valuation model. Inherent in the Black-Scholes valuation model are assumptions related to expected stock price volatility, expected life, risk-free interest rate and dividend yield. The risk-free interest rate is based on the U.S. Treasury five-year maturity yield curve in effect on the date of valuation. The dividend yield percentage is zero because the Company neither currently pays dividends nor intends to do so during the expected term of the warrants. Expected stock price volatility is based on the weighted average of the Company’s historical common stock volatility and the volatility of several peer public companies. The expected life of the warrants is assumed to be equivalent to their remaining contractual term.

Revenue Recognition

The Company recognizes revenue in accordance with the Financial Accounting Standards Board (“FASB”) Accounting Standards Codification (“ASC”) 605, Revenue Recognition, or ASC 605. The Company recognizes revenue when the following criteria are met: persuasive evidence of an arrangement exists, services have been rendered, the price is fixed or determinable, and collectability is reasonably assured.

The Company has entered into license agreements with collaborators. The terms of these agreements have included nonrefundable signing and licensing fees, as well as milestone payments and royalties on any future product sales developed by the collaborators under these licenses. The Company assesses these multiple elements in accordance with ASC 605, in order to determine whether particular components of the arrangement represent separate units of accounting.

These collaboration agreements are accounted for in accordance with Accounting Standards Update (“ASU”) No. 2009-13, Topic 605 – Multiple-Deliverable Revenue Arrangements, or ASU 2009-13. This guidance requires the application of the “relative selling price" method when allocating revenue in a multiple deliverable arrangement. The selling price for each deliverable shall be determined using vendor specific objective evidence of selling price, if it exists; otherwise, third-party evidence of selling price shall be used. If neither exists for a deliverable, the vendor shall use its best estimate of the selling price for that deliverable. The Company recognizes upfront license payments as revenue upon delivery of the license only if the license has standalone value and the fair value of the undelivered performance obligations can be determined. If the fair value of the undelivered performance obligations can be determined, such obligations are accounted for separately as the obligations are fulfilled. If the license is considered to either not have stand-alone value or have stand-alone value but the fair value of any of the undelivered performance obligations cannot be determined, the arrangement is accounted for as a single unit of accounting and the license payments and payments for performance obligations are recognized as revenue over the estimated period of when the performance obligations are performed.
Whenever the Company determines that an arrangement should be accounted for as a single unit of accounting, the Company must determine the period over which the performance obligations will be performed and revenue will be recognized, to the extent this is determinable. If the Company cannot reasonably estimate, to the extent this is determinable, the timing and the level of effort to complete its performance obligations under the arrangement, then the Company recognizes revenue under the arrangement on a straight-line basis over the period that the Company expects to complete such performance obligations.

The Company’s license agreements with Pharmstandard International S.A. (“Pharmstandard”), Green Cross Corp. (“Green Cross”), Medinet Co., Ltd. (“Medinet”), and Lummy (Hong Kong) Co. Ltd. (“Lummy HK”) provide for, and any future license agreements the Company may enter into may provide for, royalty payments. To date, the Company has not received any royalty payments and accordingly has not recognized any related revenue. The Company will recognize royalty revenue upon the sale of the related products, provided there are no remaining performance obligations under the arrangements.

In September 2006, the Company entered into a multi-year research contract with the NIH and NIAID to design, develop and clinically test an autologous HIV immunotherapy capable of eliciting therapeutic immune responses. The Company is using funds from this contract to develop AGS-004. Under this contract, as amended, the NIH and NIAID have committed to fund up to a total of $39.8 million, including reimbursement of direct expenses and allocated overhead and general and administrative expenses of up to $38.4 million and payment of other specified amounts totaling up to $1.4 million upon the Company’s achievement of specified development milestones. Since September 2010, the Company has received reimbursement of its allocated overhead and general and administrative expenses at provisional indirect cost rates equal to negotiated provisional indirect cost rates agreed to with the NIH and NIAID in September 2010. These provisional indirect cost rates are subject to adjustment based on the Company’s actual costs pursuant to the agreement with the NIH and NIAID. This commitment originally extended until May 2013. The Company agreed to an additional modification of the Company’s contract with the NIH and NIAID under which the NIH and NIAID agreed to increase their funding commitment to the Company by an additional $5.4 million in connection with the extension of the contract from May 2013 to September 2015. Additionally, a contract modification for a $0.5 million increase was agreed to by the NIH on September 18, 2014 to cover a portion of the manufacturing costs of the planned Phase 2 clinical trial of AGS-004 for long-term viral control in pediatric patients. On June 29, 2016, a contract modification was agreed to that extended the NIH and NIAID’s commitment under the contract to July 31, 2018. The Company has agreed to a statement of work under the contract, and is obligated to furnish all the services, qualified personnel, material, equipment, and facilities, not otherwise provided by the U.S. government, needed to perform the statement of work.

The Company recognizes revenue from reimbursements earned in connection with the NIH and NIAID contract as reimbursable costs are incurred. The Company recognizes revenues from the achievement of milestones under the NIH and NIAID contract upon the accomplishment of any such milestone.

For the years ended December 31, 2015, 2016 and 2017, the Company recorded revenue under the NIH and NIAID agreement of $448,273, $807,968 and $177,926, respectively. The Company has recorded total revenue of $38.3 million through December 31, 2017 under the NIH and NIAID agreement. As of December 31, 2017, there was up to $1.5 million of potential revenue remaining to be earned under the agreement with the NIH and NIAID. As of December 31, 2016 and 2017, the Company recorded a receivable from the NIH and NIAID of $136,140 and $31,977, respectively. The concentration of credit risk is equal to the outstanding accounts receivable and such risk is subject to the credit worthiness of the NIH and NIAID. There have been no credit losses under this arrangement.
Income Taxes

The Company provides for income taxes using the asset and liability method. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities, and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

Segment and Geographic Information

Operating segments are defined as components of an enterprise engaging in business activities from which it may earn revenues and incur expenses, for which discrete financial information is available and whose operating results are regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment and all of the Company operations are in North America.

Research and Development

Research and development costs include all direct costs related to the development of the Company’s technology, including salaries and related benefits of research and development ("R&D") personnel, depreciation of laboratory equipment, fees paid to consultants and contract research organizations, share-based compensation for R&D personnel, sponsored research payments and license fees. R&D costs are expensed as incurred.

Share-Based Compensation

The Company estimates the grant date fair value of its share-based awards and amortizes this fair value to compensation expense over the requisite service period or vesting term (see Note 11).

Comprehensive Income (Loss)

ASC 220, Comprehensive Income, establishes standards for reporting and display of comprehensive income and its components in a full set of financial statements. The Company’s other comprehensive income (loss) is related to foreign currency translation adjustments and unrealized gain (loss) on short-term investments.

Foreign Currency Translation

Gains and losses from foreign currency transactions are reflected in income currently.

The Company has identified the functional currency of its subsidiaries with foreign operations as the applicable local currency. The translation from the applicable local currency to United States dollars is performed using the exchange rate in effect as of the balance sheet date. Revenue and expense accounts are translated using the average exchange rate experienced during the period. Adjustments resulting from the translation of the Company’s subsidiaries’ financial statements from its functional currency to the United States dollar are not included in determining net loss, but are reported as accumulated other comprehensive gain (loss), a separate component of stockholders’ equity (deficit).

Interest Expense

During the years ended December 31, 2015, 2016 and 2017, interest expense primarily resulted from interest on the Loan Agreement with the Lenders, the Company’s convertible note payable to Pharmstandard, the Company’s note payable to Medinet and the Company’s capital lease obligations. The Company paid a total of $23.1 million under the Loan Agreement in March 2017, which represented the principal balance and accrued interest outstanding under the Loan Agreement and terminated the capital lease obligations under the power generation agreements in November 2017 (see Note 6 and 8).
In May 2014, the Financial Accounting Standards Board (“FASB”) issued Accounting Standards Update (“ASU”) 2014-09, Revenue from Contracts with Customers ("ASU 2014-09") pertaining to revenue recognition. The primary objective of ASU 2014-09 is for entities to recognize revenue to depict the transfer of goods or services to customers in amounts that reflect the consideration to which an entity expects to be entitled to in exchange for those goods or services. This new standard also requires enhanced disclosures about revenue, provides guidance for transactions that were not previously addressed comprehensively and improve guidance for multiple-element arrangements. The original effective date of this new standard was for periods beginning after December 15, 2016. In August 2015, the FASB issued ASU 2015-14, Revenue from Contracts with Customers: Deferral of the Effective Date, which deferred the effective date of ASU 2014-09 by one year to periods beginning after December 15, 2017, with early adoption permitted but not earlier than the original effective date. Accordingly, this new standard will be effective for the Company in first quarter of 2018. Additionally, the FASB issued ASU 2016-10, Identifying Performance Obligations and Licensing, which provided additional guidance and clarity on this topic. The two permitted transition methods under ASU 2014-09 are the full retrospective method, in which case the new standard would be applied to each prior period presented and the cumulative effect of applying the standard would be recognized as of the earliest period reported, or the modified retrospective method, in which case the cumulative effect of applying the new standard would be recognized as of the date of initial application.

The Company plans to adopt the full retrospective method effective January 1, 2018, and is continuing to evaluate the expected impact of the standard. The Company is currently performing an assessment of the impact of the new standard on its collaboration arrangements with third parties and its multi-year research contract with the NIH and NIAID and is in the process of mapping those activities to deliverables and tracing those deliverables to the new standard. The Company then will assess what impact the new standard will have on those deliverables. The Company expects no material impact on revenue recognized from its collaboration agreements and multi-year research contract with the NIH and NIAID. The Company is currently performing a detailed contract review that must be completed before it can quantify the expected impact of the standard. The Company also anticipates enhanced financial statement disclosures surrounding the nature, amount, timing and uncertainty of revenue and cash flows arising from its collaboration agreements and contract with the NIH and NIAID. The impact of the new standard will be finalized upon adoption in the first quarter of 2018 and is therefore subject to change.

In August 2016, the FASB issued ASU 2016-15, Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments (a consensus of the Emerging Issues Task Force). This ASU requires changes in the presentation of certain items in the statement of cash flows including but not limited to debt prepayment or debt extinguishment costs; contingent consideration payments made after a business combination; proceeds from the settlement of insurance claims; proceeds from the settlement of corporate-owned life insurance policies and distributions received from equity method investees. This guidance will be effective for annual periods and interim periods within those annual periods beginning after December 15, 2017, will require adoption on a retrospective basis and will be effective for the Company on January 1, 2018. The Company is currently evaluating the impact that adoption of this standard will have on the Company’s consolidated financial statements. The Company expects to classify cash payments for debt prepayment or extinguishment costs as financing cash flows, which are currently reported as operating cash flows.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842) ("ASU 2016-02"). The provisions of ASU 2016-02 set out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e. lessees and lessors). This 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. 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 using guidance similar to existing guidance for operating leases. Topic 842 supersedes the previous lease standard, Topic 840 Leases. This guidance will be effective for annual periods and interim periods within those annual periods beginning after December 15, 2018, and will be effective for the Company on January 1, 2019. The Company is currently evaluating the impact that the implementation of this standard will have on the Company's consolidated financial statements.
In November 2016, the FASB issued ASU 2016-18, *Restricted Cash* ("ASU 2016-18"). ASU 2016-18 requires that the statement of cash flows explain the change during the period in the total of cash, cash equivalents, and restricted cash. Accordingly, restricted cash will be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 is effective for the Company beginning in the first quarter of 2019, with early adoption permitted, and must be adopted using a retrospective approach. Other than this change in presentation within the statement of cash flows, ASU 2016-18 will not have an impact on the Company's consolidated financial statements.

**Recently Adopted Accounting Standards**

In August 2016, the FASB issued ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"). ASU 2016-09 simplifies several aspects related to the accounting for and financial statement presentation of share-based payments, including the accounting for income taxes at award settlement and forfeitures, and the classification of excess tax benefits and shares surrendered for tax withholdings in the statement of cash flows. The Company adopted this standard during the year ended December 31, 2017 with no effect on the Company’s consolidated financial statements.

### 2. Fair Value of Financial Instruments

The estimated fair values of all of the Company’s financial instruments, excluding long-term debt, approximate their carrying amounts in the consolidated balance sheets as of December 31, 2016 and December 31, 2017.

As of December 31, 2016 and December 31, 2017, the Company held certain assets and liabilities that are required to be measured at fair value on a recurring basis. These assets include money market funds included in cash equivalents. Additionally, as of December 31, 2016 and December 31, 2017, the Company had outstanding warrants recorded as a liability and measured at fair value on a recurring basis. The valuation of these financial instruments uses a three-tiered approach, which requires that fair value measurements be classified and disclosed in one of three tiers. These tiers are: Level 1, defined as quoted prices in active markets for identical assets or liabilities; Level 2, defined as valuations based on observable inputs other than those included in Level 1, such as quoted prices for similar assets and liabilities in active markets, or other inputs that are observable or can be corroborated by observable input data; and Level 3, defined as valuations based on unobservable inputs reflecting the Company’s own assumptions, consistent with reasonably available assumptions made by other market participants.

The Company’s Level 1 assets consist of money-market funds and restricted cash in a deposit account at a bank. The method used to estimate the fair value of the Level 1 assets is based on observable market data, as these money-market funds are publicly-traded. The Company has no Level 2 assets. As of each balance sheet date, observable market inputs may include trade information, broker or dealer quotes, bids, offers or a combination of these data sources.

The Company’s warrant liability is classified as a Level 3 financial liability. The fair value of the warrant liability is measured using the Black-Scholes valuation model. Inherent in the Black-Scholes valuation model are assumptions related to expected stock price volatility, expected life, risk-free interest rate and dividend yield (see Note 10).

During the years ended December 31, 2016 and 2017, there were no transfers between Levels 1, 2, and 3 assets or liabilities.

As of December 31, 2016 and 2017, these financial instruments and respective fair values were classified as follows:

<table>
<thead>
<tr>
<th></th>
<th>Quoted Prices in Active Markets for Identical Assets (Level 1)</th>
<th>Significant Other Observable Inputs (Level 2)</th>
<th>Significant Unobservable Inputs (Level 3)</th>
<th>Balance as of December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assets</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Money-market funds</td>
<td>$45,389,314</td>
<td>$—</td>
<td>$—</td>
<td>$45,389,314</td>
</tr>
<tr>
<td>Restricted cash – long-term</td>
<td>740,000</td>
<td>$—</td>
<td>$—</td>
<td>740,000</td>
</tr>
<tr>
<td><strong>Total assets at fair value</strong></td>
<td>$46,129,314</td>
<td>$—</td>
<td>$—</td>
<td>$46,129,314</td>
</tr>
<tr>
<td><strong>Liabilities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warrants</td>
<td>$—</td>
<td>$20,926,061</td>
<td>$20,926,061</td>
<td></td>
</tr>
<tr>
<td><strong>Total liabilities at fair value</strong></td>
<td>$—</td>
<td>$20,926,061</td>
<td>$20,926,061</td>
<td>$20,926,061</td>
</tr>
<tr>
<td>Assets</td>
<td>Quoted Prices in Active Markets for Identical Assets (Level 1)</td>
<td>Significant Other Observable Inputs (Level 2)</td>
<td>Significant Unobservable Inputs (Level 3)</td>
<td>Balance as of December 31, 2017</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>---------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
<td>------------------------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Money-market funds</td>
<td>$ 4,098,037</td>
<td>$ —</td>
<td>$ —</td>
<td>$ 4,098,037</td>
</tr>
<tr>
<td>Total assets at fair value</td>
<td>$ 4,098,037</td>
<td>$ —</td>
<td>$ —</td>
<td>$ 4,098,037</td>
</tr>
</tbody>
</table>

| Liabilities                |                                                               |                                               |                                          |                              |
|----------------------------|                                                               |                                               |                                          |                              |
| Warrants                   |                                                               |                                               | $ 167,636                                | $ 167,636                    |
| Total liabilities at fair value |                                                               |                                               | $ 167,636                                | $ 167,636                    |

Changes in the fair value of the Company’s Level 3 liability for warrants during the years ended December 31, 2016 and 2017 were as follows (see Note 10):

<table>
<thead>
<tr>
<th></th>
<th>Balance as of December 31, 2015</th>
<th>Issuance of warrants at fair value</th>
<th>Unrealized gain during the year</th>
<th>Balance as of December 31, 2016</th>
<th>Unrealized gain during the year</th>
<th>Balance as of December 31, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance as of December 31, 2015</td>
<td>$ —</td>
<td>21,933,413</td>
<td>(1,007,352)</td>
<td>$ 20,926,061</td>
<td>(20,758,425)</td>
<td>$ 167,636</td>
</tr>
</tbody>
</table>

The amortized cost, gross unrealized holding gains, gross unrealized holding losses, and estimated fair value of money-market funds included in cash and cash equivalents and restricted cash as of December 31, 2016 and December 31, 2017 were as follows:

<table>
<thead>
<tr>
<th></th>
<th>As of December 31, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amortized Cost Basis</td>
</tr>
<tr>
<td>Money-market funds</td>
<td>$ 45,389,314</td>
</tr>
<tr>
<td>Restricted cash – long-term</td>
<td>740,000</td>
</tr>
<tr>
<td></td>
<td>$ 46,129,314</td>
</tr>
</tbody>
</table>
As of December 31, 2017

<table>
<thead>
<tr>
<th></th>
<th>Gross Cost Basis</th>
<th>Gross Unrealized Holding Gains</th>
<th>Gross Unrealized Holding Losses</th>
<th>Aggregate Fair Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Money-market funds</td>
<td>$ 4,098,037</td>
<td>$ —</td>
<td>$ —</td>
<td>$ 4,098,037</td>
</tr>
<tr>
<td></td>
<td>$ 4,098,037</td>
<td>$ —</td>
<td>$ —</td>
<td>$ 4,098,037</td>
</tr>
</tbody>
</table>

The fair value of the Company’s debt was derived by evaluating the nature and terms of each note, considering the prevailing economic and market conditions as of each balance sheet date and based on the Level 2 valuation hierarchy of the fair value measurements standard using a present value methodology. The fair value of the Company’s debt as of December 31, 2016 was approximately $29.8 million compared with its carrying value of $30.1 million. The fair value of the Company’s debt as of December 31, 2017 was approximately $19.1 million compared with its carrying value of $19.5 million (see Note 6).

3. Restructuring Activities and Related Impairments of Property and Equipment and Leases

As discussed in Note 1, the Company’s most advanced product candidate is rocagolcencel-T, which the Company is developing for the treatment of mRCC and other cancers. The Company is currently conducting a pivotal Phase 3 clinical trial of rocagolcencel-T plus sunitinib or another therapy for the treatment of newly diagnosed mRCC. In February 2017, the IDMC for the ADAPT trial recommended that the trial be discontinued for futility based on its planned interim data analysis. The IDMC concluded that the trial was unlikely to demonstrate a statistically significant improvement in overall survival in the combination treatment arm utilizing the intent-to-treat population at the pre-specified number of 290 events (deaths), the original primary endpoint of the study. This development triggered a restructuring of the Company’s operations and impairments of property and equipment and leases. As set forth below and in Notes 4 and 8, the Company recognized restructuring costs of $6.0 million and impairment loss of property and equipment of $27.3 million during the year ended December 31, 2017.

**Workforce Action Plan**

On March 10, 2017, the Company enacted a workforce action plan designed to streamline operations and reduce the Company’s operating expenses. Under this plan, the Company reduced its workforce by 46 employees (or 38%) from 122 employees to 76 employees in March 2017. Through additional targeted reductions and attrition, the workforce was further reduced to 39 employees as of December 31, 2017. The principal objective of the reduction was to enable the Company to conserve its financial resources as the Company conducted its ongoing review of the preliminary ADAPT trial data set and discussed the data with the FDA. The Company recognized $1.2 million in severance costs during the year ended December 31, 2017, all of which was paid as of December 31, 2017. The Company also recognized $3.2 million in stock-based compensation costs from the acceleration of vesting of stock options and restricted stock held by the terminated employees during the year ended December 31, 2017.

**CTI Lease Agreement**

In January 2017, the Company entered into a ten-year lease agreement with two five-year renewal options for 40,000 square feet of manufacturing and office space at the Center for Technology Innovation, or CTI, on the Centennial Campus of North Carolina State University in Raleigh, North Carolina. The Company provided a security deposit in the amount of $2.4 million as security for obligations under the lease agreement, which was provided in the form of a letter of credit. The Company had intended to utilize this facility to prepare for a biologics license application (“BLA”), to the FDA and to support initial commercialization of rocagolcencel-T. The Company had expected to complete the initial build-out and equipping of the facility, including capacity qualification necessary for BLA filing, by the end of the first quarter of 2018. However, due to the IDMC recommendation in February 2017 to discontinue the ADAPT trial, the Company began reassessing its manufacturing plans, including initiating discussions with the landlord of its CTI facility regarding the termination of this lease.
On March 17, 2017 the landlord notified the Company that it was terminating the lease (the “Termination Notice”), effective immediately. The Company never occupied the leased space. In the Termination Notice, the landlord asserted that the Company was in default under the Lease due to nonpayment of invoices for upfit costs. The Company did not dispute the occurrence of the event of default or the termination of the Lease and did not seek to cure the default. In the Termination Notice, the landlord stated that the Company was liable for any and all costs incurred by the landlord in re-letting the premises, any deficiency between the Company’s scheduled rent for the remainder of the term of the Lease and the rent charged to the new tenant, the unamortized portion of the funded up-fit costs, rent abatement, interest at the rate of 12% per annum on the sums noted and all attorneys’ fees incurred by the landlord in enforcing the Lease. The Company instructed the landlord to begin the process of re-letting the premises in order to mitigate damages. On March 31, 2017, the Company entered into a Lease Termination Agreement (the “Termination Agreement”) with the landlord terminating the lease as of March 17, 2017. From the $2.4 million letter of credit, the landlord drew down $0.7 million to cover unpaid construction costs in March 2017 and $1.7 million in April 2017 for lease termination damages and agreed to return $0.1 million to the Company in consideration for being able to salvage some of the construction costs. During the year ended December 31, 2017, the Company recorded a lease termination fee of $1.6 million which is included in restructuring costs in the Company’s consolidated statement of operations. The Company also recorded an impairment loss on Construction-in-progress on the property of $0.9 million during the year ended December 31, 2017.

