

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

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2017

or

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

For the transaction period from _____ to _____

Commission file number: 001-36860

IOVANCE BIOTHERAPEUTICS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware

(State or Other Jurisdiction of
Incorporation or Organization)

75-3254381

(I.R.S. Employer
Identification No.)

999 Skyway Road, Suite 150, San Carlos, California

(Address of Principal Executive Offices)

94070

(Zip Code)

(650) 260-7120

(Registrant's Telephone Number, Including Area Code)

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

<u>Title of Each Class</u>	<u>Name Of Each Exchange On Which Registered</u>
Common Stock, \$ 0.000041666 Par Value per Share	The Nasdaq Global Market

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

None

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T 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) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

Large accelerated filer

Non-accelerated filer (Do not check if a smaller reporting company)

Accelerated filer

Smaller reporting company

Emerging growth company

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

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

The aggregate market value of the registrant's common stock held by non-affiliates on June 30, 2017, the last business day of the registrant's most recently completed second fiscal quarter, was approximately \$363,066,000. Shares of common stock held by directors and executive officers and any ten percent or greater stockholders and their respective affiliates have been excluded from this calculation, because such stockholders may be deemed to be "affiliates" of

the Registrant. This is not necessarily determinative of affiliate status of other purposes. As of February 28, 2018, there were 89,445,753 shares of the registrant's common stock outstanding.

Documents Incorporated By Reference

Portions of registrant's proxy statement relating to registrant's 2018 Annual Meeting of Stockholders (the "Proxy Statement") to be filed with the Securities and Exchange Commission pursuant to Regulation 14A, not later than 120 days after the close of the registrant's fiscal year, are incorporated by reference in Part III of this Annual Report on Form 10-K. Except with respect to information specifically incorporated by reference in this Annual Report on Form 10-K, the Proxy Statement is not deemed to be filed as part of this Annual Report on Form 10-K.

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Forward-Looking Statements and Market Data

This Annual Report on Form 10-K contains forward-looking statements that are based on management's beliefs and assumptions and on information currently available to management. All statements other than statements of historical facts contained in this report are forward-looking statements. In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "aim," "potential," "continue," "ongoing," "goal," or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words.

These statements involve risks, uncertainties and other factors that may cause actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this report, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Forward-looking statements in this Annual Report on Form 10-K include, but are not limited to, statements about:

- the success, cost and timing of our clinical trials;
- the success, cost and timing of our product development activities;
- the ability of our third-party contract manufactures to continue to manufacture tumor infiltrating lymphocytes, or TIL, in accordance with our selected process;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates;
- the ability and willingness of our third-party research institution collaborators to continue research and development activities relating to our product candidates;
- the potential of our other research and development and strategic collaborations;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our manufacturing methods and product candidates;
- our plans to research, develop and commercialize our product candidates;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- regulatory developments in the United States and foreign countries;
- fluctuations in the trading price of our common stock; and
- our use of cash and other resources.

We caution you that the risks, uncertainties and other factors referenced above may not contain all the risks, uncertainties and other factors that are important to you. In addition, we cannot guarantee future results, level of activity, performance or achievements. Any forward-looking statement made by us in this Annual Report on Form 10-K speaks only as of the date of this Annual Report on Form 10-K or as of the date on which it is made. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether because of new information, future events or otherwise, after the date of this Annual Report on Form 10-K.

Unless the context requires otherwise, in this report the terms "Iovance," the "Company," "we," "us" and "our" refer to Iovance Biotherapeutics, Inc.

PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of novel cancer immunotherapy products designed to harness the power of a patient's own immune system to eradicate cancer cells. Our lead product candidate, LN-144 for metastatic melanoma, is an autologous adoptive cell therapy utilizing tumor-infiltrating lymphocytes, or TIL, which are T cells derived from patients' tumors. TIL therapy is a platform technology that has already been studied for the treatment of metastatic melanoma and metastatic cervical cancer by the National Cancer Institute, or NCI. We are investigating the effectiveness and safety of TIL therapy for the treatment of metastatic melanoma, squamous cell carcinoma of the head and neck, cervical carcinoma, and metastatic non-small cell lung cancer, as well as other oncology indications.

A patient's immune system, particularly his or her TIL, plays an important role in identifying and killing cancer cells. TIL product consists of a polyclonal population of T cells that are designed to recognize a wide variety of cancer-specific mutations. TIL treatment is designed to target tumors through the polyclonal nature of the TIL product and can potentially overcome the hostile tumor microenvironment based upon (a) the non-myeloablative chemotherapy that is a component of TIL therapy and (b) the nature of the TIL cells themselves. TIL therapy involves four steps: (i) growing a patient's TIL outside the patient's body, or *ex vivo*, (ii) administering non-myeloablative chemotherapy, (iii) infusing the expanded TIL back into the patient, and (iv) subsequent infusions of up to six doses of interleukin-2, or IL-2. By expanding a patient's TIL *ex vivo*, away from the immunosuppressive tumor microenvironment, the T cells can rapidly proliferate. As a result, billions of TIL cells, when infused back into the patient, are better able to potentially eradicate tumors.

Manufacturing of TIL historically has typically taken 5-6 weeks and has yielded a non-cryopreserved TIL product. We have developed a new manufacturing method that reduces the duration of manufacture of the TIL product to 22 days and allows for production of a cryopreserved TIL product. We refer to our new manufacturing method as Generation 2, or Gen 2, manufacturing. We own the intellectual property associated with Gen 2 manufacturing. In late 2017, we selected Gen 2 as the manufacturing method for TIL product to be used in all our ongoing and upcoming trials. The cryopreserved TIL product offers greater flexibility in scheduling the dosing of patients, reduces the period for patients to wait until they receive their TIL product infusion, and reduces the cost of manufacture.

We are pursuing metastatic melanoma as our first target indication because of the promising initial results in this indication generated by Dr. Steven Rosenberg, M.D., Ph.D., Chief of the Surgery Branch of the NCI, and the commercial opportunity inherent in the significant unmet need of this patient population. Melanoma is a common type of skin cancer, accounting for 87,110 patients diagnosed and 9,730 deaths in the United States in 2017, according to the NCI's Surveillance, Epidemiology and End Results, or SEER program. Patients with metastatic melanoma following treatment under the current standards of care have a particularly dire prognosis with very few curative treatment options.

We have an on-going Phase 2 clinical trial, C-144-01, of our lead product candidate, LN-144, TIL for the treatment of metastatic melanoma. This multicenter study is enrolling patients with melanoma whose disease has progressed following treatment with at least one systemic therapy, including anti-PD-1 and if BRAF mutated, a BRAF inhibitor. The trial is currently active at fourteen U.S. sites. We anticipate initiating patient dosing in Europe during the first half of 2018. The purpose of the study is to evaluate the efficacy and safety of our autologous LN-144. As per Response Evaluation Criteria in Solid Tumors version 1.1, or RECIST 1.1 criteria, a reduction in tumor size of at least 30% qualifies as a Partial Response, or PR, while the Objective Response Rate, or ORR, is defined as the proportion of patients who have either a PR or a Complete Response, CR, to therapy. The trial's primary objective is to characterize the efficacy of LN-144 based upon ORR. Secondary outcome measures for safety and efficacy of LN-144 include Duration of Response, or DOR, and CR rates. We will evaluate other secondary or exploratory endpoints. On December 13, 2017, we reported updated results from cohort 2 of the C-144-01 study, which used our Gen 2 manufacturing process. The data reported showed clinically meaningful outcomes with a 40% ORR, which included four PRs, observed in ten evaluable patients. The evaluable patients had a high tumor burden despite a median of 3.6 prior therapies, including both anti-CTLA 4 and anti-PD-1 treatments. The most common side effects of any grade were pyrexia, anemia and decreased neutrophil count. We have decided to use our Gen 2 manufacturing process for all ongoing Phase 2 trials and in all future TIL clinical development in trials sponsored by us, and as a result, cohort 1 of the C-144-01 melanoma study is closed to enrollment, and new patients are being enrolled in cohort 2.

We have received orphan drug designation for LN-144 in the United States to treat malignant melanoma stages IIB-IV. If approved, this designation provides seven years of market exclusivity in the United States, subject to certain limited exceptions. However, the orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review or approval process. On August 31, 2017, we were granted Fast Track designation by the U.S. Food and Drug Administration, or FDA, for LN-144, TIL in advanced melanoma.

In addition to our ongoing trial in metastatic melanoma, we have initiated clinical trials of LN-145, TIL therapy in cervical, head and neck cancers, and non-small cell lung cancer, or NSCLC. C-145-03 is a Phase 2, multicenter study that will enroll up to 47 patients and will assess the safety and efficacy of LN-145 for the treatment of patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck. The primary endpoint of this study is efficacy of LN-145 based on ORR. The trial has met the threshold for the first stage of the Simon's two-stage design pursuant to which a portion of the patients would be enrolled in the first stage, and, upon achievement of a pre-specified minimal response rate, enrollment of the second stage would proceed. The trial will therefore continue to enroll patients to the full sample size of 47 per protocol. In January 2018, we announced preliminary data from C-145-03 which demonstrated that three of the eight patients treated with LN-145 had a PR, and the ORR in the study to date is 38%. These patients had a median of four prior treatments for their cancer and had all received prior anti-PD-1 therapy. The most common side effects were pyrexia, chills, and hypotension. C-145-04 is a Phase 2, multicenter study, designed as a Simon's two-stage design to enroll up to 47 patients, and will assess the safety and efficacy of LN-145 for the treatment of patients with recurrent, metastatic, or persistent cervical carcinoma. The study is open for enrollment of patients in the United States and we anticipate the start of enrollment of patients in Europe in the first half of 2018. In January 2018, we reported preliminary data from C-145-04 which showed that of the two patients that are currently evaluable, one treated with LN-145 had a confirmed PR and one patient had stable disease. We have amended the protocol so that newly-enrolled patients in both trials can be treated using TIL produced from our Gen 2 manufacturing process.

We are initiating our clinical development around NSCLC, with two studies. One of the studies is an investigator-sponsored Phase 2 study to be conducted at H. Lee Moffitt Cancer Center and Research Institute, or Moffitt, and the other will be sponsored by our company. Patient enrollment has begun in the investigator-sponsored study in collaboration with researchers at Moffitt, Stand Up To Cancer, and others. Patients who are treatment naïve to prior anti-PD-1/ PD-L1 with stage IV or recurrent NSCLC will be enrolled in a study combining TIL and nivolumab. The Iovance-sponsored Phase 2 study in NSCLC patients who are PD-1 and PD-L1 treatment naïve, will initiate in the first half of 2018, in collaboration with MedImmune, the global biologics research and development arm of AstraZeneca. The study with MedImmune will allow for enrollment with LN-145 alone or in combination with durvalumab. In the future, we plan to initiate additional indications alone or through collaborations.

We are also initiating clinical trials as part of our strategic alliance with The University of Texas M.D. Anderson Cancer Center, or M.D. Anderson, in multiple solid tumor cancers using two different TIL manufacturing processes, including our Gen 2 manufacturing process. These multi-arm clinical trials will evaluate the safety and efficacy of TIL therapy in ovarian cancer, various sarcomas, and pancreatic cancer, and are expected to begin enrollment in 2018.

Our current product candidate pipeline is summarized in the graphic below:

INDICATION	REGIMEN	N	PARTNER	PRECLINICAL	PHASE I	PHASE 2
Melanoma	TIL LN-144	60	—			
Cervical Cancer	TIL LN-145	47	—			
Head & Neck Cancer	TIL LN-145	47	—			
Non-Small Cell Lung Cancer	TIL LN-145 vs TIL LN-145 + durvalumab	24				

Our current collaboration pipeline is summarized in the graphic below:

INDICATION	REGIMEN	N	PARTNER	PRECLINICAL	PHASE I	PHASE 2
Melanoma	Combination TIL ± TBI	101				
Melanoma	Combination TIL + Yervoy					
Melanoma	Combination TIL + Keytruda	170				
Melanoma	Combination TIL + Opdivo	12				
Ocular (Uveal) Melanoma	TIL	23				
Glioblastoma	TIL					
Pancreatic Cancer	TIL					
Ovarian, Sarcomas, Pancreatic	TIL					
Non-small cell lung cancer	Combination TIL + Opdivo	18				

For the studies listed in our collaboration pipeline table, the partner listed above is the sponsor of the clinical trial. Such partner may not use our Gen 2 manufacturing process, and/or the therapeutic dosing may differ from our clinical trials. As a result, such partner data may not be representative of our data.

2017 Developments

In 2017, we reported several significant events, including the following:

Clinical

- We presented clinical data from the first cohort of our Phase 2 trial in metastatic melanoma, known as C-144-01, at the 2017 ASCO Annual Meeting in June.
- We began patient dosing in the second cohort of C-144-01, our Phase 2 trial investigating LN-144 for the treatment of patients with metastatic melanoma and reported preliminary data at the SITC Annual Meeting in November.
- We began patient dosing in C-145-03, our Phase 2 trial of LN-145 for the treatment of patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck.
- We began patient dosing in C-145-04, our Phase 2 trial of LN-145 for the treatment of patients with recurrent, metastatic or persistent cervical carcinoma.
- We entered into a new Clinical Grant Agreement, or CGA, with Moffitt to provide funding for a clinical study of TIL therapy in lung cancer and began patient enrollment in a study in patients with advanced non-small cell lung cancer, or NSCLC, combining TIL and nivolumab in patients who have progressed on nivolumab.
- We entered into a multi-year strategic alliance with M.D. Anderson.

Regulatory

- We received Fast Track designation for LN-144 for the treatment of advanced melanoma.
- We submitted Clinical Trial Applications, or CTAs, in multiple countries in Europe in support of our Phase 2 clinical trials and received approval to commence clinical trials in the Netherlands.

Research

- We entered into a collaboration with the Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, or OSUCCC – James, or Ohio State University, to evaluate TILs, marrow infiltrating lymphocytes, or MILs, and peripheral-blood associated lymphocytes in acute myeloid leukemia, or AML, and chronic lymphocytic leukemia, or CLL.

Manufacturing

- We entered in to a new three-year Manufacturing Services Agreement, or MSA, with PharmaCell B.V., or PharmaCell, now a subsidiary of Lonza Group Ltd., in the Netherlands.
- We entered in to a new two-year MSA with Moffitt Cancer Center.
- We commenced a partnership with TrakCel Ltd., or TrakCel, to build a scheduling and logistics software tool that automates the supply chain for our TIL therapy.

Corporate

- We changed our corporate name from Lion Biotechnologies, Inc. to Iovance Biotherapeutics, Inc. and reincorporated from a Nevada corporation to a Delaware corporation.
- We appointed Timothy E. Morris as our Chief Financial Officer in August 2017.
- We raised approximately \$53.7 million in net proceeds, after deducting underwriting discounts and offering expenses, through a public offering that closed in September 2017.

Recent Developments

In January 2018, we closed an underwritten public offering of 15,000,000 shares of our common stock at a public offering price of \$11.50 per share, before underwriting discounts. The shares sold at closing included 1,956,521 shares issued upon the exercise in full by the underwriter of its option to purchase additional shares at the public offering price less the underwriting discount. The gross proceeds from the offering, before deducting the underwriting discounts and commissions and other estimated offering expenses payable by us, are \$172.5 million with estimated net proceeds to us of approximately \$161.7 million.

On February 26, 2018, Jay Venkatesan, M.D., resigned from our board of directors, effective March 1, 2018. Separately, on March 1, 2018, our board of directors appointed Michael Weiser, M.D., Ph.D., as a director, effective March 15, 2018. Upon joining our board of directors, Dr. Weiser will become a member of its audit committee and nominating and governance committee, and will become the chair of its compensation committee.

Corporate Strategy

Our goal is to be a leader in the development and commercialization of TIL-based immunotherapies to treat solid tumors. We are developing a portfolio of TIL-based product candidates with the potential to meaningfully improve survival and quality of life for cancer patients. Key elements of our strategy include:

Expedite clinical development, regulatory approval, and commercialization of our lead product candidate LN-144 for the treatment of metastatic melanoma.

Based on results of TIL therapy from NCI-sponsored and our own clinical trials in metastatic melanoma, we are focused on expediting the development, regulatory approval and commercialization of our lead product candidate, LN-144, for the treatment of patients with metastatic melanoma. We filed an IND with the FDA in December 2014 to initiate a company-sponsored Phase 2 single-arm, multicenter clinical trial of LN-144 in patients with metastatic melanoma. We began enrollment of this study in the second half of 2015 and expanded it into three cohorts in 2017. Cohort 1 evaluated our first-generation TIL manufacturing process, cohort 2 is evaluating our second-generation, Gen 2, TIL manufacturing process and cohort 3 is evaluating retreatment of certain patients with a second dose of TIL. We announced initial data from the first two arms of this trial at the ASCO and SITC Annual Meetings in 2017 and presented updated data from ongoing cohort 2 in December 2017. In 16 and 10 evaluable patients, the ORRs were 29% and 40% from cohorts 1 and 2, respectively.

If results from this company-sponsored multi-center Phase 2 trial present clinically meaningful results for TIL therapy in patients with metastatic melanoma who have failed to respond to or progressed on at least one line of prior therapy, we plan to initiate discussions with the FDA in 2018 about a registration path for LN-144 and, when applicable, the filing of a Biologic License Application, or BLA, for approval of LN-144 as a treatment for patients with metastatic melanoma. We may also initiate discussions with the FDA concerning expedited development pathways, such as accelerated approval, which we believe may be warranted, given the limited options for patients with advanced melanoma. However, even if the FDA grants accelerated approval, confirmatory post-approval trials may still be required by the FDA.

Continue to improve our TIL manufacturing process and develop new TIL manufacturing technology to become the preferred provider of TIL therapy in the U.S. and the rest of the world.

We believe we are the only company in the United States to have a centralized TIL manufacturing process and location. In 2017, we announced that our internal research and process development efforts had resulted in a second generation TIL manufacturing process, known as Gen 2, which reduced TIL manufacturing time from 5-6 weeks to 22 days. Gen 2 also produces a cryopreserved product for ease of administration and handling. The Gen 2 manufacturing process is now being utilized in cohort 2 of our ongoing LN-144 trial and has been selected for all ongoing and future TIL clinical development. We also intend to include Gen 2 as the manufacturing process for registration for our discussions with the FDA and eventually the anticipated BLA filing.

Collaborate with governmental, academic and corporate partners to improve and develop TIL therapies for new indications, for use in combination with other therapies and to evaluate new manufacturing methods.

In addition to our own research and process development efforts, we seek to collaborate with government, academic research institutions, and corporate partners to improve TIL manufacturing and to develop TIL therapies for new indications. In 2017, we also announced collaborations with Moffitt, M.D. Anderson, and Ohio State University to evaluate several new solid tumor and hematologic indications for TIL therapy in clinical and preclinical studies as well as, in some cases, new TIL manufacturing approaches. In September 2016, we entered into a license agreement with PolyBioCept AB, a corporation organized under the laws of Sweden, or PolyBioCept, and a related clinical trial with Karolinska University Hospital to evaluate a new cytokine cocktail for TIL manufacturing and the treatment of patients with pancreatic cancer and glioblastoma. In August 2016, we expanded our Cooperative Research and Development Agreement, or CRADA, with the NCI for another 5-year term. This collaboration with the NCI is directed at identifying new indications for, and variations of, unmodified TIL therapy based on human proof-of-concept data. Our CRADA with the NCI addresses human papilloma virus, or HPV-associated cancers (cervical and head and neck), lung, bladder, and breast cancer.

Academic research institutions

We currently have three CGAs with Moffitt involving investigator-sponsored trials. In December 2017, we announced an agreement with Moffitt to evaluate TIL therapy in a clinical trial that combines TIL with nivolumab in NSCLC. Dosing in this clinical trial began in late 2017. The Phase 1 study (NCT03215810) is being conducted by Moffitt and is designed to enroll up to 18 patients with advanced NSCLC. In December 2016, we entered into a three-year Sponsored Research Agreement, or SRA, with Moffitt. The SRA covers research aimed at better understanding the characterization of T cell subsets that comprise TIL products and to enhance the therapeutic efficacy of TIL. Also in December 2016, we announced a new clinical grant agreement with Moffitt under which we provide support for an ongoing clinical trial at Moffitt that combines TIL therapy with nivolumab for the treatment of patients with metastatic melanoma.

In September 2017, we entered into a preclinical research collaboration with OSUCCC – James focused on TIL, MIL and peripheral blood-associated lymphocyte technologies. The collaboration will initially focus on hematologic malignancies in areas of poor prognostic cancers with high unmet medical need, which include AML and CLL.

In April 2017, we entered into a Strategic Alliance Agreement, or SAA, with M.D. Anderson to conduct clinical and preclinical research studies of TIL therapies in several new indications, including sarcomas, ovarian cancer, and pancreatic cancer. The collaboration with M.D. Anderson has multiple components including preclinical research to expand our understanding of TIL and two clinical trials. The trials will be conducted by M.D. Anderson and will include one study with TIL manufactured (LN-145) by Iovance and one study with TIL manufactured by M.D. Anderson. In the latter study, Bristol-Myers Squibb Co. will supply a 4-1BB (CD137) agonist antibody, urelumab, for use in the manufacturing of TIL by M.D. Anderson pursuant to an agreement with us and M.D. Anderson. Both studies will enroll patients with various sarcomas or platinum-resistant ovarian cancer. We plan to initiate dosing in these studies in 2018. Iovance has rights to certain intellectual property related to the M.D. Anderson manufacturing method expected to be utilized in the study.

Corporate partners

In December 2017, we announced a new clinical trial under our collaboration with MedImmune. The Phase 2 multicenter study will be sponsored by us and will enroll up to 24 PD-1/PD-L1 naïve patients and be composed of two cohorts to assess the efficacy and safety of LN-145 alone and in combination with anti-PD-L1 inhibitor, (durvalumab) (MED14736), in patients with locally advanced or metastatic NSCLC. This clinical trial is expected to begin enrolling patients in 2018 and will evaluate TIL therapy in combination with durvalumab. We entered into our collaboration with MedImmune in December 2015 to conduct clinical and preclinical research in immuno-oncology. Under the terms of the agreement, we will fund and conduct at least one clinical trial combining durvalumab with TIL, for the treatment of patients. MedImmune will supply durvalumab for the clinical trials. The purpose of the study is to assess the efficacy and safety of TIL alone in this patient population as well as TIL in combination with durvalumab.

In 2016, we entered into an exclusive license agreement with PolyBioCept to license certain rights to patent applications related to a cytokine cocktail for expansion of TIL. In connection with this license, we entered into a clinical trial agreement with Karolinska University Hospital in Sweden to conduct two clinical trials in patients with pancreatic cancer and glioblastoma with TIL manufactured using the cytokine cocktail. Due to personnel changes at the Karolinska University Hospital, we expect the start of these clinical trials will be delayed to dates that have not yet been determined. In connection with this license, we also agreed to enter into a sponsored research agreement with the Karolinska Institute within 90 days after the date of the PolyBioCept Agreement, which date has been extended by amendments to the license. Failure to amend the license will give PolyBioCept the right to terminate the license (and we will have the right to repayment of \$2.2 million).

Establish initial manufacturing capacity for TIL products with contract manufacturing organizations.

We continue to invest in improving the process and efficiency of manufacturing our product candidates and to build a centralized manufacturing capability in the United States and Europe for TIL manufacturing. Currently we use several contract manufacturing organizations, or CMOs, to supply our TIL-based products for our clinical trials. CMOs limit the amount of upfront capital investment; however, we may establish our own manufacturing facilities in the future for better margins and rapid implementation of innovative changes. We intend to carefully manage our cost structure, and reduce the long-term cost of manufacturing our products, although there can be no assurance that we will be able to reduce our manufacturing costs to commercially attractive levels.

In 2017, we entered into a three-year MSA and related statements of work with PharmaCell B.V., or PharmaCell, a contract manufacturing services company based in the Netherlands, to manufacture our autologous cell therapy products for use in European clinical trials. PharmaCell was subsequently acquired by Lonza Group Ltd., or Lonza. Lonza will manufacture TIL products in its clinical and commercial facility in Geleen, the Netherlands.

Also in 2017, we entered into a two-year MSA and related statements of work with Moffitt, to manufacture our autologous cell therapy products. Currently, we do not anticipate extending the term of this agreement.

In 2016, we entered into a three-year MSA and related statements of work with WuXi AppTec, Inc., or WuXi, in order to increase our TIL manufacturing capacity in facilities with both clinical and commercial capability. We have extended the term of the related statements of work until May 2020.

Iovance-Sponsored Trials

We currently have three ongoing Phase 2 clinical studies and intend to initiate an additional Phase 2 study in the first half of 2018. The three ongoing studies include LN-144 for metastatic melanoma, LN-145 for recurrent, metastatic or persistent cervical carcinoma and LN-145 for recurrent and/or metastatic squamous cell carcinoma of the head and neck. We plan to initiate a study with LN-145 in NSCLC in 2018. Each of the clinical trials includes autologous TIL infusion followed by IL-2 after a non-myeloablative chemotherapy preparative regimen for the treatment of patients with metastatic melanoma. Additional information about the clinical studies is as follows:

LN-144 - Metastatic Melanoma

We are developing LN-144 to treat metastatic melanoma. Melanoma is a common type of skin cancer, accounting for approximately 87,110 patients diagnosed and 9,730 deaths each year in the United States according to the American Cancer Society, Cancer Facts and Figures estimates for 2017. Our ongoing Phase 2 trial, C-144-01, (NCT02360579), is a prospective, 3-cohort interventional study evaluating LN-144 in metastatic melanoma patients who have progressed after prior anti-PD-1 therapy and if BRAF mutant, after BRAF inhibitor. Patients enrolled in this trial to date have typically failed several prior treatment regimens.

Patients with metastatic melanoma who have failed at least one treatment under the current standards of care have an unfavorable prognosis with very few curative treatment options. The National Comprehensive Cancer Network, or NCCN, has updated its recommendations for the treatment of patients with unresectable or metastatic melanoma. Initial therapy can include checkpoint inhibitors either alone or in combination (ipilimumab, nivolumab, pembrolizumab), targeted therapies for patients with BRAF mutations (dabrafenib/trametinib, vemurafenib/cobimetinib combinations or single agents) or participating in a clinical trial. For patients not responding or progressing and who have an adequate clinical status, agents selected from the previous list but of a different therapeutic class can be used as well as high dose IL-2. NCCN experts also recommend participating in a clinical trial at any stage of disease. Patients who do not respond to the current second-line therapies have very few treatment options and typically have a very poor prognosis, with limited median survival measured in months.

LN-145 - Head and Neck Cancer

We are developing LN-145 to treat head and neck cancers. In June 2017, we enrolled our first patient in our ongoing Phase 2 trial, C-145-03, (NCT03083873) for the treatment of patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck, who have failed one prior therapy. The trial has met the initial efficacy threshold for the first stage of the Simon's two stage design, which is an initial evaluation of patient response. The trial will therefore continue to enroll patients to the full sample size of 47 per protocol. We have amended the protocol so that newly enrolled patients can be treated using LN-145 produced from the Gen 2 manufacturing process. In January 2018, we announced preliminary data from this study which demonstrated that three of the eight patients treated with LN-145 had a reduction in tumor size of at least 30% and qualified as a PR, and the ORR in the study to date is 38%. These patients had a median of 4 prior treatments for their cancer and had all received prior anti-PD-1 therapy. The most common side effects were pyrexia, chills, and hypotension.

According to estimates from the SEER program, approximately 63,030 people were diagnosed with head- and neck-related cancers, and approximately 13,360 head- and neck-related cancer deaths occurred in the United States in 2017.

LN-145 - Cervical Cancer

We are developing LN-145 to treat cervical cancer. In August 2017, we enrolled our first patient in our ongoing Phase 2 trial, C-145-04 (NCT03108495) for the treatment of patients with recurrent, metastatic or persistent cervical carcinoma who have failed one prior therapy. The study is enrolling patients in the United States and is expected to start enrollment of patients in Europe in the first half of 2018. We have amended the protocol so that newly enrolled patients can be treated with LN-145 produced from the Gen 2 manufacturing process. In January 2018, we reported preliminary data from C-145-04 which showed that of the two patients that are currently evaluable, one treated with LN-145 had a confirmed PR and one patient had stable disease.

According to estimates from the SEER program, approximately 12,820 women were diagnosed with cervical cancer, and approximately 4,210 cervical cancer-related deaths occurred in the United States in 2017.

LN-145 - Non-Small Cell Lung Cancer

We are developing LN-145 for NSCLC. Under our collaboration with MedImmune, we plan to initiate a two-cohort Phase 2 trial, IOV-LUN-201, alone or in combination with durvalumab for the treatment of patients with locally advanced metastatic NSCLC. Patients in this study will be naïve to PD-1 or PD-L1 therapy. The study is expected to begin enrollment in 2018. Patients will be treated with LN-145 produced from the Gen 2 manufacturing process.

According to estimates from the SEER program, approximately 222,500 people were diagnosed with lung and bronchus cancers, and approximately 155,870 deaths occurred related to these cancers in the United States in 2017.

Other Trials

TIL in Other Solid Tumor Indications

We are collaborating with M.D. Anderson on clinical trials to evaluate TIL therapy in sarcomas, ovarian cancer and pancreatic cancer. These trials are expected to begin enrolling patients in the first half of 2018. Patients in these studies will be treated with LN-145 or TIL manufactured by M.D. Anderson.

We are also collaborating with Karolinska University Hospital to conduct clinical trials of TIL manufactured using a novel cytokine cocktail for TIL expansion in pancreatic cancer and glioblastoma. Due to personnel changes at the Karolinska University Hospital, we expect the start of these clinical trials will be delayed to dates that have not yet been determined.

TIL in Combination with Other Immunotherapy Drugs

Checkpoint inhibitors are a new class of immunotherapy drugs which seek to overcome one of cancer's main defenses against an immune system attack. PD-1 is a checkpoint protein found on immune cells called T cells. It normally acts as a type of "off switch" that helps prevent T cells from attacking other cells in the body. It does this by attaching to PD-L1, a protein found on both normal and cancerous cells, which may then shut down an attack by a T cell. Some cancer cells have large amounts of PD-L1 expressed on their surfaces, which helps them evade T cell attack.

We are collaborating with Moffitt on a clinical trial (NCT03215810) that is currently enrolling patients to evaluate TIL therapy in combination with the checkpoint inhibitor nivolumab in NSCLC. An additional clinical trial (NCT03374839) is being conducted by Moffitt to evaluate TIL therapy in combination with nivolumab in metastatic melanoma. We have also previously collaborated with Moffitt on a clinical trial (NCT01701674) to evaluate TIL therapy in combination with the checkpoint inhibitor ipilimumab. This trial has been completed and we await publication of the results.

Under our CRADA, we are collaborating with the NCI (NCT02621021) to evaluate TIL therapy in combination with the checkpoint inhibitor pembrolizumab in a 170-patient clinical trial in patients with advanced melanoma. This study is currently enrolling.

Immune system

The immune system recognizes danger signals and responds to threats at a cellular level. The most significant components of the cellular aspect of the adaptive immune response are T cells, or T lymphocytes, so called because they mature in the thymus and are distinguished from B cells which mature in the bone marrow. T cells can be distinguished from other white blood cells by T cell receptors present on their cell surface. These receptors contribute to tumor surveillance by helping T cells recognize infected cells as well as cancerous cells. T cells are involved in both sensing and killing infected or cancerous cells, as well as coordinating the activation of other cells in an immune response.

Although the immune system is designed to identify foreign or abnormal proteins expressed on tumor cells, this process is often defective, or not operating optimally, in cancer patients. The defective process sometimes occurs when the cancer cells closely resemble healthy cells and go unnoticed or if tumors lose their protein expression. Additionally, cancer cells employ a number of mechanisms to escape immune detection to suppress the effect of the immune response. Some tumors also encourage the production of regulatory T cells that prevent cytotoxic T cells from attacking the cancer.

Cancer immunotherapy

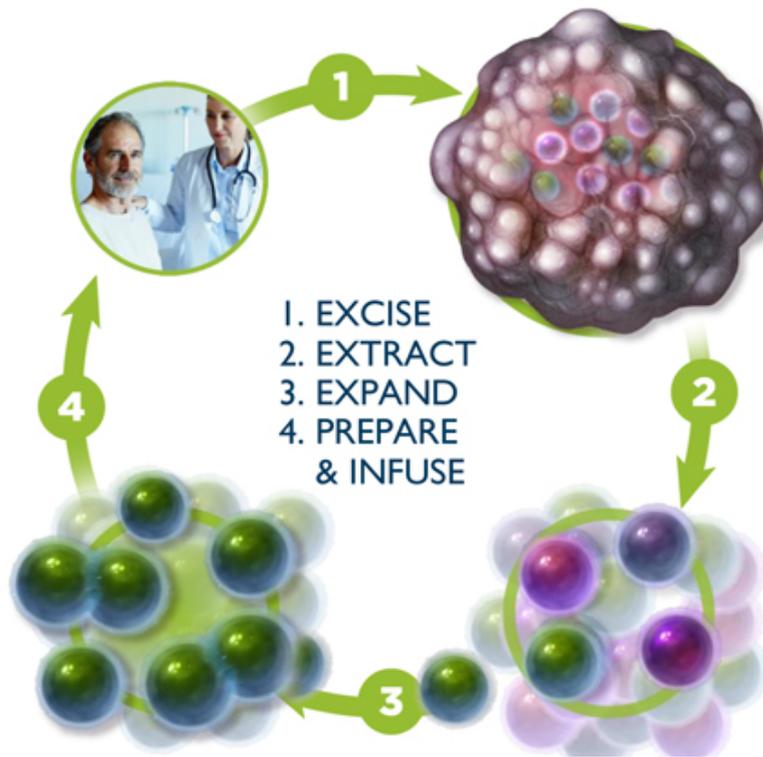
Despite the progress that has been made over the past several decades, effective treatment of cancer, especially solid tumors, continues to be challenging. Some reasons solid tumors are so difficult to treat are: (i) in many solid tumors, multiple genes (as many as hundreds or thousands of genes) are mutated, and solid tumors are heterogeneous, (ii) it is not always clear which particular mutations are critical, and (iii) tumors can adapt and find a way to evade treatments that target a single mutation. In addition, the tumor can suppress the patient's natural immune response. When T cells with cancer-specific receptors are absent, present in low numbers, of poor quality, or rendered inactive by suppressive mechanisms employed by tumor tissue, the cancer can grow and spread to various organs. In addition, standard of care treatments for cancer can be deleterious to T cells' ability to kill cancer.

We believe that adoptive cell therapy, with the use of human cells as therapeutic entities to reengage the immune system, may be the next significant advancement in the treatment of cancer. These cellular therapies may avoid the long-term side effects associated with current treatments and have the potential to be effective regardless of the type of previous treatments patients have experienced. We believe TIL therapy, in particular, has the potential to treat solid tumors by increasing the effectiveness and number of a patient's cancer-specific T cells. TIL therapy is polyclonal, and we believe that it is capable of targeting multiple tumor antigens on cancer cells. Furthermore, the non-myeloablative lymphodepleting chemotherapy administered prior to TIL infusion is capable of suppressing the hostile tumor microenvironment, which we believe will enhance the efficacy of TIL therapy.

Tumor-infiltrating lymphocytes

Adoptive cell therapy with TIL involves the following steps:

1. Excision: After a surgical resection of a lesion, a patient's TIL are removed from suppressive tumor microenvironment
2. Extraction: Tumor is fragmented and placed in media for TIL to leave the tumor
3. Expansion: TIL expanded exponentially *ex vivo* to yield $10^9 - 10^{11}$ TIL
4. Preparation and Infusion: Patient receives non-myeloablative lymphodepletion to eliminate potentially suppressive tumor microenvironment and maximize engraftment and potential potency of TIL therapy; patient is infused with their expanded TIL and up to 6 doses of IL-2 to promote activation, proliferation and anti-tumor cytolytic activity of TIL.



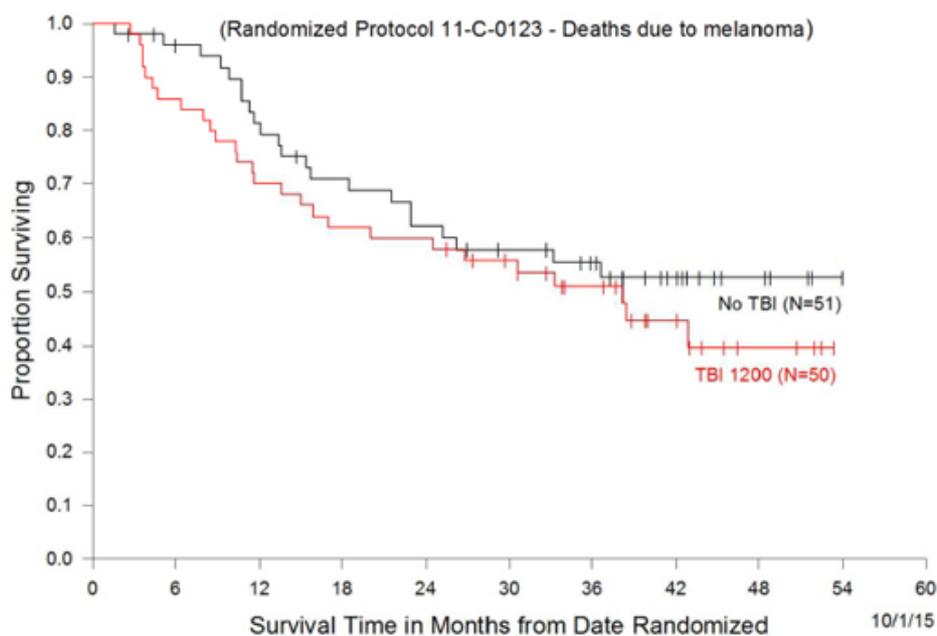
Currently, our Gen 2 manufacturing process takes 22 days from receipt of the patient's tumor. The final TIL product is shipped to the institution for infusion of the TIL back into the patient. We currently treat patients with a single infusion of TIL, although our protocols allow for evaluation of more than one administration of TIL. After infusion, TIL can potentially infiltrate the tumor microenvironment to eliminate large numbers of cancer cells. TIL can also further proliferate in the body. TIL therapy can potentially overcome several mechanisms of tumor escape to which endogenous T cells may be susceptible due to the hostile tumor microenvironment.

Historical clinical results with TIL in metastatic melanoma

To date, hundreds of metastatic melanoma patients have already been treated with TIL therapy produced locally using different manufacturing methods at different academic institutions and hospitals in the United States, Europe, Canada, and Israel. At NCI, clinical responses have been relatively consistent in several trials: over 50% of the melanoma patients treated with TIL have an objective response (i.e. tumor regression of 50% or more, as defined by RECIST criteria) and approximately 22-24% of patients have a complete response with no evidence of disease remaining after only one administration. Many patients respond to TIL therapy despite experiencing tumor progression after previously being treated with other therapies.

In September 2015, Dr. Rosenberg, a recognized pioneer in immuno-oncology and adoptive cell therapy using TIL, presented updated findings from a Phase 2 clinical trial of TIL therapy in metastatic melanoma at the American Association for Cancer Research Inaugural International Cancer Immunotherapy Conference. Data was presented from a 101 patient, Phase 2 clinical trial conducted at the NCI. In the trial, patients with advanced metastatic melanoma were equally divided in two groups. Both groups were treated according to a standard TIL protocol using nonmyeloablative, or NMA, chemotherapy, with the second group also receiving total body irradiation. 54% of the patients treated with TIL therapy achieved an objective response. An objective response occurs when there is a complete remission or a partial remission of the tumor. Out of the 101 patients, 24, or 24%, had experienced a complete remission and 23 of the 24, or 96%, showed ongoing durability of this response at 30 to 47 months following treatment, at the time of publication. Median follow-up time was approximately 40.9 months. Overall survival, or OS, was approximately 80% at 12 months, and median OS had not yet been achieved. Median progression-free survival was approximately 8-10 months. This observation was also presented by Dr. Stephanie Goff at the 2016 ASCO meeting and published in the *Journal of Clinical Oncology* in June 2016.

Overall Survival of patients in TIL ± TBI study



Source: Goff, S.L. et al. Randomized, Prospective Evaluation Comparing Intensity of Lymphodepletion Before Adoptive Transfer of Tumor-Infiltrating Lymphocytes for Patients With Metastatic Melanoma. *Journal of Clinical Oncology*, 34(20), 2389-2397.

Clinical results with TIL in other solid tumor indications

Under our CRADA with the NCI, we are providing research and development and clinical funding for the development of unmodified TIL therapy for a variety of solid tumor indications, including HPV-associated cancers (cervical, head and neck), bladder, breast, and lung cancers. The NCI has completed a clinical trial involving TIL therapy to treat advanced HPV-positive cervical cancer. Data from this trial was published in the *Journal of Clinical Oncology* in April 2015 and in *Science* in April 2017. Out of nine cervical cancer patients treated with HPV-TIL, two experienced complete remissions reported as ongoing at 54 and 46 months. Another patient experienced a three-month partial remission. Additionally, the NCI has ongoing trials to treat patients using TIL with colorectal cancer, gastric cancer, pancreatic cancer, hepatocellular carcinoma and cholangiocarcinoma and lung cancer. Depending on results from the research and development and clinical trials conducted at the NCI under our CRADA, we may pursue the development and regulatory approval of TIL therapy for additional indications.

Safety

We continue to enroll patients in our ongoing TIL programs and we closely monitor our studies to learn about all safety events occurring. Some of such events may be associated with TIL therapy. To date, however, the largest set of data for TIL therapy was generated by the NCI as part of their multiple clinical studies. Per publications from the NCI, toxicities or adverse events during TIL therapy have been mostly associated with either the lymphodepletion regimen or the high-dose IL-2 therapy given after TIL infusion as described by Goff et al. in the *Journal of Clinical Oncology* in June 2016. The standard approach to the administration of high-dose IL-2 is to continue dosing until patients can no longer tolerate treatment. Our trials, however, have limited administration of IL-2 to up to 6 doses. Treatment-related toxicities reported by Goff et al. included febrile neutropenia, bacteremia, atrial fibrillation, sepsis, and cardiac arrhythmia in the NMA arm.