**Impairment of Centerpoint Facility and Construction-in-Progress**

During the three months ended March 2017, the Company also determined that it would no longer need to develop its facility in Durham County, North Carolina (“Centerpoint”), which the Company intended to be built to house the Company’s corporate headquarters and primary manufacturing facility. The Company recorded an impairment loss for the net carrying value of the facility asset of $0.7 million during the year ended December 31, 2017. In the Company’s consolidated statement of operations for the year ended December 31, 2017, the Company recorded an impairment loss of $18.3 million for the Construction-in-progress on the property. In November 2017, TKC Properties, the landlord of the Centerpoint facility completed the sale of the facility to a third party. In connection with this transaction, the Company entered into a lease termination agreement with TKC Properties pursuant to which the Company received cash proceeds of $1.8 million and recorded a gain on disposition of $1.8 million in the Company’s consolidated statement of operations during the year ended December 31, 2017.

The restructuring liability during the year ended December 31, 2017 consisted of the following:

<table>
<thead>
<tr>
<th></th>
<th>Severance and Other Employee Costs</th>
<th>Lease and Other Facility Costs</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance as of December 31, 2016</td>
<td>$ —</td>
<td>$ —</td>
<td>$ —</td>
</tr>
<tr>
<td>Restructuring costs</td>
<td>4,416,189</td>
<td>1,615,590</td>
<td>6,031,779</td>
</tr>
<tr>
<td>Acceleration of stock options and restricted stock</td>
<td>(3,171,751)</td>
<td>—</td>
<td>(3,171,751)</td>
</tr>
<tr>
<td>Cash payments</td>
<td>(1,244,438)</td>
<td>(1,615,590)</td>
<td>(2,860,028)</td>
</tr>
<tr>
<td>Balance as of December 31, 2017</td>
<td>$ —</td>
<td>$ —</td>
<td>$ —</td>
</tr>
</tbody>
</table>

**4. Property and Equipment**

Property and equipment consisted of the following as of December 31, 2016 and 2017:

<table>
<thead>
<tr>
<th></th>
<th>Useful Life (Years)</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office furniture and equipment</td>
<td>7</td>
<td>$657,875</td>
<td>$639,603</td>
</tr>
<tr>
<td>Computer equipment</td>
<td>3</td>
<td>1,018,173</td>
<td>989,137</td>
</tr>
<tr>
<td>Computer software</td>
<td>3</td>
<td>3,146,978</td>
<td>3,146,978</td>
</tr>
<tr>
<td>Laboratory equipment</td>
<td>7</td>
<td>5,709,215</td>
<td>6,050,640</td>
</tr>
<tr>
<td>Leasehold improvements</td>
<td>5</td>
<td>2,435,530</td>
<td>2,435,530</td>
</tr>
<tr>
<td>Assets related to facility lease obligation</td>
<td>8</td>
<td>8,070,033</td>
<td>—</td>
</tr>
<tr>
<td>Construction-in-progress</td>
<td></td>
<td>28,807,957</td>
<td>—</td>
</tr>
<tr>
<td>Total property and equipment, net</td>
<td></td>
<td>49,845,761</td>
<td>13,261,888</td>
</tr>
<tr>
<td>Less: Accumulated depreciation and amortization</td>
<td>(8,894,184)</td>
<td>(9,679,565)</td>
<td>—</td>
</tr>
<tr>
<td>Property and equipment, net</td>
<td></td>
<td>$40,951,577</td>
<td>$3,582,323</td>
</tr>
</tbody>
</table>
The Company reviews its property and equipment for impairment whenever events or changes indicate its carrying value may not be recoverable. As discussed in Note 3, the Company determined during the three months ended March 31, 2017 that it would no longer need to develop various equipment included in Construction-in-progress under its current manufacturing plans. The Company has agreements and understandings with various vendors to attempt to sell or dispose this equipment at prices less than the Company’s carrying value. Accordingly, the Company determined that the fair value of this equipment held for sale was $0.7 million as of December 31, 2017 and recorded an impairment loss of $1.1 million during the year ended December 31, 2017. Additionally, the Company recorded a $6.1 million impairment loss on other equipment included in Construction-in-progress during the year ended December 31, 2017 that had to be abandoned or had no net realizable value.

During the year ended December 31, 2016, the Company changed its manufacturing plans for the product launch of rocapuldencel-T. As a result of this change in plans for manufacturing rocapuldencel-T, the Company determined in the fourth quarter of 2016 that it would not require three isolator machines that were under construction and in various stages of completion by a vendor for the semi-automated manufacturing process. In March 2017, the Company sold the three isolator machines on the Company’s behalf to third parties at prices less than the Company’s carrying value. Accordingly, the Company determined that the fair value of these three isolator machines held for sale was $1,452,172 as of December 31, 2016 and an impairment loss of $741,114 was recognized during the year ended December 31, 2016.

**Centerpoint Facility and Construction-in-Progress**

As of December 31, 2016, assets related to the Centerpoint facility lease obligation and Construction-in-progress were recognized primarily due to the Company being deemed to be the accounting owner of the Centerpoint facility being built to be the Company’s corporate headquarters and primary manufacturing facility during its construction period under build-to-suit lease accounting (see Note 8). As discussed in Note 3, the Company determined that it would no longer need to develop the Centerpoint facility. The Company recorded an impairment loss of $18.3 million for the Construction-in-progress on the property during the year ended December 31, 2017.

In November 2017, TKC, the landlord of the Centerpoint facility, successfully completed the sale of the facility to a third party. In connection with this transaction, the Company entered into a lease termination agreement with TKC pursuant to which the Company received cash proceeds of $1.8 million and recorded a gain on disposition of $1.8 million in the Company’s consolidated statement of operations during the year ended December 31, 2017.

Construction-in-progress under capital leases included $2.4 million and $0 as of December 31, 2016 and December 31, 2017, respectively. As of December 31, 2016 and December 31, 2017, Construction-in-progress included $2.7 million and $0, respectively, of capitalized interest.

Depreciation and amortization expense was as follows:

<table>
<thead>
<tr>
<th>Year ended December 31</th>
<th>$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year ended December 31, 2015</td>
<td>680,444</td>
</tr>
<tr>
<td>Year ended December 31, 2016</td>
<td>952,341</td>
</tr>
<tr>
<td>Year ended December 31, 2017</td>
<td>967,891</td>
</tr>
</tbody>
</table>

5. **Income Taxes**

No provision for U.S. federal, state or foreign income taxes has been recorded as the Company has incurred net operating losses (“NOL”) since its inception in 1997.
Significant components of the Company’s deferred tax assets and liabilities consisted of the following:

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2016</th>
<th>December 31, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. federal and state net operating loss carryforwards</td>
<td>$89,445,428</td>
<td>$69,850,442</td>
</tr>
<tr>
<td>Foreign net operating loss carryforwards</td>
<td>1,526,207</td>
<td>1,649,765</td>
</tr>
<tr>
<td>Contribution carryforwards</td>
<td>4,245</td>
<td>2,202</td>
</tr>
<tr>
<td>Research and development credits</td>
<td>7,705,933</td>
<td>8,477,318</td>
</tr>
<tr>
<td>Investment tax credits</td>
<td>30,363</td>
<td>32,473</td>
</tr>
<tr>
<td>Share-based compensation</td>
<td>1,586,780</td>
<td>2,725,223</td>
</tr>
<tr>
<td>Other accruals</td>
<td>917,376</td>
<td>84,357</td>
</tr>
<tr>
<td>Deferred revenue</td>
<td>1,120,772</td>
<td>1,044,788</td>
</tr>
<tr>
<td>Property and equipment</td>
<td>257,192</td>
<td>27,628</td>
</tr>
<tr>
<td><strong>Total deferred tax assets</strong></td>
<td><strong>102,594,296</strong></td>
<td><strong>83,894,196</strong></td>
</tr>
<tr>
<td>Valuation allowance for deferred assets</td>
<td>(102,594,296)</td>
<td>(83,894,196)</td>
</tr>
<tr>
<td><strong>Net deferred tax assets</strong></td>
<td><strong>$—</strong></td>
<td><strong>$—</strong></td>
</tr>
</tbody>
</table>

As of December 31, 2016 and 2017, the Company provided a full valuation allowance against its net deferred tax assets since as of that time, the Company could not assert that it was more likely than not that these deferred tax assets would be realized. There was an increase in the valuation allowance in the year ended December 31, 2017 of $18,700,100, all of which was allocable to current operating activities.

As of December 31, 2017, the Company had U.S. federal and state, and Canadian federal and provincial NOL carryforwards of approximately $300.8 million, $338.5 million, $6.1 million and $6.1 million, respectively. These NOL carryforwards begin to expire in 2018, 2017, 2026 and 2026, respectively. As of December 31, 2017, the Company also had unlimited Luxembourg NOL carryforwards of approximately $0.2 million. As of December 31, 2017, the Company had U.S. federal and state tax credit carryforwards of approximately $8.2 million and $0.3 million, respectively. These credit carryforwards begin to expire in 2020 and 2024, respectively. As of December 31, 2017, the Company had Canadian investment tax credit carryforwards of approximately $32,500 that begin to expire in 2024.

The utilization of the NOL and tax credit carryforwards may be subject to limitation under the rules regarding a change in stock ownership as determined by the Internal Revenue Code, and state and foreign tax laws. Section 382 of the Internal Revenue Code of 1986, as amended, imposes annual limitations on the utilization of NOL carryforwards, other tax carryforwards, and certain built-in losses upon an ownership change as defined under that section. In general terms, an ownership change may result from transactions that increase the aggregate ownership of certain stockholders in the Company’s stock by more than 50 percentage points over a three year testing period (“Section 382 Ownership Change”). If the Company has undergone a Section 382 Ownership Change, an annual limitation would be imposed on certain of the Company’s tax attributes, including NOL and capital loss carryforwards, and certain other losses, credits, deductions or tax basis. Management has determined that the Company experienced an ownership change during 2014 for purposes of Section 382. Due to the Section 382 limitation resulting from the ownership change, approximately $28,156,600 of the Company’s federal NOLs are expected to expire unused. The federal tax credits and state NOLs would potentially be limited as well. The estimated amount of federal NOLs expected to expire due to the limitation has not been recognized in the consolidated financial statements.

As of December 31, 2017, the Company had no foreign unremitted earnings from its foreign subsidiaries.
Taxes computed at the statutory U.S. federal income tax rate of 34.0% are reconciled to the provision for income taxes for the years ended December 31, 2015, 2016 and 2017 as follows:

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. federal tax statutory rate</td>
<td>$(25,428,097)</td>
<td>$(18,029,558)</td>
<td>$(13,796,353)</td>
</tr>
<tr>
<td>Statutory U.S. federal income</td>
<td>34.0%</td>
<td>34.0%</td>
<td>34.0%</td>
</tr>
<tr>
<td>income tax rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>State taxes (net of federal</td>
<td>(1,936,719)</td>
<td>(1,034,566)</td>
<td>(801,406)</td>
</tr>
<tr>
<td>benefit)</td>
<td>2.6%</td>
<td>2.0%</td>
<td>2.0%</td>
</tr>
<tr>
<td>U.S. federal research and</td>
<td>(2,135,940)</td>
<td>(1,368,171)</td>
<td>(1,038,768)</td>
</tr>
<tr>
<td>development tax credits</td>
<td>2.9%</td>
<td>2.6%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Other non deductible expenses</td>
<td>1,032,480</td>
<td>760,287</td>
<td>1,973,462</td>
</tr>
<tr>
<td></td>
<td>(1.4%)</td>
<td>(1.5%)</td>
<td>(4.9%)</td>
</tr>
<tr>
<td>Increase in unrecognized tax</td>
<td>640,782</td>
<td>410,451</td>
<td>311,630</td>
</tr>
<tr>
<td>benefits</td>
<td>(0.9%)</td>
<td>(0.8%)</td>
<td>(0.8%)</td>
</tr>
<tr>
<td>Change in effective state tax</td>
<td>1,190,519</td>
<td>1,655,991</td>
<td>12,871</td>
</tr>
<tr>
<td>rate</td>
<td>(1.6%)</td>
<td>(3.1%)</td>
<td>(0.0%)</td>
</tr>
<tr>
<td>Expiration of NOL &amp;</td>
<td>9,590,101</td>
<td>—</td>
<td>136,325</td>
</tr>
<tr>
<td>contribution carryforwards</td>
<td>(12.8%)</td>
<td>(0.0%)</td>
<td>(0.3%)</td>
</tr>
<tr>
<td>Adjustment for change in</td>
<td>—</td>
<td>—</td>
<td>41,255,460</td>
</tr>
<tr>
<td>effective tax rate</td>
<td>(0.0%)</td>
<td>(0.0%)</td>
<td>(101.7%)</td>
</tr>
<tr>
<td>Change in fair value of</td>
<td>—</td>
<td>—</td>
<td>(7,467,843)</td>
</tr>
<tr>
<td>warrant liability</td>
<td>(0.0%)</td>
<td>(0.0%)</td>
<td>(18.4%)</td>
</tr>
<tr>
<td>Change in valuation allowance</td>
<td>16,705,784</td>
<td>17,691,710</td>
<td>(18,700,100)</td>
</tr>
<tr>
<td></td>
<td>(22.3%)</td>
<td>(33.4%)</td>
<td>(46.1%)</td>
</tr>
<tr>
<td>Deferred tax asset true-ups</td>
<td>341,090</td>
<td>(86,144)</td>
<td>(1,885,278)</td>
</tr>
<tr>
<td></td>
<td>(0.5%)</td>
<td>(0.2%)</td>
<td>(4.6%)</td>
</tr>
<tr>
<td>Provision for income taxes</td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td></td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

On September 18, 2015, North Carolina enacted House Bill 97, which reduced the corporate income tax rate from 5% to 4% in 2016. As a result of the new enacted tax rate, the Company adjusted its deferred tax assets in 2015 by applying the lower rate, which resulted in a decrease in the deferred tax assets and a corresponding decrease to the valuation allowance of approximately $1,190,500. On August 4, 2016, North Carolina issued a notice confirming that the corporate income tax rate would be further reduced from 4% to 3% in accordance with House Bill 97. As a result of the new enacted tax rate, the Company adjusted its deferred tax assets in 2016 by applying the lower rate, which resulted in a decrease in the deferred tax assets and a corresponding decrease to the valuation allowance of approximately $1,656,000. On June 28, 2017, North Carolina issued a notice confirming that the corporate income tax rate would be further reduced from 3% to 2.5% in accordance with House Bill 97. As a result of the new enacted tax rate, the Company adjusted its deferred tax assets in 2017 by applying the lower rate, which resulted in a decrease in the deferred tax assets and a corresponding decrease to the valuation allowance of approximately $16,810.

On December 22, 2017, the Tax Cuts and Jobs Act was enacted into law (the “Tax Legislation”), which reduced the federal corporate income tax rate to 21% for tax years beginning after December 31, 2017. As a result of the new enacted tax rate, the Company adjusted its deferred tax assets as of December 31, 2017 by applying the new 21% rate, which resulted in a decrease to the deferred tax assets and a corresponding decrease to the valuation allowance of approximately $41.3 million.

The Tax Legislation also implements a territorial tax system. Under the territorial tax system, in general, the Company’s foreign earnings will no longer be subject to tax in the United States. As part of transition to the territorial tax system the Tax Legislation includes a mandatory deemed repatriation of all undistributed foreign earnings that are subject to a U.S. income tax. The Company estimates that the deemed repatriation will not result in any additional U.S. income tax liability as it estimates it currently has no undistributed foreign earnings.

The SEC staff issued Staff Accounting Bulletin 118, or SAB 118, which will allow the Company to record provisional amounts related to accounting for the Tax Legislation during a measurement period which is similar to the measurement period used when accounting for business combinations. The Company is following the guidance set forth by SAB 118 and any amounts calculated are provisional estimates and will be reevaluated as more information or guidance becomes available.
As of December 31, 2017, the Company considers the accounting for the change in income tax rates on deferred tax assets and liabilities as a result of the Tax Reform Act to be provisional and, accordingly, subject to adjustment in future periods. The calculated provisional amount of $41.3 million impact on the deferred tax assets and valuation allowance will be finalized in conjunction with the filing of the Company's U.S. federal income tax return for the year ended December 31, 2017 that will not be finalized until later in 2018.

The Company also considers it likely that further technical guidance regarding certain aspects of the new provisions included in the Tax Reform Act, as well as clarity regarding state income tax conformity to current federal tax code, may be issued which could result in changes to the provisional amounts reported as of December 31, 2017 and related state income tax effects. Any adjustments made during the measurement period will likely not have any impact on the effective tax rate due to the full valuation allowance offset to deferred tax assets.

The Company will continue to assess the impact of the recently enacted tax law on its business and consolidated financial statements.

The Company had gross unrecognized tax benefits of $3,206,300 as of January 1, 2017. As of December 31, 2017, the total gross unrecognized tax benefits were $3,517,900 and of this total, none would affect the Company’s effective tax rate if recognized. The Company does not anticipate a significant change in total unrecognized tax benefits or the Company’s effective tax rate due to the settlement of audits or the expiration of statutes of limitations within the next 12 months.

The Company’s policy is to recognize interest and penalties related to uncertain tax positions in the provision for income taxes. As of December 31, 2016 and 2017, the Company had no accrued interest or penalties related to uncertain tax positions.

The Company has analyzed its filing positions in all significant federal and state jurisdictions where it is required to file income tax returns, as well as open tax years in these jurisdictions. With few exceptions, the Company is no longer subject to U.S. federal, state, and local tax examinations by tax authorities for years before 2014 although carryforward attributes that were generated prior to 2014 may still be adjusted upon examination by the Internal Revenue Service if they either have been or will be used in a future period. No income tax returns are currently under examination by taxing authorities.

The following is a tabular reconciliation of the Company’s change in gross unrecognized tax positions during the years ended December 31, 2015, 2016 and 2017:

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beginning balance</td>
<td>$2,155,000</td>
<td>$2,795,800</td>
<td>$3,206,300</td>
</tr>
<tr>
<td>Gross increase for tax positions related to current periods</td>
<td>640,800</td>
<td>410,500</td>
<td>311,600</td>
</tr>
<tr>
<td>Gross (decrease) increase for tax positions related to prior periods</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Ending balance</td>
<td>$2,795,800</td>
<td>$3,206,300</td>
<td>$3,517,900</td>
</tr>
</tbody>
</table>

6. Notes Payable and Convertible Notes Payable

Notes payable and convertible notes payable consisted of the following as of December 31, 2016 and 2017:

| Notes payable under the venture loan and security agreement, including accrued interest | 24,035,029 | 23,714,620 |
| Less debt discount and debt issuance costs | (320,409) | — |
| Notes payable under the venture loan and security agreement, net | 23,714,620 | 24,035,029 |
| Convertible note payable to Pharmstandard, including accrued interest | — | 6,302,959 |
| Convertible note payable to Invetech, including accrued interest | — | 5,845,655 |
| Convertible note payable to Saint-Gobain, including accrued interest | — | 2,334,929 |
| Note payable to Medinet, including accrued interest | 6,403,186 | 4,958,824 |
| Other notes payable | 30,972 | 13,825 |
| Total debt | 30,148,778 | 19,456,192 |
| Less current portion of convertible note payable to Invetech, including accrued interest | — | (1,300,000) |
| Less current portion of convertible note payable to Saint-Gobain, including accrued interest | — | (1,050,000) |
| Less current portion of note payable to Medinet, including accrued interest | — | (4,958,824) |
| Less current portion of other notes payable | (11,475,480) | (13,825) |
| Long-term portion of notes payable and convertible notes payable | $18,673,298 | $12,133,543 |

Convertible Note Payable to Invetech. As discussed in Note 7, the Company had recorded a manufacturing research and development obligation payable to Invetech on its consolidated balance sheet of approximately $8.3 million, representing $5.2 million in deferred fees, $2.3 million in estimated bonus payments and $0.7 million in accrued interest.
On September 22, 2017, the Company entered into the Satisfaction and Release Agreement with Invtech. Under the Satisfaction and Release Agreement, the Company agreed to make, issue and deliver to Invtech (i) a cash payment of $0.5 million, (ii) 57,142 shares of the Company’s common stock with a fair value of $0.2 million on the date of issuance and (iii) an unsecured convertible promissory note in the original principal amount of $5.2 million on account of and in full satisfaction and release of all of the Company’s payment obligations to Invtech arising under the Invtech prior to the date of the Satisfaction and Release Agreement, including the Company’s obligation to pay Invtech up to a total of $8.3 million in deferred fees, bonus payments and accrued interest. As a result, the Company recognized a gain on the early extinguishment of debt of $1.5 million in the Company’s statement of operations during the year ended December 31, 2017. Following is a summary the terms of the convertible note payable to Invtech (the “Invtech Note”).

The original principal amount of the Invtech Note is $5.2 million. The maturity date for the payment of principal and interest under the Invtech Note is September 30, 2020. The Invtech Note bears interest at a rate of 6.0% per annum, which interest will compound annually. The Invtech Note is not secured by any assets of the Company.

The Company is required to make quarterly installment payments under the Invtech Note for the fiscal quarters ending December 31, 2017 and March 31, 2018, each in an aggregate amount of up to $0.4 million, consisting of (i) cash in the amount of $0.2 million and (ii) if certain specified conditions are met as of the corresponding payment date, up to $0.2 million of shares of the Company’s common stock. For the fiscal quarters ending June 30, 2018 through March 31, 2019, the Company is required to make quarterly installment payments under the Invtech Note, each in an aggregate amount of up to $0.3 million, consisting of (i) cash in the amount of $150,000 and (ii) if certain specified conditions are met as of the corresponding payment date, up to $150,000 of shares of the Company’s common stock. For the fiscal quarters ending June 30, 2019 through June 30, 2020, the Company is required to make quarterly installment payments under the Invtech Note, each in an amount of $150,000, payable in cash. For the year ended December 31, 2017, the Company made an installment payment of $0.2 million in cash to Invtech.