In our ongoing C-144-01 trial with LN-144 in metastatic melanoma, pyrexia, anaemia, neutrophil and platelet count decrease, febrile neutropenia, and fatigue were, thus far, observed as the most common treatment emergent adverse events of any grade in cohort 2, and febrile neutropenia and neutrophil and platelet count decrease were, thus far, observed as the most common treatment emergent serious adverse events of any grade in cohort 1. Pyrexia, chills, hyponatremia, and hypotension were the most common treatment emergent adverse events by preferred term in our ongoing C-145-03 trial in recurrent and/or metastatic squamous cell carcinoma of the head and neck. As additional patients are enrolled in the program, the safety profile of TIL therapy may change.

Next Generation TIL Product Strategies

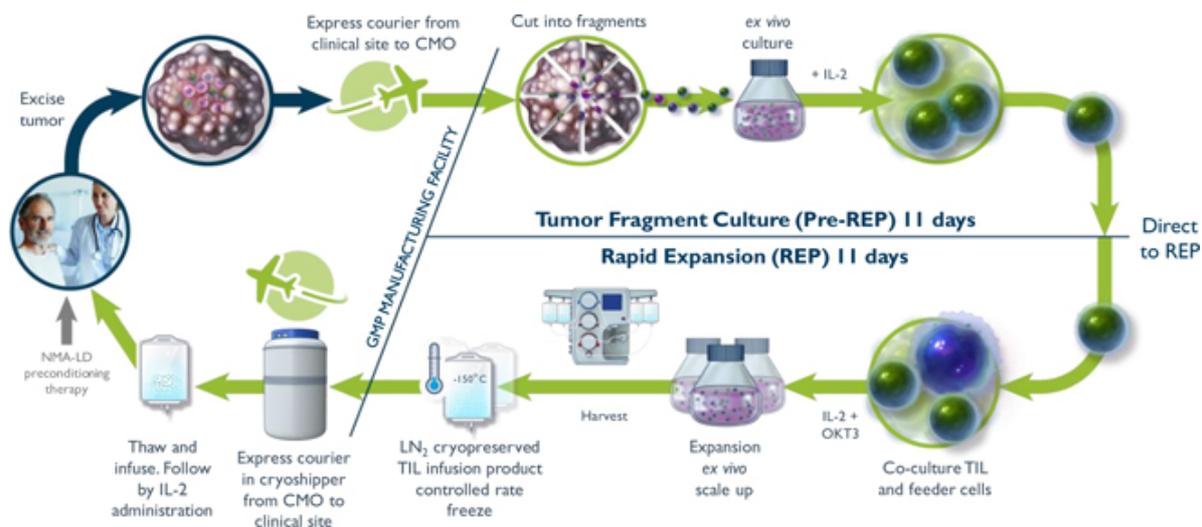
We hold an exclusive license from the NCI to a patent family directed to select TIL for various cell surface markers in order to treat patients with metastatic melanoma. The license to this next-generation TIL technology was developed to achieve a potentially more potent and efficient TIL production by selecting for TIL that express various activating receptors, including 4-1BB and PD-1. TIL that express these proteins are associated with higher tumor reactivity, so potentially fewer of the enriched cells are needed to be therapeutically effective. Selected TIL technology has the potential to reduce the time and cost of manufacturing. We have not yet progressed this technology into clinical trials.

In addition to selected TIL, we are evaluating strategies to genetically engineer TIL, and to pre-condition tumors from which we expand TIL so that more TIL are present at the time of tumor excision.

Process Development, Manufacturing, and Manufacturing Agreements

Our first generation TIL manufacturing process was based on the NCI's original manufacturing and processing of TIL, which we modified so that it could be reproduced in a Good Manufacturing Process, or cGMP, environment. This first-generation process expanded the number of TIL over a 5-6-week period and produced a non-cryopreserved product for administration to the patient. Our Gen 2 TIL manufacturing process was developed by our internal research and process development team. This process, is currently in use in cohort 2 of the C-144-01 trial with LN-144 in metastatic melanoma. We presented early data from cohort 2 late in 2017 and have selected Gen 2 for product registration and all ongoing and future TIL clinical development.

The Gen 2 manufacturing process begins with the collection of the patient's tumor, which is then sent to a central manufacturing facility, where the T cells are isolated. These cells are stimulated to proliferate, then propagated in cell culture flasks until sufficient cells are available for infusion back into the patient. The TIL is then washed and put in media suitable for cryopreservation and infusion. The final product is shipped back to the clinical center where they can be administered to the patient. The following diagram illustrates our Gen 2 TIL manufacturing process.



We have entered into MSAs with WuXi, Moffitt and PharmaCell, pursuant to which they have agreed to manufacture, package, ship and handle quality assurance and quality control of certain clinical trials for our TIL products working closely with our employees. We have two suites for clinical manufacturing at WuXi, and one of those suites is also available to manufacture TIL for commercial use. Cell processing activities will be conducted at all companies under cGMP, using qualified equipment and materials. We believe that all materials and components utilized in the production of the final TIL product are readily available from qualified suppliers. We have also commenced a partnership with TrakCel to build a scheduling and logistics software tool that automates the supply chain for our TIL therapy. We expect to rely on these CMOs, to meet anticipated clinical trial demands. In the future, we may rely on them or other third parties, or develop our own manufacturing capabilities for the manufacturing and processing of TIL-based product candidates for our clinical trials. To meet projected needs for commercial sale quantities, we may develop our own commercial manufacturing facility to supply and process products. Developing our own manufacturing capabilities may be costlier than we anticipate or result in significant delays. If we are unable to develop our own manufacturing capabilities, we will rely on CMOs, including both current and alternate suppliers, to ensure sufficient capacity is available for commercial purposes.

Personalized Patient Product Management

In September 2017, we entered into a partnership with TrakCel to build a scheduling and logistics software tool that automates the supply chain for our TIL therapy products. The TrakCel software will electronically link us with our clinical sites, CMOs and couriers to schedule and track TIL therapies for each patient. The TrakCel software is also intended to help manage capacity utilization and throughput and will provide efficiencies in the delivery of TIL treatment.

The TrakCel software is also designed to ensure chain of identity for each patient's product. Because our product candidates are specifically manufactured for each individual patient, we will be required to maintain a chain of identity with respect to the patient's tumor as it moves from the patient to the manufacturing facility, through the manufacturing process, and back to the patient.

Orphan Drug Designation

During 2015, we received an orphan drug designation for LN-144 in the United States to treat malignant melanoma stages IIB-IV. If approved, this designation provides seven years of market exclusivity in the United States, subject to certain limited exceptions. However, the orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process.

Fast Track Designation

In August 2017, we announced that the FDA had granted Fast Track designation for LN-144, for the treatment of advanced melanoma. The FDA's Fast Track process is designed to facilitate the development and expedite the review of drugs that treat serious conditions and fill an unmet medical need. Fast Track designation allows more frequent meetings and communications with the FDA to discuss the drug's development plans and review process. The Fast Track designation also allows for a rolling review of a company's BLA.

Commercialization Plan

We currently have no sales, marketing or commercial product distribution capabilities. As we make progress towards registration of LN-144, we plan to build our own sales and commercialization capabilities in support of commercialization of TIL.

We have not yet decided on a commercial strategy for our TIL products. Our commercial strategy for markets outside the U.S. may include the use of strategic partners, distributors, a contract sales force or the establishment of our own commercial infrastructure. We plan to further evaluate these alternatives as we approach approval for one of our product candidates.

As additional product candidates advance through our pipeline, our commercial plans may change. Clinical data, size of the development programs, size of the target market, size of a commercial infrastructure, intellectual property protection and manufacturing needs may all influence our U.S., Europe and rest-of-world strategies.

Intellectual Property

Intellectual property is of importance in our field and in biotechnology generally. We seek to protect and enhance proprietary technology, inventions, and improvements that are commercially important to the development of our business by seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also plan to rely on regulatory protection afforded through orphan drug designations, available regulatory exclusivities and patent term extensions where available. To achieve this objective, a strategic focus for us has been to identify and license key patents that provide protection and serve as an optimal platform to enhance our intellectual property and technology base.

We have also engaged in the development of our own patent portfolio based on internal research and development activities in 2016. As a result, we now own a number of pending patent applications in the fields of TIL therapy, TIL manufacturing processes, and TIL expansion methods, and we expect to further develop our patent portfolio as a strategic focus in 2018.

Research, Development and License Agreements

Currently, preclinical research and development is conducted with the NCI under the CRADA, with Moffitt under our SRA, and at our own internal research and development laboratory in Tampa, Florida. We also have preclinical collaborations with M.D. Anderson and Ohio State University. We sponsor our own clinical trials and also have clinical collaborations with the NCI under our CRADA, and with Moffitt, M.D. Anderson, and Karolinska University Hospital under clinical trial agreements.

In addition, we own the exclusive, co-exclusive, and non-exclusive licenses to certain patent and other intellectual property rights with the National Institutes of Health, or NIH, Moffitt, M.D. Anderson Cancer Center and PolyBioCept described below in this Annual Report on Form 10-K.

National Institutes of Health and the National Cancer Institute

Cooperative Research and Development Agreement

In August 2011, we signed a five-year CRADA with the NCI to work with Dr. Steven Rosenberg on developing adoptive cell immunotherapies that are designed to destroy metastatic melanoma cells using a patient's tumor infiltrating lymphocytes.

In January 2015, we executed an amendment to the CRADA to include four new indications. As amended, in addition to metastatic melanoma, the CRADA included the development of TIL therapy for the treatment of patients with bladder, lung, triple-negative breast, and HPV-associated cancers.

In August 2016, we entered into a second amendment to the CRADA. The principal changes effected by the second amendment included (i) extending the term of the CRADA by another five years to August 2021, and (ii) modifying the focus on the development of unmodified TIL as a stand-alone therapy or in combination with FDA-licensed products and commercially available reagents routinely used for adoptive cell therapy. The parties will continue the development of improved methods for the generation and selection of unmodified TIL with anti-tumor reactivity in metastatic melanoma, bladder, lung, breast, and HPV-associated cancers.

Pursuant to the terms of the CRADA, as amended, we are currently required to make quarterly payments of \$0.5 million to the NCI for support of research activities. To the extent we license patent rights relating to TIL-based product candidates under this agreement, we will be responsible for all patent-related expenses and fees, past and future, relating to the TIL-based product candidate. The extended CRADA has a five-year term expiring in August 2021. Either party may unilaterally terminate the CRADA for any reason or for no reason at any time by providing written notice at least 60 days before the desired termination date. We recorded costs associated with the CRADA of \$2.0 million, \$1.8 million and \$2.0 million in the years ended December 31, 2017, 2016 and 2015, respectively. These costs were recorded as research and development expenses.

Patent License Agreement Related to the Development and Manufacture of TIL

Effective October 5, 2011, we entered into a Patent License Agreement with the NIH which was subsequently amended on February 9, 2015 and October 2, 2015. Pursuant to the Patent License Agreement as amended, or the Patent License Agreement, the NIH granted us licenses, including exclusive, co-exclusive, and non-exclusive licenses, to certain technologies relating to unmodified autologous TIL adoptive cell therapy products for the treatment of metastatic melanoma, lung, breast, bladder and HPV-positive cancers. In consideration for the exclusive rights granted under the Patent License Agreement, we agreed to pay the NIH a non-refundable upfront licensing fee in the amount of \$0.4 million. We also agreed to pay customary royalties based on a percentage of net sales of a licensed product (which percentage is in the mid-single digits), a percentage of revenues from sublicensing arrangements, and lump sum benchmark payments upon the successful completion of clinical studies involving licensed technologies, the receipt of the first FDA approval or foreign equivalent for a licensed product or process resulting from the licensed technologies, the first commercial sale of a licensed product or process in the United States, and the first commercial sale of a licensed product or process in any foreign country. We will also be responsible for all costs associated with the preparation, filing, maintenance and prosecution of the patent applications and patents covered by the Patent License Agreement.

Exclusive Patent License Agreement Related to TIL Selection

On February 10, 2015, we entered into an Exclusive Patent License Agreement with the NIH under which we received an exclusive license to the NIH's rights to patent-pending technologies related to methods for improving adoptive cell therapy through potentially more potent and efficient production of TIL from melanoma tumors by selecting for T-cell populations that express various inhibitory receptors. Unless terminated sooner, the license shall remain in effect until the last licensed patent right expires.

In consideration for the exclusive rights granted under the Exclusive Patent License Agreement, we agreed to pay the NIH a non-refundable upfront licensing fee in the amount of \$0.8 million. We also agreed to pay customary royalties based on a percentage of net sales of a licensed product (which percentage is in the mid-single digits), a percentage of revenues from sublicensing arrangements, and lump sum benchmark payments upon the successful completion of clinical studies involving licensed technologies, the receipt of the first FDA approval or foreign equivalent for a licensed product or process resulting from the licensed technologies, the first commercial sale of a licensed product or process in the United States, and the first commercial sale of a licensed product or process in any foreign country. We will also be responsible for all costs associated with the preparation, filing, maintenance and prosecution of the patent applications and patents covered by the Exclusive Patent License Agreement.

The costs associated with the NIH patent licenses in the year ended December 31, 2017 were immaterial, while there were \$0.4 million in costs associated with these licenses in each of the years ended December 31, 2016 and 2015.

H. Lee Moffitt Cancer Center

Research Collaboration and Clinical Grant Agreements with Moffitt Cancer Center

In September 2014, we entered into a research collaboration agreement with Moffitt to jointly engage in translational research and development of adoptive cell therapy with TIL for improved anti-tumor properties and manufacturing process.

In December 2016, we entered into an SRA with Moffitt, or the Moffitt SRA. At the same time, we entered into a CGA with Moffitt to support an ongoing clinical trial at Moffitt that combines TIL therapy with nivolumab for the treatment of patients with metastatic melanoma. In June 2017, we entered into a second CGA with Moffitt to support a new clinical trial at Moffitt that combines TIL therapy with nivolumab for the treatment of patients with non-small cell lung cancer. In the years ended December 31, 2017, 2016 and 2015, we recorded research and development costs of \$1.2 million, \$0.7 million, and \$0.7 million, respectively, in connection with the research collaboration and clinical grant agreements with Moffitt.

Exclusive License Agreement with Moffitt

We entered into a license agreement with Moffitt, or the Moffitt License, effective as of June 28, 2014, under which we received a world-wide license to Moffitt's rights to patent-pending technologies related to methods for improving TIL for adoptive cell therapy. Unless earlier terminated, the term of the license extends until the earlier of the expiration of the last issued patent related to the licensed technology or 20 years after the effective date of the license agreement.

Pursuant to the Moffitt License, we paid an upfront licensing fee in the amount of \$0.1 million. A patent issuance fee will also be payable under the Moffitt License, upon the issuance of the first U.S. patent covering the subject technology. In addition, we agreed to pay milestone license fees upon completion of specified milestones, customary royalties based on a specified percentage of net sales (which percentage is in the low single digits) and sublicensing payments, as applicable, and annual minimum royalties beginning with the first sale of products based on the licensed technologies, which minimum royalties will be credited against the percentage royalty payments otherwise payable in that year. We will also be responsible for all costs associated with the preparation, filing, maintenance and prosecution of the patent applications and patents covered by the Moffitt License related to the treatment of any cancers in the United States, Europe and Japan and in other countries we may designate in agreement with Moffitt.

PolyBioCept and Karolinska University Hospital

PolyBioCept Exclusive and Co-Exclusive License Agreement

In September 2016, we entered into an Exclusive and Co-Exclusive License Agreement, or the PolyBioCept Agreement, with PolyBioCept. PolyBioCept has filed two patent applications with claims related to a cytokine cocktail for use in expansion of lymphocytes, one of which has been abandoned. Under the PolyBioCept Agreement, we received the exclusive right and license to PolyBioCept's intellectual property to develop, manufacture, market and genetically engineer TIL produced by expansion, selection and enrichment using a proprietary cytokine cocktail. We also received a co-exclusive license (with PolyBioCept) to develop, manufacture and market genetically engineered TIL under the same intellectual property. The licenses are for the use in all cancers and are worldwide in scope, with the exception that the uses in melanoma are not included for certain countries of the former Soviet Union.

We paid PolyBioCept a total of \$2.5 million as an upfront exclusive license payment. We will also have to make additional milestone payments to PolyBioCept under the PolyBioCept Agreement if, and when, (i) certain product development milestones are achieved, (ii) certain regulatory approvals have been obtained from the FDA and/or the European Medicines Agency, and (iii) certain product sales targets are achieved. The milestone payments will be payable both in cash (U.S. dollars) and in shares of our common stock. If all the foregoing product development, regulatory approval and sales milestone payments are met, we will have to pay PolyBioCept an additional \$8.7 million and will have to issue to PolyBioCept a total 2,219,376 shares of unregistered common stock. In addition to these potential payments, we reimbursed PolyBioCept \$0.2 million in expenses related to the transfer of know-how and paid PolyBioCept \$0.1 million as a clinical trials management fee. We also agreed to separately engage PolyBioCept as a consultant to provide certain product development and research related services in a one-year agreement for up to \$0.2 million, subject to the consent of the Karolinska Institute to the services to be performed by its employees thereunder. Such consent was not granted, so this one-year services agreement was not entered into with PolyBioCept. The PolyBioCept Agreement has an initial term of 30 years and may be extended for additional five-year periods. We recognized \$0.2 million in costs associated with this agreement in the year ended December 31, 2017, while we recognized \$2.7 million in connection with this agreement in the year ended December 31, 2016, as research and development expense. The \$2.5 million upfront exclusive license payment was included in the \$2.7 million expensed during 2016.

Karolinska University Hospital and Karolinska Institute Agreements

In connection with the execution of the PolyBioCept Agreement, we also (i) entered into a clinical trials agreement with the Karolinska University Hospital to conduct clinical trials in glioblastoma and pancreatic cancer at the Karolinska University Hospital, and (ii) agreed to enter into a sponsored research agreement with the Karolinska Institute for the research of the cytokine cocktail in additional indications. We agreed to enter into the sponsored research agreement within 90 days after the date of the PolyBioCept Agreement, which date has been extended by amendments to the PolyBioCept Agreement. To date we have not executed this sponsored research agreement. Failure to enter into the sponsored research agreement or further amend the PolyBioCept Agreement will give PolyBioCept the right to terminate the PolyBioCept Agreement (and we shall be entitled to repayment of \$2.2 million in payments previously made). We will pay the Karolinska Institute an additional \$2.6 million in connection with these other related agreements. In the year ended December 31, 2016, we paid Karolinska University Hospital \$1.6 million to conduct these clinical trials. The \$1.6 million payment was classified as prepaid expense and is being expensed in accordance with our research and development expense accounting policy (see Note 1 in the Notes to Financial Statements in Part IV of this Annual Report on Form 10-K). Accordingly, we recognized \$0.3 million, and \$0.1 million in connection with this agreement as research and development expense in the years ended December 31, 2017 and 2016, respectively.

M.D. Anderson Cancer Center

Strategic Alliance Agreement

In April 2017, we entered into the SAA with M.D. Anderson under which we and M.D. Anderson agreed to conduct clinical and preclinical research studies. Per the terms of the SAA, we agreed to provide total funding not to exceed approximately \$14.2 million for the performance of the multi-year studies under the SAA. In return, we will acquire all rights to inventions resulting from the studies and have been granted a non-exclusive, sub-licensable, royalty-free, and perpetual license to specified background intellectual property of M.D. Anderson reasonably necessary to exploit, including the commercialization of, any invention. We have also been granted certain rights in clinical data generated by M.D. Anderson outside of the clinical trials to be performed under the SAA. The SAA's term shall continue in effect until the later of the fourth anniversary of the SAA or the completion or termination of the research and receipt of all deliverables due to us from M.D. Anderson thereunder. In the year ended December 31, 2017, we paid \$1.4 million under the SAA which amount has been classified as a long-term asset and will be amortized to research and development expenses in accordance with our research and development accounting policy, based on enrollment and other factors. There were no costs recognized in association with the SAA with M.D. Anderson in the year ended December 31, 2017.

The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute

In September 2017, we entered into a preclinical research collaboration with OSUCCC – James focused on TIL, MIL and peripheral blood-associated lymphocyte technologies. The collaboration will initially focus on hematologic malignancies in areas of poor prognostic cancers with high unmet medical need, which include AML and CLL. There were no costs recognized in association with this preclinical research collaboration in the year ended December 31, 2017.

MedImmune

In December 2015, we entered into a collaboration agreement to conduct clinical and preclinical research in immuno-oncology with MedImmune, or the MedImmune Agreement. Under the terms of the MedImmune Agreement, we will fund and conduct at least one clinical trial combining MedImmune's PD-L1 inhibitor, durvalumab, with TIL for the treatment of patients. MedImmune will supply durvalumab for the clinical trials. The purpose of the trials is to establish a potential dosing regimen for this combination therapy and assess its safety and efficacy. In December 2017, we announced that we would conduct a trial of TIL therapy in combination with durvalumab in non-small cell lung cancer. The trial will enroll patients with Stage III or IV NSCLC who are PD-1 and PD-L1 naïve. This trial is expected to start enrolling patients in 2018.

Competition

The biotechnology and pharmaceutical industries put significant resources in developing novel and proprietary therapies for the treatment of cancer. We compete with multiple entities who have developed and are developing immuno-oncology therapies, including large and specialty pharmaceutical and biotechnology companies, academic research institutions and governmental agencies and public and private research institutions, as well as companies developing novel targeted therapies for cancer. Universities and public and private research institutions in the U.S. and Europe are also potential competitors. For example, a Phase 3 study comparing TIL to standard ipilimumab in patients with metastatic melanoma is currently being conducted in Europe by the Netherlands Cancer Institute, the Copenhagen County Herlev University Hospital, and the University of Manchester. While these universities and public and private research institutions primarily have educational objectives, they may develop proprietary technologies that lead to other FDA-approved therapies or that secure patent protection. We anticipate that we will face possibly increasing competition as new drugs and therapies enter the market and advanced technologies become available.

Due to their promising clinical therapeutic effect in clinical exploratory trials, we anticipate substantial direct competition from other organizations developing advanced T-cell therapies. In particular, we expect to compete with other new therapies for our lead indications, such as melanoma, developed by companies such as Bristol-Myers Squibb, Merck, Nektar Therapeutics, Incyte, and others. We also may compete with therapies based on genetically engineered T cells rendered reactive against tumor-associated antigens prior to their administration to patients. Genetically engineered T cells are being pursued by several companies, including Adaptimmune, Celgene (in collaboration with bluebird bio as well as through Celgene's subsidiary Juno Therapeutics), Gilead Sciences, Novartis and others. To date, these technologies have been applicable to hematologic malignancies, but it is conceivable that such genetic modification may be applied for solid tumor indications and create competition with us.

Competition for late stage melanoma patients may come, if approved, from several compounds currently under development. NKTR-214, a pegylated version of IL-2, a CD122 agonist, under development by Nektar Therapeutics, in combination with nivolumab has reported 7 out of 11 stage 4 treatment naïve melanoma patients reported a partial or complete response. NKTR-214 activates cancer-fighting T cells and natural killer cells directly in the tumor, and it boosts PD-1 expression. Several companies are targeting Indoleamine 2,3-dioxygenase (known as IDO) a protein that suppresses the immune system that cancer cells sometimes hijack. NewLink Genetics reported results from a 60-person phase 2 study evaluating indoximod in combination with pembrolizumab showing 52% of patients had either a complete response or partial response. Incyte Corporation has also reported results from its IDO inhibitor, epacadostat in combination with pembrolizumab showing a 58% overall response rate in advanced melanoma patients.

While other types of cancer immunotherapies may potentially be used in combination with TIL, such as checkpoint inhibitors, to enhance efficacy, we also expect substantial direct competition from other types of immunotherapies. We face competition from immunotherapy treatments offered by companies such as Amgen, AstraZeneca, Bristol-Myers Squibb, Merck, and Roche. Immunotherapy is also being pursued by several biotechnology companies as well as by large-cap pharmaceutical companies. We cannot predict whether other types of immunotherapies may be enhanced and show greater efficacy. As a result, we may have direct and substantial competition from such immunotherapies in the future.

Many potential competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do. Accordingly, our competitors may be more successful than us in obtaining approval for treatments and achieving widespread market acceptance and may render our treatments obsolete or non-competitive. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical study sites and patient registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same. We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect.

We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While 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.

Government Regulations

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

Biologic products are regulated by the FDA under a combination of the Federal Food, Drug, and Cosmetic Act, or FFDC, and Public Health Services Act, or PHSA, and the FDA's implementing regulations. Failure to comply with regulatory requirements may result in significant regulatory actions. Such actions may include refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, imposition of a clinical hold or termination of clinical trials, warning letters, untitled letters, cyber letters, modification of promotional materials or labeling, provision of corrective information, imposition of post-market requirements including the need for additional testing, imposition of distribution or other restrictions under Risk Evaluation and Mitigation Strategies, or REMS, product recalls, product seizures or detentions, refusal to allow imports or exports, total or partial suspension of production or distribution, FDA debarment, injunctions, fines, consent decrees, corporate integrity agreements, debarment from receiving government contracts and new orders under existing contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement, or civil or criminal penalties, including fines and imprisonment, and adverse publicity, among other adverse consequences.

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

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's current Good Laboratory Practices, or GLP, regulation, as well as manufacturing development and formulation studies;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent Institutional Review Board, or IRB, or ethics committee at each clinical site centrally before the trial is begun;
- performance of adequate and well-controlled human clinical trials to establish the safety, and efficacy of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA, after completion of pivotal clinical trial(s);
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with current Good Manufacturing Practices, or cGMP, and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical sites to assess compliance with current Good Clinical Practices, or cGCPs; and
- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States, which must be updated periodically when changes are made.

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. Prior to beginning the first clinical trial with a new product candidate, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during trials due to safety concerns or non-compliance. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Human immunotherapy products are a new category of therapeutics. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the trial period, the number of patients the FDA will require to be enrolled in the trials in order to establish the safety, efficacy, purity and potency of immunotherapy products, or that the data generated in these trials will be acceptable to the FDA to support marketing approval.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with cGCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated, and a statistical analysis plan. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Investigators must also provide certain information to the clinical trial sponsors to allow the sponsors to make certain financial disclosures to the FDA.

Furthermore, an independent IRB for each site proposing to conduct the clinical trial or centrally must review and approve the plan for any clinical trial, its informed consent form and any subject communications, before the clinical trial begins at that site, and upon amendment of the trial, and must monitor the study until completed. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and are reasonable in relation to anticipated benefits and whether the planned human subject protections are adequate. Informed consent must be received from each study subject prior to participation in a clinical study. Progress reports detailing the results of the clinical trials must also be submitted at least annually to the FDA and the IRB and more frequently if serious adverse events or other significant safety information is found.

Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk, that the trial is not being conducted in accordance with regulatory or IRB requirements, or that the trial is unlikely to meet its stated objectives. Sponsors may also discontinue studies or development programs for many reasons, including changing business objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, or DSMB, which provides recommendations and assessments for whether or not a study should move forward at designated check points based on access to certain data from the study. Following a review by a DSMB, the study may be halted if there is an unacceptable safety risk for subjects or on other grounds, such as failure to demonstrate efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries. For instance, we are required to register certain clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in enforcement actions and adverse publicity.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1 - The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2 - The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3 - The investigational product is administered to an expanded patient population in adequate and well-controlled studies to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval. Typically, two Phase 3 studies are required by the FDA for product approval.
- Phase 4 - In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA.

Additional types of data may also help to support a BLA, such as real-world evidence and patient experience data. Phase 1, Phase 2 and Phase 3, and Phase 4 testing, if applicable, may not be completed successfully within a specified period, if at all, and there can be no assurance that the data collected will support FDA approval or licensure of the product. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life and manufacturing processes must be validated.

The manufacture of investigational biologics for the conduct of human clinical trials is subject to cGMP requirements. Investigational biologics and active ingredients imported into the United States are also subject to regulation by the FDA relating to their labeling and distribution. Further, the export of investigational products outside of the United States is subject to regulatory requirements of the importing country as well as U.S. export requirements under the FFDCa. Additional United States and foreign laws and regulations may also be applicable to the handling, import, export, and transportation of biological materials, including tissue samples.

During the development of a new therapeutic, a sponsor may be able to request a Special Protocol Assessment, or SPA, the purpose of which is to reach an agreement with the FDA on the Phase 3 clinical trial protocol design and analysis that will form the primary basis of product approval and an efficacy claim, as well as preclinical carcinogenicity trials and stability studies. An SPA may only be modified with the agreement of the FDA and the trial sponsor, or if the director of the FDA reviewing division determines that a substantial scientific issue essential to determining the safety or efficacy of the product was identified after the testing began. An SPA is intended to provide assurance that, in the case of clinical trials, if the agreed upon clinical trial protocol is followed, the clinical trial endpoints are achieved, and there is a favorable risk-benefit profile, the data may serve as the primary basis for an efficacy claim in support of a BLA. However, SPA agreements are not a guarantee of approval of a product candidate or any permissible claims about the product candidate. In particular, SPAs are not binding on the FDA if, among other reasons, previously unrecognized public health concerns arise during the performance of the clinical trial, other new scientific concerns regarding the product candidate's safety or efficacy arise, or if the sponsoring company fails to comply with the agreed upon clinical trial protocol.

In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA for a new active ingredient, indication, dosage form, dosage regimen, or route of administration, must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Also, under the FDA Reauthorization Act of 2017, beginning in 2020, sponsors submitting applications for product candidates intended for the treatment of adult cancer which are directed at molecular targets that the FDA determines to be substantially relevant to the growth or progression of pediatric cancer must submit, with the application, reports from molecularly targeted pediatric cancer investigations designed to yield clinically meaningful pediatric study data, using appropriate formulations, to inform potential pediatric labeling. 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. Orphan products are also exempt from PREA requirements.

The FDA also may require submission of REMS, to ensure that the benefits of the biologic outweigh the risks. The REMS plan could include medication guides, physician communication plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools. An assessment of the REMS must also be conducted at set intervals. Following product approval, a REMS may also be required by the FDA if new safety information is discovered and the FDA determines that a REMS is necessary to ensure that the benefits of the biologic outweigh the risks.

BLA Submission and Review by the FDA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by investigators. The submission of a BLA requires payment of a substantial User Fee to the FDA, and the sponsor of an approved BLA is also subject to annual program fees. These fees are typically increased annually. A waiver of user fees may be obtained under certain limited circumstances.

Once a BLA has been submitted, the FDA has sixty days to determine whether it will accept the application for filing. The FDA accepts applications for filing if it determines that the application is substantially complete to permit a substantive review. The FDA may request additional information rather than accept a 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's goal is to review the application within ten months after it accepts the application for filing, or, if the application relates to a serious or life-threatening indication and, if approved, the product would provide a significant improvement in safety and efficacy, six months after the FDA accepts the application for filing, which is referred to as priority review. The review process is often significantly extended if the FDA requests additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency.

The FDA may convene an advisory committee to provide clinical insight on application review questions. Before approving a novel biologic, the FDA must either refer that biologic to an external advisory committee or provide in an action letter, a summary of the reasons why the FDA did not refer the product candidate to an advisory committee. An advisory committee is typically a panel that includes clinicians and other experts, which review, evaluate, and make 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 a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP.

If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing, clinical studies, application modifications, or information in a complete response letter, or CRL. A CRL indicates that the review cycle for the application is complete and that the application is not ready for approval. If a CRL is issued, the applicant may either: resubmit the BLA, addressing all the deficiencies identified in the letter; withdraw the application; or request an opportunity for a hearing. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than an applicant interprets the same data.

If the FDA finds that a BLA is approvable, the FDA may issue an approval letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. However, even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings, or precautions be included in the product labeling, including a boxed warning, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a product's safety and efficacy 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 under a REMS which can materially affect the potential market and profitability of the product. The FDA may also not approve label statements that are necessary for successful commercialization and marketing.

If compliance with the pre- and post-marketing regulatory standards are not maintained or if problems occur after the product reaches the marketplace, the FDA may also withdraw the product approval. Further, should new safety information arise, additional testing, product labeling, or FDA notification may be required.

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

Under the accelerated approval program, the FDA may approve a BLA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. To qualify for accelerated approval, the product must be intended to treat a serious condition and must generally provide a meaningful advantage over available therapies. Post-marketing studies or completion of ongoing studies after marketing approval are required to verify the biologic's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. If this trial is not conducted, if it fails to verify the benefit, if other evidence demonstrates that the product is not safe, pure or potent, or if the applicant disseminates false or misleading promotional material, the FDA may withdraw approval of the application on an expedited basis. Sponsors of accelerated approval products must further submit promotional materials to the FDA before dissemination.

In addition, the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted and signed into law in 2012, established the new breakthrough therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Sponsors may request the FDA to designate a breakthrough therapy at the time of or any time after the submission of an IND, but ideally before an end-of-Phase 2 meeting with the FDA. If the FDA designates a breakthrough therapy, it may take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and considering alternative clinical trial designs when scientifically appropriate, which may result in smaller trials or more efficient trials that require less time to complete and may minimize the number of patients exposed to a potentially less efficacious treatment. Breakthrough designation also allows the sponsor to file sections of the BLA for review on a rolling basis.

Recently, through the 21st Century Cures Act, or Cures Act, Congress also established another expedited program, called a Regenerative Medicine Advanced Therapy, or RMAT, designation. The Cures Act directs the FDA to facilitate an efficient development program for and expedite review of RMATs. To qualify for this program, the product must be a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or a combination of such products, and not a product solely regulated as a human cell and tissue product. The product must be intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, and preliminary clinical evidence must indicate that the product has the potential to address an unmet need for such disease or condition. Advantages of the RMAT designation include all the benefits of the Fast Track and breakthrough therapy designation programs, including early interactions with the FDA. These early interactions may be used to discuss potential surrogate or intermediate endpoints to support accelerated approval.

In August 2017, we announced that the FDA had granted Fast Track designation for LN-144, for advanced metastatic melanoma. The Fast Track designation does not change the standards for approval but may expedite the development or approval process.

Orphan Drugs

During 2015, we received an orphan drug designation for LN-144 in the United States to treat malignant melanoma stages IIB-IV. We plan to seek orphan drug designation for some or all our other product candidates in specific orphan indications in which there is a medically plausible basis for the use of such products.

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

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic, as sameness is defined in FDA's regulations, for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research, opportunities for certain research grant funding, and a waiver of the BLA application fees. The tax credit, however, was recently limited through Congress's tax reform efforts. Despite these benefits, the orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review or approval process.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. The FDA may also approve a product deemed to be the same as an approved orphan product for the same orphan indication, despite periods of exclusivity, if the new product is demonstrated to be clinically superior to the former product.

Market and Data Exclusivity and Biosimilars

While the FDA may eventually license products, as further described below, that are biosimilar to any of our product candidates that are approved, our products may receive periods of regulatory exclusivity, in addition to orphan drug exclusivity for those products with orphan drug designations, providing additional protection from certain forms of competition. For instance, our products may receive 12 years of reference product exclusivity that begins running at the time of first licensure. During this time, the FDA may not make an approval of a biosimilar product effective and may not accept a biosimilar application for four years from the date of licensure. However, certain changes and supplements to an approved BLA, and subsequent applications filed by the same sponsor, manufacturer, licensor, predecessor in interest, or other related entity do not qualify for the exclusivity period. The PHSa also includes provisions to protect reference products that have patent protection. The biosimilar product sponsor and reference product sponsor may, but are not required to, exchange certain patent and product information for the purpose of determining whether there should be a legal patent challenge. Based on the outcome of negotiations surrounding the exchanged information, the reference product sponsor may bring a patent infringement suit and injunction proceedings against the biosimilar product sponsor. The biosimilar applicant may also be able to bring an action for declaratory judgment concerning the patent.

The Biologics Price Competition and Innovation Act, or BPCIA, created an abbreviated approval pathway for biological products shown to be highly similar to or interchangeable with an FDA-licensed reference biological product. Accordingly, if we receive FDA licensure, we may face competition from biosimilar products. Biosimilarity sufficient to reference a prior FDA-approved product requires a high similarity to the reference product notwithstanding minor differences in clinically inactive components, and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Biosimilarity must be shown through analytical studies, animal studies, and at least one clinical trial, absent a waiver by the FDA. There must be no difference between the reference product and a biosimilar in conditions of use, route of administration, dosage form, and strength. A biosimilar product may be deemed interchangeable with a prior approved product if it meets the higher hurdle of demonstrating that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, 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.

Pediatric Exclusivity and Patent Term Extension

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

If approved, biologics may also be eligible for periods of U.S. patent term restoration. If granted, patent term restoration extends the patent life of a single unexpired patent that has not previously been extended, for a maximum of five years. The total patent life of the product with the extension also cannot exceed fourteen years from the product's approval date. Subject to the prior limitations, the period of the extension is calculated by adding half of the time from the effective date of an IND to the initial submission of a marketing application, and all the time between the submission of the marketing application and its approval. This period may also be reduced by any time that the applicant did not act with due diligence. Whether any of our product candidates will be eligible for patent term restoration is currently unknown. Even if any of our product candidates are found to be eligible for patent term protection, the applicable authorities may subsequently determine that we are not eligible for such restoration periods.

Post-Approval Requirements

Any products for which we receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product and deviations, annual reporting and monitoring and providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, certain electronic records and signatures, fulfilling post-marketing study and REMS commitments, and complying with FDA promotion and advertising requirements, which include, among other things, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved uses (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available products for off-label use, if they deem such use to be appropriate in their professional medical judgment, manufacturers may not market or promote such off-label uses.

In addition, quality control and manufacturing procedures must continue to conform to applicable manufacturing requirements after approval to ensure the long-term stability of the product. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved products are required to register their establishments with the FDA and certain state agencies that list their products, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including, among other things, withdrawal of approval, recall or withdrawal of the product from the market. In addition, changes to the manufacturing process are strictly regulated, and depending on the significance of the change, may require prior FDA approval or notification before being implemented. Other types of changes to the approved product, such as adding new indications and claims, are also subject to further FDA review and approval.

Moreover, the Drug Quality and Security Act, or DQSA, imposes obligations on manufacturers of biopharmaceutical products related to product tracking and tracing. As part of this legislation, manufacturers are required to provide certain information regarding the products to individuals and entities to which product ownership is transferred, label products with a product identifier, and keep certain records regarding the product. The transfer of information to subsequent product owners by manufacturers must be done electronically. Manufacturers must also verify that purchasers of the manufacturers' products are appropriately licensed. Further, under this legislation, manufacturers have product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products that would result in serious adverse health consequences of death to humans, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death. Similar requirements additionally are and will be imposed through this legislation on other companies within the biopharmaceutical product supply chain, distributors and dispensers. With regard to manufacturers, however, the FDA recently delayed its enforcement of the provisions of the law related to the use of product identifiers until November 2018.

As previously mentioned, the FDA may also require Phase 4 testing and surveillance to monitor the effects of an approved product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Additional Biologic Requirements

To help reduce the increased risk of the introduction of adventitious agents, the PHSA emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases in the United States and between states.

After a BLA is approved, the product may also be subject to official lot release as a condition of approval. As part of the manufacturing process, 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 by the FDA, the manufacturer submits samples of each lot of product to the FDA, together with a release protocol showing the results of all the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products before releasing the lots for distribution by the manufacturer.

In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products. After approval of biologics, manufacturers must address any safety issues that arise, are subject to recalls or a halt in manufacturing, and are subject to periodic inspection after approval.

Other Healthcare Laws and Compliance Requirements

Our sales, promotion, medical education and other activities following product approval will be subject to regulation by numerous regulatory and law enforcement authorities in the United States in addition to the FDA, including potentially the Federal Trade Commission, the Department of Justice, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services and state and local governments. Our promotional and scientific/educational programs must comply with the federal Anti-Kickback Statute, the Foreign Corrupt Practices Act, or FCPA, the False Claims Act, or FCA, the Veterans Health Care Act, physician payment transparency laws, privacy laws, security laws, and additional state laws similar to the foregoing.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs, in whole or in part. The term remuneration has been interpreted broadly to include anything of value. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Our practices may not in all cases meet all the criteria for protection under a statutory exception or regulatory safe harbor.

Additionally, the intent standard under the federal Anti-Kickback Statute was amended by the Patient Protection Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, which is collectively referred to as the Affordable Care Act, or ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

The civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal healthcare program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Additionally, the FCPA, and similar worldwide anti-bribery laws, generally prohibit companies and their intermediaries from making, offering or authorizing improper payments or other items of value, directly or indirectly, to foreign officials, political parties, or candidates for the purpose of obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts. We cannot assure you that our internal control policies and procedures will protect us from reckless or negligent acts committed by our employees, future distributors, partners, collaborators or agents. Violations of these laws, or allegations of such violations, could result in fines, penalties or prosecution and have a negative impact on our business, results of operations and reputation.

The FCA imposes liability on persons who, among other things, knowingly present or cause to be presented false or fraudulent claims for payment to, or approval by the federal government knowingly making or using, or causing to be made or used a false statement or record material to a claim to the federal government, or avoiding, decreasing or concealing an obligation to pay money to the federal government. The civil FCA has been or can be used to assert liability on the basis of kickbacks and other improper referrals, improperly reported government pricing metrics such as Best Price and Average Manufacturer Price, improper promotion of uses not expressly approved by the FDA in a drug's label, false statements associated with government grants, and allegations of misrepresentations with respect to services rendered, as well as claims for payment that are inaccurate or fraudulent, that are for services not provided as claimed, or for services that are not medically necessary. FCA claims may be based on noncompliance with regulatory requirements under an implied certification theory if material to the government's decision to buy or pay for a drug. Intent to deceive is not required to establish liability under the civil FCA. Civil FCA liability may also be imposed for Medicare or Medicaid overpayments caused by understated rebate amounts that are not refunded within 60 days of discovering the overpayment, even if the overpayment was not caused by a false or fraudulent act. Actions under the FCA may be brought by the government or as a qui tam action by a private individual in the name of the government. If the government intervenes in a qui tam action, and prevails, the qui tam plaintiff will share in the proceeds from damages and fines or settlement funds. If the government declines to intervene, the qui tam plaintiff may pursue the case alone. Violations of the FCA can result in significant monetary penalties and treble damages. The government may further prosecute conduct under the criminal FCA, which prohibits the making or presenting of a claim to the government knowing the claim to be false, fictitious or fraudulent. Unlike the civil FCA, conviction requires proof of intent to submit a false claim.