The Invtech Note also provides that on the anniversary of the issue date of the Invtech Note for each of the first three years following the issue date, the outstanding principal amount of the Invtech Note, if any, plus accrued and unpaid interest thereon shall automatically be deemed to be reduced by $250,000, if and only if the Company has paid all debt service payments due under the Invtech Note on or prior to the relevant anniversary date and no event of default, fundamental transaction or change of control, each as defined in the Invtech Note, has occurred on or prior to such anniversary date.

As detailed further below, Invtech may exercise its conversion rights upon: (i) maturity of the Invtech Note, (ii) certain change of control events, and (iii) certain events of default. In each case, the number of shares of common stock issuable upon such complete or partial conversion of the Invtech Note is determined by dividing the portion of the principal and accrued or unpaid interest to be converted by $10.00 per share (as adjusted for any stock dividend, stock split, stock combination, reclassification or similar transaction).

- **Maturity of the Invtech Note.** Upon maturity of the Invtech Note or at any time within 75 days of such maturity, Invtech may, at its option, elect to convert any amount of the outstanding principal and accrued interest into shares of the Company’s common stock. The Company will be required to pay any amount not so converted in cash.

- **Change of Control.** Upon a change of control pursuant to which Invtech has a redemption right, Invtech may, at its option, elect to convert any amount of the outstanding principal and accrued interest, less any remaining installment payments required to be made in cash, into shares of the Company’s common stock. The Company will be required to pay any amount not so converted in cash.

- **Default.** Upon the occurrence of certain events of default, Invtech may, at its option, elect to convert any amount of the outstanding principal and accrued interest into shares of the Company’s common stock. The Company will be required to pay any amount not so converted in cash.

Subject to the aforementioned conversion rights of Invtech, the Company may prepay the Invtech Note in whole or in part at any time without penalty or premium.
Convertible Note Payable to Saint-Gobain. On November 22, 2017, the Company entered into the Saint-Gobain Satisfaction and Release Agreement with Saint-Gobain. Under the Saint-Gobain Satisfaction and Release Agreement, the Company agreed to make, issue and deliver to Saint-Gobain (i) a cash payment of $0.5 million, (ii) 34,499 shares of common stock, (iii) an unsecured convertible promissory note in the original principal amount of $2.4 million, and (iv) certain specified equipment originally provided to the Company by Saint-Gobain under the Saint-Gobain Development Agreement, on account of and in full satisfaction and release of all of the Company’s payment obligations to Saint-Gobain arising under the Saint-Gobain Development Agreement, prior to the date of the Saint-Gobain Satisfaction and Release Agreement, including the development fees and charges. In connection with entering into the Saint-Gobain Satisfaction and Release Agreement, the Company and Saint-Gobain entered into an amendment to the Saint-Gobain Development Agreement to extend the term to December 31, 2019. Following is a summary of the terms of the convertible note payable to Saint-Gobain (the “Saint-Gobain Note”).

The original principal amount of the Note is $2,360,000. The maturity date for the payment of principal and interest under the Note is September 30, 2020. The Note bears interest at a rate of 6.0% per annum, which interest will compound quarterly. The Note is not secured by any assets of the Company.

The Company is required to make quarterly installment payments under the Saint-Gobain Note for the fiscal quarters ending December 31, 2017 and March 31, 2018, each in an aggregate amount of up to $340,000, consisting of (i) cash in the amount of $200,000 and (ii) if certain specified conditions are met as of the corresponding payment date, up to $140,000 of shares of the Company’s common stock. For the fiscal quarters ending June 30, 2018 and September 30, 2018, the Company is required to make quarterly installment payments under the Saint-Gobain Note, each in an aggregate amount of up to $245,000, consisting of (i) cash in the amount of $125,000 and (ii) if certain specified conditions are met as of the corresponding payment date, up to $120,000 of shares of the Company’s common stock. For the fiscal quarters ending December 31, 2018 and March 31, 2019, the Company is required to make quarterly installment payments under the Saint-Gobain Note, each in an aggregate amount of up to $220,000, consisting of (i) cash in the amount of $100,000 and (ii) if certain specified conditions are met as of the corresponding payment date, up to $120,000 of shares of the Company’s common stock. For the fiscal quarter ending December 31, 2017, March 31, 2018, June 30, 2018, September 30, 2018, December 31, 2018 and March 31, 2019, if the conditions required for the issuance of common stock are not met solely because the stock price of the common stock at the time is less than $4.06 per share (as adjusted for any stock dividend, stock split, stock combination, reclassification or similar transaction), then the Company will be required to pay in each such quarter cash equal to 50% of the value of the common stock that would otherwise have been issued. For the fiscal quarters ending June 30, 2019 through June 30, 2020, the Company is required to make quarterly installment payments under the Saint-Gobain Note, each in an amount of $100,000, payable in cash. For the year ended December 31, 2017, the Company made an installment payment of $270,000 in cash to Saint-Gobain.

As detailed further below, Saint-Gobain may exercise its conversion rights upon: (i) maturity of the Saint-Gobain Note, (ii) certain change of control events (as defined in the Saint-Gobain Note), and (iii) certain events of default (as defined in the Saint-Gobain Note). In each case, the number of shares of common stock issuable upon such complete or partial conversion of the Saint-Gobain Note is determined by dividing the portion of the principal and accrued or unpaid interest to be converted by $0.50 per share (as adjusted for any stock dividend, stock split, stock combination, reclassification or similar transaction).

- **Maturity of the Note**. Upon maturity of the Saint-Gobain Note or at any time during the 75 day period prior to the maturity date of the note, Saint-Gobain may, at its option, elect to convert any amount of the outstanding principal and accrued interest into shares of the Company’s common stock. The Company will be required to pay any amount not so converted in cash.

- **Change of Control**. Upon a change of control pursuant to which Saint-Gobain has a redemption right, Saint-Gobain may, at its option, elect to convert any amount of the outstanding principal and accrued interest, less any remaining installment payments required to be made in cash, into shares of the Company’s common stock. The Company will be required to pay any amount not so converted in cash.

- **Default**. Upon the occurrence of certain events of default, Saint-Gobain may, at its option, elect to convert any amount of the outstanding principal and accrued interest into shares of the Company’s common stock. The Company will be required to pay any amount not so converted in cash.
Subject to the aforementioned conversion rights of Saint-Gobain, the Company may prepay the Saint-Gobain Note in whole or in part at any time without penalty or premium.

**Convertible Note Payable to Pharmstandard.** On June 15, 2017, the Company entered into a note purchase agreement (the “Note Purchase Agreement”) with Pharmstandard, pursuant to which the Company agreed to issue and sell to Pharmstandard a secured convertible promissory note in the original principal amount of $6.0 million (the “Pharmstandard Note”).

The Company issued the Pharmstandard Note on June 21, 2017, the closing date of the financing. Under the Pharmstandard Note, the maturity date for the payment of principal and interest is the fifth anniversary of the issue date. The Pharmstandard Note bears interest at a rate of 9.5% per annum, which interest compounds annually. The Pharmstandard Note is secured by a lien on and security interest in all of the Company’s intellectual property. The Company may prepay the Pharmstandard Note in whole or in part at any time without penalty or premium. Upon the occurrence of certain events of default, Pharmstandard will have the option to require the Company to repay the unpaid principal amount of the Pharmstandard Note and any unpaid accrued interest.

In addition, at Pharmstandard’s election, Pharmstandard may convert the entire principal and interest on the Pharmstandard Note into shares of the Company’s common stock at a price per share equal to $10.00. However, Pharmstandard will not be permitted to convert the entire Pharmstandard Note if such conversion would result in Pharmstandard and its affiliates holding shares that exceed 39.9% of the total number of outstanding shares of common stock of the Company or 39.9% of the combined voting power of all outstanding securities of the Company. To the extent that conversion of the entire Pharmstandard Note would cause Pharmstandard and its affiliates to exceed these thresholds, Pharmstandard may convert a portion of the Pharmstandard Note to the extent these thresholds are not exceeded by such partial conversion.

Pharmstandard is the Company’s largest stockholder, and beneficially owned, in the aggregate, shares representing approximately 17.3% of the Company’s outstanding common stock as of February 28, 2018. In addition, two members of the Company’s board of directors are closely associated with Pharmstandard.

**Venture Loan Facility.** In September 2014, the Company entered into the Loan Agreement with the Lenders under which the Company could borrow up to $25.0 million in two tranches of $12.5 million each (the “Loan Facility”).

The Company borrowed the first tranche of $12.5 million upon the closing of the Loan Facility in September 2014 and borrowed the second tranche of $12.5 million in August 2015. The per annum interest rate for each tranche was a floating rate equal to 9.25% plus the amount by which the one-month London Interbank Offered Rate (“LIBOR”) exceeds 0.50% (effectively a floating rate equal to 8.75% plus the one-month LIBOR Rate). The total per annum interest rate was not to exceed 10.75%.

The Company incurred $0.4 million in debt issuance costs in connection with the closing of the Loan Facility. Debt issuance costs were presented in the Company’s consolidated balance sheet as a direct deduction from the associated liability and amortized to interest expense over the terms of the related debt. Debt issuance costs were eliminated on the Company’s consolidated balance sheet as of December 31, 2017 as a result of the early extinguishment of debt under the payoff letter discussed below.

The Company made payments with respect to the first tranche of $12.5 million on an interest-only basis monthly through October 31, 2016, and was obligated to make monthly payments of principal and accrued interest through the scheduled maturity date for the first tranche loan on September 30, 2018. In addition, a final payment for the first tranche loan equal to $0.6 million was due on September 30, 2018, or such earlier date specified in the Loan Agreement. The Company was recognizing the final payment of $0.6 million as accrued interest over the expected life of the first tranche loan. The Company agreed to repay the second tranche loan of $12.5 million in 18 monthly payments of interest only until February 7, 2017, followed by 24 monthly payments of principal and accrued interest through the scheduled maturity date for the second tranche loan on February 7, 2019. In addition, a final payment of $0.6 million was due on February 7, 2019, or such earlier date specified in the Loan Agreement. The Company was recognizing the final payment of $0.6 million as accrued interest over the expected life of the second tranche loan. In addition, the Company agreed that if the Company repaid all or a portion of the loan prior to the applicable maturity date, it would pay the Lenders a prepayment penalty fee based on a percentage of the then outstanding principal balance, equal to 3% if the prepayment occurs on or before 24 months after the funding date, 2% if the prepayment occurs more than 24 months after, but on or before 36 months after, the funding date thereof, or 1% if the prepayment occurs more than 36 months after the funding date thereof.
On March 3, 2017, the Company entered into a payoff letter with the Lenders, pursuant to which the Company paid on March 6, 2017, a total of $23.1 million to the Lenders, representing the principal balance and accrued interest outstanding under the Loan Agreement in repayment of the Company’s outstanding obligations under the Loan Agreement. In addition, the Company issued to the Lenders five year warrants to purchase an aggregate of 5,000 shares of the Company’s common stock at an exercise price of $26.00 per share in consideration of the Lenders accepting the $23.1 million. The Company recognized a gain on this early extinguishment of debt of $0.2 million during the year ended December 31, 2017 which is included in Other income (expense) on the statement of operations. The payoff of the debt was considered a troubled debt restructuring because of the doubt surrounding the Company’s ability to continue as a going concern and the fact that the final payment of $1.25 million and the pre-payment penalty of $0.6 million were waived by the Lenders in exchange for the issuance of the warrants.

Upon the payment of the $23.1 million and the issuance of the warrants pursuant to the payoff letter, all outstanding indebtedness and obligations of the Company owing to the Lenders under the Loan Agreement were deemed paid in full, and the Loan Agreement and the notes thereunder were terminated.

In connection with the Loan Agreement, the Company issued to the Lenders and their affiliates warrants to purchase a total of 4,139 shares of the Company’s common stock at a per share exercise price of $181.20 (the “Venture Loan Warrants”). Upon the Company’s satisfaction of the conditions precedent to the making of the second tranche loan, the Venture Loan Warrants became exercisable in full. The Venture Loan Warrants will terminate on September 29, 2021 or such earlier date as specified in the Venture Loan Warrants. As of September 29, 2014, the Company recorded a debt discount of $0.3 million equal to the value of these Venture Loan Warrants. This debt discount was offset against the long-term portion of the note payable balance and included in additional paid-in capital on the Company’s consolidated balance sheet. Debt discount was amortized to interest expense over the terms of the related debt. Debt discount was eliminated on the Company’s balance sheet as of December 31, 2017 as a result of the early extinguishment of debt discussed above.

**Medinet Loan.** In December 2013, in connection with a license agreement currently with Medinet Co., Ltd and its wholly-owned subsidiary, MEDcell Co., Ltd. (together "Medinet"), as described in Note 13, the Company borrowed $9.0 million pursuant to an unsecured promissory note that bears interest at a rate of 3.0% per annum. The principal and interest under the note are due and payable on December 31, 2018. Under the terms of the note and the license agreement, any milestone payments related to the developmental and regulatory milestones that become due will be applied first to the repayment of the loan. The Company has the right to prepay the loan at any time. If the Company has not repaid the loan by December 31, 2018, then the Company has agreed to grant to Medinet a non-exclusive, royalty-bearing license to make and sell Arcelis products in Japan for the treatment of cancer. In such event, the amounts owing under the loan as of December 31, 2018 may constitute pre-paid royalties under the license or would be due and payable. Royalties under this license would be paid until the expiration of the licensed patent rights in Japan at a rate to be negotiated. If the Company and Medinet cannot agree on the royalty rate, they have agreed to submit the matter to arbitration. Because the $9.0 million promissory note was issued at a below market interest rate, the Company allocated the proceeds of the loan between the license agreement and the debt at the time of issuance. Accordingly, as of the borrowing date, December 31, 2013, the Company recorded $6.9 million to notes payable, based upon an effective interest rate of 8.0%, and $2.1 million as a deferred liability.

During the year ended December 31, 2015, the Company recognized a $1.0 million milestone payment as deferred revenue under the Medinet license agreement and reduced the related note payable by $0.8 million and the deferred liability by $0.2 million. During the year ended December 31, 2016, the Company recognized a $2.0 million milestone payment as deferred revenue under the Medinet license agreement and reduced the related note payable by $1.5 million and the deferred liability by $0.5 million. During the year ended December 31, 2017, the Company recognized an additional $2.0 million milestone payment as deferred revenue under the Medinet license agreement and reduced the related note payable by $1.5 million and the deferred liability by $0.5 million. As of December 31, 2016, the amount of the note payable was $6.4 million, including $1.8 million of accrued interest. As of December 31, 2017, the amount of the note payable was $5.0 million, including $1.9 million of accrued interest. As of December 31, 2016 and 2017, the total deferred liability associated with the Medinet note was $5.4 million and $6.9 million, respectively (see Note 13).
During November 2013, the Company borrowed $77,832 from a lending institution to finance the purchase of computer equipment, of which $46,754, $30,972 and $13,825 in principal was outstanding as of December 31, 2015, December 31, 2016 and December 31, 2017, respectively. Borrowings are collateralized by substantially all of the computer equipment financed under the agreement, bear interest at a rate of 8.31% per annum and are to be repaid in 60 equal monthly installments commencing on the date of borrowing.

7. Manufacturing Research and Development Obligation

In October 2014, the Company entered into the Invotech Development Agreement. Under the Invotech Development Agreement, Invotech agreed to develop and provide prototypes of the automated production system to be used for the manufacture of the Company’s Arcelis-based products. Invotech agreed to defer 30% of its fees, up to $5.0 million, under the Invotech Development Agreement subject to payment by the Company in installments over 2017 and 2018.

As of December 31, 2016, the Company recorded this manufacturing research and development obligation on its consolidated balance sheet at $8.2 million, representing $5.2 million in deferred fees, $2.3 million in estimated bonus payments and $0.6 million in accrued interest, of which $3.7 million is included in the current liabilities as the current portion of the obligation.

On September 22, 2017, the Company entered into the Satisfaction and Release Agreement with Invotech. Under the Satisfaction and Release Agreement, the Company agreed to make, issue and deliver to Invotech (i) a cash payment of $0.5 million, (ii) 57,142 shares of the Company’s common stock and (iii) an unsecured convertible promissory note in the original principal amount of $5.2 million on account of and in full satisfaction and release of all of the Company’s payment obligations to Invotech arising under the Invotech Development Agreement prior to the date of the Satisfaction and Release Agreement, including the Company’s obligation to pay Invotech up to a total of $8.3 million in deferred fees, bonus payments and accrued interest. As a result, the Company recognized a gain on the early extinguishment of debt of $1.5 million in the Company’s consolidated statement of operations during the year ended December 31, 2017.

8. Facility Lease Obligation, Capital Lease Obligations, Assets Held for Sale and Sold

Centerpoint Lease Obligation

In August 2014, the Company entered into a Lease Agreement (the “Centerpoint Lease Agreement”) with TKC LXXII, LLC, a North Carolina limited liability company (“TKC”). Under the Centerpoint Lease Agreement, the Company agreed to lease certain land and an approximately 125,000 square-foot building to be constructed in Durham County, North Carolina, which the Company refers to as Centerpoint. The Company intended this facility to be built to house the Company’s corporate headquarters and primary manufacturing facility. The shell of the new facility was constructed on a build-to-suit basis by TKC in accordance with agreed upon specifications and plans as set forth in the Centerpoint Lease Agreement and at the expense of TKC, other than those costs resulting from changes requested by the Company, for which the Company was responsible and for which the Company paid $1.7 million.

The term of the Centerpoint Lease Agreement was 10 years from the commencement date of July 1, 2015. The Company had an option to extend the Centerpoint Lease Agreement by six five-year renewal terms. Current rent payments in the third year were $49,052 per month, subject to certain fixed increases over the course of the term as set forth in the Centerpoint Lease Agreement.

The Centerpoint Lease Agreement required the Company to provide TKC with a letter of credit. The Company provided the bank that issued the letter of credit on its behalf a security deposit of $1.3 million to guarantee the letter of credit. In accordance with the Centerpoint Lease Agreement, this deposit was reduced to $0.7 million as of December 31, 2015 under a purchase and sale agreement with TKC. The deposit was recorded as restricted cash as of December 31, 2016 on the Company’s consolidated balance sheet.
Under the Centerpoint Lease Agreement, the Company was involved in the construction of the building. To the extent the Company was involved with the structural improvements of the construction project or takes construction risk prior to the commencement of a lease, ASC 840-40-05-5 requires for accounting purposes that the Company be considered the owner of this project during the construction period. Therefore, the Company recorded an asset in property and equipment, net on the Company’s consolidated balance sheets for the cost of the Company’s portion of the building plus the amount of estimated structural construction costs incurred by TKC and the Company as of the applicable balance sheet date. The Company recorded a corresponding facility lease obligation on its consolidated balance sheets representing the amounts paid by TKC.

The initial recording of these assets and liabilities was classified as non-cash investing and financing items, respectively, for purposes of the Company’s consolidated statements of cash flows.

Under the Centerpoint Lease Agreement, the Company had an option to purchase the property. In February 2015, the Company exercised this purchase option and entered into a Purchase and Sale Agreement (the “Purchase Agreement”) with TKC. The purchase price to be paid by the Company at closing was $7.4 million plus the amount of any additional costs incurred by TKC as a result of changes requested by the Company, for which the Company paid $1.7 million, and the amount of any improvement allowances advanced to the Company by TKC prior to the closing. Under the terms of the Purchase Agreement, the Company had until October 31, 2016 to consummate the purchase of the property. The Company did not purchase the property by such date. As a result, the Company had no further right to purchase the property and remained subject to the lease under the Centerpoint Lease Agreement.

As of December 31, 2016, assets related to the Company’s facility lease obligation were recognized primarily due to the Company being deemed to be the accounting owner of the Centerpoint facility which was being built to be the Company’s corporate headquarters and primary manufacturing facility during its construction period under build-to-suit lease accounting. As discussed in Note 3, the Company determined that it would no longer need to develop the Centerpoint facility. The Company recorded an impairment loss for the net carrying value of the facility asset of $0.7 million during the year ended December 31, 2017. The Company recorded an asset related to the facility lease obligation included in property and equipment of $7.9 million as of December 31, 2016. The facility lease obligation on the Company’s consolidated balance sheet was $7.4 million as of December 31, 2016. The Company also recorded an impairment loss of $18.3 million for the Construction-in-progress on the property during the year ended December 31, 2017 (see Note 3).

In November 2017, TKC, the landlord of the Centerpoint facility, successfully completed the sale of the facility to a third party. In connection with this transaction, the Company entered into a lease termination agreement with TKC pursuant to which the Company received cash proceeds of $1.8 million and recorded a gain on disposition of $1.8 million in the Company’s consolidated statement of operations during the year ended December 31, 2017. Additionally, the Company was no longer required to maintain restricted cash of $0.7 million as a security deposit under the lease.

**Capital Lease Obligations**

In August 2016, the Company entered into two agreements (the “Power Generation Agreements”) with an electric utility company. The Power Generation Agreements are being accounted for as capital leases for financial reporting purposes. Under the lease agreements, the electric utility company agreed to design, procure, install, own and maintain electrical equipment at Centerpoint to provide required electrical loads. The Power Generation Agreements required monthly minimum payments of $32,948 for a period of 128 months, or a total of $4.2 million ending in March 2027. Property, plant and equipment included $2.4 million as of December 31, 2016 under the Power Generation Agreements in the Construction-in-progress account. Since the capital leases were for electrical equipment held for sale on the Centerpoint property, the Company recorded an impairment loss of $0.1 million during the year ended December 31, 2017 (see Note 3). In connection with the sale of the Centerpoint facility discussed above, the capital leases and related equipment were transferred to the buyer of the Centerpoint facility and the related assets and obligations were eliminated from the Company’s consolidated balance sheet as of December 31, 2017.
9. Common Stock

Issuance of Common Stock in 2017

At-the-Market Offering in 2017

In May 2015, the Company entered into a sales agreement, with Cowen, pursuant to which the Company could issue and sell shares of the Company’s common stock from time to time having an aggregate offering price of up to $30 million through Cowen, acting as the Company’s agent. In February 2018, the Company amended and restated the sales agreement with Cowen to increase the maximum aggregate offering price from $30 million to up to $45 million (the “Sales Agreement”). Sales of the Company’s common stock through Cowen may be made by any method permitted that is deemed an “at-the-market offering” as defined in Rule 415 under the Securities Act of 1933, as amended. Cowen is not required to sell any specific number or dollar amount of securities, but acts as a sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, and in accordance with the terms of the Sales Agreement. There is no arrangement for funds to be received in any escrow, trust or similar arrangement. Under the Sales Agreement, the Company has agreed to pay Cowen a commission of up to 3% of the gross proceeds of any sales made pursuant to the Sales Agreement. During the year ended December 31, 2017, the Company sold 3,373,967 shares of common stock pursuant to the Sales Agreement, resulting in proceeds of $15.5 million, net of commissions and issuance costs. The Company sold an additional 3,982,865 shares resulting in $7.3 million of proceeds between January 1, 2018 and March 16, 2018. During the year ended December 31, 2016, the Company sold 43,634 shares of common stock pursuant to the Sales Agreement, resulting in proceeds of $5.5 million, net of commissions and issuance costs. As of March 16, 2018, $15.8 million of stock remained to be sold under the Sales Agreement.

Other Common Stock Issued in 2017

In lieu of paying certain annual cash bonuses for 2016, in January 2017 the Company granted restricted stock awards to certain of its executive officers and employees. The number of shares granted to each executive officer and employee was calculated by dividing 25% of the amount of the 2016 annual cash bonus that would otherwise have been paid by the closing price of the Company’s common stock on January 13, 2017. A total of 4,005 restricted shares of common stock with an aggregate fair value of $0.4 million were issued. Each of the restricted stock awards was subject to a lapping right of repurchase in the Company’s favor, which right lapsed with respect to 100% of the underlying shares of each award on April 17, 2017, for those executive officers and employees still providing services to the Company on such date. During the year ended December 31, 2017, 368 shares of common stock were forfeited back to the Company.

During the year ended December 31, 2017, the Company granted restricted stock awards for an aggregate of 369,998 shares of common stock with a fair value of $1.4 million to 43 employees resulting in stock-based compensation expense of $0.8 million and $0.5 million included in research and development and general and administrative expenses, respectively. Awards for 28,689 shares of common stock vested upon termination of the recipients’ employment during the year ended December 31, 2017 with such costs of $0.1 million included in restructuring expenses. As of December 31, 2017, there were 91,923 unvested restricted shares of common stock outstanding which vest in full during January 2018. Unrecognized compensation for these restricted shares of common stock totaled $14,848 as of December 31, 2017 and was recognized as services were provided during January 2018. Additionally, in June 2017, one grant of 2,333, fully vested shares of common stock was awarded to an employee resulting in stock-based compensation expense of $20,999 included in general and administrative expenses during the year ended December 31, 2017.

In September 2017, under the Invotech Satisfaction and Release Agreement, the Company issued to Invotech .57,142 shares of common stock in partial satisfaction and release of the Company’s payment obligations to Invotech arising under the Company’s development agreement with Invotech.

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In November 2017, under the Saint-Gobain Satisfaction and Release Agreement, the Company issued to Saint-Gobain 34,499 shares of common stock on account of and in partial satisfaction and release of the Company’s payment obligations to Saint-Gobain arising under the Saint-Gobain Development Agreement.

**Issuance of Common Stock in 2016**

**PIPE Financing**

On March 4, 2016, the Company entered into a securities purchase agreement with certain investors pursuant to which the Company agreed to issue and sell an aggregate of up to $60 million of its common stock and warrants to purchase shares of common stock in a PIPE financing. At the closing of the initial tranche in March 2016, the Company sold and the investors purchased, for a total purchase price of approximately $19.9 million, a total of 182,621 shares of common stock and warrants to purchase a total of 136,966 shares of common stock (0.75 shares of common stock for each share of common stock purchased), based on a purchase price per share of common stock and accompanying warrant equal to $108.875. At the closing of the second tranche in June 2016, the Company sold and the investors purchased, for a total purchase price of approximately $29.8 million, a total of 273,933 shares of common stock and warrants to purchase a total of 205,450 shares of common stock at the same price and on the same terms as the first tranche. The warrants issued in each closing have an exercise price of $107.00 per share and expire five years from the date of issuance.

In connection with entering into the securities purchase agreement, the Company entered into a registration rights agreement with the investors pursuant to which the Company registered for resale the shares issued in the financing and the shares issuable upon exercise of the warrants issued in the financing.

**Follow-On Public Offering**

On August 2, 2016, the Company issued and sold 454,545 shares of common stock and warrants to purchase an aggregate of 340,909 shares of common stock, or the August 2016 Warrants, in an underwritten public offering at a price to the public of $110.00 per share and accompanying warrant. The shares of common stock and warrants were sold in combination, with one warrant to purchase up to 0.75 of a share of common stock accompanying each share of common stock sold. The August 2016 Warrants have an exercise price of $110.00 per share, became immediately exercisable upon issuance and will expire on August 2, 2021. The aggregate net proceeds to the Company of the offering were approximately $48.2 million after deducting underwriting discounts and commissions and offering expenses.

**Other Common Stock Issued in 2016**

In lieu of paying certain annual cash bonuses for 2015, in January 2016 the Company granted restricted stock awards to certain of its executive officers and employees. The number of shares granted to each executive officer and employee was calculated by dividing the amount of the 2015 annual cash bonus that would otherwise have been paid to such executive officer or employee by the closing price of the Company’s common stock on January 8, 2016 of $2.24 per share. A total of 296,936 shares of restricted common stock with a value of $665,137 were issued. Each of the restricted stock awards was subject to a lapsing right of repurchase in the Company’s favor, which right will lapse with respect to 100% of the underlying shares of each award on November 20, 2016. All such awards vested.

For 2016, the Company’s board of directors determined that each non-employee director will receive shares of the Company’s common stock under the Company’s 2014 stock incentive plan in lieu of cash board fees on the last day of each calendar quarter in 2016. The number of shares to be granted to each non-employee director on a quarterly basis shall be that number of whole shares of the Company’s common stock equal to the dollar amount of such director’s fees for a given calendar quarter divided by the closing share price of the Company’s common stock on the last trading day of such calendar quarter. During the year ended December 31, 2016, the Company issued 52,173 shares of its common stock as board compensation to non-employee directors in lieu of $288,999 in cash board fees and such amounts are included in general and administrative expenses.
During the year ended December 31, 2016, the Company recorded share-based expense in connection with the grant of restricted stock and restricted stock units to certain executive employees and a consultant of $169,504 and $1,999, respectively, or a total of $171,503. Of these amounts, during the year ended December 31, 2016, $134,388 is included in general and administrative expenses, and $37,115 is included in research and development expenses. During the year ended December 31, 2016, 22,783 shares of restricted stock were granted, 14,514 shares of restricted stock vested and 1,350 shares of restricted stock were forfeited resulting in 6,919 shares of unvested restricted stock as of December 31, 2016. During the year ended December 31, 2016, 21,848 restricted stock units each representing one share of common stock were granted from which 12,744 shares of common stock were vested and issued resulting in 9,104 restricted stock units outstanding as of December 31, 2016.

Issuance of Common Stock in 2015

Lummy License Agreement

In connection with the Company’s entry into the Lummy License Agreement (see Note 12), on April 7, 2015, the Company entered into stock purchase agreements with Tianyi Lummy International Holdings Group, Ltd. and China BioPharma Capital I, L.P. (the “Lummy Entities”), of which Lummy (Hong Kong) Co. Ltd.’s parent company is an affiliate and limited partner, respectively. Pursuant to the purchase agreements, the Lummy Entities purchased an aggregate of 50,000 shares of the Company’s common stock at a per share price of $202.20. The closing price of the Company’s common stock on April 7, 2015 was $171.40 per share, or approximately 18% lower than the $202.20 purchase price per share. The cash proceeds received of $10,110,000 from the issuance of the Company’s common stock were allocated $8,570,000 to common stock and additional paid-in capital and $1,540,000 representing the premium to fair market value paid by the Lummy Entities to deferred revenue attributable to the Lummy License Agreement.

The Lummy Entities have also agreed to purchase approximately $10.0 million in additional shares of the Company’s common stock, for a total aggregate investment of approximately $20.0 million, within 31 days of and subject to the Company reaching full enrollment of the ADAPT trial of rocapuldencel-T for mRCC, receiving a recommendation of the review board for the continuation of the ADAPT trial following 50% of events and receiving positive feedback from the FDA on a qualified protocol to demonstrate comparability of the Company’s automated manufacturing process for rocapuldencel-T to the manufacturing process used by Company in its ADAPT trial. However, on March 4, 2016, the Company entered into a letter agreement with each of the Lummy Entities pursuant to which the Company agreed that upon their purchase of shares and warrants in the PIPE Financing they would have no further obligation to purchase shares pursuant to the purchase agreements.

Cellscript Agreement

On December 22, 2015, the Company entered into a Master Process Development and Supply Agreement with Cellscript, LLC (“Cellscript”). Under the agreement, Cellscript has agreed to develop cGMP processes for the manufacture and production of CD40L RNA, a ribonucleic acid used in the production of the Company’s Arcelis-based products, and to manufacture and produce CD40L RNA for the Company, in each case in accordance with the agreement and a project work agreement previously agreed to by the Company and Cellscript.

In consideration for these development and production services, the Company has agreed to pay Cellscript total fees of $4,600,000. Upon the execution of the agreement and in exchange for research and development services, the Company made a payment to Cellscript of $2,111,432 through the issuance to Cellscript of 45,309 shares of the Company’s common stock. The balance of the owed fees are payable to Cellscript, at the Company’s option, in cash, common stock or a combination of cash and common stock upon the achievement of development milestones. Any shares of common stock issued pursuant to the Cellscript agreement are subject to a lock-up period of 180 days from the date of issuance of such shares to Cellscript.

10. Warrants

In March 2016, the Company sold and certain investors purchased for a total purchase price of $19.9 million a total of 182,621 shares of common stock and warrants to purchase a total of 136,966 shares of common stock at a per share exercise price of $107.00. These warrants will terminate on March 14, 2021 or such earlier date as specified in the warrants. Additionally, in June 2016, the Company sold and such investors purchased for a total purchase price of $29.8 million a total of 273,933 shares of common stock and warrants to purchase a total of 205,450 shares of common stock at a per share exercise price of $107.00. These warrants will terminate on June 29, 2021 or such earlier date as specified in the warrants. In June 2016, warrants to purchase 2,803 shares of common stock were exercised for proceeds of $0.3 million to the Company.
In August 2016, the Company sold and certain investors purchased for a total purchase price of $50.0 million a total of 454,545 shares of common stock and warrants to purchase a total of 340,909 shares of common stock at a per share exercise price of $110.00 (the “August 2016 Warrants”). These warrants will terminate on August 2, 2021 or such earlier date as specified in the warrants.

As discussed in Note 6 regarding the Company’s notes payable, in connection with the Loan Agreement in September 2014, the Company issued to the Lenders and their affiliates the Venture Loan Warrants. Upon the Company’s satisfaction of the conditions precedent to the making of the second tranche loan, the Venture Loan Warrants became exercisable in full. The Venture Loan Warrants will terminate on September 29, 2021 or such earlier date as specified in the Venture Loan Warrants. In addition, in March 2017, the Company issued to the Lenders five year warrants to purchase an aggregate of 5,000 shares of the Company’s common stock at an exercise price of $26.00 per share in consideration of the Lenders accepting the early pay-off of the indebtedness under the Loan Agreement. These warrants were recorded at a fair value of $87,100 and included in additional paid-in capital as of December 31, 2017.

All outstanding warrants were issued with an original life of five years.

As of December 31, 2017, outstanding warrants to purchase a total of 689,661 shares of the Company’s common stock were as follows:

<table>
<thead>
<tr>
<th>Type of Warrant and Classification</th>
<th>Date of Issuance</th>
<th>Number of Shares</th>
<th>Exercise Price</th>
<th>Expiration Date(s)</th>
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<tbody>
<tr>
<td>Common stock - Equity</td>
<td>9/29/14</td>
<td>4,139</td>
<td>$181.20</td>
<td>9/29/21</td>
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<td>Common stock - Equity</td>
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<td>$107.00</td>
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<td>Common stock - Equity</td>
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<td>205,450</td>
<td>$107.00</td>
<td>6/29/21</td>
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<tr>
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<td>340,909</td>
<td>$110.00</td>
<td>8/02/21</td>
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<tr>
<td>Common stock - Equity</td>
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<td>$26.00</td>
<td>3/06/22</td>
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The following warrants were issued in August 2016 and remained outstanding as of December 31, 2017, and include provisions that could require cash settlement of the August 2016 warrants. The August 2016 Warrants are therefore recorded as liabilities of the Company at the estimated fair value as of the date of issuance. The August 2016 Warrants are required to be recorded at fair value as of the end of each subsequent reporting period, with changes in fair value recorded as other income or expense in the Company’s consolidated statement of operations in each subsequent period:

<table>
<thead>
<tr>
<th>August 2016 Warrants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise price</td>
</tr>
<tr>
<td>Expiration date</td>
</tr>
<tr>
<td>Total shares issuable on exercise</td>
</tr>
</tbody>
</table>

The fair value of the August 2016 Warrants is measured using the Black-Scholes valuation model. Inherent in the Black-Scholes valuation model are assumptions related to expected stock price volatility, expected life, risk-free interest rate and dividend yield. The risk-free interest rate is based on the U.S. Treasury five-year maturity yield curve in effect on the date of valuation. The dividend yield percentage is zero because the Company neither currently pays dividends nor intends to do so during the expected term of the August 2016 Warrants. Expected stock price volatility is based on the weighted average of the Company’s historical common stock volatility and the volatility of several peer public companies. The expected life of the August 2016 Warrants is assumed to be equivalent to their remaining contractual term.
The assumptions used by the Company to determine the fair value of the August 2016 Warrants are summarized in the following table as of December 31, 2016 and 2017:

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2016</th>
<th>December 31, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exercise price of warrants</strong></td>
<td>$110.00</td>
<td>$110.00</td>
</tr>
<tr>
<td><strong>Closing underlying stock price on date of valuation</strong></td>
<td>$98.00</td>
<td>$3.00</td>
</tr>
<tr>
<td><strong>Expected stock price volatility</strong></td>
<td>84%</td>
<td>112%</td>
</tr>
<tr>
<td><strong>Expected life (in years)</strong></td>
<td>4.58</td>
<td>3.58</td>
</tr>
<tr>
<td><strong>Risk-free interest rate</strong></td>
<td>1.93%</td>
<td>2.04%</td>
</tr>
<tr>
<td><strong>Expected dividend yield</strong></td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td><strong>Valuation per common share underlying each warrant</strong></td>
<td>$61.38</td>
<td>$0.49</td>
</tr>
<tr>
<td><strong>Total liability for warrants on the consolidated balance sheet</strong></td>
<td>$20,926,061</td>
<td>$167,636</td>
</tr>
<tr>
<td><strong>Decrease in fair value in the years ended December 31, 2016 and 2017</strong></td>
<td>$1,007,352</td>
<td>$20,758,425</td>
</tr>
</tbody>
</table>

In 2013, the Company agreed to enter into a manufacturing rights agreement for the manufacturing of rocapuldencel-T in the European market with Pharmstandard, which also provided for the issuance of warrants to Pharmstandard to purchase 24,989 shares of the Company’s common stock at an exercise price of $116.40 per share. As of March 31, 2018, the Company had not entered into this manufacturing rights agreement or issued such warrants.

**11. Stock Options and Employee Stock Purchase Plan**

**2014 Stock Incentive Plan and 2014 Employee Stock Purchase Plan**

In January 2014, the Company’s board of directors and stockholders approved, effective upon the closing of the Company’s initial public offering, the 2014 Stock Incentive Plan (the “2014 Plan”). Under the 2014 Plan, the Company is authorized to grant incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards for 570,746 shares of common stock plus an annual increase in the number of shares of our common stock available for issuance under the plan on the first day of each fiscal year beginning with the fiscal year ending December 31, 2018 and continuing each fiscal year until, and including, the fiscal year ending December 31, 2024, equal to the lowest of 250,000 shares of common stock, four percent (4%) of the outstanding shares of common stock on such date or an amount determined by our board of directors.

At the July 28, 2017 stockholders’ meeting, the stockholders approved an amendment to the 2014 Plan to increase the number of shares of common stock authorized for issuance under the 2014 Plan by 300,000 and to increase the maximum number of shares that automatically may be added to the 2014 Plan on the first day of each fiscal year until the fiscal year ending December 31, 2024 by 134,548 shares, such that the total number of shares of common stock authorized for issuance under the 2014 Plan is equal to the sum of 570,746 shares, plus an annual increase to be added on the first day of each of the fiscal year, beginning with the fiscal year ending December 31, 2018 and continuing each fiscal year until, and including, the fiscal year ending December 31, 2024, equal to the lowest of (i) 250,000 shares of Common Stock, (ii) four percent (4%) of the outstanding shares of Common Stock on such date or (iii) an amount determined by the Company’s board of directors.

Also in January 2014, the Company’s board of directors and stockholders approved, effective upon the closing of the Company’s initial public offering, a 2014 Employee Stock Purchase Plan (the “2014 ESPP”). Under the 2014 ESPP, on the offering commencement date of each plan period (the “Purchase Plan Period”), the Company will grant to each eligible employee who is then a participant in the 2014 ESPP an option to purchase shares of common stock. The employee may authorize up to a maximum of 10% of his or her base pay to be deducted by the Company during each Purchase Plan Period. Each employee who continues to be a participant in the 2014 ESPP on the last business day of the Purchase Plan Period is deemed to have exercised the option, to the extent of accumulated payroll deductions within the 2014 ESPP ownership limits.
Under the terms of the 2014 ESPP, the option exercise price shall be determined by the Company’s board of directors for each Purchase Plan Period and the option exercise price will be at least 85% of the applicable closing price of the common stock. The option exercise price will be 85% of the lower of the Company’s closing stock price on the first and last business day of each Purchase Plan Period. The Company’s first Purchase Plan Period commenced on September 2, 2014 and ended on February 27, 2015. For the first Purchase Plan Period, 652 shares were purchased with employee withholdings at an option exercise price based upon 85% of the lower of the closing price at the beginning of the first Purchase Plan Period of $196.60 and the closing price on February 27, 2015 of $180.40, resulting in the recognition of share-based compensation expense of $54,508. The Company’s second Purchase Plan Period commenced on March 2, 2015 and ended on August 31, 2015. For the second Purchase Plan Period, 1,015 shares were purchased with employee withholdings at an option exercise price based upon 85% of the lower of the closing price at the beginning of the second Purchase Plan Period of $180.40 and the closing price on August 31, 2015 of $124.20, resulting in the recognition of share-based compensation expense of $72,800. The Company’s third Purchase Plan Period commenced on September 1, 2015 and ended on February 29, 2016. For the third Purchase Plan Period, 1,814 shares were purchased with employee withholdings at an option exercise price based upon 85% of the lower of the closing price at the beginning of the third Purchase Plan Period of $124.80 and the closing price of $88.80 on February 29, 2016, resulting in the recognition of share-based compensation expense of $107,455. The Company’s fourth Purchase Plan Period commenced on March 1, 2016 and ended on August 31, 2016. For the fourth Purchase Plan Period, 1,507 shares were purchased with employee withholdings at an option exercise price based upon 85% of the lower of the closing price at the beginning of the fourth Purchase Plan Period of $98.20 and the closing price of $99.00 on August 31, 2016, resulting in the recognition of share-based compensation expense of $63,788. The Company’s fifth Purchase Plan Period commenced on September 1, 2016 and ended on February 28, 2017. For the fifth Purchase Plan Period, 428 shares were purchased with employee withholdings at an option exercise price based upon 85% of $23.00 on February 28, 2017, resulting in the recognition of share-based compensation expense of $30,064. The Company’s sixth Purchase Plan Period commenced on March 1, 2017 and ended on August 31, 2017. For the sixth Purchase Plan Period, 999 shares were purchased with employee withholdings at an option exercise price based upon 85% of $4.00 on August 31, 2017, resulting in the recognition of share-based compensation expense of $17,711. The Company did not commence a new Purchase Plan Period after September 1, 2017.

Upon the exercise of stock options, vesting of other awards and purchase of shares through the 2014 ESPP or under the 2014 Plan, the Company issues new shares of common stock. All awards granted under the 2014 Plan that are canceled prior to vesting or expire unexercised are returned to the approved pool of reserved shares under the 2014 Plan and made available for future grants. As of December 31, 2017, there were 252,898 shares of common stock remaining available for future issuance under the 2014 Plan and 10,899 shares of common stock remaining available for future issuance under the 2014 ESPP.

The Company recorded the following share-based compensation expense:

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research and development</td>
<td>$2,104,401</td>
<td>$2,818,618</td>
<td>$2,424,924</td>
</tr>
<tr>
<td>General and administrative</td>
<td>$1,910,537</td>
<td>$2,575,874</td>
<td>$3,226,844</td>
</tr>
<tr>
<td>Restructuring costs</td>
<td>—</td>
<td>—</td>
<td>3,215,848</td>
</tr>
<tr>
<td>Total share-based compensation expense</td>
<td>$4,014,938</td>
<td>$5,394,492</td>
<td>$8,867,616</td>
</tr>
</tbody>
</table>

Allocations to research and development and general and administrative expense are based upon the department to which the associated employee reported. No related tax benefits of the share-based compensation expense have been recognized. Share-based payments issued to nonemployees are recorded at their fair values, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period.