Payment or reimbursement of prescription drugs by Medicaid or Medicare requires manufacturers of the drugs to submit pricing information to the Centers for Medicare & Medicaid Services, or CMS. The Medicaid Drug Rebate statute requires manufacturers to calculate and report price points, which are used to determine Medicaid rebate payments shared between the states and the federal government and Medicaid payment rates for the drug. For drugs paid under Medicare Part B, manufacturers must also calculate and report their Average Sales Price or ASP, which is used to determine the Medicare Part B payment rate for the drug. Drugs that are approved under a Biologic License Application, or BLA, or an NDA, including 505(b)(2) drugs, are subject to an additional inflation penalty which can substantially increase rebate payments. In addition, for BLA and NDA drugs, the Veterans Health Care Act, or VHCA, requires manufacturers to calculate and report to the Veterans Administration, or VA, a different price called the Non-Federal Average Manufacturing Price, which is used to determine the maximum price that can be charged to certain federal agencies, referred to as the Federal Ceiling Price, or FCP. Like the Medicaid rebate amount, the FCP includes an inflation penalty. A Department of Defense regulation requires manufacturers to provide this discount on drugs dispensed by retail pharmacies when paid by the TRICARE Program. All these price reporting requirements create risk of submitting false information to the government, and potential FCA liability.

The VHCA also requires manufacturers of covered drugs participating in the Medicaid program to enter into Federal Supply Schedule contracts with the VA through which their covered drugs must be sold to certain federal agencies at FCP and to report pricing information. This necessitates compliance with applicable federal procurement laws and regulations and subjects us to contractual remedies as well as administrative, civil, and criminal sanctions. In addition, the VHCA requires manufacturers participating in Medicaid to agree to provide different mandatory discounts to certain Public Health Service grantees and other safety net hospitals and clinics.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, also created federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, a healthcare benefit program, regardless of whether the payor is public or private, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense, and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items, or services relating to healthcare matters. The ACA amended the intent requirement of certain of these criminal statutes under HIPAA so that a person or entity no longer needs to have actual knowledge of the statute, or the specific intent to violate it, to have committed a violation.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The ACA, among other things, imposed new reporting requirements on drug manufacturers for payments or other transfers of value made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians, other healthcare providers, and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of \$150,000 per year (or up to an aggregate of \$1 million per year for “knowing failures”), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Certain states also mandate implementation of commercial compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians and other healthcare professionals.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA’s privacy and security standards directly applicable to “business associates,” defined as a person or entity that performs certain functions or activities that involve the use or disclosure of protected health information in connection with providing a service for or on behalf of, or provide services to, a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney’s fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect.

To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Coverage and Reimbursement

Sales of pharmaceutical products depend significantly on the availability of third-party coverage and reimbursement. Third-party payors include Medicare, Medicaid, and other government programs at the federal and state level, managed care providers, private health insurers and other organizations. Third party payors decide which drugs they will pay for on behalf of their beneficiaries and establish reimbursement levels for health care. Although we currently believe that third-party payors will provide coverage and reimbursement for our product candidates, if approved, these third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare products. We may need to conduct expensive clinical studies to demonstrate the comparative cost-effectiveness of our products. The product candidates that we develop may not be considered cost-effective. It is time consuming and expensive for us to seek coverage and reimbursement from third-party payors. Moreover, a payor’s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved, especially for product candidates such as ours, which are used in the inpatient setting, usually resulting in no separate reimbursement for pharmaceuticals. Reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

Medicare is a federally-funded program managed by CMS through local contractors that administer coverage and reimbursement for certain healthcare items and services furnished to the elderly and disabled. Medicare Part A covers inpatient hospitalization and Medicare Part B covers outpatient medical services. Medicare coverage of drugs and biological products and payment rates to providers are established by federal law and regulations. Medicaid is an insurance program for certain categories of low income patients who are otherwise uninsured and is both federally and state funded and managed by each state. The federal government sets general guidelines for Medicaid and requires rebates on outpatient drugs and biological products, including those administered by physicians if the cost is billed separately. Each state creates specific regulations that govern its individual program, including supplemental rebate programs that prioritize coverage for drugs on the state Preferred Drug List. Government laws and regulations also establish price controls on prescription drugs purchased by government agencies that provide health care and certain federally funded hospital outpatient departments and clinics. In the United States, private health insurers and other third-party payors often provide reimbursement for products and services based on the level at which the government provides reimbursement through the Medicare or Medicaid programs for such products and services. These restrictions and limitations influence the purchase of healthcare services and products. In addition, government programs like Medicaid include substantial penalties for increasing commercial prices over the rate of inflation which can affect realization and return on investment.

In the United States, the European Union, and other potentially significant markets for our product candidates, government authorities and private third-party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which often has resulted in average selling prices lower than they would otherwise be. Manufacturers frequently must rebate a portion of the prescription price to the third-party payors as a condition of coverage, which can greatly reduce realization on the sale. Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy, and are developing increasingly sophisticated methods of controlling healthcare costs. They may limit coverage to specific drug products on an approved list, or formulary, which might not include all the FDA-approved drug products for a particular indication, or they may control costs, particularly for new expensive therapies, by requiring prior authorization or imposing other restrictions before covering certain products, or they may condition payment based on achieving performance metrics. Legislative proposals to reform healthcare or reduce costs under government programs may result in lower reimbursement for our product candidates or exclusion of our product candidates from coverage.

Achieving favorable CMS coverage and reimbursement is usually a significant gating issue for successful introduction of a new product, because Medicare and Medicaid can represent a sizeable share of the market and because private payors often rely on the lead of the governmental payors in rendering coverage and reimbursement determinations. Further, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the European Union will likely put additional pressure on product pricing, reimbursement, and utilization, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, competition within therapeutic classes, availability of generic equivalents, judicial decisions and governmental laws and regulations related to Medicare, Medicaid, and healthcare reform, pharmaceutical coverage and reimbursement policies, and pricing in general. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Sales of our product candidates will therefore depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, such as Medicare and Medicaid, private health insurers, and other third-party payors.

As a result of the above, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA 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. Adequate third-party reimbursement may not be available to ensure acceptance and use of our products and product candidates or enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development. Legislative and regulatory proposals to reform healthcare or reduce costs under government insurance programs may result in lower reimbursement for our products and product candidates or exclusion of our products and product candidates from coverage. The cost containment measures that healthcare payors and providers are instituting and any healthcare reform could significantly reduce our revenues from the sale of any approved product candidates. We cannot provide any assurances that we will be able to obtain and maintain third-party coverage or adequate reimbursement for our product candidates in whole or in part.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major federal and state legislative initiatives.

In addition, other legislative and regulatory changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013, which will remain in effect through 2025 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In 2017, CMS promulgated a rule reducing Medicare Part B reimbursement to hospitals for drugs purchased under the 340B program by 30%. Although hospital trade associations filed a lawsuit challenging the regulation, the final rule is now in effect. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our product candidates, if approved, and, accordingly, our financial operations.

Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

The cost of pharmaceuticals continues to generate substantial governmental and third-party payor interest and states have begun to take action to increase transparency in drug pricing through mandatory reporting requirements. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations, and additional legislative proposals. Our results of operations could be adversely affected by current and future healthcare reforms. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could have a material adverse effect on our ability to obtain adequate prices for our product candidates and operate profitably.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products to the extent we choose to develop or sell any products outside of the United States. The approval process varies from country to country and the time may be longer or shorter than that required to obtain FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

In the EU, member states require both regulatory clearances by the national competent authority and a favorable ethics committee opinion prior to the commencement of a clinical trial. Under the EU regulatory systems, marketing authorization applications may be submitted under either a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all EU member states. It is compulsory for medicines produced by certain biotechnological processes. Because our products are produced in that way, we would be subject to the centralized process. Under the centralized procedure, pharmaceutical companies submit a single marketing authorization application to the European Medicines Agency. Once granted by the European Commission, a centralized marketing authorization is valid in all EU member states, as well as the European Economic Area countries of Iceland, Liechtenstein and Norway. By law, a company can only start to market a medicine once it has received a marketing authorization.

Employees

As of December 31, 2017, we had 63 employees, 46 of whom were engaged in research and development activities and 17 of whom were engaged in business development, finance, or administrative support. None of our employees are subject to a collective bargaining agreement. We consider our relationship with our employees to be good. Our future performance depends significantly upon the continued service of our key scientific, technical and senior management personnel.

Available Information

We maintain a website at www.iovance.com and make available there, free of charge, our periodic reports filed with the Securities and Exchange Commission (SEC), as soon as is reasonably practicable after filing. The public may read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains a website at <http://www.sec.gov> that contains reports, proxy and information statements, and other information regarding issuers such as us that file electronically with the SEC.

Item 1A. Risk Factors

The risks described below may not be the only ones relating to our company. Additional risks that we currently believe are immaterial may also impair our business operations. Our business, financial conditions and future prospects and the trading price of our common stock could be harmed as a result of any of these risks. Investors should also refer to the other information contained or incorporated by reference in this Annual Report on Form 10-K, including our financial statements and related notes, and our other filings from time to time with the Securities and Exchange Commission.

Risks Related to Our Business

We have a history of operating losses; we expect to continue to incur losses and we may never be profitable.

We are a clinical-stage biotechnology company focused on the development and commercialization of novel cancer immunotherapy products designed to harness the power of a patient's own immune system to eradicate cancer cells. We do not have products approved for commercial sale and have not generated revenue from operations. As of December 31, 2017, we had an accumulated deficit of \$249.2 million. In addition, during the fiscal year ended December 31, 2017, we incurred a net loss of \$92.1 million. Since our inception we have not generated any revenues from operations. We do not expect to generate any meaningful product sales or royalty revenues for the foreseeable future. We expect to incur significant additional operating losses in the future as we expand our development and clinical trial activities in support of demonstrating the effectiveness of our products.

Our ability to achieve long-term profitability is dependent upon obtaining regulatory approvals for our products and successfully commercializing our products alone or with third parties. However, our operations may not be profitable even if any of our products under development are successfully developed and produced and thereafter commercialized.

We have limited experience in operating our current business, which makes it difficult to evaluate our business plan and our prospects.

We have only a limited operating history in our current line of business on which a decision to invest in our company can be based. The future of our company currently is dependent upon our ability to implement our business plan, as that business plan may be modified from time to time by our management. While we believe that we have a sound business plan and research and development strategy, we have only a limited operating history against which we can test our plans and assumptions, and investors therefore cannot evaluate the likelihood of our success.

We face the problems, expenses, difficulties, complications and delays normally associated with a small, biotechnology company, many of which are beyond our control. Accordingly, our prospects should be considered in light of the risks, expenses and difficulties frequently encountered in the establishment of a new business developing technologies in an industry that is characterized by a number of market entrants and intense competition. Because of our size and limited resources, we may not possess the ability to successfully overcome many of the risks and uncertainties frequently encountered by early stage companies involved in the rapidly evolving field of immunotherapy. If our research and development efforts are successful, we may also face the risks associated with the shift from development to commercialization of new products based on innovative technologies. There can be no assurance that we will be successful in developing our new business.

We are substantially dependent on the success of our product candidates and cannot guarantee that these product candidates will successfully complete development, receive regulatory approval, or be successfully commercialized.

We currently have no products approved for commercial distribution. We have invested a significant portion of our efforts and financial resources in the development of our current product candidates, LN-144 and LN-145 and expect that we will continue to invest heavily in our current product candidates, as well as in any future product candidates we may develop. Our business depends entirely on the successful development and commercialization of our product candidates, which may never occur. Our ability to generate revenues in the future is substantially dependent on our ability to develop, obtain regulatory approval for, and then successfully commercialize our product candidates. We currently generate no revenue from the sale of any products, and we may never be able to develop or commercialize a marketable product.

Our product candidates will require additional clinical and non-clinical development, regulatory approval, commercial manufacturing arrangements, establishment of a commercial organization, significant marketing efforts, and further investment before we generate any revenue from product sales. We cannot assure you that we will meet our timelines for our current or future clinical trials, which may be delayed or not completed for a number of reasons.

We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates or regulatory approval that will allow us to successfully commercialize our product candidates. If we do not receive FDA approval with the necessary conditions to allow successful commercialization, and then successfully commercialize our product candidates, we will not be able to generate revenue from those product candidates in the United States in the foreseeable future, or at all. Any significant delays in obtaining approval for and commercializing our product candidates will have a material adverse impact on our business and financial condition.

We have not previously submitted a Biologics License Application, or BLA to the FDA, or similar marketing application to comparable foreign authorities, for any product candidate, and we cannot be certain that our current or any future product candidates will be successful in clinical trials or receive regulatory approval.

Our product candidates are susceptible to the risks of failure inherent at any stage of product development, including the appearance of unexpected adverse events or failure to achieve primary endpoints in clinical trials. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials.

If approved for marketing by applicable regulatory authorities, our ability to generate revenues from our product candidates will depend on our ability to:

- create market demand for our product candidates through our own marketing and sales activities, and any other arrangements to promote these product candidates that we may otherwise establish;
- receive regulatory approval for claims that are necessary or desirable for successful marketing;
- hire, train, and deploy a sales force or contract with a third party for a sales force to commercialize product candidates in the United States;
- manufacture product candidates in sufficient quantities and at acceptable quality and manufacturing cost to meet commercial demand at launch and thereafter;
- establish and maintain agreements with wholesalers, distributors, and group purchasing organizations on commercially reasonable terms;
- create partnerships with, or offer licenses to, third parties to promote and sell product candidates in foreign markets where we receive marketing approval;
- maintain patent and trade secret protection and regulatory exclusivity for our product candidates;
- launch commercial sales of our product candidates, whether alone or in collaboration with others;
- achieve market acceptance of our product candidates by patients, the medical community, and third-party payors;
- achieve appropriate reimbursement for our product candidates;
- effectively compete with other therapies or competitors; and maintain a continued acceptable safety profile of our product candidates following launch.

We have limited experience as a company conducting clinical trials and face risks due to the need to rely on third parties.

We have limited experience conducting pre-clinical and clinical trials and have no experience as a company in filing and supporting the applications necessary to gain marketing approvals. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety, purity, and potency for that indication. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities and clinical trial sites by, applicable regulatory authorities. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval.

Prior to 2015, all the preclinical and clinical trials relating to our product candidates had been conducted by the NCI. We have recruited a team that has experience with clinical trials; however, we as a company have limited experience in conducting clinical trials. In part because of this lack of experience, we cannot be certain that our ongoing clinical trials will be completed on time, if at all, will progress according to our plans or expectations, or that our planned clinical trials will be initiated, progress according to our plans or expectations, or be completed on time, if they are completed at all.

Large-scale trials require significant financial and management resources, and reliance on third-party clinical investigators, CROs, CMOs, or consultants. Relying on third-party clinical investigators, CROs or CMOs may force us to encounter delays and challenges that are outside of our control.

We rely on third party CROs and clinical trial sites to conduct, supervise, and monitor our clinical trials for our product candidates. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct our clinical trials. While we have agreements governing their activities, we have limited influence over their actual performance and control only certain aspects of their activities. The failure of these third parties to successfully carry out their contractual duties or meet expected deadlines could substantially harm our business because we may be delayed in completing or unable to complete the clinical trials required to support future approval of our product candidates, or we may not obtain marketing approval for or commercialize our product candidates in a timely manner or at all. Moreover, these agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that could delay our product development activities and adversely affect our business.

Our reliance on these third parties for development activities will reduce our control over these activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards and our reliance on the CROs, clinical trial sites, and other third parties does not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial and for ensuring that our preclinical trials are conducted in accordance with GLPs, as appropriate. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with standards, commonly referred to as GCPs, 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. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, clinical investigators, and trial sites. If we, our CROs, clinical trial sites, or other third parties fail to comply with applicable GCPs or other regulatory requirements, we or they may be subject to enforcement or other legal actions, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations.

In addition, we will be required to report certain financial interests of our third-party investigators if these relationships exceed certain financial thresholds or meet other criteria. The FDA or comparable foreign regulatory authorities may question the integrity of the data from those clinical trials conducted by investigators that are determined to have conflicts of interest.

In addition, our clinical trials must be conducted with product candidates that were produced under cGMP regulations. Our or our contractors' failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register certain clinical trials and post the results of certain completed clinical trials on a government sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in enforcement actions and adverse publicity.

Our CROs, clinical trial sites, and other third parties may also have relationships with other entities, some of which may be our competitors, for whom they may also be conducting clinical trials or other therapeutic development activities that could harm our competitive position. In addition, these third parties are not our employees, and except for remedies available to us under our agreements with them, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, non-clinical, and preclinical programs. 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, if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements or for other reasons, our trials may be repeated, extended, delayed, or terminated and we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates, or we or they may be subject to regulatory enforcement actions. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. To the extent we are unable to successfully identify and manage the performance of third party service providers in the future, our business may be materially and adversely affected.

If any of our relationships with these third parties terminate, we may not be able to enter into arrangements or do so on commercially reasonable terms. Switching or adding additional contractors involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays could occur, which could compromise our ability to meet our desired development timelines. Though we carefully manage our relationships with our third-party service providers, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects or results of operations.

We also rely on other third parties to distribute our products for the clinical trials that we conduct. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or any additional product candidates or commercialization of our product candidates, if approved, producing additional losses and depriving us of potential product revenue.

We may encounter substantial delays in our clinical trials or may not be able to conduct our trials on the timelines we expect and we may be required to conduct additional clinical trials or modify current or future clinical trials based on feedback we receive from the FDA.

Clinical testing is expensive, time consuming, and subject to uncertainty. We cannot guarantee that any current or future clinical studies will be conducted as planned or completed on schedule, if at all, or that any of our product candidates will receive regulatory approval. We initiated clinical trials in patients with metastatic melanoma, cervical and head and neck cancers. We plan to initiate trials in new indications. Even as these trials progress, issues may arise that could require us to suspend or terminate such clinical trials. A failure of one or more clinical studies can occur at any stage of testing, and our future clinical studies may not be successful. Events that may prevent successful or timely initiation or completion of clinical development, or product approval include:

- inability to generate sufficient preclinical data to support the initiation of clinical studies;
- regulators or Institutional Review Boards, or IRBs may not authorize us or our investigators to commence a clinical trial, conduct a clinical trial at a prospective trial site, or amend trial protocols, or regulators or IRBs may require that we modify or amend our clinical trial protocols;
- delays in reaching a consensus with regulatory agencies on study design;
- the FDA or comparable foreign regulatory authorities may disagree with our intended indications, study design or our interpretation of data from preclinical studies and clinical trials or find that a product candidate's benefits do not outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may not accept data from studies with clinical trial sites in foreign countries;
- the FDA may not allow us to use the clinical trial data from a research institution to support an IND if we cannot demonstrate the comparability of our product candidates with the product candidate used by the relevant research institution in its clinical studies;
- delays in or failure to reach an agreement on acceptable terms with prospective CROs and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical study sites;
- delays in obtaining required IRB approval at each clinical study site;
- imposition of a temporary or permanent clinical hold, suspensions or terminations by regulatory agencies, IRBs, or us for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects, or other unexpected characteristics of the product candidate, or due to findings of undesirable effects caused by a chemically or mechanistically similar therapeutic or therapeutic candidate;
- delays in recruiting suitable patients to participate in our clinical studies;
- we may have delays in adding new investigators or clinical trial sites, or we may experience a withdrawal of clinical trial sites;
- failure by our CROs, clinical trial sites, patients, or other third parties, or us to adhere to clinical study requirements, including regulatory, contractual or protocol requirements;
- failure to perform in accordance with the FDA's current good clinical practices, or cGCPs, requirements, or applicable regulatory guidelines in other countries;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate or enrollment in these clinical trials may be slower than we anticipate;
- patients that enroll in our studies may misrepresent their eligibility or may otherwise not comply with the clinical trial protocol, resulting in the need to drop such patients from the study or clinical trial, increase the needed enrollment size for the study or clinical trial or extend the study's or clinical trial's duration;
- patients dropping out of a study;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols to regulatory authorities and IRBs, and which may cause delays in our development programs, or changes to regulatory review times;
- there may be regulatory questions or disagreements regarding interpretations of data and results, or new information may emerge regarding our product candidates;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical studies of our product candidates being greater than we anticipate, or we may have insufficient funds for a clinical trial or to pay the substantial user fees required by the FDA upon the filing of a BLA;
- clinical studies of our product candidates producing negative or inconclusive results may fail to provide sufficient data and information to support product approval, or our studies may fail to reach the necessary level of statistical or clinical significance, which may result in our deciding, or regulators requiring us, to conduct additional clinical studies, or preclinical studies, or abandon product development programs;
- we may not be able to demonstrate that a product candidate provides an advantage over current standards of care or current or future competitive therapies in development;

- there may be changes to the therapeutics or their regulatory status which we are administering in combination with our product candidates;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or our manufacturing facilities for clinical and future commercial supplies;
- the FDA or comparable regulatory authorities may take longer than we anticipate to make a decision on our product candidates;
- transfer of our manufacturing processes to our contract manufacturers or other larger-scale facilities operated by a CMO and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical studies or the inability to do any of the foregoing, including as a result of any quality issues associated with the contract manufacturer.