Valuation Assumptions for Stock Option Plans and the 2014 ESPP

The stock-based compensation expense recognized for stock option plans was determined using the Black-Scholes option valuation model. Option valuation models require the input of subjective assumptions and these assumptions can vary over time. The weighted average assumptions used were as follows:

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-free interest rate</td>
<td>2.05%</td>
<td>1.50%</td>
<td>2.26%</td>
</tr>
<tr>
<td>Expected dividend yield</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Expected stock option term (in years)</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Expected volatility</td>
<td>87%</td>
<td>82%</td>
<td>86%</td>
</tr>
</tbody>
</table>
The risk-free interest rate is based on the U.S. Treasury yield curve in effect on the date of grant. The dividend yield percentage is zero because the Company neither currently pays dividends nor intends to do so during the expected option term. The Company’s historical share option exercise experience does not provide a reasonable basis upon which to estimate an expected term because of a lack of sufficient data. Therefore, the Company estimates the expected term by using the simplified method allowed by the SEC. Expected stock price volatility is based on the weighted average of the Company’s historical common stock volatility and the volatility of several peer public companies. The weighted average grant date fair value of stock options was $115.20, $76.80 and $72.91 in the years ended December 31, 2015, 2016 and 2017, respectively.

The share-based compensation expense recognized for the 2014 ESPP was determined using the Black-Scholes option valuation model. The range of assumptions used were as follows:

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-free interest rate</td>
<td>0.07% - 0.26%</td>
<td>0.47 - 0.50%</td>
<td>0.69 - 0.79%</td>
</tr>
<tr>
<td>Expected dividend yield</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Expected ESPP rights term (in years)</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Expected volatility</td>
<td>45% - 58%</td>
<td>113% - 141%</td>
<td>141% - 210%</td>
</tr>
</tbody>
</table>

**Other Information for Stock Option Plans**

The following table summarizes the Company’s stock option activity during the year ended December 31, 2017:

<table>
<thead>
<tr>
<th></th>
<th>Number of Shares</th>
<th>Weighted Average Exercise Price</th>
<th>Weighted Average Contractual Term (in years)</th>
<th>Aggregate Intrinsic Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outstanding as of December 31, 2016</td>
<td>245,141</td>
<td>$121.40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Granted</td>
<td>70,604</td>
<td>$95.38</td>
<td>$95.38</td>
<td></td>
</tr>
<tr>
<td>Exercised</td>
<td>—</td>
<td>$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancelled</td>
<td>(46,231)</td>
<td>$97.58</td>
<td>$97.58</td>
<td></td>
</tr>
<tr>
<td>Outstanding as of December 31, 2017</td>
<td>269,514</td>
<td>$111.91</td>
<td>5.58</td>
<td>$</td>
</tr>
<tr>
<td>Exercisable as of December 31, 2017</td>
<td>182,039</td>
<td>$117.01</td>
<td>4.14</td>
<td>$</td>
</tr>
<tr>
<td>Vested and expected to vest as of December 31, 2017</td>
<td>262,778</td>
<td>$112.19</td>
<td>5.66</td>
<td>$</td>
</tr>
</tbody>
</table>

The aggregate intrinsic value of stock options in the table above represents the difference between the $3.00 closing price of the Company’s common stock as of December 31, 2017 and the exercise price of outstanding, exercisable, and vested and expected to vest in-the-money stock options. Since all stock options outstanding have exercise prices higher than $3.00 per share, aggregate intrinsic value is zero as of December 31, 2017.

Included in amounts in the table above, the Company granted performance-based options to three executives to purchase a total of 6,495 shares of the Company’s common stock at an exercise price of $121.80 per share in July 2014. These options vested based on the successful completion of various performance requirements of each of the three executives at various times through December 31, 2017.
The following table summarizes information about the Company’s stock options as of December 31, 2017:

<table>
<thead>
<tr>
<th>Exercise Price or Range of Exercise Price</th>
<th>Options Outstanding</th>
<th>Weighted Average Contractual Life (Years)</th>
<th>Options Exercisable</th>
</tr>
</thead>
<tbody>
<tr>
<td>$3.40</td>
<td>1,500</td>
<td>9.74</td>
<td>125</td>
</tr>
<tr>
<td>$27.00 to $99.00</td>
<td>87,411</td>
<td>5.74</td>
<td>44,601</td>
</tr>
<tr>
<td>$101.00 to $185.60</td>
<td>179,740</td>
<td>5.80</td>
<td>130,825</td>
</tr>
<tr>
<td>$217.22 to $221.80</td>
<td>800</td>
<td>6.87</td>
<td>800</td>
</tr>
<tr>
<td>$705.97 to $733.20</td>
<td>63</td>
<td>3.69</td>
<td>63</td>
</tr>
</tbody>
</table>

Stock options with a fair value of $3.4 million, $4.4 million and $7.4 million completed vesting in the years ended December 31, 2015, 2016 and 2017, respectively. As of December 31, 2017, the Company had a total of $6.0 million in unrecognized compensation expense from unvested stock option awards, of which $2.6 million is expected to be recognized in 2018, $2.0 million in 2019, $1.3 million in 2020, and $0.05 million in 2021.

12. Collaboration Agreements

**Pharmstandard License Agreement**

In August 2013, Pharmstandard purchased shares of the Company’s series E preferred stock. Concurrently with such purchase, the Company entered into an exclusive royalty-bearing license agreement with Pharmstandard. Under this license agreement, the Company granted Pharmstandard and its affiliates a license, with the right to sublicense, develop, manufacture and commercialize rocapuldencel-T and other products for the treatment of human diseases, which are developed by Pharmstandard using the Company’s individualized immunotherapy platform, in the Russian Federation, Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Turkmenistan, Ukraine and Uzbekistan, which the Company refers to as the Pharmstandard Territory. The Company also provided Pharmstandard with a right of first negotiation for development and commercialization rights in the Pharmstandard Territory to specified additional products the Company may develop.

Under the terms of the license agreement, Pharmstandard licensed the Company rights to clinical data generated by Pharmstandard under the agreement and granted the Company an option to obtain an exclusive license outside of the Pharmstandard Territory to develop and commercialize improvements to the Company’s Arcelis technology generated by Pharmstandard under the agreement, a non-exclusive worldwide royalty-free license to Pharmstandard improvements to manufacture products using the Company’s Arcelis technology and a license to specified follow-on licensed products generated by Pharmstandard outside of the Pharmstandard Territory, each on terms to be negotiated upon the Company’s request for a license. In addition, Pharmstandard agreed to pay the Company pass-through royalties on net sales of all licensed products in the low single digits until it has generated a specified amount of aggregate net sales. Once the net sales threshold is achieved, Pharmstandard will pay the Company royalties on net sales of specified licensed products, including rocapuldencel-T, in the low double digits below 20%. These royalty obligations last until the later of the expiration of specified licensed patent rights in a country or the twelfth anniversary of the first commercial sale in such country on a country by country basis and no further royalties on specified other licensed products. After the net sales threshold is achieved, Pharmstandard has the right to offset a portion of the royalties Pharmstandard pays to third parties for licenses to necessary third party intellectual property against the royalties that Pharmstandard pays to the Company.

The agreement will terminate upon expiration of the royalty term, upon which all licenses will become fully paid-up perpetual exclusive licenses. Either party may terminate the agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy and the Company may terminate the agreement if Pharmstandard challenges or assists a third party in challenging specified patent rights of the Company. If Pharmstandard terminates the agreement upon the Company’s material breach or bankruptcy, Pharmstandard is entitled to terminate the Company’s licenses to improvements generated by Pharmstandard, upon which the Company may come to rely for the development and commercialization of rocapuldencel-T and other licensed products outside of the Pharmstandard Territory, and to retain its licenses from the Company and to pay the Company substantially reduced royalty payments following such termination.

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In November 2013, the Company entered into an agreement with Pharmstandard under which Pharmstandard purchased shares of the Company’s series E preferred stock. Under this agreement, the Company agreed to enter into a manufacturing rights agreement for the European market with Pharmstandard, which also provided for the issuance of warrants to Pharmstandard to purchase 24,989 shares of the Company’s common stock at an exercise price of $116.40 per share. The Company has not entered into this manufacturing rights agreement or issued the warrants. All outstanding shares of the Company’s preferred stock converted into shares of the Company’s common stock upon the closing of its initial public offering in February 2014.

**Pharmstandard and Actigen Option Agreement**

On February 1, 2018, the Company entered into an option agreement with Pharmstandard and Actigen Limited to evaluate, with an option to license, certain patent rights and know-how related to a group of fully human PD1 monoclonal antibodies and related technology held by Actigen. Actigen previously granted Pharmstandard an option to exclusively license these patent rights. Under the option agreement, Pharmstandard granted to the Company (i) an exclusive license for evaluation purposes only to make, have made, use and import the PD1 monoclonal antibodies covered by these patent rights (but not offer to sell or sell products and processes covered by or incorporating the patent rights) for a period of one year from the date of the agreement and (ii) an option exercisable during the one-year period to obtain an exclusive license (with the right to sublicense) under the patent rights to make, have made, use, offer for sale, sell and import (with a right to grant sublicenses) the PD1 monoclonal antibodies for all prophylactic, therapeutic and diagnostic uses and for all human diseases and conditions in the United States and Canada. The parties have agreed that, if the Company exercises the option during the option exercise period, the parties will negotiate in good faith a license agreement on the terms and conditions outlined in the option agreement, including payments by us to Pharmstandard of (i) an upfront license fee of $3.6 million, payable upon execution of the license agreement in our common stock of the Company, (ii) various development and regulatory milestone payments totaling $8.5 million, and (iii) upper single digit percentage royalties on net sales of any pharmaceutical product or therapeutic regimen incorporating the licensed PD1 monoclonal antibodies that will apply on a country-by-country basis until the later of the last to expire patent or ten years from the date of first commercial sale, against which the first $5.0 million of our development expenditures will be credited as prepaid royalties.

In consideration for the rights granted under the option agreement, the Company agreed to issue to Pharmstandard, on or before April 2, 2018, 169,014 shares of our common stock, the value of which will be creditable against the upfront license fee if the Company entered into a license agreement. Unless earlier terminated by any party for uncured material breach or by us without cause upon thirty days prior written notice, the option agreement will terminate upon the later of the end of the option exercise period if the Company decides not to exercise the option or sixty days after the Company exercises the option.

**Green Cross License Agreement**

In July 2013, the Company entered into an exclusive royalty-bearing license agreement with Green Cross Corp. ("Green Cross"). Under this agreement, the Company granted Green Cross a license to develop, manufacture and commercialize rocapuldencl-T for mRCC in South Korea. The Company also provided Green Cross with a right of first negotiation for development and commercialization rights in South Korea to specified additional products the Company may develop.

Under the terms of the license, Green Cross has agreed to pay the Company $0.5 million upon the initial submission of an application for regulatory approval of a licensed product in South Korea, $0.5 million upon the initial regulatory approval of a licensed product in South Korea and royalties ranging from the mid-single digits to low double digits below 20% on net sales until the fifteenth anniversary of the first commercial sale in South Korea. In addition, Green Cross has granted the Company an exclusive royalty free license to develop and commercialize all Green Cross improvements to the Company’s licensed intellectual property in the rest of the world, excluding South Korea, except that, as to such improvements for which Green Cross makes a significant financial investment and that generate significant commercial benefit in the rest of the world, the Company is required to negotiate in good faith a reasonable royalty that the Company will be obligated to pay to Green Cross for such license. Under the terms of the agreement, the Company is required to continue to develop and to use commercially reasonable efforts to obtain regulatory approval for rocapuldencl-T in the United States.
The agreement will terminate upon expiration of the royalty term, which is 15 years from the first commercial sale, upon which all licenses will become fully paid up perpetual non-exclusive licenses. Either party may terminate the agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy and the Company may terminate the agreement if Green Cross challenges or assists a third party in challenging specified patent rights of the Company. If Green Cross terminates the agreement upon the Company’s material breach or bankruptcy, Green Cross is entitled to terminate the Company’s licenses to improvements and retain its licenses from the Company and to pay the Company substantially reduced milestone and royalty payments following such termination.

Medinet License Agreement

In December 2013, the Company entered into a license agreement with Medinet Co., Ltd. This agreement was subsequently novated, amended and restated among the Company, Medinet Co., Ltd. and MEDcell Co., Ltd. in October 2014. Pursuant to the novation, Medinet Co., Ltd. assigned and transferred all of its rights and obligations under the original license agreement, including the rights to receive payments under the $9.0 million note in favor of Medinet Co., Ltd., to MEDcell Co., Ltd. without any substantive change in the underlying rights or obligations. Medinet Co., Ltd. and MEDcell Co., Ltd. together are referred to herein as “Medinet.” Under this agreement, the Company granted Medinet an exclusive, royalty-free license to manufacture in Japan rocapuldencel-T and other products using the Company’s Arcelis technology solely for the purpose of the development and commercialization of rocapuldencel-T and these other products for the treatment of mRCC. The Company refers to this license as the manufacturing license.

In addition, under this agreement, the Company granted Medinet an option to acquire a nonexclusive, royalty-bearing license under the Company’s Arcelis technology to sell in Japan rocapuldencel-T and other products for the treatment of mRCC. The Company refers to the option as the sale option and the license as the sale license. This option expired on April 30, 2016. As a result, Medinet may only manufacture rocapuldencel-T and these other products for the Company or its designee. The Company and Medinet have agreed to negotiate in good faith a supply agreement under which Medinet would supply the Company or its designee with rocapuldencel-T and these other products for development and sale for the treatment of mRCC in Japan. During the term of the manufacturing license, the Company may not manufacture rocapuldencel-T or these other products for the Company or any designee for development or sale for the treatment of mRCC in Japan.

In consideration for the manufacturing license, Medinet paid the Company $1.0 million. Medinet also loaned the Company $9.0 million in connection with the Company entering into the agreement. The Company has agreed to use these funds in the development and manufacturing of rocapuldencel-T and the other products. Medinet also agreed to pay the Company milestone payments of up to a total of $9.0 million upon the achievement of developmental and regulatory milestones and $5.0 million upon the achievement of a sales milestone related to rocapuldencel-T and these products. Under the terms of the note and the manufacturing license agreement, any milestone payments related to the developmental and regulatory milestones that become due will be applied first to the repayment of the loan. The first milestone was achieved in July 2015 and resulted in a $1.0 million payment. The second milestone was achieved in June 2016 and resulted in a $2.0 million payment. The third milestone was achieved in March 2017 and resulted in a $2.0 million payment. Together, these milestone payments reduced the outstanding principal under the loan as of December 31, 2017 to $4.0 million.

In December 2013, in connection with the manufacturing license agreement with Medinet, the Company borrowed $9.0 million pursuant to an unsecured promissory note that bears interest at a rate of 3.0% per annum. The principal and interest under the note are due and payable on December 31, 2018. The Company has the right to prepay the loan at any time. If the Company has not repaid the loan by December 31, 2018, then the Company has agreed to grant to Medinet a non-exclusive, royalty-bearing license to make and sell Arcelis products in Japan for the treatment of cancer. In such event, the amounts owing under the loan as of December 31, 2018 may constitute pre-paid royalties under the license or would be due and payable. Royalties under this license would be paid until the expiration of the licensed patent rights in Japan at a rate to be negotiated. If the Company and Medinet cannot agree on the royalty rate, the Company and Medinet have agreed to submit the matter to arbitration.

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The Company recorded the initial $1.0 million payment from Medinet as a deferred liability. In addition, because the $9.0 million promissory note was issued at a below market interest rate, the Company allocated the proceeds of the loan between the manufacturing license agreement and the debt at the time of issuance. Accordingly, as of December 31, 2013, the date of borrowing, the Company recorded $6.9 million to notes payable, based upon an effective interest rate of 8.0%, and $2.1 million as a deferred liability. During the year ended December 31, 2015, the Company recognized a $1.0 million milestone payment as deferred revenue under the license agreement and reduced the related note payable by $0.8 million and the deferred liability by $0.2 million. During the year ended December 31, 2016, the Company recognized a $2.0 million milestone payment as deferred revenue under this license agreement and reduced the related note payable by $1.5 million and the deferred liability by $0.5 million. During the year ended December 31, 2017, the Company recognized an additional $2.0 million milestone payment as deferred revenue under this license agreement and reduced the related note payable by $1.5 million and the deferred liability by $0.5 million. As of December 31, 2016, the amount of the note payable was $6.4 million, including $1.8 million accrued interest. As of December 31, 2017, the amount of the note payable was $5.0 million, including $1.9 million accrued interest. As of December 31, 2016 and 2017, the total deferred liability associated with the Medinet note was $5.4 million, and $6.9 million, respectively.

The agreement will terminate upon expiration of the royalty term, upon which all licenses will become fully paid up, perpetual non-exclusive licenses. Either party may terminate the agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy, and the Company may terminate the agreement if Medinet challenges or assists a third party in challenging specified patent rights of the Company. If Medinet terminates the agreement upon the Company’s material breach or bankruptcy, Medinet is entitled to terminate the Company’s licenses to improvements and retain its royalty-bearing licenses from the Company.

**Lummy License Agreement**

On April 7, 2015, the Company and Lummy (Hong Kong) Co. Ltd. (“Lummy HK”), a wholly owned subsidiary of Chongqing Lummy Pharmaceutical Co. Ltd., entered into a license agreement (the “License Agreement”) whereby the Company granted to Lummy HK an exclusive license under the Arcelis technology, including patents, know-how and improvements to manufacture, develop and commercialize products for the treatment of cancer (“Licensed Product”) in China, Hong Kong, Taiwan and Macau (the “Territory”). Under the License Agreement, Lummy HK also has a right of first negotiation to manufacture, develop, and commercialize products for the territory of the U.S. and Canada for the treatment of cancer (“Licensed Product”) in China, Hong Kong, Taiwan and Macau (the “Territory”). Under the License Agreement, Lummy HK also has a right of first negotiation with respect to a license under the Arcelis technology for the treatment of infectious diseases in the Territory. This agreement was subsequently amended in December 2016 and also in October 2017.

Under the terms of the License Agreement, the parties will share relevant data, and the Company will have a right to reference Lummy HK data for purposes of its development programs under the Arcelis technology. In addition, Lummy HK has granted to the Company an exclusive, royalty-free license under and to any and all Lummy HK improvements to the Arcelis technology conceived or reduced to practice by Lummy HK (“Lummy HK Improvements”) and Lummy HK data to develop and/or commercialize products (“Arcelis-Based Products”) outside the Territory, an exclusive, royalty-free license under and to any and all investigational new drug applications (“INDs”) and other regulatory approvals and Lummy HK trademarks used for an Arcelis-Based Product to develop and/or commercialize an Arcelis-Based Product outside the Territory and a non-exclusive, worldwide, royalty-free license under any Lummy HK Improvements and Lummy HK data to manufacture Arcelis-Based Products anywhere in the world. Lummy HK has the right to reference the Company’s data, INDs and other regulatory filings and submissions for the purpose of developing and obtaining regulatory approval of Licensed Products in the Territory.

Pursuant to the License Agreement, Lummy HK will pay the Company royalties on net sales and an aggregate of up to $22.3 million upon the achievement of manufacturing, regulatory and commercial milestones. The License Agreement will terminate upon expiration of the last to expire royalty term for all Arcelis-Based Products, with each royalty term being the longer of the expiration of the last valid patent claim covering the applicable Arcelis-Based Product and 10 years from the first commercial sale of such Arcelis-Based Product. Either party may terminate the License Agreement for the other party’s uncured material breach or if specified conditions occur relating to the other party’s insolvency or bankruptcy. The Company may terminate the License Agreement if Lummy HK challenges or assists a third party in challenging specified patent rights of the Company. If Lummy HK terminates the License Agreement upon the Company’s material breach or bankruptcy, Lummy HK is entitled to terminate the licenses it granted to the Company and retain its licenses from the Company with respect to Arcelis-Based Products then in development or being commercialized, subject to Lummy HK’s continued obligation to pay royalties and milestones with respect to such Arcelis-Based Products.
Pursuant to the license agreement, Lummy HK paid the Company a $1.5 million upon the achievement of a manufacturing milestone in October 2017. The milestone payment was made in consideration of the successful initiation of transfer of technology related to the manufacturing of Rocapulデンシ-T, to which Lummy HK has a license for commercialization in China and other Asian territories. The Company recorded the $1.5 million payment from Lummy HK as revenue.

13. Commitments

The Company rents laboratory and office space and equipment under operating leases that expire in various years through 2023. Future minimum lease payments under noncancelable operating leases as of December 31, 2017 are as follows:

<table>
<thead>
<tr>
<th>Year</th>
<th>Payment ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>602,177</td>
</tr>
<tr>
<td>2019</td>
<td>640,309</td>
</tr>
<tr>
<td>2020</td>
<td>656,272</td>
</tr>
<tr>
<td>2021</td>
<td>650,607</td>
</tr>
<tr>
<td>2022</td>
<td>376,205</td>
</tr>
<tr>
<td>Thereafter</td>
<td>29,699</td>
</tr>
<tr>
<td>Total minimum lease payments</td>
<td>2,955,269</td>
</tr>
</tbody>
</table>

Rent expense related to operating leases for the years ended December 31, 2015, 2016 and 2017 was $536,932, $1,098,452 and $1,296,280, respectively.

The Company has entered into various licensing agreements with universities and other research institutions under which the Company receives substantially all rights of the inventors or co-assignee to produce and market technology protected by certain patents and patent applications. The Company also entered into various assignment agreements with a scientist under which the Company receives exclusive rights to produce and market technology protected by certain patents and patent applications.

The Company is generally required to make royalty payments ranging from 1% to 4% of future sales of products employing the technology or falling under claims of a patent. If future sales require the use of technology licensed from multiple different sources, the total royalty rates could be higher. As royalty payments are directly related to future sales volume, future commitments cannot be determined. No accrual for future payments under these agreements has been recorded, as the Company cannot estimate if, when or in what amount payments may become due.

14. Employee Benefit Plan

The Company provides a retirement plan qualified under section 401(k) of the Internal Revenue Code of 1986, as amended (“IRC”). Participants may elect to contribute a portion of their annual compensation to the plan, after complying with certain limitations set by the IRC. All employees are eligible to participate in the plan after attaining the age of 21. The Company matched 25% of the first 6% contributed by eligible participants in the plan during the years ended December 31, 2015, 2016 and 2017, or $334,487, $350,646 and $243,598, respectively.
The following table presents the computation of basic and diluted net loss per share of common stock:

<table>
<thead>
<tr>
<th>Year Ended December 31</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net loss attributable to common stockholders</td>
<td>$(74,788,521)</td>
<td>$(53,028,110)</td>
<td>$(40,577,510)</td>
</tr>
<tr>
<td>Weighted average common shares outstanding, basic and diluted</td>
<td>1,022,862</td>
<td>1,600,286</td>
<td>3,017,409</td>
</tr>
<tr>
<td>Net loss per share attributable to common stockholders, basic and diluted</td>
<td>$(73.12)</td>
<td>$(33.14)</td>
<td>$(13.45)</td>
</tr>
</tbody>
</table>

The following potentially dilutive securities have been excluded from the computation of diluted weighted average shares outstanding, as they would be antidilutive:

<table>
<thead>
<tr>
<th>Year Ended December 31</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stock options outstanding</td>
<td>157,451</td>
<td>211,509</td>
<td>283,443</td>
</tr>
<tr>
<td>Warrants outstanding</td>
<td>4,139</td>
<td>356,339</td>
<td>688,771</td>
</tr>
<tr>
<td>Convertible notes outstanding</td>
<td>—</td>
<td>—</td>
<td>518,382</td>
</tr>
</tbody>
</table>

16. Selected Quarterly Data (unaudited)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenue</td>
<td>$146,429</td>
<td>$488,643</td>
<td>$146,756</td>
<td>$163,640</td>
</tr>
<tr>
<td>Operating expenses:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>9,501,976</td>
<td>9,164,184</td>
<td>9,340,018</td>
<td>10,301,058</td>
</tr>
<tr>
<td>General and administrative</td>
<td>2,975,024</td>
<td>3,389,479</td>
<td>3,010,518</td>
<td>4,828,280</td>
</tr>
<tr>
<td>Impairment of property and equipment (1)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>741,114</td>
</tr>
<tr>
<td>Operating loss</td>
<td>(12,330,571)</td>
<td>(12,065,020)</td>
<td>(12,203,780)</td>
<td>(15,706,812)</td>
</tr>
<tr>
<td>Other income (expense), net</td>
<td>(489,617)</td>
<td>(541,225)</td>
<td>(43,061)</td>
<td>(351,976)</td>
</tr>
<tr>
<td>Net loss</td>
<td>$(12,820,188)</td>
<td>$(12,606,245)</td>
<td>$(12,246,841)</td>
<td>$(15,354,836)</td>
</tr>
<tr>
<td>Net loss per share, basic and diluted</td>
<td>$(11.34)</td>
<td>$(9.67)</td>
<td>$(6.46)</td>
<td>$(7.45)</td>
</tr>
<tr>
<td>Weighted average shares outstanding, basic and diluted</td>
<td>1,130,331</td>
<td>1,303,308</td>
<td>1,896,911</td>
<td>2,062,257</td>
</tr>
</tbody>
</table>

(1) Represents impairment loss on property and equipment held for sale in the three months ended December 31, 2016; none present in other periods presented.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenue</td>
<td>$105,259</td>
<td>$69,693</td>
<td>$53,497</td>
<td>$1,670,949</td>
</tr>
<tr>
<td>Operating expenses:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research and development</td>
<td>7,913,829</td>
<td>5,120,952</td>
<td>4,550,353</td>
<td>4,070,962</td>
</tr>
<tr>
<td>General and administrative</td>
<td>3,962,891</td>
<td>2,679,867</td>
<td>2,879,011</td>
<td>2,661,466</td>
</tr>
<tr>
<td>Impairment of property and equipment (1)</td>
<td>27,204,349</td>
<td>—</td>
<td>—</td>
<td>50,036</td>
</tr>
<tr>
<td>Restructuring costs (2)</td>
<td>5,008,292</td>
<td>344,474</td>
<td>679,013</td>
<td>—</td>
</tr>
<tr>
<td>Gain on disposal of impaired property (3)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(2,767,540)</td>
</tr>
<tr>
<td>Operating loss</td>
<td>(43,984,102)</td>
<td>(8,075,600)</td>
<td>(8,054,880)</td>
<td>(2,343,975)</td>
</tr>
<tr>
<td>Other income (expense), net (4)</td>
<td>(19,904,021)</td>
<td>(463,011)</td>
<td>1,988,933</td>
<td>451,104</td>
</tr>
<tr>
<td>Net loss</td>
<td>$(24,080,081)</td>
<td>$(8,538,611)</td>
<td>$(6,065,947)</td>
<td>$(1,892,871)</td>
</tr>
<tr>
<td>Net loss per share, basic and diluted</td>
<td>$(11.66)</td>
<td>$(4.13)</td>
<td>$(2.08)</td>
<td>$(0.38)</td>
</tr>
<tr>
<td>Weighted average shares outstanding, basic and diluted</td>
<td>2,065,676</td>
<td>2,068,743</td>
<td>2,911,800</td>
<td>4,992,418</td>
</tr>
</tbody>
</table>

(1) Represents impairment loss on property and equipment held for sale in the three months ended March 31, 2017 and March 31, 2016; none present in other periods presented.
(2) Represents costs of a reduction-in-force and early termination of a lease agreement implemented in March 2017.

(3) Represents a gain on sale of impaired property in the three months ended December 31, 2017 from the disposal of the Centerpoint property and certain other property in the Saint-Gobain debt restructuring.

(4) Primarily represents gain on change in value of warrants classified as liabilities of $20,357,323 in the three months ended March 31, 2017 and a gain on early extinguishment of debt of $1,506,901 and $600,119 in the three months ended September 30, 2017 and December 31, 2017, respectively.

17. Legal Proceedings

The Company is not a party to any legal proceedings and is not aware of any claims or actions pending or threatened against it. In the future, the Company might from time to time become involved in litigation relating to claims arising from its ordinary course of business.

18. Subsequent Events

On January 8, 2018, the Company announced that, on January 6, 2018, it signed a Stock Purchase Agreement with Lummy under which the Company agreed to issue and sell to Lummy in a private financing 375,000 shares of the Company’s common stock for an aggregate purchase price of $1,500,000. In March 2018, the Company and Lummy amended the stock purchase agreement to reduce the aggregate price for the shares to $450,000. Concurrent with such amendment, the Company entered into an amendment to the license agreement with Lummy pursuant to which Lummy agreed to pay us a $1.05 million milestone payment.

On February 14, 2018, the Company notified Medinet that the Company irrevocably agreed to have no further right under the license agreement to revoke the manufacturing and sale license, or the sale license only. In all other respects, the Medinet license agreement will remain in full force and effect. As a result of the revocation right no longer being of force and effect, the Company expects to recognize $5.8 million of deferred milestone revenue as revenue under ASU 2014-09 in the first quarter of 2018. As noted in Note 1, the impact of the new standard has not been finalized and is therefore subject to change.
**Deferred Tax Asset Valuation Allowance**

Information presented below is in thousands:

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>Balance at Beginning of Year</th>
<th>Charged to Expenses (a)</th>
<th>Charged to Other Accounts</th>
<th>Increases</th>
<th>Balance at End of Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>$102,594</td>
<td>$(18,700)</td>
<td>$</td>
<td>— $</td>
<td>83,894</td>
</tr>
<tr>
<td>2016</td>
<td>$84,903</td>
<td>$17,691</td>
<td>$</td>
<td>— $</td>
<td>102,594</td>
</tr>
<tr>
<td>2015</td>
<td>$68,197</td>
<td>$16,706</td>
<td>$</td>
<td>— $</td>
<td>84,903</td>
</tr>
</tbody>
</table>

(a) Impact of providing full valuation allowance against all deferred tax assets since the Company could not assert that it was more likely than not that these deferred tax assets would be realized.
FIRST: The name of the Corporation is Argos Therapeutics, Inc.

SECOND: The address of the Corporation’s registered office in the State of Delaware is 2711 Centerville Road, Suite 400, in the City of Wilmington, County of New Castle, 19808. The name of its registered agent at that address is Corporation Service Company.

THIRD: The nature of the business or purposes to be conducted or promoted by the Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of the State of Delaware.

FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is 205,000,000 shares, consisting of (i) 200,000,000 shares of Common Stock, $0.001 par value per share (“Common Stock”), and (ii) 5,000,000 shares of Preferred Stock, $0.001 par value per share (“Preferred Stock”).

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A COMMON STOCK

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights of the holders of the Preferred Stock of any series as may be designated by the Board of Directors upon any issuance of the Preferred Stock of any series.

2. Voting. The holders of the Common Stock shall have voting rights at all meetings of stockholders, each such holder being entitled to one vote for each share thereof held by such holder; provided, however, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Certificate of Incorporation (which, as used herein, shall mean the certificate of incorporation of the Corporation, as amended from time to time, including the terms of any certificate of designations of any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon pursuant to this Certificate of Incorporation. There shall be no cumulative voting.

The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

3. Dividends. Dividends may be declared and paid on the Common Stock from funds lawfully available therefor as and when determined by the Board of Directors and subject to any preferential dividend or other rights of any then outstanding Preferred Stock.

4. Liquidation. Upon the dissolution or liquidation of the Corporation, whether voluntary or involuntary, holders of Common Stock will be entitled to receive all assets of the Corporation available for distribution to its stockholders, subject to any preferential or other rights of any then outstanding Preferred Stock.
Preferred Stock may be issued from time to time in one or more series, each of such series to have such terms as stated or expressed herein and in the resolution or resolutions providing for the issue of such series adopted by the Board of Directors of the Corporation as hereinafter provided. Any shares of Preferred Stock which may be redeemed, purchased or acquired by the Corporation may be reissued except as otherwise provided by law.

Authority is hereby expressly granted to the Board of Directors from time to time to issue the Preferred Stock in one or more series, and in connection with the creation of any such series, by adopting a resolution or resolutions providing for the issuance of the shares thereof and by filing a certificate of designations relating thereto in accordance with the General Corporation Law of the State of Delaware, to determine and fix the number of shares of such series and such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitations or restrictions thereof, including without limitation thereof, dividend rights, conversion rights, redemption privileges and liquidation preferences, as shall be stated and expressed in such resolutions, all to the full extent now or hereafter permitted by the General Corporation Law of the State of Delaware. Without limiting the generality of the foregoing, the resolutions providing for issuance of any series of Preferred Stock may provide that such series shall be superior or rank equally or be junior to any other series of Preferred Stock to the extent permitted by law.

The number of authorized shares of Preferred Stock may be increased or decreased (but not below the number of shares then outstanding) by the affirmative vote of the holders of a majority of the voting power of the capital stock of the Corporation entitled to vote thereon, voting as a single class, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

FIFTH: Except as otherwise provided herein, the Corporation reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by statute and this Certificate of Incorporation, and all rights conferred upon stockholders herein are granted subject to this reservation.

SIXTH: In furtherance and not in limitation of the powers conferred upon it by the General Corporation Law of the State of Delaware, and subject to the terms of any series of Preferred Stock, the Board of Directors shall have the power to adopt, amend, alter or repeal the By-laws of the Corporation by the affirmative vote of a majority of the directors present at any regular or special meeting of the Board of Directors at which a quorum is present. The stockholders may not adopt, amend, alter or repeal the By-laws of the Corporation, or adopt any provision inconsistent therewith, unless such action is approved, in addition to any other vote required by this Certificate of Incorporation, by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes that all the stockholders would be entitled to cast in any annual election of directors or class of directors. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article SIXTH.

SEVENTH: Except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty, no director of the Corporation shall be personally liable to the Corporation or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability. No amendment to or repeal of this provision shall apply to or have any effect on the liability or alleged liability of any director of the Corporation for or with respect to any acts or omissions of such director occurring prior to such amendment or repeal. If the General Corporation Law of the State of Delaware is amended to permit further elimination or limitation of the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law of the State of Delaware as so amended.
EIGHTH: The Corporation shall provide indemnification as follows:

1. Actions, Suits and Proceedings Other than by or in the Right of the Corporation. The Corporation shall indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the Right of the Corporation) by reason of the fact that he or she is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) (all such persons being referred to hereafter as an “Indemnitee”), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys’ fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974), and amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that Indemnitee did not act in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his or her conduct was unlawful.

2. Actions or Suits by or in the Right of the Corporation. The Corporation shall indemnify any Indemnitee who was or is a party to or threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that Indemnitee is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys’ fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, except that no indemnification shall be made under this Section 2 in respect of any claim, issue or matter as to which Indemnitee shall have been adjudged to be liable to the Corporation, unless, and only to the extent, that the Court of Chancery of Delaware or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of such liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnity for such expenses (including attorneys’ fees) which the Court of Chancery of Delaware or such other court shall deem proper.

3. Indemnification for Expenses of Successful Party. Notwithstanding any other provisions of this Article EIGHTH, to the extent that an Indemnitee has been successful, on the merits or otherwise, in defense of any action, suit or proceeding referred to in Sections 1 and 2 of this Article EIGHTH, or in defense of any claim, issue or matter therein, or on appeal from any such action, suit or proceeding, Indemnitee shall be indemnified against all expenses (including attorneys’ fees) actually and reasonably incurred by or on behalf of Indemnitee in connection therewith. Without limiting the foregoing, if any action, suit or proceeding is disposed of, on the merits or otherwise (including a disposition without prejudice), without (i) the disposition being adverse to Indemnitee, (ii) an adjudication that Indemnitee was liable to the Corporation, (iii) a plea of guilty or nolo contendere by Indemnitee, (iv) an adjudication that Indemnitee did not act in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the Corporation, and (v) with respect to any criminal proceeding, an adjudication that Indemnitee had reasonable cause to believe his or her conduct was unlawful, Indemnitee shall be considered for the purposes hereof to have been wholly successful with respect thereto.

4. Notification and Defense of Claim. As a condition precedent to an Indemnitee’s right to be indemnified, such Indemnitee must notify the Corporation in writing as soon as practicable of any action, suit, proceeding or investigation involving such Indemnitee for which indemnity will or could be sought. With respect to any action, suit, proceeding or investigation of which the Corporation is so notified, the Corporation will be entitled to participate therein at its own expense and/or to assume the defense thereof at its own expense, with legal counsel reasonably acceptable to Indemnitee. After notice from the Corporation to Indemnitee of its election so to assume such defense, the Corporation shall not be liable to Indemnitee for any legal or other expenses subsequently incurred by Indemnitee in connection with such action, suit, proceeding or investigation, other than as provided below in this Section 4. Indemnitee shall have the right to employ his or her own counsel in connection with such action, suit, proceeding or investigation, but the fees and expenses of such counsel incurred after notice from the Corporation of its assumption of the defense thereof shall be at the expense of Indemnitee unless (i) the employment of counsel by Indemnitee has been authorized by the Corporation, (ii) counsel to Indemnitee shall have reasonably concluded that there may be a conflict of interest or position on any significant issue between the Corporation and Indemnitee in the conduct of the defense of such action, suit, proceeding or investigation or (iii) the Corporation shall not in fact have employed counsel to assume the defense of such action, suit, proceeding or investigation, in each of which cases the fees and expenses of counsel for Indemnitee shall be at the expense of the Corporation, except as otherwise expressly provided by this Article EIGHTH. The Corporation shall not be entitled, without the consent of Indemnitee, to assume the defense of any claim brought by or in the right of the Corporation or as to which counsel for Indemnitee shall have reasonably made the conclusion provided for in clause (ii) above. The Corporation shall not be required to indemnify Indemnitee under this Article EIGHTH for any amounts paid in settlement of any action, suit, proceeding or investigation effected without its written consent. The Corporation shall not settle any action, suit, proceeding or investigation in any manner which would impose any penalty or limitation on Indemnitee without Indemnitee’s written consent. Neither the Corporation nor Indemnitee will unreasonably withhold or delay its consent to any proposed settlement.
5. **Advance of Expenses.** Subject to the provisions of Section 6 of this Article EIGHTH, in the event of any threatened or pending action, suit, proceeding or investigation of which the Corporation receives notice under this Article EIGHTH, any expenses (including attorneys' fees) incurred by or on behalf of Indemnitee in defending an action, suit, proceeding or investigation or any appeal therefrom shall be paid by the Corporation in advance of the final disposition of such matter; provided, however, that the payment of such expenses incurred by or on behalf of Indemnitee in advance of the final disposition of such matter shall be made only upon receipt of an undertaking by or on behalf of Indemnitee to repay all amounts so advanced in the event that it shall ultimately be determined by final judicial decision from which there is no further right to appeal that Indemnitee is not entitled to be indemnified by the Corporation as authorized in this Article EIGHTH; and provided further that no such advancement of expenses shall be made under this Article EIGHTH if it is determined (in the manner described in Section 6) that (i) Indemnitee did not act in good faith and in a manner he or she reasonably believed to be in, or not opposed to, the best interests of the Corporation, or (ii) with respect to any criminal action or proceeding, Indemnitee had reasonable cause to believe his or her conduct was unlawful. Such undertaking shall be accepted without reference to the financial ability of Indemnitee to make such repayment.

6. **Procedure for Indemnification and Advancement of Expenses.** In order to obtain indemnification or advancement of expenses pursuant to Section 1, 2, 3 or 5 of this Article EIGHTH, an Indemnitee shall submit to the Corporation a written request. Any such advancement of expenses shall be made promptly, and in any event within 60 days after receipt by the Corporation of the written request of Indemnitee, unless (i) the Corporation has assumed the defense pursuant to Section 4 of this Article EIGHTH (and none of the circumstances described in Section 4 of this Article EIGHTH that would nonetheless entitle the Indemnitee to indemnification for the fees and expenses of separate counsel have occurred) or (ii) the Corporation determines within such 60-day period that Indemnitee did not meet the applicable standard of conduct set forth in Section 1, 2 or 5 of this Article EIGHTH, as the case may be. Any such indemnification, unless ordered by a court, shall be made with respect to requests under Section 1 or 2 only as authorized in the specific case upon a determination by the Corporation that the indemnification of Indemnitee is proper because Indemnitee has met the applicable standard of conduct set forth in Section 1 or 2, as the case may be. Such determination shall be made in each instance (a) by a majority vote of the directors of the Corporation consisting of persons who are not at that time parties to the action, suit or proceeding in question (“disinterested directors”), whether or not a quorum, (b) by a committee of disinterested directors designated by majority vote of disinterested directors, whether or not a quorum, (c) if there are no disinterested directors, or if the disinterested directors so direct, by independent legal counsel (who may, to the extent permitted by law, be regular legal counsel to the Corporation) in a written opinion, or (d) by the stockholders of the Corporation.

7. **Remedies.** The right to indemnification or advancement of expenses as granted by this Article EIGHTH shall be enforceable by Indemnitee in any court of competent jurisdiction. Neither the failure of the Corporation to have made a determination prior to the commencement of such action that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Corporation pursuant to Section 6 of this Article EIGHTH that Indemnitee has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct. In any suit brought by Indemnitee to enforce a right to indemnification, or brought by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the Corporation shall have the burden of proving that Indemnitee is not entitled to be indemnified, or to such advancement of expenses, under this Article EIGHTH. Indemnitee’s expenses (including attorneys’ fees) reasonably incurred in connection with successfully establishing Indemnitee’s right to indemnification, in whole or in part, in any such proceeding shall also be indemnified by the Corporation. Notwithstanding the foregoing, in any suit brought by Indemnitee to enforce a right to indemnification hereunder it shall be a defense that the Indemnitee has not met any applicable standard for indemnification set forth in the General Corporation Law of the State of Delaware.
8. **Limitations.** Notwithstanding anything to the contrary in this Article EIGHTH, except as set forth in Section 7 of this Article EIGHTH, the Corporation shall not indemnify an Indemnitee pursuant to this Article EIGHTH in connection with a proceeding (or part thereof) initiated by such Indemnitee unless the initiation thereof was approved by the Board of Directors of the Corporation. Notwithstanding anything to the contrary in this Article EIGHTH, the Corporation shall not indemnify an Indemnitee to the extent such Indemnitee is reimbursed from the proceeds of insurance, and in the event the Corporation makes any indemnification payments to an Indemnitee and such Indemnitee is subsequently reimbursed from the proceeds of insurance, such Indemnitee shall promptly refund indemnification payments to the Corporation to the extent of such insurance reimbursement.

9. **Subsequent Amendment.** No amendment, termination or repeal of this Article EIGHTH or of the relevant provisions of the General Corporation Law of the State of Delaware or any other applicable laws shall adversely affect or diminish in any way the rights of any Indemnitee to indemnification under the provisions hereof with respect to any action, suit, proceeding or investigation arising out of or relating to any actions, transactions or facts occurring prior to the final adoption of such amendment, termination or repeal.

10. **Other Rights.** The indemnification and advancement of expenses provided by this Article EIGHTH shall not be deemed exclusive of any other rights to which an Indemnitee seeking indemnification or advancement of expenses may be entitled under any law (common or statutory), agreement or vote of stockholders or disinterested directors or otherwise, both as to action in Indemnitee’s official capacity and as to action in any other capacity while holding office for the Corporation, and shall continue as to an Indemnitee who has ceased to be a director or officer, and shall inure to the benefit of the estate, heirs, executors and administrators of Indemnitee. Nothing contained in this Article EIGHTH shall be deemed to prohibit, and the Corporation is specifically authorized to enter into, agreements with officers and directors providing indemnification rights and procedures different from those set forth in this Article EIGHTH. In addition, the Corporation may, to the extent authorized from time to time by its Board of Directors, grant indemnification rights to other employees or agents of the Corporation or other persons serving the Corporation and such rights may be equivalent to, or greater or less than, those set forth in this Article EIGHTH.

11. **Partial Indemnification.** If an Indemnitee is entitled under any provision of this Article EIGHTH to indemnification by the Corporation for some or a portion of the expenses (including attorneys’ fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with any action, suit, proceeding or investigation and any appeal therefrom but not, however, for the total amount thereof, the Corporation shall nevertheless indemnify Indemnitee for the portion of such expenses (including attorneys’ fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement to which Indemnitee is entitled.

12. **Insurance.** The Corporation may purchase and maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of the Corporation or another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) against any expense, liability or loss incurred by him or her in any such capacity, or arising out of his or her status as such, whether or not the Corporation would have the power to indemnify such person against such expense, liability or loss under the General Corporation Law of the State of Delaware.
13. **Savings Clause.** If this Article EIGHTH or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Corporation shall nevertheless indemnify each Indemnitee as to any expenses (including attorneys’ fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) and amounts paid in settlement in connection with any action, suit, proceeding or investigation, whether civil, criminal or administrative, including an action by or in the right of the Corporation, to the fullest extent permitted by any applicable portion of this Article EIGHTH that shall not have been invalidated and to the fullest extent permitted by applicable law.