We also may conduct clinical and preclinical research in collaboration with other biotechnology and biologics entities in which we combine our technologies with those of our collaborators. Such collaborations may be subject to additional delays because of the management of the trials, contract negotiations, the need to obtain agreement from multiple parties, and the necessity of obtaining additional approvals for therapeutics used in the combination trials. These combination therapies will require additional testing and clinical trials will require additional FDA regulatory approval and will increase our future cost of expenses.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to, or we may elect to, conduct additional studies to bridge our modified product candidates to earlier versions. These changes may require the FDA approval or notification, may not have their desired effect and the FDA may not accept data from prior versions of the product to support an application, delaying our clinical trials or programs or necessitating additional clinical or preclinical studies. By example, we changed our manufacturing process from Gen 1 to Gen 2 to decrease the production time and allow for the cryopreservation of the product. We may find that this update has unintended consequences that necessitates additional development and manufacturing work, additional clinical and preclinical studies, or that results in non-approval of a BLA.

Clinical study delays could shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Regulatory authorities have 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. The number and types of preclinical studies and clinical trials that will be required for regulatory approval also varies depending on the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. Approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. It is possible that neither of our product candidates nor any product candidates we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us or any future collaborators to commence product sales. Any delay in completing development, obtaining or failure to obtain required approvals could also materially adversely affect our ability or that of any of our collaborators to generate revenue from any such product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

It may take longer and cost more to complete our clinical trials than we project, or we may not be able to complete them at all.

For budgeting and planning purposes, we have projected the date for the commencement of future trials, and continuation and completion of our ongoing clinical trials. However, a number of factors, including scheduling conflicts with participating clinicians and clinical institutions, and difficulties in identifying and enrolling patients who meet trial eligibility criteria, may cause significant delays. We may not commence or complete clinical trials involving any of our products as projected or may not conduct them successfully.

We have opened enrollment of our company-sponsored, Phase 2 clinical trials to establish the feasibility of our product, and to assess its overall safety in patients with metastatic melanoma, cervical and head and neck cancers. However, we may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Accordingly, we cannot guarantee that the trial will progress as planned or as scheduled. Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our ongoing clinical trial and planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

We expect to rely on medical institutions, academic institutions or CROs to conduct, supervise or monitor some or all aspects of clinical trials involving our products. We will have less control over the timing and other aspects of these clinical trials than if we conducted them entirely on our own. If we fail to commence or complete, or experience delays in, any of our planned clinical trials, our stock price and our ability to conduct our business as currently planned could be harmed.

We currently anticipate that we will have to rely on our CMOs to manufacture our adoptive cell therapy products for clinical trials. If they fail to commence or complete, or experiences delays in, manufacturing our adoptive cell therapy products, our planned clinical trials will be delayed, which will adversely affect our stock price and our ability to conduct our business as currently planned.

Clinical trials are expensive, time-consuming and difficult to design and implement, and our clinical trial costs may be higher than for more conventional therapeutic technologies or drug products.

Clinical trials are expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. Because our product candidates are based on new cell therapy technologies and manufactured on a patient-by-patient basis, we expect that they will require extensive research and development and have substantial manufacturing costs. In addition, costs to treat patients with relapsed/refractory cancer and to treat potential side effects that may result from our product candidates can be significant. Some clinical trial sites may not bill, or obtain coverage from, Medicare, Medicaid, or other third-party payors for some or all of these costs for patients enrolled in our clinical trials, and we may be required by those trial sites to pay such costs. Accordingly, our clinical trial costs are likely to be significantly higher per patient than those of more conventional therapeutic technologies or drug products. In addition, our proposed personalized product candidates involve several complex and costly manufacturing and processing steps, the costs of which will be borne by us. Depending on the number of patients we ultimately enroll in our trials, and the number of trials we may need to conduct, our overall clinical trial costs may be higher than for more conventional treatments.

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

The clinical trials of our product candidates are, and the manufacturing and marketing of our products will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and market our product candidates. Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are both safe and effective for use in each target indication. Because our product candidates are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure, and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use. The risk/benefit profile required for product licensure will vary depending on these factors and may include not only the ability to show tumor shrinkage, but also adequate duration of response, a delay in the progression of the disease, and/or an improvement in survival. For example, response rates from the use of our product candidates may not be sufficient to obtain regulatory approval unless we can also show an adequate duration of response. Regulatory authorities may ultimately disagree with our chosen endpoints or may find that our studies or study results do not support product approval. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates with small patient populations may not be predictive of the results of later-stage clinical trials or the results once the applicable clinical trials are completed. Preliminary, single cohort, or top-line results from clinical studies may not be representative of the final study results. The results of studies in one set of patients or line of treatment may not be predictive of those obtained in another and the results in various human clinical trials reported in scientific and medical literature may not be indicative of results we obtain in our clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. Preclinical studies may also reveal unfavorable product candidate characteristics, including safety concerns.

We expect there may be greater variability in results for products processed and administered on a patient-by-patient basis, as anticipated for our product candidates, than for “off-the-shelf” products, like many other drugs. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. Many companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. Our current and future clinical trial results may not be successful. Moreover, should there be a flaw in a clinical trial, it may not become apparent until the clinical trial is well advanced. Further, because we currently plan to develop our product candidates for use with other oncology products, the design, implementation, and interpretation of the clinical trials necessary for marketing approval may be more complex than if we were developing our product candidates alone.

In addition, even if such trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates.

We have reported preliminary results for clinical trials of our product candidates, including TIL for the treatment of metastatic melanoma, cervical cancer, and head and neck cancers. These preliminary results, which include assessments of efficacy such as ORR, are subject to substantial risk of change due to small sample sizes, and may change as patients are evaluated or as additional patients are enrolled in these clinical trials. These outcomes may be unfavorable, deviate from our earlier reports, and/or delay or prevent regulatory approval or commercialization of our product candidates, including candidates for which we have reported preliminary efficacy results. In clinical studies where a staged expansion is expected, such as studies using a Simon's two stage design, these outcomes may result in the failure to meet an initial efficacy threshold for the first stage. Furthermore, other measures of efficacy for these clinical trials and product candidates may not be as favorable.

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

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

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the patient eligibility criteria defined in the protocol;
- the size of the study population required for analysis of the trial's primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the efforts to facilitate timely enrollment in clinical trials and the effectiveness of recruiting publicity;
- the patient referral practices of physicians;
- competing clinical trials for similar therapies or other new therapeutics not involving cell-based immunotherapy;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating;
- clinical investigators enrolling patients who do not meet the enrollment criteria, requiring the inclusion of additional patients in the clinical trial;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will not complete a clinical trial, return for post-treatment follow-up, or follow the required study procedures. For instance, patients, including patients in our control groups, may withdraw from the clinical trial if they are not experiencing improvement in their underlying disease or condition. Withdrawal of patients from our clinical trials may compromise the quality of our data.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Because the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitor's use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Moreover, because our product candidates represent a departure from more commonly used methods for cancer treatment, potential patients and their doctors may be inclined to use conventional therapies, such as chemotherapy and approved immunotherapies, rather than enroll patients in any future clinical trial. In addition, potential enrollees may opt to participate in alternate clinical trials because of the length of time between the time that their tumor is excised and the TIL is infused back into the patient.

Even if we are able to enroll a sufficient number of patients in our clinical trials, delays in patient enrollment or small population size may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

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

Results of our trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could cause us, IRBs, or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. Even if we were to receive product approval, such approval could be contingent on inclusion of unfavorable information in our product labeling, such as limitations on the indicated uses for which the products may be marketed or distributed, a label with significant safety warnings, including boxed warnings, contraindications, and precautions, a label without statements necessary or desirable for successful commercialization, or requirements for costly post marketing testing and surveillance, or other requirements, including REMS, to monitor the safety or efficacy of the products, and in turn prevent us from commercializing and generating revenues from the sale of our current or future product candidates.

If unacceptable toxicities arise in the development of our product candidates, we, an IRB or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials, order our clinical trials to be placed on clinical hold, or deny approval of our product candidates for any or all targeted indications. The FDA or comparable foreign regulatory authorities may also require additional data, clinical, or pre-clinical studies should unacceptable toxicities arise. We may need to abandon development or limit development of that product candidate 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. Toxicities associated with our trials and products may also negatively impact our ability to conduct clinical trials using TIL therapy in larger patient populations, such as in patients that have not yet been treated with other therapies or have not yet progressed on other therapies.

Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete our trials or result in potential product liability claims. Such toxicities, which may arise from TIL therapy in general, including co-therapies, may include, for example, pyrexia, anaemia, neutrophil and platelet count decrease, febrile neutropenia, fatigue, chills, hyponatremia, and hypotension. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from personalized cell therapy are not normally encountered in the general patient population and by medical personnel. Any of these occurrences may harm our business, financial condition and prospects significantly.

The manufacture of our product candidates is complex, and we may encounter difficulties in production, particularly with respect to process development or scaling-out of our manufacturing capabilities. If we, or any of our third-party manufacturers encounter such difficulties, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

Our product candidates are biologics and the process of manufacturing our products is complex, highly-regulated and subject to multiple risks. The manufacture of our product candidates involves complex processes, including harvesting tumor fragments from patients, multiplying the T cells to obtain the desired dose, and ultimately infusing the T cells back into a patient. As a result of the complexities, the cost to manufacture biologics is generally higher than traditional small molecule chemical compounds, and the manufacturing process is less reliable and is more difficult to reproduce. Our manufacturing process will be susceptible to product loss or failure due to logistical issues associated with the collection of tumor cells, or starting material, from the patient, shipping such material to the manufacturing site, shipping the final product back to the patient, and infusing the patient with the product, manufacturing issues associated with the differences in patient starting tumors, interruptions in the manufacturing process, contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in cell growth, and variability in product characteristics. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. If for any reason we lose a patient's tumor, or later-developed product at any point in the process, or if any product does not meet the applicable specifications, the manufacturing process for that patient will need to be restarted and the resulting delay may adversely affect that patient's outcome. If microbial, viral, or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.

Because our product candidates are manufactured specifically for each individual patient, we will be required to maintain a chain of identity with respect to the patient's tumor as it moves from the patient to the manufacturing facility, through the manufacturing process, and back to the patient. Maintaining such a chain of identity is difficult and complex, and failure to do so could result in adverse patient outcomes, loss of product, or regulatory action including withdrawal of our products from the market. Further, as product candidates are developed through preclinical to late stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials or otherwise necessitate the conduct of additional studies.

Currently, our product candidates are manufactured using processes developed or modified by us or by our third-party research institution collaborators that we may not intend to use for more advanced clinical trials or commercialization. We have selected Gen 2 as the manufacturing process for product registration, and all ongoing and future company-sponsored clinical trials. Although we believe Gen 2 is a commercially viable process, there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, cost overruns, potential problems with process scale-out, process reproducibility, stability issues, lot consistency, and timely availability of raw materials. As a result of these challenges, we may experience delays in our clinical development and/or commercialization plans. We may ultimately be unable to reduce the cost of goods for our product candidates to levels that will allow for an attractive return on investment if and when those product candidates are commercialized.

Our current manufacturing strategy involves the use of CMOs. Currently our product candidates are manufactured by WuXi, PharmaCell, and Moffitt. Should we continue to use CMOs, we may not succeed in maintaining our relationships with our current CMOs or establishing relationships with additional or alternative CMOs. Our product candidates may compete with other products and product candidates for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that are both capable of manufacturing for us and willing to do so. If our CMOs should cease manufacturing for us, we would experience delays in obtaining sufficient quantities of our product candidates for clinical trials and, if approved, commercial supply. Further, our CMOs may breach, terminate, or not renew these agreements. If we were to need to find alternative manufacturing facilities it would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. The commercial terms of any new arrangement could be less favorable than our existing arrangements and the expenses relating to the transfer of necessary technology and processes could be significant.

Reliance on third-party manufacturers entails exposure to risks to which we would not be subject if we manufactured the product candidate ourselves, including:

- inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reduced day-to-day control over the manufacturing process for our product candidates as a result of using third-party manufacturers for all aspects of manufacturing activities;
- reduced control over the protection of our trade secrets and know-how from misappropriation or inadvertent disclosure;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that may be costly or damaging to us or result in delays in the development or commercialization of our product candidates; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

In the future, we may seek to establish our own manufacturing capabilities and infrastructure, including a manufacturing facility. We would expect that development of our own manufacturing facility would provide us with enhanced control of material supply for both clinical trials and the commercial market, enable the more rapid implementation of process changes, and allow for better long-term margins. However, we have no experience as a company in developing a manufacturing facility and may never be successful in developing our own manufacturing facility or capability. We may establish multiple manufacturing facilities as we expand our commercial footprint to multiple geographies, which may lead to regulatory delays or prove costly. Even if we are successful, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, labor shortages, natural disasters, power failures, and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

The manufacture of biopharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of therapeutics often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel, and compliance with strictly enforced federal, state, and foreign regulations.

Moreover, any problems or delays we or our CMOs experience in preparing for commercial scale manufacturing of a product candidate or component may result in a delay in FDA approval of the product candidate or may impair our ability to manufacture commercial quantities or such quantities at an acceptable cost, which could result in the delay, prevention, or impairment of clinical development and commercialization of our product candidates and could adversely affect our business. Furthermore, if we or our commercial manufacturers fail to deliver the required commercial quantities of our product candidates on a timely basis and at reasonable costs, we would likely be unable to meet demand for our products and we would lose potential revenues.

In addition, the manufacturing process and facilities for any products that we may develop is subject to FDA and foreign regulatory authority approval processes, and we or our CMOs will need to meet all applicable FDA and foreign regulatory authority requirements, including cGMPs, on an ongoing basis. The cGMP requirements include quality control, quality assurance, and the maintenance of records and documentation. The FDA and other regulatory authorities enforce these requirements through facility inspections. Manufacturing facilities must be approved by the FDA pursuant to inspections that will be conducted after we submit our marketing applications to the agency. Manufacturers are also subject to continuing FDA and other regulatory authority inspections following marketing approval. Further, we, in cooperation with our CMOs, must supply all necessary chemistry, manufacturing, and control documentation in support of a BLA on a timely basis.

Our, or our CMO's, manufacturing facilities may be unable to comply with our specifications, cGMPs, and with other FDA, state, and foreign regulatory requirements. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of product candidate that may not be detectable in final product testing. If we or our CMOs are unable to reliably produce products to specifications acceptable to the FDA or other regulatory authorities, or in accordance with the strict regulatory requirements, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CMOs will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Deviations from manufacturing requirements may further require remedial measures that may be costly and/or time-consuming for us or a third party to implement and may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

Even to the extent we use and continue to use CMOs, we are ultimately responsible for the manufacture of our products and product candidates. A failure to comply with these requirements may result in regulatory enforcement actions against our manufacturers or us, including fines and civil and criminal penalties, which could result in imprisonment, suspension or restrictions of production, suspension, injunctions, delay or denial of product approval or supplements to approved products, clinical holds or termination of clinical studies, warning or untitled letters, regulatory authority communications warning the public about safety issues with the biologic, refusal to permit the import or export of the products, product seizure, detention, or recall, operating restrictions, suits under the civil False Claims Act, corporate integrity agreements, consent decrees, or withdrawal of product approval.

Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and growth prospects.

Cell-based therapies rely on the availability of reagents, specialized equipment, and other specialty materials, which may not be available to us on acceptable terms or at all. For some of these reagents, equipment, and materials, we rely or may rely on sole source vendors or a limited number of vendors, which could impair our ability to manufacture and supply our products.

Manufacturing our product candidates will require many reagents, which are substances used in our manufacturing processes to bring about chemical or biological reactions, and other specialty materials and equipment, some of which are manufactured or supplied by small companies with limited resources and experience to support commercial biologics production. We currently depend on a limited number of vendors for certain materials and equipment used in the manufacture of our product candidates. Some of these suppliers may not have the capacity to support clinical trials and commercial products manufactured under cGMP by biopharmaceutical firms or may otherwise be ill-equipped to support our needs. We also do not have supply contracts with many of these suppliers and may not be able to obtain supply contracts with them on acceptable terms or at all. Accordingly, we may experience delays in receiving key materials and equipment to support clinical or commercial manufacturing.

For some of these reagents, equipment, and materials, we rely and may in the future rely on sole source vendors or a limited number of vendors. An inability to continue to source product from any of these suppliers, which could be due to a number of issues, including regulatory actions or requirements affecting the supplier, adverse financial or other strategic developments experienced by a supplier, labor disputes or shortages, unexpected demands, or quality issues, could adversely affect our ability to satisfy demand for our product candidates, which could adversely and materially affect our product sales and operating results or our ability to conduct clinical trials, either of which could significantly harm our business.

As we continue to develop and scale our manufacturing process, we expect that we will need to obtain rights to and supplies of certain materials and equipment to be used as part of that process. We may not be able to obtain rights to such materials on commercially reasonable terms, or at all, and if we are unable to alter our process in a commercially viable manner to avoid the use of such materials or find a suitable substitute, it would have a material adverse effect on our business. Even if we are able to alter our process so as to use other materials or equipment, such a change may lead to a delay in our clinical development and/or commercialization plans. If such a change occurs for product candidate that is already in clinical testing, the change may require us to perform both *ex vivo* comparability studies and to collect additional data from patients prior to undertaking more advanced clinical trials.

The deviations in our proposed new products from existing products may require us to perform additional testing, which will increase the cost, and extend the time for obtaining approval.

Our TIL based therapy is based on the adoptive cell therapy technology that we licensed from the NIH and that is presently in use as a physician-sponsored investigational therapy for the treatment of Stage IV metastatic melanoma in the United States at the NCI, M.D. Anderson Cancer Center, and Moffit. These current methods of treatment are very labor intensive and expensive, which has limited its widespread application. We have developed a new process, Gen 2, that we anticipate will enable more efficient manufacturing of TIL. We may have difficulty demonstrating that the products produced from our new processes are identical to the existing products. The FDA may require additional clinical testing before permitting a larger clinical trial with the new processes, and the product may not be as efficacious in the new clinical trials. Cellular products are not considered as well characterized products because there are hundreds of markers present on these cells, and even small changes in manufacturing processes could alter the cell types. It is unclear at this time which of those markers are critical for success of these cells to combat cancer, so our ability to predict the outcomes with newer manufacturing processes is limited. The changes that we have made to the historical manufacturing process may require additional testing, which may increase costs and timelines associated with these developments.

In addition to developing a TIL based therapy on existing ACT technology, we are currently evaluating the desirability of conducting clinical trials of our products in combination with other existing drugs. These combination therapies will require additional testing and clinical trials will require additional FDA regulatory approval and will increase our future cost of development.

We will be unable to commercialize our products if our trials are not successful.

Our research and development programs are at an early stage. We must demonstrate our products' safety and efficacy in humans through extensive clinical testing. We may experience numerous unforeseen events during, or as a result of, the testing process that could delay or prevent commercialization of our products, including but not limited to the following:

- safety and efficacy results in various human clinical trials reported in scientific and medical literature may not be indicative of results we obtain in our clinical trials;
- after reviewing test results, we or our collaborators may abandon projects that we might previously have believed to be promising;
- we, our collaborators or regulators, may suspend or terminate clinical trials if the participating subjects or patients are being exposed to unacceptable health risks;
- the effects our potential products have may not be the desired effects or may include undesirable side effects or other characteristics that preclude regulatory approval or limit their commercial use if approved;

- manufacturers may not meet the necessary standards for the production of the product candidates or may not be able to supply the product candidates in a sufficient quantity; and
- regulatory authorities may find that our clinical trial design or conduct does not meet the applicable approval requirements.

Clinical testing is very expensive, can take many years, and the outcome is uncertain. It can take as much as 12 months or more before we learn the results from any clinical trial using our adoptive cell therapy with TIL. The data collected from our clinical trials may not be sufficient to support approval by the FDA of our TIL-based product candidates for the treatment of solid tumors. The clinical trials for our products under development may not be completed on schedule and the FDA may not ultimately approve any of our product candidates for commercial sale. If we fail to adequately demonstrate the safety and efficacy of any product candidate under development, we may not receive regulatory approval for those products, which would prevent us from generating revenues or achieving profitability.

Our research and development efforts have been to a large extent dependent upon the CRADA.

Although we opened our own research and development laboratory in 2014, we are continuing to fully develop our research and development capabilities. In addition, we conduct a portion of our research and development under the CRADA with the NCI. Under the CRADA, the NCI currently engage in research and development related to the development of improved methods of large scale unmodified TIL generation for the treatment of patients with metastatic melanoma, bladder, lung, breast, and HPV-associated cancers. We are obligated to make annual payments of \$2.0 million under the CRADA. In addition, although the CRADA has a five-year term, either party to the CRADA has the right to terminate the CRADA upon 60 days' notice to the other party. As a result, no assurance can be given that the NCI will not terminate, or that we will renew, the CRADA that expires in August 2021 and that the CRADA will, therefore, remain in effect until we complete our desired research thereunder.