14. **Definitions.** Terms used herein and defined in Section 145(h) and Section 145(i) of the General Corporation Law of the State of Delaware shall have the respective meanings assigned to such terms in such Section 145(h) and Section 145(i).

NINTH: This Article NINTH is inserted for the management of the business and for the conduct of the affairs of the Corporation.

1. **General Powers.** The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors.

2. **Number of Directors; Election of Directors.** Subject to the rights of holders of any series of Preferred Stock to elect directors, the number of directors of the Corporation shall be established by the Board of Directors. Election of directors need not be by written ballot, except as and to the extent provided in the By-laws of the Corporation.

3. **Classes of Directors.** Subject to the rights of holders of any series of Preferred Stock to elect directors, the Board of Directors shall be and is divided into three classes, designated Class I, Class II and Class III. Each class shall consist, as nearly as may be possible, of one-third of the total number of directors constituting the entire Board of Directors. The Board of Directors is authorized to assign members of the Board of Directors already in office to Class I, Class II or Class III at the time such classification becomes effective.

4. **Terms of Office.** Subject to the rights of holders of any series of Preferred Stock to elect directors, each director shall serve for a term ending on the date of the third annual meeting of stockholders following the annual meeting of stockholders at which such director was elected; provided that each director initially assigned to Class I shall serve for a term expiring at the Corporation’s first annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; each director initially assigned to Class II shall serve for a term expiring at the Corporation’s second annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; and each director initially assigned to Class III shall serve for a term expiring at the Corporation’s third annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; provided further, that the term of each director shall continue until the election and qualification of his or her successor and be subject to his or her earlier death, resignation or removal.

5. **Quorum.** The greater of (a) a majority of the directors at any time in office and (b) one-third of the number of directors fixed pursuant to Section 2 of this Article NINTH shall constitute a quorum of the Board of Directors. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of the directors present may adjourn the meeting from time to time without further notice other than announcement at the meeting, until a quorum shall be present.

6. **Action at Meeting.** Every act or decision done or made by a majority of the directors present at a meeting duly held at which a quorum is present shall be regarded as the act of the Board of Directors unless a greater number is required by law or by this Certificate of Incorporation.

7. **Removal.** Subject to the rights of holders of any series of Preferred Stock, directors of the Corporation may be removed only for cause and only by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors.

8. **Vacancies.** Subject to the rights of holders of any series of Preferred Stock, any vacancy or newly created directorship in the Board of Directors, however occurring, shall be filled only by vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director and shall not be filled by the stockholders. A director elected to fill a vacancy shall hold office until the next election of the class for which such director shall have been chosen, subject to the election and qualification of a successor and to such director’s earlier death, resignation or removal.
9. **Stockholder Nominations and Introduction of Business, Etc.** Advance notice of stockholder nominations for election of directors and other business to be brought by stockholders before a meeting of stockholders shall be given in the manner provided by the By-laws of the Corporation.

10. **Amendments to Article.** Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article NINTH.

**TENTH:** Stockholders of the Corporation may not take any action by written consent in lieu of a meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article TENTH.

**ELEVENTH:** Special meetings of stockholders for any purpose or purposes may be called at any time by only the Board of Directors, the Chairman of the Board or the Chief Executive Officer, and may not be called by any other person or persons. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article ELEVENTH.

**TWELFTH:** Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall, to the fullest extent permitted by law, be the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of the Corporation, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the Corporation to the Corporation or the Corporation’s stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, or (iv) any action asserting a claim governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of capital stock of the Corporation shall be deemed to have notice of and consented to the provisions of this Article TWELFTH.

IN WITNESS WHEREOF, this Restated Certificate of Incorporation, which restates, integrates and amends the certificate of incorporation of the Corporation, and which has been duly adopted in accordance with Sections 228, 242 and 245 of the General Corporation Law of the State of Delaware, has been executed by its duly authorized officer this 12th day of February, 2014.

ARGOS THERAPEUTICS, INC.

By:  /s/ Jeffrey D. Abbey

Name:  Jeffrey D. Abbey
Title:  President and Chief Executive Officer
ARGOS Therapeutics, Inc. (the “Corporation”), a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the “General Corporation Law”), does hereby certify as follows:

1. The current name of the Corporation is Argos Therapeutics, Inc.

2. The Board of Directors of the Corporation duly adopted resolutions pursuant to Section 242 of the General Corporation Law proposing this Amendment of the Corporation’s Restated Certificate of Incorporation (the “Restated Certificate”), declaring the advisability of this Amendment of the Restated Certificate and authorizing the appropriate officers of the Corporation to solicit the consent of the stockholders therefor, which resolution setting forth the proposed amendment is as follows:

RESOLVED, that the first paragraph of Article FOURTH of the Restated Certificate of the Corporation be and hereby is deleted in its entirety and the following is inserted in lieu thereof:

“FOURTH: Effective at 5:00 p.m., Eastern Time, on the date of filing this Certificate of Amendment to the Restated Certificate of Incorporation with the Secretary of State of the State of Delaware (the “Effective Time”), a one-for-twenty reverse stock split of the Corporation’s common stock, $0.001 par value per share (the “Common Stock”), shall become effective, pursuant to which each twenty shares of Common Stock issued or outstanding (including treasury shares) immediately prior to the Effective Time shall be reclassified and combined into one validly issued, fully paid and nonassessable share of Common Stock automatically and without any action by the holder thereof upon the Effective Time and shall represent one share of Common Stock from and after the Effective Time (such reclassification and combination of shares, the “Reverse Stock Split”). The par value of the Common Stock following the Reverse Stock Split shall remain at $0.001 par value per share. No fractional shares of Common Stock shall be issued as a result of the Reverse Stock Split and, in lieu thereof, upon surrender after the Effective Time of a certificate which formerly represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time, any person who would otherwise be entitled to a fractional share of Common Stock as a result of the Reverse Stock Split, following the Effective Time, shall be entitled to receive a cash payment equal to the fraction of a share of Common Stock to which such holder would otherwise be entitled multiplied by the fair value per share of the Common Stock immediately prior to the Effective Time as determined by the Board of Directors of the Corporation.

Each stock certificate that, immediately prior to the Effective Time, represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall, from and after the Effective Time, automatically and without the necessity of presenting the same for exchange, represent that number of whole shares of Common Stock after the Effective Time into which the shares formerly represented by such certificate have been reclassified (as well as the right to receive cash in lieu of fractional shares of Common Stock after the Effective Time); provided, however, that each person of record holding a certificate that represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall receive, upon surrender of such certificate, a new certificate evidencing and representing the number of whole shares of Common Stock after the Effective Time into which the shares of Common Stock formerly represented by such certificate shall have been reclassified.
The total number of shares of all classes of stock which the Corporation shall have authority to issue is 205,000,000 shares, consisting of (i) 200,000,000 shares of Common Stock, $0.001 par value per share (“Common Stock”), and (ii) 5,000,000 shares of Preferred Stock, $0.001 par value per share (“Preferred Stock”).

This Certificate of Amendment of the Restated Certificate has been duly adopted by the stockholders of the Corporation in accordance with the provisions of Section 242 of the Delaware General Corporation Law.

IN WITNESS WHEREOF, the Corporation has caused its duly authorized officer to execute this Certificate of Amendment on this 18th day of January, 2018.

ARGOS THERAPEUTICS, INC.

By: /s/ Richard D. Katz
Name: Richard D. Katz
Title: Chief Financial Officer
Evaluation and Option Agreement for a Patent License

This Evaluation and Option Agreement for a Patent License ("Agreement"), dated as of February 1, 2018 ("Effective Date"), is by and between Actigen Limited ("Patent Holder") Pharmstandard International, S.A. ("Prospective Licensor") and Argos Therapeutics, Inc. ("Prospective Sublicensee").

WHEREAS, Patent Holder has the exclusive right to license the Patent Rights (as defined below) related to anti-PD-1 antibodies and the Technology (as defined below);

WHEREAS, Patent Holder has granted Prospective Licensor an option (with the right to sub-option) to exclusively license (with the right to sublicense) the Patent Rights and Technology (including at least all of the rights set forth in Section 2.1(a)(i-ii) below) under the option agreement effective January 29, 2018 (the “Option Agreement”) and the right to evaluate the Patent Rights and Technology prior to the exercise of such option;

WHEREAS, Prospective Sublicensee is interested in obtaining an exclusive license to the Patent Rights and the Technology and desires a period of time to evaluate them; and

WHEREAS, Prospective Licensor is willing to grant Prospective Sublicensee the right to conduct the evaluation for a reasonable period of time during which neither Patent Holder nor Prospective Licensor will negotiate a grant of rights, or grant any rights, under the Patent Rights or the Technology to a third party.

NOW, THEREFORE, in consideration of the mutual covenants, terms and conditions set forth herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties agree as follows:

1. Definitions. For purposes of this Agreement, the following terms shall have the following meanings:

   "Affiliate" of a Person means any other Person that directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with, such Person. For purposes of this Agreement, the term "control" (including the terms "controlled by" and "under common control with") means the direct or indirect power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise/ownership of more than 50% percent (50%) of the voting securities of a Person.

   "Field" has the meaning set forth in Exhibit A.

   "Law" means any statute, law, ordinance, regulation, rule, code, order, constitution, treaty, common law, judgment, decree, other requirement or rule of law of any federal, state, local, or foreign government or political subdivision thereof, or any arbitrator, court, or tribunal of competent jurisdiction.
"Patent License Agreement" means the definitive agreement, having the terms set forth in Exhibit A, pursuant to which Prospective Licensor will grant Prospective Sublicensee an exclusive license to the Patent Rights and the Technology.

"Patent Rights" means: (a) the patents and patent applications listed in Schedule 1, all patents issuing from the patent applications listed in Schedule 1 and all continuations, continuations-in-part, divisions, extensions, substitutions, reissues, re-examinations, and renewals of any of the foregoing; (b) any patents in the Territory that issue from any applications filed after the Effective Date and claim priority from any of the patents or patent applications identified in section (a) or from which any of the patents or patent applications identified in section (a) claim priority; and (c) any patents or patent applications owned or controlled by Prospective Licensor and/or Patent Holder, as applicable, relating to the Technology that are useful for (i) manufacturing any product or using any process claimed by the Patent Rights or (ii) otherwise commercializing any Patent Rights.

"Person" means an individual, corporation, partnership, joint venture, limited liability entity, governmental authority, unincorporated organization, trust, association, or other entity.

"Product" has the meaning set forth in Exhibit A.

"Representative" means a Party's and its Affiliates' employees, directors, consultants, agents, contractors, and legal advisors.

"Technology" means trade secrets, know-how, and any other technical information and materials comprising or relating to Prospective Licensor and Patent Holder's anti-PD-1 antibodies, their manufacture, use, or development.

"Territory" means the United States of America and Canada.

2. Exclusive Option Grant.

2.1 Grant.

(a) Prospective Licensor grants to Prospective Sublicensee an (i) exclusive license for evaluation purposes only to make, have made, use and import, but not offer to sell or sell products and processes covered by or incorporating the Patent Rights and the Technology for a period of one (1) year from the Effective Date, and any extension thereof ("Option Period"), and (ii) option exercisable during the Option Period to obtain an exclusive license under the Patent Rights and the Technology to make, have made, use, offer for sale, sell, and import with the right to grant sublicenses in the Field in the Territory Products as more fully set forth in Exhibit A (the "Option"). This grant is irrevocable subject only to a termination of this Agreement pursuant to Section 8.2(b).
In consideration for the rights granted in Section 2.1(a), Prospective Sublicensor shall issue to Prospective Licensor, within sixty (60) days after the Effective Date the number of shares of ARGS common stock valued at market close on the Effective Date at three hundred sixty thousand US Dollars ($360,000) (the “Option Fee”).

2.2 Exclusivity. During the Option Period, Patent Holder and Prospective Licensor:

(a) Shall neither grant to any Person (other than Prospective Sublicensor) nor directly or indirectly, solicit, initiate, facilitate, encourage, or participate in any discussions or negotiations with any Person concerning entering into, continuing, or consummating any transaction under which any Person other than Prospective Sublicensor does or will obtain (i) any contingent or non-contingent assignment, right, license, interest, shop right, or privilege under or relating to any of the Patent Rights or the Technology in the Field of Use in the Territory, or

(b) Shall continue to maintain and hold in its own name sole ownership and control of the Patent Rights and the Technology, as applicable provided that Patent Holder may be free to assign license or transfer to an Affiliate at any time.

2.3 Exercise of Option. Prospective Sublicensor may exercise the Option by delivering to Prospective Licensor during the Option Period written notice of Prospective Sublicensor's intent to enter into the Patent License Agreement.

2.4 No Obligation. Prospective Sublicensor has no obligation or commitment to enter into the Patent License Agreement or any other agreement relating to the subject matter hereof. However, Prospective Licensor (or Patent Holder, if applicable) shall be bound by to enter into the Patent License Agreement if Prospective Sublicensor exercises the Option and to negotiate such sublicense in good faith. Further, Patent Holder and Prospective Licensor agree to negotiate in good faith a license that will allow Prospective Licensor to enter into a sublicense agreement with Prospective Sublicensor according to the terms set forth in Exhibit A.

2.5 Off-Set of Payments. All sums payable by Prospective Sublicensor hereunder shall be credited towards any fees, royalties, or other payments required to be paid by Prospective Sublicensor pursuant to the Patent License Agreement.

2.6 Contingent Option. Patent Holder grants Prospective Sublicensor a contingent option to obtain an exclusive license under the Patent Rights and the Technology to make, have made, use, offer for sale, sell, and import with the right to grant sublicenses in the Field in the Territory Products as more fully set forth in Exhibit A (“Contingent Option”). The Contingent Option is exercisable by Prospective Sublicensor only if Patent Holder and Prospective Licensor fail to execute a license agreement as set forth in Section 4.1 during or prior to the end of the Exclusive License Negotiation Period, as defined herein. Upon exercise of the Contingent Option, Patent Holder shall negotiate in good faith a license in accordance with the terms set forth in Exhibit A, and substituting Patent Holder for “Pharmstandard” as used therein. If Patent Holder and Prospective Sublicensor fail to enter into a license within sixty (60) days of the exercise of the Contingent Option, then for a period of one (1) year, Prospective Sublicensor shall have the right of first refusal to enter into an agreement for any rights set forth in Exhibit A on the best terms that Patent Holder offers to Prospective Licensor or a third party.
2.7 Patent Holder shall use reasonable efforts to ensure that the PCT application listed in Schedule 1 enters national phase in the U.S. and Canada.

3. Disclosure of Information.

3.1 Patent Information. Within fifteen (15) days after the Effective Date, Prospective Licensor shall provide (or shall cause Patent Holder to provide) Prospective Sublicensee with:

(a) A copy of each patent application filed by or on behalf of Patent Holder included in the Patent Rights;

(b) A copy of the prosecution file history of each patent and patent application identified in Section 3.1(a); and

(c) Such other patent information as Prospective Sublicensee reasonably requests to support its efforts to evaluate the Patent Rights.

3.2 Technology Information. After signing of this Agreement, as soon as reasonably practicable, the Patent Holder shall use its reasonable efforts to provide Prospective Sublicensee with samples of the PD-1 antibodies as reasonably requested, but in any case, not more than 500 mg. If the Prospective Sublicensee needs a quantity in excess of 500 mg, then the Parties shall negotiate supply of such samples separately. If Patent Holder is unable to provide the material it shall not be considered a breach of this Agreement.

3.3 Reasonable Assistance. During the Option Period, Prospective Licensor and Patent Holder shall provide all reasonable cooperation with and assistance to Prospective Sublicensee in connection with Prospective Sublicensee's evaluation of the Patent Rights and the Technology including information that:

(a) Prospective Licensor or Patent Holder knows or has reasonable basis to believe are material to Prospective Sublicensee's evaluation of the Patent Rights or the Technology; or

(b) Prospective Sublicensee reasonably requests for purposes of its evaluation of the Patent Rights or the Technology pursuant to this Agreement.
Such information, documents, and materials may include design, manufacturing, clinical, quality, regulatory, and financial information and all other documents, materials, and other information (whether tangible or intangible) evidencing or relating to any Patent Rights or the Technology, including all patent applications, patent filings, communications with the US, PCT or any foreign patent office, licenses, assignments, agreements and other instruments, opinions of legal counsel, cease and desist letters, offers of licenses, and legal notices.

4. **Exclusive Negotiation.**

4.1 **Exclusive Negotiation Periods.** Prior to or promptly after, but in no case more than sixty (60) days after Prospective Sublicensee exercises the Option pursuant to Section 2.3 ("Exclusive License Negotiation Period"), Prospective Licensor and Patent Holder shall execute and record a license agreement that enables Prospective Licensor to grant Prospective Sublicensee a sublicense on the terms set forth in Exhibit A. For a period of sixty (60) days after Prospective Licensor executes such license with Patent Holder ("Exclusive Sublicense Negotiation Period"), Prospective Licensor shall (a) upon signing, provide Prospective Sublicensee with a copy of the license with Patent Holder and (b) for a period of sixty (60) days, in good faith and with the object of entering into a definitive Patent License Agreement with Prospective Sublicensee incorporating the essential terms set forth in Exhibit A, negotiate exclusively with Prospective Sublicensee the remaining terms and conditions of such Patent License Agreement. Prospective Licensor and Prospective Sublicensee may extend the Exclusive Sublicense Negotiation Period upon mutual written consent. Prospective Licensor shall not enter into negotiations with any third party to sublicense the Patent Rights and technology in the Field in the Territory during the Exclusive Sublicense Negotiation Period. If Prospective Licensor and Prospective Sublicensee fail to execute the Patent License Agreement during the Exclusive Sublicense Negotiation Period, then for a period of the following two (2) years, Prospective Licensor grants Prospective Sublicensee the right of first refusal to enter into an agreement that would grant any of the rights set forth in Exhibit A, on the same terms that a third party offers to Prospective Licensor. Prospective Licensor shall promptly notify Prospective Sublicensee of such third party offer and offer a sublicense under the same or better terms to Prospective Sublicensee. Prospective Sublicensee shall have thirty (30) days to accept or reject such offer. If Prospective Sublicensee accepts such offer, then Prospective Licensor and Prospective Sublicensee shall enter into a definitive sublicense agreement within thirty (30) days of such acceptance.

4.2 If Prospective Licensor fails during the Exclusive License Negotiation Period to execute a license agreement with Patent Holder that gives Prospective Licensor the full right and authority to grant Prospective Sublicensee the sublicense in accordance with Exhibit A or fails to enter into a sublicense with Prospective Sublicensee during the Exclusive Sublicense Negotiation Period, then Prospective Licensor shall pay Prospective Sublicensee three hundred sixty thousand U.S. Dollars ($360,000.00 USD) within two (2) weeks of the expiration of the Exclusive License Negotiation Period or the Exclusive Sublicense Negotiation Period, as applicable.
4.3 **Enforceable Agreement.** The parties acknowledge and agree that the terms set forth in Exhibit A create a binding agreement between the parties obligate Prospective Licensor to exclusively license at the latest within one hundred twenty (120) days following the Exercise of Option (defined in cl. 2.3.) the Patent Rights and the Technology to Prospective Sublicensee pursuant to those terms and without requiring the parties to further execute a separate written agreement, and that the terms of Exhibit A will be fully enforceable upon Prospective Sublicensee's exercise of the Option by written notice of Prospective Sublicensee's intent to enter into the Patent License Agreement.

5. **Non-Assertion.** Prospective Licensor and Patent Holder shall not at any time assert against Prospective Sublicensee, any of its Affiliates, or any of their respective Representatives, successors or assigns, any claims of infringement of any of the Patent Rights or misappropriation of any Technology in the Field of Use in the Territory based on any activities in the Territory that are related to Prospective Sublicensee's evaluation of the Patent Rights or the Technology.

6. **Confidentiality.** Prospective Licensor and Prospective Sublicensee shall be bound under the obligations of confidentiality set forth in the Confidential Disclosure Agreement between the Parties dated June 1, 2014. Patent Holder and Prospective Sublicensee shall be bound under the obligations of confidentiality set forth in the Confidential Disclosure Agreement dated January 18, 2017.

7. **Representations and Warranties.**

7.1 **Mutual Representations and Warranties.** Each party represents and warrants to the other party that:

   (a) It is duly organized, validly existing, and in good standing as a corporation or other entity as represented herein under the laws and regulations of its jurisdiction of incorporation, organization, or chartering;

   (b) It has the full right, power, and authority to enter into this Agreement and to perform its obligations hereunder;

   (c) The execution of this Agreement by a Representative whose signature is set forth at the end hereof has been duly authorized by all necessary corporate action of the party; and

   (d) When executed and delivered by the party, this Agreement shall constitute the legal, valid, and binding obligation of that party, enforceable against that party in accordance with its terms.

7.2 **Prospective Licensor's and Patent Holders Representations and Warranties.** Prospective Licensor, severally and not jointly, represent and warrant that:

   (a) Patent Holder and Prospective Licensor have executed an option agreement with each other of even date providing Prospective Licensor with an exclusive option to acquire an exclusive license, with the right to sublicense the Patent Rights and the Technology, including all intellectual property rights relating thereto;
(b) Prospective Licensor has and, throughout the Term, shall retain the unconditional and irrevocable right, power, and authority to
grant the Option to license the Patent Rights and the Technology contemplated hereunder in accordance with the Patent License Agreement;

(c) Neither its performance of any of its obligations under this Agreement nor the grant of the license to the Patent Rights and the
Technology contemplated hereunder does or shall at any time:

(i) conflict with or violate any applicable Law;

(ii) require the consent, approval, or authorization of any governmental or regulatory authority or other third party; or

(iii) require from the Prospective Sublicensee the provision of any payment or other consideration to any third party;

(d) It is, and throughout the Term shall remain, under no obligation, that does or will conflict with or otherwise affect this
Agreement, including any of Prospective Licensor's or Patent Holder’s representations, warranties, or obligations or Prospective Sublicensee's rights or
licenses hereunder;

8. **Term and Termination.**

8.1 **Term.** This Agreement shall commence as of the Effective Date and, unless terminated earlier in accordance with Section 8.2, shall
remain in force until the expiration of the Exclusive Negotiation Period and any extension thereof ("**Term**").

8.2 **Termination.**

(a) Prospective Sublicensee may terminate this Agreement at any time without cause, and without incurring any obligation, liability,
or penalty by reason of such termination on giving Prospective Licensor and Patent Holder not less than thirty (30) days prior written notice.

(b) Any party may terminate this Agreement effective upon written notice to the other parties if a party materially breaches this
Agreement and such breach: (i) is incapable of cure; or (ii) being capable of cure (by a breaching or non-breaching party), remains uncured [**] days
after the breaching party receives written notice thereof.

8.3 **Survival.** The rights and obligations of the parties set forth in this Section 8.3 (Survival) and Section 1 (Definitions), Section 6
(Confidentiality), Section 7 (Representations and Warranties) and Section 9 (Miscellaneous), and any right, obligation, or required performance of the parties
in this Agreement which by its express terms or nature and context is intended to survive termination or expiration of this Agreement, will survive any such
termination or expiration.
9. **Miscellaneous.**

9.1 **Force Majeure.** No party shall be liable or responsible to the other parties, or be deemed to have defaulted under or breached this Agreement, for any failure or delay in fulfilling or performing any term hereof, when and to the extent such failure or delay is caused by: acts of God, flood, fire or explosion, war, terrorism, invasion, riot or other civil unrest, embargoes or blockades in effect on or after the Effective Date, national or regional emergency or any passage of law or governmental order, rule, regulation or direction, or any action taken by a governmental or public authority, including imposing an embargo, export or import restriction, quota or other restriction or prohibition, in each case provided that: (a) such event is outside the reasonable control of the affected party; (b) the affected party gives prompt written notice to the other parties, stating the period of time the occurrence is expected to continue; and (c) the affected party uses diligent efforts to end the failure or delay and minimize the effects of such event.

9.2 **Further Assurances.** Each party shall, upon the reasonable request execute and deliver such further documents and instruments and perform such further actions, necessary to give full effect to the terms of this Agreement.

9.3 **Independent Contractors.** The relationship between the parties is that of independent contractors. Nothing contained in this Agreement shall be construed as creating any agency, partnership, joint venture, or other form of joint enterprise, employment, or fiduciary relationship between the parties, and neither party shall have authority to contract for or bind the other party in any manner whatsoever.

9.4 **Notices.** All notices, requests, consents, claims, demands, waivers, and other communications hereunder shall be in writing and shall be deemed to have been given in accordance with this Section:

If to Prospective Licensor:  
Pharmstandard International S.A.  
10A, rue Henri Schnadt,  
L-2530, Luxembourg  
Attention: Director

If to Prospective Sublicensee:  
Argos Therapeutics, Inc.  
4233 Technology Dr.  
Durham, NC 27704 USA  
Attention: CEO
If to Patent Holder:  
Actigen Limited  
St John's Innovation Centre,  
Cowley Road, Cambridge, CB4 0WS  
Attention: Director

Notices sent in accordance with this Section shall be deemed effectively given:

(a) When delivered by hand (with written confirmation of receipt);
(b) When received, if sent by a nationally recognized courier (receipt requested); or
(c) On the date sent by e-mail with confirmation of transmission if sent during normal business hours of the recipient, and on the next business day if sent after normal business hours of the recipient.

9.5 **Interpretation.** This Agreement shall be construed without regard to any presumption or rule requiring construction or interpretation against the party drafting an instrument or causing any instrument to be drafted.

9.6 **Headings.** The headings in this Agreement are for reference only and shall not affect its interpretation.

9.7 **Entire Agreement.** This Agreement, together with all Exhibits and, Schedules and any other documents incorporated herein by reference, constitute the sole and entire agreement of the parties to this Agreement with respect to the subject matter contained herein, and supersedes all prior and contemporaneous understandings and agreements, both written and oral, with respect to such subject matter.

9.8 **Assignment.** Prospective Sublicensor may freely assign or otherwise transfer all or any of its rights, or delegate or otherwise transfer all or any of its obligations or performance, under this Agreement with Prospective Licensor's or Patent Holder's consent in neither case not to be unreasonably withheld. Patent Holder may freely assign or otherwise transfer all or any of its rights or delegate or otherwise transfer all or any of its obligations or performance under this Agreement without Patent Holder's consent. Both parties shall promptly advise the other of any action under this paragraph. This Agreement is binding upon and inures to the benefit of the parties hereto and their respective permitted successors and assigns.
9.9 **No Third Party Beneficiaries.** This Agreement is for the sole benefit of the parties hereto and their respective successors and permitted assigns and nothing herein, express or implied, is intended to or shall confer upon any other Person any legal or equitable right, benefit, or remedy of any nature whatsoever, under or by reason of this Agreement.

9.10 **Amendment; Modification; Waiver.** This Agreement may only be amended, modified, or supplemented by an agreement in writing signed by each party hereto. No waiver by any party of any of the provisions hereof shall be effective unless explicitly set forth in writing and signed by the waiving party. Except as otherwise set forth in this Agreement, no failure to exercise, or delay in exercising, any rights, remedy, power, or privilege arising from this Agreement shall operate or be construed as a waiver thereof; nor shall any single or partial exercise of any right, remedy, power, or privilege hereunder preclude the exercise, or further exercise, of any other right, remedy, power, or privilege.

9.11 **Severability.** If any term or provision of this Agreement is invalid, illegal, or unenforceable in any jurisdiction, the invalidity, illegality, or unenforceability shall not affect any other term or provision of this Agreement or invalidate or render unenforceable that term or provision in any other jurisdiction. Upon a determination that any term or other provision is invalid, illegal, or unenforceable, the parties hereto shall negotiate in good faith to modify this Agreement to effect the original intent of the parties as closely as possible in a mutually acceptable manner so that the transactions contemplated hereby can be consummated as originally contemplated to the greatest extent possible.

9.12 **Governing Law.** This Agreement is governed by, and construed in accordance with, the laws of England and Wales and the parties agree that any dispute including any dispute under Clause 9.13 shall be exclusively heard in the High Court of England and Wales.

9.13 **Equitable Relief.** Each party to this Agreement acknowledges and agrees that (a) a breach or threatened breach by such party of any of its obligations under this Agreement would give rise to irreparable harm to the other party for which monetary damages would not be an adequate remedy and (b) in the event of a breach or a threatened breach by such party of any such obligations, the other party hereto shall, in addition to any and all other rights and remedies that may be available to such party at law, at equity, or otherwise in respect of such breach, be entitled to equitable relief, including a temporary restraining order, an injunction, specific performance, and any other relief that may be available from a court of competent jurisdiction, without any requirement to post a bond or other security, and without any requirement to prove actual damages or that monetary damages will not afford an adequate remedy. Each party to this Agreement agrees that such party will not oppose or otherwise challenge the appropriateness of equitable relief or the entry by a court of competent jurisdiction of an order granting equitable relief, in either case, consistent with the terms of this Section 9.13. However, each party has the right to appeal above any equitable relief in case the party disagrees with such equitable relief.
9.14 **Counterparts.** This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together shall be deemed to be one and the same agreement. A signed copy of this Agreement delivered by e-mail, or other means of electronic transmission shall be deemed to have the same legal effect as delivery of an original signed copy of this Agreement.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the Effective Date by their respective officers thereunto duly authorized.

PHARMSTANDARD INTERNATIONAL S.A.

By /s/ Eriks Martinovskis
Name: Eriks Martinovskis
Title: Director

ARGOS THERAPEUTICS, INC.

By /s/ Jeffrey D. Abbey
Name: Jeffrey D. Abbey
Title: President and Chief Executive Officer

ACTIGEN LIMITED

By /s/ Michael Braunagel
Name: Michael Braunagel
Title: Managing Director
1. **Background**

Pharmstandard has exclusively in-licensed monoclonal antibodies to human PD-1 from Actigen, Ltd (the “Pharmstandard Antibodies”). Argos Therapeutics (herein “Argos”) has an interest in such molecules and would like to make a non-binding offer to sub-license the Pharmstandard Antibodies for use in the Field, including in combination with Argos’ proprietary tumor vaccines in a limited set of countries (the “Licensed Rights”) on the terms and conditions described herein. Pharmstandard and Argos are sometimes referred to hereinafter as “the Parties.” The objective of this term sheet is to guide and direct the Parties toward the execution of a more formal and complete agreement between the Parties (the “License Agreement”).

2. **License Rights**

Pharmstandard grants to Argos an exclusive license (with the right to sublicense, subject to Section 10) to make, have made, use, offer for sale, sell, import, research, develop, and produce the Pharmstandard Antibodies for the purpose of developing and commercializing Products in the Field in the United States of America and Canada (the “Licensed Territory”).

3. **Field**

All prophylactic, therapeutic, and diagnostic uses of the Product for all human diseases and conditions.

4. **Product**

Any pharmaceutical product or therapeutic regimen incorporating a Pharmstandard Antibody.
5. **Research and Development Costs**

Argos shall be responsible for funding all activities required to produce, develop and commercialize Products in the Licensed Territory, including technology transfer from Pharmstandard or its licensor, Actigen.

6. **Third Party License Agreements**

Argos shall be responsible for obtaining any necessary licenses in the Licensed Territory under third party intellectual property, subject to the royalty offset provisions below.

7. **Financial Terms**

**Milestones.** Argos will pay Pharmstandard the following fees upon the first achievement of the designated milestone events for each Product:

<table>
<thead>
<tr>
<th>Development Milestones (for each Product)</th>
<th>Payment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upfront payment (on signing license agreement)</td>
<td>Shares of ARGS common stock equal to $3.24 million</td>
</tr>
</tbody>
</table>

**Total Development Milestone Fees** $11.74 million

[**].
**Royalties.** Argos will pay to Pharmstandard Royalties on net sales of each Product in the Licensed Territory at a rate of [*%*] (*%* percent). Argos’ development costs, up to a maximum of $5 million, shall be credited as prepaid royalties. Nothing in this clause shall be construed as Pharmstandard’s obligation to compensate Argos’ development costs in case of any Product Approval is not received by Argos.

Royalty payment obligations set forth herein shall expire on the later of: (a) the last to expire patent covering the manufacture, use, sale, import, export, or offer for sale of the Product; or (b) ten (10) years from the date of first sale of the Product in a given country. Upon expiration of the royalty payment obligations for the Product in a given geographical area, Argos shall have a fully paid-up, exclusive license for the Product in such geographical area.

**Royalty Offset for Third Party Royalties.** Argos shall be entitled to offset against royalties owed to Pharmstandard on sales [*%*] of the royalties paid to third parties on such Product sales under agreements entered into by Argos, provided that the third party license is required to commercialize the Pharmstandard Antibodies being part of the Product. For clarity, in no case the Royalties payable to Pharmstandard shall be lower than [*%*] on net sales.

8. **Intellectual Property**

All intellectual property related to improvements of the Pharmstandard Antibodies made by Argos, or a sublicensee or subcontractor of Argos, in the performance of this Agreement shall be owned by Argos, and Pharmstandard shall have a royalty-free license to such improvements. All inventions regarding the vaccine or the use of Pharmstandard Antibodies and vaccine as Product shall be owned by Argos.

9. **Data and Material Transfer**

Argos will provide Pharmstandard with a copy of all information, materials and data for the Pharmstandard Antibodies and the Product, which contains information relevant to IND/BLA filings or clinical trials. Pharmstandard is free to use this data in the development of the Pharmstandard Antibodies both at Pharmstandard or its sublicensees, free of charge, as a monotherapy or in any combination outside the scope of this license.

Also, the GMP Master Cell Bank, to be created by Argos and/or its sublicensees in connection with IND/BLA filing, shall be made available to Pharmstandard at Argos’ cost with a right to sublicense.
10. **Performance**

   The minimal Diligence obligation for Argos (i.e. the funding allocated to develop the Product) shall be either: 1) at least [***], or 2) at least [**]. The license expires if this condition is not met.

11. **Good Faith and Timeline**

   All further negotiations leading to the final contract, including discussions to modify terms of this agreement will be done in good faith between the partners.

   The Parties intend to conclude a licensing agreement by the end of January 2018

12. **Governing Law and Confidentiality**

   The Parties expressly acknowledge and agree that the details of Terms are confidential information (except to the extent disclosure is required by law) and that they will be handled to the standard rules of handling confidential information in place at the Parties.

   The License Agreement shall be governed in accordance with the laws of the England and Wales, without regard to any conflicts of laws principles.
### SCHEDULE 1

#### PATENT RIGHTS

<table>
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<tr>
<th>PCT application number</th>
<th>Title</th>
<th>Priority date</th>
<th>Priority ID</th>
<th>Status</th>
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Licensed Know-How

Sequences of antibody that binds to PD-1:

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16
Second Amendment

to
License Agreement

between

Argos Therapeutics, Inc.
(hereinafter “Argos”)

- and -

Lummy (Hong Kong) Co., Ltd.
(hereinafter “China Company”)

This Amendment is made as of and effective __2017-10-18____ (“Effective Date”), contingent on the full execution of the Second Stock Purchase Agreement between China Company and Argos “Second SPA”).

WHEREAS, Argos and China Company entered into a license agreement dated April 7, 2015 (the “License Agreement”), as first amended on December 5, 2016;

WHEREAS, the original License Agreement set forth certain royalties and milestones, which the parties wish to amend contingent on the full execution of the Second SPA;

WHEREAS the parties now require that the Agreement be amended as set forth herein,

the parties agree to amend the Agreement as follows:

1. Section 3.2.1 shall be deleted and replaced with the following (Section 3.2.1.1 shall not be affected):

3.2.1 Royalties Payable on a Licensed Product. Subject to the terms and conditions of this Agreement and beginning immediately after the aggregate Net Sales by China Company and its Related Parties of Licensed Products reach the Recoupment Threshold, China Company shall pay to Argos a royalty of (i) [**] percent ([**]%) of Net Sales of Licensed Products, provided that such Licensed Product is approved in by the FDA or any Regulatory Authority in the Argos Territory prior to its approval by a Regulatory Authority in the China Company Territory; or (ii) [**] percent ([**]%) of Net Sales of Licensed Product if such licensed product is first approved by a Regulatory Authority in the China Company Territory prior to its approval by a Regulatory Authority in the Argos Territory, which royalty shall be increased to [**] percent ([**]%) upon approval of the Licensed Product by the FDA.
2. Section 3.3 is amended to read in its entirety as follows:

3.3 Milestones. Subject to the terms and conditions of this Agreement, China Company shall make the non-refundable, non-creditable milestone payments to Argos set forth below no later than [**] days after the earliest date on which the corresponding milestone event has first been achieved with respect to a Licensed Product.

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<th>Milestone Event</th>
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The following shall be deemed to be material breaches of this Agreement, subject, however to the notice and cure period set forth in 10.2.1(a): (a) the Milestone Event set forth in (i) above is not completed within [**] months after the Trigger Event, (b) the Milestone Event set forth in (ii) above is not completed within [**] months after the Trigger Event, or (c) the Milestone Event set forth in (v) above is not completed within [**] months after the Trigger Event, and, in each case, the failure to complete the applicable Milestone Event is not directly related to acts or omissions by Argos. In addition, failure to achieve the following shall be deemed to be material breaches of this Agreement: (i) within [**] months of the first [**] U.S. FDA approvals obtained by Argos for a Licensed Product, China Company must Initiate Clinical Study of said Licensed Products, and (ii) within [**] months from Initiation of a Pivotal Clinical Study for said Licensed Products, China Company must submit the relevant application(s) for the Regulatory Approval to Commercialize said Licensed Products. Notwithstanding the foregoing, the Parties acknowledge and agree that the regulatory process to obtain Regulatory Approval for the Licensed Product in the China Company Territory has a high level of uncertainty and in the event that the failure to achieve a milestone set forth in (v), (vi), or (vii) is primarily attributable to regulatory requirements or delays caused by Regulatory Authorities in the China Company Territory which are out of the control of China Company and which could not reasonably be anticipated as of the Effective Date (an “Intervening Regulatory Event”), the Parties agree to renegotiate the relevant Milestone Events in good faith in a manner reasonably taking into consideration the Intervening Regulatory Event.
All other terms and conditions will remain the same.

IN WITNESS WHEREOF, the parties hereto have caused this Amendment to be executed by their duly authorized corporate officers or representatives as of the Effective Date of this Amendment.

Argos Therapeutics, Inc.                         Lummy (Hong Kong) Co., Ltd.

By: /s/ Jeff Abbey                                By: /s/ Xuefeng Leng

Name: Jeff Abbey                                    Name: Xuefeng Leng

Title: President and CEO                            Title: Director
Third Amendment

to
License Agreement

between

Argos Therapeutics, Inc.
(hereinafter “Argos”)

- and -

Lummy (Hong Kong) Co., Ltd.
(hereinafter “China Company”)

This Amendment is made as of and effective March 23rd, 2018 (“Effective Date”), contingent on the full execution of the Amended Second Stock Purchase Agreement between China Company and Argos “Second SPA”).

WHEREAS, Argos and China Company entered into a license agreement dated April 7, 2015 (the “License Agreement”), as first amended on December 5, 2016, and amended a second time on October 19, 2017;

WHEREAS, the License Agreement, as amended, set forth certain royalties and milestones, which the parties wish to amend contingent on the full execution of the Amended Second SPA;

WHEREAS the parties now require that the License Agreement be amended as set forth herein, the parties agree to amend the License Agreement as follows:

1. Section 3.3 is amended to read in its entirety as follows:

3.3 Milestones. Subject to the terms and conditions of this Agreement, China Company shall make the non-refundable, non-creditable milestone payments to Argos set forth below no later than [**] days after the earliest date on which the corresponding milestone event has first been achieved with respect to a Licensed Product.

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The following shall be deemed to be material breaches of this Agreement, subject, however to the notice and cure period set forth in 10.2.1(a): (a) the Milestone Event set forth in (i) above is not completed within [**] months after the Trigger Event, (b) the Milestone Event set forth in (iii) above is not completed within [**] months after the Trigger Event, or (c) the Milestone Event set forth in (vi) above is not completed within [**] months after the Trigger Event, and, in each case, the failure to complete the applicable Milestone Event is not directly related to acts or omissions by Argos. In addition, failure to achieve the following shall be deemed to be material breaches of this Agreement: (i) within [**] months of the first [**] U.S. FDA approvals obtained by Argos for a Licensed Product, China Company must Initiate Clinical Study of said Licensed Products, and (ii) within [**] months from Initiation of a Pivotal Clinical Study for said Licensed Products, China Company must submit the relevant application(s) for the Regulatory Approval to Commercialize said Licensed Products. Notwithstanding the foregoing, the Parties acknowledge and agree that the regulatory process to obtain Regulatory Approval for the Licensed Product in the China Company Territory has a high level of uncertainty and in the event that the failure to achieve a milestone set forth in (vi), (vii), or (viii) is primarily attributable to regulatory requirements or delays caused by Regulatory Authorities in the China Company Territory which are out of the control of China Company and which could not reasonably be anticipated as of the Effective Date (an “Intervening Regulatory Event”), the Parties agree to renegotiate the relevant Milestone Events in good faith in a manner reasonably taking into consideration the Intervening Regulatory Event.

All other terms and conditions will remain the same.

IN WITNESS WHEREOF, the parties hereto have caused this Amendment to be executed by their duly authorized corporate officers or representatives as of the Effective Date of this Amendment.

Argos Therapeutics, Inc.                              Lummy (Hong Kong) Co., Ltd.

By: /s/ Jeff Abbey                                   By: /s/ Xuefeng Leng

Name: Jeff Abbey                                     Name: Xuefeng Leng

Title: President and CEO                             Title: Director
CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Forms S-3 (Nos. 333-204016, 333-211364, 333-212645, 333-215480, 333-220001, 333-221343 and 333-222414) and Forms S-8 (Nos. 333-208055, 333-210522, 333-211403, 333-213137, 333-216985 and 333-220261) of Argos Therapeutics, Inc. of our report dated April 2, 2018 relating to the financial statements and financial statement schedule, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Raleigh, North Carolina
April 2, 2018
CERTIFICATIONS

I, Jeffrey D. Abbey, certify that:

1. I have reviewed this Annual Report on Form 10-K of Argos Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant’s other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rule 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant’s internal control over financial reporting that occurred during the registrant’s most recent fiscal quarter (the registrant’s fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting; and

5. The registrant’s other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant’s auditors and the audit committee of the registrant’s board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant’s ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

Date: April 2, 2018

By: /s/ JEFFREY D. ABBEY

Jeffrey D. Abbey
President and Chief Executive Officer
(Principal Executive Officer)
CERTIFICATIONS

I, Richard D. Katz, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Argos Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant’s other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rule 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant’s internal control over financial reporting that occurred during the registrant’s most recent fiscal quarter (the registrant’s fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting; and

5. The registrant’s other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant’s auditors and the audit committee of the registrant’s board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant’s ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

Date: April 2, 2018

By: /s/ RICHARD D. KATZ, M.D.

Richard D. Katz, M.D.
Vice President and Chief Financial Officer
(Principal Financial Officer)
CERTIFICATIONS PURSUANT TO 18 U.S.C. 1350

The undersigned, the Chief Executive Officer and the Vice President of Finance (principal financial officer) of Argos Therapeutics, Inc. (the “Company”), each hereby certifies that, to his knowledge on the date hereof:

(a) the Annual Report on Form 10-K of the Company for the period ended December 31, 2017 filed on the date hereof with the Securities and Exchange Commission (the “Report”) fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(b) information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

By: /S/ JEFFREY D. ABBEY

Jeffrey D. Abbey
Chief Executive Officer
April 2, 2018

By: /S/ RICHARD D. KATZ, M.D.

Richard D. Katz, M.D.
Vice President and Chief Financial Officer
April 2, 2018