We have limited control over the nature or timing of the NCI's clinical trials and limited visibility into their day-to-day activities. The research we are funding constitutes only a small portion of the NCI's overall research. Other research being conducted by Dr. Rosenberg may at times receive higher priority than research on our programs. These factors could adversely affect the timing of our IND filings and our ability to conduct future planned clinical trials.

Under the CRADA, we have an option to negotiate commercialization licenses from the NIH to intellectual property relating to TIL-based product candidates developed as part of the CRADA research plan. However, we would have to negotiate with the NIH for such a license. There can be no assurance that we would be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. Further, to the extent we would like to negotiate a license to a patent filed before the CRADA was entered into, another party may object to the NIH granting us a license during a 30-day public notification period, and the NIH may decide not to grant us the license.

We collaborate with governmental, academic and corporate partners to improve and develop TIL therapies for new indications for use in combination with other therapies and to evaluate new TIL manufacturing methods, the results of which, because the manufacturing processes are not within our control, may be incorrect or unreliable.

In addition to our own research and process development efforts, we seek to collaborate with government, academic research institutions and corporate partners to improve TIL manufacturing and to develop TIL therapies for new indications. In 2017, we announced collaborations with Moffitt, M.D. Anderson and Ohio State University to evaluate several new solid tumor and hematologic indications for TIL therapy in clinical and preclinical studies as well as, in some cases, new TIL manufacturing approaches. In September 2016, we entered into a license agreement with PolyBioCept and a related clinical trial with Karolinska University Hospital to evaluate a new cytokine cocktail for TIL manufacturing and the treatment of patients with pancreatic cancer and glioblastoma. The results of these collaborations may be used to support our filing with the FDA of INDs to conduct more advanced clinical trials of our product candidates, or to otherwise analyze or make predictions or decisions with respect to our current or future product candidates. However, because the majority of our collaborations are conducted at outside laboratories and we do not have complete control over how the studies are conducted or the manufacturing methods used to manufacture TIL product, the results of such studies, which we may use as the basis for our conclusions, projections or decisions with respect to our current or future product candidates, may be incorrect or unreliable. Additionally, we may use third party data to analyze, reach conclusions or make predictions or decisions with respect to our product candidates that may be incomplete, inaccurate or otherwise unreliable.

We will need additional financing to fund our operations and complete the development and commercialization of our various product candidates, and if we are unable to obtain such financing, we may be unable to complete the development and commercialization of our product candidates. 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.

Our operations have consumed substantial amounts of cash since inception. From our inception to December 31, 2017, we have an accumulated deficit of \$249.2 million. In addition, our research and development and our operating costs have also been substantial and are expected to increase. We expect to continue to spend substantial amounts to continue the clinical development of our product candidates. As of December 31, 2017, we had \$145.4 million in cash and cash equivalents. In January 2018, we closed an underwritten public offering of our common stock. The net proceeds from the offering, after deducting the underwriting discounts and commissions and other estimated offering expenses payable by us, were \$161.7 million. Accordingly, we believe that our existing cash, cash equivalents and short-term investments will be sufficient to fund our operations for at least the next 24 months from the date this Annual Report on Form 10-K is issued. However, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may require additional capital for the further development and commercialization of our product candidates and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate. Moreover, our fixed expenses such as rent, minimum payments to our contract manufacturers, and other contractual commitments, including those for our research collaborations, are substantial and are expected to increase in the future.

We will need to obtain additional financing to fund our future operations, including completing the development and commercialization of our product candidates. Our future funding requirements will depend on many factors, including, but not limited to:

- Progress, timing, scope and costs of our clinical trials, including the ability to timely initiate clinical sites, enroll subjects and manufacture TIL for treatment for patients in our ongoing, planned and potential future clinical trials;
- Time and cost necessary to obtain regulatory approvals that may be required by regulatory authorities to execute clinical trials or commercialize our product;
- Our ability to successfully commercialize our product candidates, if approved;
- Our ability to have clinical and commercial product successfully manufactured consistent with FDA and European Medicines Agency, or EMA, regulations;
- Amount of sales and other revenues from product candidates that we may commercialize, if any, including the selling prices for such potential products and the availability of adequate third-party coverage and reimbursement for patients;
- Sales and marketing costs associated with commercializing our products, if approved, including the cost and timing of building our marketing and sales capabilities;
- Terms and timing of our current and any potential future collaborations, licensing or other arrangements that we have established or may establish;
- Cash requirements of any future acquisitions or the development of other product candidates;
- Costs of operating as a public company;
- Time and cost necessary to respond to technological, regulatory, political and market developments;
- Costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and
- Costs associated with any potential business or product acquisitions, strategic collaborations, licensing agreements or other arrangements that we may establish.

Until we can generate a sufficient amount of revenue, we may finance future cash needs through public or private equity offerings, license agreements, debt financings, collaborations, strategic alliances and marketing or distribution arrangements. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may be required to delay or reduce the scope of or eliminate one or more of our research or development programs or our commercialization efforts. Our current license and collaboration agreements may also be terminated if we are unable to meet the payment obligations under those agreements. As a result, we may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time.

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

Subject to various spending levels approved by the Board of Directors, our management will have broad discretion in the use of the net proceeds from our capital raises, including our January 2018 and September 2017 public offerings, and may not use them effectively.

Our management will have discretion in the application of the net proceeds from our capital raises, including our January 2018 and September 2017 public offerings, and our stockholders will not have the opportunity as part of their investment decision to assess whether the net proceeds from those capital raises are being used appropriately. You may not agree with our decisions, and our use of the proceeds from our capital raises may not yield any return to stockholders. Because of the number and variability of factors that will determine our use of the net proceeds from our capital raises, including our January 2018 and September 2017 public offerings, their ultimate use may vary substantially from their currently intended use. Our failure to apply the net proceeds of our capital raises, including our January 2018 and September 2017 public offerings, effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of those net proceeds. Stockholders will not have the opportunity to influence our decisions on how to use our net proceeds from capital raises, including our January 2018 and September 2017 public offerings. Pending their use, we may invest the net proceeds from our capital raises, including our January 2018 and September 2017 public offerings, in short-term, investment-grade, interest-bearing instruments and U.S. government securities. These temporary investments are not likely to yield a significant return.

The use of our net operating loss carryforwards and research tax credits may be limited.

Our net operating loss carryforwards and any future research and development tax credits may expire and not be used. As of December 31, 2017, we had U.S. federal net operating loss carryforwards of approximately \$143.3 million. Our net operating loss carryforwards arising in taxable years ending on or prior to December 31, 2017 will begin expiring in 2027 if we have not used them prior to that time. Net operating loss carryforwards arising in taxable years ending after December 31, 2017 are no longer subject to expiration under the Internal Revenue Code of 1986, as amended, or the Code. Additionally, our ability to use any net operating loss and credit carryforwards to offset taxable income or tax, respectively, in the future will be limited under Sections 382 and 383 of the Code, respectively, if we have a cumulative change in ownership of more than 50% within a three-year period.

We have performed an IRC Section 382 analysis as of December 31, 2017. Per the analysis, the May 2013 recapitalization, private placements in 2014 and 2016 may have already triggered such an ownership change. As a result, the federal and state carryforwards associated with the net operating loss and credit deferred tax assets were reduced by the amount of tax attributes estimated to expire during their respective carryforward periods. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo further ownership changes in the future. Any such annual limitation may significantly reduce the utilization of the net operating loss carryforwards and research tax credits before they expire. In addition, certain states have suspended use of net operating loss carryforwards for certain taxable years, and other states are considering similar measures. As a result, we may incur higher state income tax expense in the future. Depending on our future tax position, continued suspension of our ability to use net operating loss carryforwards in states in which we are subject to income tax could have an adverse impact on our results of operations and financial condition.

Recently enacted tax reform legislation in the U.S. could adversely affect our business and financial condition.

On December 22, 2017, the Tax Cuts and Jobs Act of 2017 (“Tax Act”) was signed into law, making significant changes to the Internal Revenue Code. Changes under the Tax Act include, but are not limited to, a corporate tax rate decrease from 35% to 21% effective for tax years beginning after December 31, 2017, a one-time transition tax on the mandatory deemed repatriation of cumulative foreign earnings, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of orphan drugs). The overall impact of the new federal tax law is uncertain, and our business and financial condition could be adversely affected. For example, because of the tax rate decrease, our deferred tax assets and our corresponding valuation allowance against these deferred tax assets have been reduced and may continue to be adversely impacted. In addition, it is uncertain if and to what extent various states will conform to Tax Act and what effect that legal challenges will have on the Tax Act, including litigation in the U.S. and international challenges brought at organizations such as the World Trade Organization. The impact of the Tax Act on holders of our common stock is also uncertain and could be adverse. Investors should consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

We are subject to extensive regulation, which can be costly, time consuming and can subject us to unanticipated delays; even if we obtain regulatory approval for some of our products, those products may still face regulatory difficulties.

Our potential products, cell processing and manufacturing activities, are subject to comprehensive regulation by the FDA in the United States and by comparable authorities in other countries. The process of obtaining FDA and other required regulatory approvals, including foreign approvals, is expensive and often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved. In addition, regulatory agencies may lack experience with our technologies and products, which may lengthen the regulatory review process, increase our development costs and delay or prevent their commercialization.

No adoptive cell therapy using TIL has been approved for marketing in the FDA. Consequently, there is no precedent for the successful commercialization of products based on our technologies. In addition, we have had only limited experience in filing and pursuing applications necessary to gain regulatory approvals, which may impede our ability to obtain timely FDA approvals, if at all. We have not yet sought FDA approval for any adoptive cell therapy product. We will not be able to commercialize any of our potential products until we obtain FDA approval, and so any delay in obtaining, or inability to obtain, FDA approval would harm our business.

If we violate regulatory requirements at any stage, whether before or after marketing approval is obtained, we may face a number of regulatory consequences, including refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, imposition of a clinical hold or termination of clinical trials, warning letters, untitled letters, cyber letters, modification of promotional materials or labeling, provision of corrective information, imposition of post-market requirements including the need for additional testing, imposition of distribution or other restrictions under a REMS, product recalls, product seizures or detentions, refusal to allow imports or exports, total or partial suspension of production or distribution, FDA debarment, injunctions, fines, consent decrees, corporate integrity agreements, debarment from receiving government contracts, and new orders under existing contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement, or civil or criminal penalties, including fines and imprisonment, and adverse publicity, among other adverse consequences. Additionally, we may not be able to obtain the labeling claims necessary or desirable for the promotion of our products. We may also be required to undertake post-marketing trials. In addition, if we or others identify side effects after any of our adoptive cell therapies are on the market, or if manufacturing problems occur, regulatory approval may be withdrawn, and reformulation of our products may be required.

We may not be able to license new TIL technology from the NIH and others.

An element of our intellectual property portfolio is to license additional rights and technologies from the NIH. Our inability to license the rights and technologies that we have identified, or that we may in the future identify, could have a material adverse impact on our ability to complete the development of our products or to develop additional products. No assurance can be given that we will be successful in licensing any additional rights or technologies from the NIH and others. Failure to obtain additional rights and licenses may detrimentally affect our planned development of additional product candidates and could increase the cost, and extend the timelines associated with our development of such other products.

The market opportunities for our product candidates may be limited to those patients who are ineligible for or have failed prior treatments and may be small.

The FDA often approves new therapies initially only for use in patients with relapsed or refractory metastatic disease. We expect to initially seek approval of our product candidates in this setting and are currently studying these patient populations. Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek approval in earlier lines of treatment and potentially as a first line therapy, but there is no guarantee that our product candidates, even if approved, would be approved for earlier lines of therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers who are in a position to receive second or third line therapy, and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations, or market research by third parties, and may prove to be incorrect. Further, new studies or approvals of new therapeutics may change the estimated incidence or prevalence of these cancers. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates and may also be limited by the cost of our treatments and the reimbursement of those treatment costs by third-party payors. For instance, we expect LN-144 to initially target a small patient population that suffers from metastatic melanoma. Even if we obtain significant market share for our product candidates, because the potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications.

We are required to pay substantial royalties and lump sum benchmark payments under our license agreements with the NIH and PolyBioCept, and we must meet certain milestones to maintain our license rights.

Under our license agreements with the NIH for our adoptive cell therapy technologies, we are currently required to pay both substantial benchmark payments and royalties to that institution based on our revenues from sales of our products utilizing the licensed technologies. Likewise, under our license agreement with PolyBioCept, we are required to make lump sum payments if, and when certain product sales targets are achieved. These payments could adversely affect the overall profitability for us of any products that we may seek to commercialize under the NIH or PolyBioCept licenses. In order to maintain our license rights under the NIH and PolyBioCept license agreements, we will need to meet certain specified milestones, subject to certain cure provisions, in the development of our product candidates. There is no assurance that we will be successful in meeting these milestones on a timely basis, or at all.

Because our current products represent, and our other potential product candidates will represent novel approaches to the treatment of disease, there are many uncertainties regarding the development, the market acceptance, third-party reimbursement coverage and the commercial potential of our product candidates.

Human immunotherapy products are a new category of therapeutics. Because this is a relatively new and expanding area of novel therapeutic interventions, there are many uncertainties related to development, marketing, reimbursement, and the commercial potential for our product candidates. There can be no assurance as to the length of the trial period, the number of patients the FDA will require to be enrolled in the trials in order to establish the safety, efficacy, purity and potency of immunotherapy products, or that the data generated in these trials will be acceptable to the FDA to support marketing approval. The FDA may take longer than usual to come to a decision on any BLA that we submit and may ultimately determine that there is not enough data, information, or experience with our product candidates to support an approval decision. The FDA may also require that we conduct additional post-marketing studies or implement risk management programs, such as REMS until more experience with our product candidates is obtained. Finally, after increased usage, we may find that our product candidates do not have the intended effect or have unanticipated side effects, potentially jeopardizing initial or continuing regulatory approval and commercial prospects.

We may also find that the manufacture of our product candidates is more difficult than anticipated, resulting in an inability to produce a sufficient amount of our product candidates for our clinical trials or, if approved, commercial supply. Moreover, because of the complexity and novelty of our manufacturing process, there are only a limited number of manufacturers who have the capability of producing our product candidates. Should any of our contract manufacturers no longer produce our product candidates, it may take us significant time to find a replacement, if we are able to find a replacement at all.

There is no assurance that the approaches offered by our products will gain broad acceptance among doctors or patients or that governmental agencies or third-party medical insurers will be willing to provide reimbursement coverage for proposed product candidates. Moreover, we do not have verifiable internal marketing data regarding the potential size of the commercial market for our product candidates, nor have we obtained current independent marketing surveys to verify the potential size of the commercial markets for our current product candidates or any future product candidates. Since our current product candidates and any future product candidates will represent novel approaches to treating various conditions, it may be difficult, in any event, to accurately estimate the potential revenues from these product candidates. Accordingly, we may spend significant capital trying to obtain approval for product candidates that have an uncertain commercial market. The market for any products that we successfully develop will also depend on the cost of the product. We do not yet have sufficient information to reliably estimate what it will cost to commercially manufacture our current product candidates, and the actual cost to manufacture these products could materially and adversely affect the commercial viability of these products. Our goal is to reduce the cost of manufacturing and providing our therapies. However, unless we can reduce those costs to an acceptable amount, we may never be able to develop a commercially viable product. If we do not successfully develop and commercialize products based upon our approach or find suitable and economical sources for materials used in the production of our products, we will not become profitable, which would materially and adversely affect the value of our common stock.

Our TIL therapy may be provided to patients in combination with other agents provided by third parties. The cost of such combination therapy may increase the overall cost of TIL therapy and may result in issues regarding the allocation of reimbursements between our therapy and the other agents, all of which may affect our ability to obtain reimbursement coverage for the combination therapy from third party medical insurers.

No assurance can be given that we will be able to develop a new, FDA-compliant, more efficient, lower cost manufacturing process upon which our business plan to commercialize TIL-based products is dependent.

Pursuant to the CRADA, and in cooperation with our contract manufacturers and potentially other manufacturers, we have developed and are developing improved methods for the generating and selecting autologous TILs, and to develop methods for large-scale production of autologous TILs that are in accord with current cGMP procedures. Developing a new, scaled-up, pharmaceutical manufacturing process that can more efficiently and cost effectively, and in a more automated manner measure, produce and control the physical and/or chemical attributes of our products in a cGMP facility is subject to many uncertainties and difficulties. We have never manufactured our adoptive cell therapy product candidate on a commercial scale, nor have our partners. As a result, we cannot give any assurance that we will be able to establish a manufacturing process that can produce our products in compliance with the applicable regulatory requirements, at a cost or in quantities necessary to make them commercially viable. Moreover, our third-party manufacturers will have to continually adhere to current cGMP regulations enforced by the FDA through its facilities inspection program. If the facilities of these manufacturers cannot pass a pre-approval plant inspection, the FDA pre-market approval of our products will not be granted. In complying with cGMP and foreign regulatory requirements, we and any of our third-party manufacturers will be obligated to expend time, money and effort in production, record-keeping and quality control to assure that our products meet applicable specifications and other requirements. If we or any of our third-party manufacturers fail to comply with these requirements, we may be subject to regulatory action. No assurance can be given that we will be able to develop such a manufacturing process, or that our partners will thereafter be able to establish and operate such a production facility.

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

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. Large judgements have also been awarded in class action lawsuits based on therapeutics that had unanticipated side effects. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants or sites and potential termination of clinical trial sites or entire clinical programs;
- initiation of investigations by regulators, refusal to approve marketing applications or supplements, and withdrawal or limitation of product approvals;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- significant negative media attention;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate; and
- a decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with corporate collaborators. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. While we have obtained clinical trial insurance for our Phase 2 clinical trials, we may have to pay amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

We face significant competition from other biotechnology and pharmaceutical companies and from non-profit institutions.

Competition in the field of cancer therapy is intense and is accentuated by the rapid pace of technological development. Research and discoveries by others may result in breakthroughs which may render our products obsolete even before they generate any revenue. There are products that are approved and currently under development by others that could compete with the products that we are developing. Many of our potential competitors have substantially greater research and development capabilities and approval, manufacturing, marketing, financial and managerial resources and experience than we do. Our competitors may:

- develop safer, more convenient or more effective immunotherapies and other therapeutic products;
- develop therapies that are less expensive or have better reimbursement from private or public payors;
- reach the market more rapidly, reducing the potential sales of our products; or
- establish superior proprietary positions.

Potential competitors in the market for treating metastatic melanoma are companies such as Bristol-Myers Squibb, Roche/Genentech, Merck, Amgen, Pfizer, and Novartis, which already have products on the market or in development. Other companies, such as Celgene, Juno Therapeutics, Gilead Sciences and Adaptimmune, which are focused on genetically engineered T-cell technologies to treat cancer, may also be competitors. All of these companies, and most of our other current and potential competitors have substantially greater research and development capabilities and financial, scientific, regulatory, manufacturing, marketing, sales, human resources, and experience than we do. Many of our competitors have several therapeutic products that have already been developed, approved and successfully commercialized, or are in the process of obtaining regulatory approval for their therapeutic products in the United States and internationally. Our competitors may obtain regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in competitors establishing a strong market position before we are able to enter the market.

Universities and public and private research institutions in the U.S. and Europe are also potential competitors. For example, a Phase 3 study comparing TIL to standard ipilimumab in patients with metastatic melanoma is currently being conducted in Europe by the Netherlands Cancer Institute, the Copenhagen County Herlev University Hospital, and the University of Manchester. While these universities and public and private research institutions primarily have educational objectives, they may develop proprietary technologies that lead to other FDA approved therapies or that secure patent protection that we may need for the development of our technologies and products.

Our lead product candidate, LN-144, is a therapy for the treatment of metastatic melanoma. Currently, there are numerous companies that are developing various alternate treatments for melanoma. Accordingly, LN-144 faces significant competition in the melanoma treatment space from multiple companies. Even if we obtain regulatory approval of LN-144, the availability and price of our competitors' products could limit the demand and the price we are able to charge for our melanoma therapy. We may not be able to implement our business plan if the acceptance of our products is inhibited by price competition or the reluctance of physicians to switch from other methods of treatment to our product, or if physicians switch to other new therapies, drugs or biologic products or choose to reserve our product for use in limited circumstances.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. 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 and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We are dependent on third parties to support our research, development and manufacturing activities and, therefore, are subject to the efforts of these parties and our ability to successfully collaborate with these third parties.

As a result of our current strategy to outsource most of our manufacturing, we rely very heavily on third parties to perform for us the manufacturing of our products for our clinical trials. We also license a significant portion of our technology from others and, except for the Gen 2 process which we have developed internally, at this time, we do not own any intellectual properties or technologies. We intend to rely upon our contract manufacturers to produce large quantities of materials needed for clinical trials and potentially product commercialization. Third party manufacturers may not be able to meet our needs with respect to timing, quantity or quality. If we are unable to contract for a sufficient supply of needed materials on acceptable terms, or if we should encounter delays or difficulties in our relationships with manufacturers, our clinical testing may be delayed, thereby delaying the submission of products for regulatory approval or the market introduction and subsequent sales of our products. Any such delay may lower our revenues and potential profitability.

In addition, in order to supplement our own efforts to improve TIL manufacturing and develop TIL therapies in new indications in clinical trials, we currently work and collaborate with government and academic research institutions, medical institutions and corporate partners such as the NCI, Moffitt, MedImmune, and the Karolinska University Hospital. We also intend to continue to enter into additional third-party collaborative agreements in the future. However, we may not be able to successfully negotiate any additional collaborative arrangements. If established, these relationships may not be scientifically or commercially successful. The success of these and future collaborations and joint development arrangements may be subject to numerous risks and uncertainties, including the inability or unwillingness of our partners to perform in the manner, or to the extent anticipated, and may also be subject to disagreements regarding the rights, interests, and performance of the counterparties under our licenses and development agreements. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercialization of the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority under the collaboration agreement.

With regard to future collaboration efforts, we face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for 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, an evaluation by the proposed collaborator of a number of similar or unique factors.

Collaborations with biopharmaceutical companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation. Any collaboration may pose a number of risks, including the following:

- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create 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 fail to make timely regulatory submissions for a product candidate;
- collaborators may not comply with all applicable regulatory requirements or may fail to report safety data in accordance with all applicable regulatory requirements;
- 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;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product candidate or product;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time consuming and expensive;
- 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 intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- collaborator may be involved in a business combination, resulting in the decreased emphasis or termination of development or commercialization of any product candidate subject to the collaboration agreement;
- termination of a collaboration agreement may make it more difficult to attract new collaborators and our and our products' or product candidates' reputation in the medical, business, and financial communities could be adversely affected.

If any third-party collaborator breaches or terminates its agreement with us or fails to conduct its activities in a timely manner, the commercialization of our products under development could be slowed down or blocked completely. It is possible that our collaborators will change their strategic focus, pursue alternative technologies or develop alternative products, either on their own or in collaboration with others, as a means for developing treatments for the diseases targeted by our collaborative programs. The effectiveness of our collaborators in marketing our products will also affect our revenues and earnings.

Our collaborators will also be required to comply with the applicable regulatory requirements, and, as such, are subject to the same risks as we are. If they do not or are not able to comply with these requirements, we may not be able to use the data generated through their studies to support our future investigational or marketing applications. Collaborator noncompliance may also expose them and us to regulatory enforcement actions.

No assurance can be given that we will be able to successfully collaborate with our partners as anticipated and that our current or future collaborations and clinical trials will be completed as contemplated, support the regulatory approval of our current product candidates, or result in any viable additional product candidates. For instance, to the extent that these collaborators conduct their studies with manufacturing processes that are different than ours or product that is different than ours, the results generated from their studies may not be seen in our current or future studies that employ our manufacturing processes and the results generated from their studies may not support approval of our product candidates.

If we are unable to obtain or maintain suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense.

Development of a product candidate intended for use in combination with an already approved product may present more or different challenges than development of a product candidate for use as a single agent.

We are currently developing LN-144 and LN-145 for use along with IL-2. We and our collaborators are also studying TIL therapy along with other products, such as durvalumab. The development of product candidates for use in combination with another product may present challenges. For example, the FDA may require us to use more complex clinical trial designs, in order to evaluate the contribution of each product and product candidate to any observed effects. It is possible that the results of these studies could show that any positive study results are attributable to the already approved product. Moreover, following product approval, the FDA may require that products used in conjunction with each other be cross labeled for combined use. To the extent that we do not have rights to already approved products, this may require us to work with another company to satisfy such a requirement. Moreover, developments related to the already approved products may impact our clinical trials for the combination as well as our commercial prospects should we receive marketing approval. Such developments may include changes to the approved product's safety or efficacy profile, changes to the availability of the approved product, and changes to the standard of care.

A Fast Track product designation or other designation to facilitate product candidate development may not lead to faster development or a faster regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We were granted Fast Track designation by the FDA for LN-144 in advanced melanoma. We may seek Fast Track designation for other of our current or future product candidates. Receipt of a designation to facilitate product candidate development is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for a designation, the FDA may disagree. In any event, the receipt of such a designation for a product candidate may not result in a faster development process, review, or approval compared to product candidates considered for approval under conventional the FDA procedures and does not assure ultimate marketing approval by the FDA. In addition, the FDA may later decide that the products no longer meet the designation conditions.

While LN-144 has received orphan drug designation, there is no guarantee that we will be able to maintain this designation, receive this designation for any of our other product candidates, or receive or maintain any corresponding benefits, including periods of exclusivity.

We received orphan drug designation for LN-144 in the United States to treat malignant melanoma stages IIB-IV. We may also seek orphan drug designation for our other product candidates, as appropriate. Orphan designation, however, may be lost if the indication for which we develop our designated product candidates do not meet the orphan criteria. Moreover, following product approval, orphan exclusivity may be lost if the FDA determines, among other reasons, that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Even if we obtain orphan exclusivity, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition and the same product can be approved for different conditions. Even after an orphan product is approved, the FDA can subsequently approve a product containing the same principal molecular features for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer or more effective or makes a major contribution to patient care.

Moreover, the FDA may grant orphan drug designations to multiple of the same products for the same indication. If another sponsor receives FDA approval for an orphan drug designated product that is the same as our product candidates and intended for the same indication before we do, we would be prevented from launching our product in the United States for this indication for a period of at least 7 years.

In response to a court decision regarding the plain meaning of the exclusivity provision of the Orphan Drug Act, the FDA may undertake a reevaluation of aspects of its orphan drug regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business, financial condition, results of operations, and prospects could be harmed.

As a condition of approval, the FDA may require that we implement various post-marketing requirements and conduct post-marketing studies, any of which would require a substantial investment of time, effort, and money, and which may limit our commercial prospects.

As a condition of biologic licensing, the FDA is authorized to require that sponsors of approved BLAs implement various post-market requirements, including REMS and Phase 4 studies. By example, when the FDA approved Novartis' Kymriah in August 2017, a CAR-T cell therapy for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse, the FDA required significant post-marketing commitments, including a Phase 4 study, revalidation of a test method, and a substantial REMS program that included, among other requirements, the certification of hospitals and their associated clinics that dispense Kymriah, which certification includes a number of requirements, the implementation of a Kymriah training program, and limited distribution only to certified hospitals and their associated clinics. If we receive approval of our product candidates, the FDA may determine that similar or additional post-approval requirements are necessary to ensure that our product candidates are safe, pure, and potent. To the extent that we are required to establish and implement any post-approval requirements, we will likely need to invest a significant amount of time, effort, and money. Such post-approval requirements may also limit the commercial prospects of our product candidates.

If we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if they are approved, we may be unable to generate product revenues.

We currently do not have a commercial infrastructure for the marketing, sale, and distribution of biopharmaceutical products. If approved, in order to commercialize our products, we must build our marketing, sales, and distribution capabilities or make arrangements with third parties to perform these services, which will take time and require significant financial expenditures and we may not be successful in doing so. Even if we are able to effectively establish a sales force and develop a marketing and sales infrastructure, our sales force and marketing teams may not be successful in commercializing our current or future product candidates. To the extent we rely on third parties to commercialize any products for which we obtain regulatory approval, we would have less control over their sales efforts, and could be held liable if they failed to comply with applicable legal or regulatory requirements.

We have no prior experience in the marketing, sale, and distribution of biopharmaceutical products, and there are significant risks involved in the building and managing of a commercial infrastructure. The establishment and development of commercial capabilities, including compliance plans, to market any products we may develop will be expensive and time consuming and could delay any product launch, and we may not be able to successfully develop this capability. We, or our collaborators, will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train, manage, and retain marketing and sales personnel. In the event we are unable to develop a marketing and sales infrastructure, we may not be able to commercialize our current or future product candidates, which would limit our ability to generate product revenues. Factors that may inhibit our efforts to commercialize our current or future product candidates include:

- the inability to recruit, train, manage, and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe our current or future product candidates;
- our inability to effectively oversee a geographically dispersed sales and marketing team;
- the costs associated with training sales and marketing personnel on legal and regulatory compliance matters and monitoring their actions;
- an inability to secure adequate coverage and reimbursement by government and private health plans;
- the clinical indications for which the products are approved and the claims that we may make for the products;
- limitations or warnings, including distribution or use restrictions, contained in the products' approved labeling;
- any distribution and use restrictions imposed by the FDA or to which we agree as part of a mandatory REMS or voluntary risk management plan;
- liability for sales or marketing personnel who fail to comply with the applicable legal and regulatory requirements;
- 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; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization or engaging a contract sales organization.

If our product candidates do not achieve broad market acceptance, the revenues that we generate from their sales will be limited.

We have never commercialized a product candidate for any indication. Even if our product candidates are approved by the appropriate regulatory authorities for marketing and sale, they may not gain acceptance among physicians, patients, third-party payors, and others in the medical community. If any product candidate for which we obtain regulatory approval does not gain an adequate level of market acceptance, we may not generate significant product revenues or become profitable. Market acceptance of our product candidates by the medical community, patients, and third-party payors will depend on a number of factors, some of which are beyond our control. For example, physicians are often reluctant to switch their patients and patients may be reluctant to switch from existing therapies even when new and potentially more effective or safer treatments enter the market.

Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of any of our product candidates will depend on a number of factors, including:

- the efficacy of our product candidates;
- the prevalence and severity of adverse events associated with such product candidates;
- the clinical indications for which the products are approved and the approved claims that we may make for the products;
- limitations or warnings contained in the Product's FDA-approved labeling, including potential limitations or warnings for such products that may be more restrictive than other competitive products;
- changes in the standard of care for the targeted indications for such product candidates;
- the relative difficulty of administration of such product candidates;
- cost of treatment versus economic and clinical benefit in relation to alternative treatments or therapies;
- the availability of adequate coverage or reimbursement by third parties, such as insurance companies and other healthcare payors, and by government healthcare programs, including Medicare and Medicaid;
- the extent and strength of our marketing and distribution of such product candidates;
- the safety, efficacy, and other potential advantages over, and availability of, alternative treatments already used or that may later be approved for any of our intended indications;
- distribution and use restrictions imposed by the FDA with respect to such product candidates or to which we agree as part of a mandatory risk evaluation and mitigation strategy or voluntary risk management plan;
- the timing of market introduction of such product candidates, as well as competitive products;
- our ability to offer such product candidates for sale at competitive prices;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the extent and strength of our third-party manufacturer and supplier support;
- the approval of other new products for the same indications;
- adverse publicity about the product or favorable publicity about competitive products; and
- potential product liability claims.

Our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful. Even if the medical community accepts that our product candidates are safe and effective for their approved indications, physicians and patients may not immediately be receptive to such product candidates and may be slow to adopt them as an accepted treatment of the approved indications. If our current or future product candidates are approved but do not achieve an adequate level of acceptance among physicians, patients, and third-party payors, we may not generate meaningful revenues from our product candidates, and we may not become profitable.

Our product candidates may face competition sooner than anticipated.

The enactment of the Biologics Price Competition and Innovation Act, or BPCIA, created an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCIA, the FDA cannot make an approval of an application for a biosimilar product effective until 12 years after the original branded product was approved under a BLA. Certain changes, however, and supplements to an approved BLA, and subsequent applications filed by the same sponsor, manufacturer, licensor, predecessor in interest, or other related entity do not qualify for the 12-year exclusivity period.

Our product candidates may qualify for the BPCIA's 12-year period of exclusivity. However, there is a risk that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Additionally, this period of regulatory exclusivity does not block companies pursuing regulatory approval via their own traditional BLA, rather than via the abbreviated pathway. Changes may also be made to this exclusivity period as a result of future legislation as there has been ongoing efforts to reduce the period of exclusivity. Even if we receive a period of BPCIA exclusivity for our first licensed product, if subsequent products do not include a modification to the structure of the product that impacts safety, purity, or potency, we may not receive additional periods of exclusivity for those products. 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. Medicare Part B encourages use of biosimilars by paying the provider the same percentage of the reference product, average sale price, or ASP as a mark-up, regardless of which product is reimbursed. It is also possible that payors will give reimbursement preference to biosimilars even over reference biologics absent a determination of interchangeability.

We will need to obtain FDA approval of any proposed product names, and any failure or delay associated with such approval may adversely affect our business.

Any name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the U.S. Patent and Trademark Office, or USPTO. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. The FDA may also object to a product name if it believes the name inappropriately implies medical claims or contributes to an overstatement of efficacy. If the FDA objects to any of our proposed product names, we may be required to adopt alternative names for our product candidates. If we adopt alternative names, we would lose the benefit of any existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

Our internal computer systems, or those used by our contract research organizations or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our contract research organizations and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event was to occur and cause interruptions in our operations, it could result in a disruption of our drug development programs. For example, the loss of clinical study data from completed or ongoing clinical studies for a product candidate could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of any product candidates could be delayed.

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

Our operations are dependent upon the services of our executives and our employees who are engaged in research and development. The loss of the services of our executive officers or senior research personnel could delay our product development programs and our research and development efforts. In order to develop our business in accordance with our business plan, we will have to hire additional qualified personnel, including in the areas of research, manufacturing, clinical trials management, regulatory affairs, and sales and marketing. We are continuing our efforts to recruit and hire the necessary employees to support our planned operations in the near term. However, competition for qualified employees among companies in the biotechnology and biopharmaceutical industry is intense, and no assurance can be given that we will be able to attract, hire, retain and motivate the highly skilled employees that we need. Future growth will impose significant added responsibilities on members of management, including:

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

Our future financial performance and our ability to commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities. Our efforts to manage our growth are complicated by the fact that nearly all of our executive officers have joined us since June 2016. This lack of long-term experience working together may adversely impact our senior management team's ability to effectively manage our business and growth.

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

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development, and commercialization goals on a timely basis, or at all.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

We may evaluate various acquisitions and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;

- the diversion of our management's attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

Depending on the size and nature of future strategic acquisitions, we may acquire assets or businesses that require us to raise additional capital or to operate or manage businesses in which we have limited experience. Making larger acquisitions that require us to raise additional capital to fund the acquisition will expose us to the risks associated with capital raising activities. Acquiring and thereafter operating larger new businesses will also increase our management, operating and reporting costs and burdens. In addition, if we undertake acquisitions, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

We may rely on third parties to perform many essential services for any products that we commercialize, including services related to warehousing and inventory control, distribution, government price reporting, customer service, accounts receivable management, cash collection, and adverse event reporting. If these third parties fail to perform as expected or to comply with legal and regulatory requirements, our ability to commercialize our current or future product candidates will be significantly impacted and we may be subject to regulatory sanctions.

We may retain third-party service providers to perform a variety of functions related to the sale and distribution of our current or future product candidates, key aspects of which will be out of our direct control. These service providers may provide key services related to warehousing and inventory control, distribution, customer service, accounts receivable management, and cash collection. If we retain a service provider, we would substantially rely on it as well as other third-party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical or natural damage at their facilities, our ability to deliver product to meet commercial demand would be significantly impaired and we may be subject to regulatory enforcement action.

In addition, we may engage third parties to perform various other services for us relating to adverse event reporting, safety database management, fulfillment of requests for medical information regarding our product candidates and related services. If the quality or accuracy of the data maintained by these service providers is insufficient, or these third parties otherwise fail to comply with regulatory requirements related to adverse event reporting, we could be subject to regulatory sanctions.

Additionally, we may contract with a third-party to calculate and report pricing information mandated by various government programs. If a third party fails to timely report or adjust prices as required or errs in calculating government pricing information from transactional data in our financial records, it could impact our discount and rebate liability, and potentially subject us to regulatory sanctions or False Claims Act lawsuits.

The SEC has issued an administrative order against us that may make it more difficult for us to raise capital in the future.

On April 10, 2017, the SEC issued an administrative order that requires us to cease and desist from committing or causing any violations and any future violations of Sections 5(b), 17(a), and 17(b) of the Securities Act of 1933, as amended, or the Securities Act, and of Section 10(b) of the Securities Exchange Act of 1934 and Rule 10b-5 thereunder. The order was entered into as part of our settlement with the SEC in the investigation titled *In the Matter of Certain Stock Promotion*. The SEC's investigation, in part, involved the conduct of our former Chief Executive Officer and director, Manish Singh, during the period between September 2013 and April 2014, and the failure by authors of certain articles about our company to disclose that they were compensated by one of our former investor relations firms. The foregoing order may negatively impact our reputation with current and future investors, will disqualify us from effecting private placement transactions in reliance upon any of the exemptions from Securities Act registration afforded by Regulation D, and will limit our ability to make certain communications in future public offerings. As a result, the SEC's order will make it more difficult for us to raise capital in future private and public offerings. We currently anticipate that we will have to raise additional capital in the future to fund our future research, development and commercialization efforts.

We are, and in the future may be, subject to Federal or state securities or related legal actions that could adversely affect our results of operations and our business.

Shortly after the SEC announced settlements with us, with other public companies, and with unrelated parties in the *In the Matter of Certain Stock Promotion* investigation, two securities class action complaints were filed in the U.S. District Court for the Northern District of California against our company, Manish Singh, and two of our other former officers. On July 20, 2017, the plaintiff in one of the cases filed a notice to voluntarily dismiss that case, and the court entered an order dismissing the complaint on July 21, 2017. On July 26, 2017, the court appointed a movant as lead plaintiff. On September 8, 2017, the lead plaintiff, individually and on behalf of all others similarly situated, filed an amended complaint seeking class action status in the United States District Court for the Northern District of California (*Jay Rabkin v. Lion Biotechnologies, Inc., et al.*, case no. 3:17cv0286) against us, two of our former officers, and the managing member of our former investor relations firm. The amended complaint alleges, among other things, that the defendants violated various provisions of the Securities Exchange Act of 1934 by making materially false and misleading statements, or by failing to make certain disclosures, regarding the actions taken by Manish Singh, our former Chief Executive Officer and a former director, and our former investor relations firm that were the subject of the *In the Matter of Certain Stock Promotions* SEC investigation. On December 15, 2017, a purported shareholder derivative complaint, *Kevin Fong v. Manish Singh, et al.* (case no. 17:1806), was filed against us, as nominal defendant, and certain of our current and former officers and directors, and others, as defendants, in the U.S. District Court for the District of Delaware. The complaint alleges breaches of fiduciary duties, unjust enrichment, and violations of Section 14(a) of the Securities Exchange Act of 1934 and Rule 14a-9 promulgated thereunder arising from the Securities and Exchange Commission's investigation in the *In the Matter of Certain Stock Promotions* matter and our April 10, 2017 settlement thereof, and seeks unspecified damages on behalf of our company and injunctive relief. We intend to vigorously defend against these complaints. However, based on the very early stage of the aforementioned litigation, it is not possible to estimate the amount or range of possible loss that might result from an adverse judgment or a settlement of these matters. Furthermore, litigation is inherently uncertain, and there is no assurance as to the outcome of this, or other future cases. We could incur substantial unreimbursed legal fees, settlements, judgments and other expenses in connection with these or other legal and regulatory proceedings that may not qualify for coverage under, or may exceed the limits of, our applicable directors' and officers' liability insurance policies and could have a material adverse effect on our financial condition, liquidity and results of operations. The currently pending cases also may distract the time and attention of our officers and directors or divert our other resources away from our ongoing commercial and development programs. An unfavorable outcome in these matters could damage our business and reputation or result in additional claims or proceedings against us.

Risks Related to Government Regulation

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

We have not previously submitted a BLA to the FDA, or similar approval filings to comparable foreign authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and effectiveness for each desired indication. The BLA must also include significant information regarding the chemistry, manufacturing and controls for the product. We expect the novel nature of our product candidates to create further challenges in obtaining regulatory approval. For example, the FDA has limited experience with commercial development of cell therapies for cancer. Accordingly, the regulatory approval pathway for our product candidates may be uncertain, complex, expensive and lengthy, and approval may not be obtained.

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

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

We could also encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, the IRBs for the institutions in which such trials are being conducted by the FDA or other regulatory authorities, or recommended for suspension or termination by Data Monitoring Committees due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of our product candidates, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

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

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

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

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

Any regulatory approvals that we receive for our product candidates will require surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a risk evaluation and mitigation strategy, or REMS, to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA may also require post-approval Phase 4 studies. Moreover, the FDA and comparable foreign regulatory authorities will continue to closely monitor the safety profile of any product even after approval. If the FDA or comparable foreign regulatory authorities become aware of new safety information after approval of any of our product candidates, they may withdraw approval, require labeling changes or establishment of a REMS or similar strategy, impose significant restrictions on a product's indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. Any such restrictions could limit sales of the product.

In addition, we, our contractors, and our collaborators are and will remain responsible for FDA compliance, including requirements related to product design, testing, clinical and pre-clinical trials approval, manufacturing processes and quality, labeling, packaging, distribution, adverse event and deviation reporting, storage, advertising, marketing, promotion, sale, import, export, submissions of safety and other post-marketing information and reports such as deviation reports, registration, product listing, annual user fees, and recordkeeping for our product candidates. We and any of our collaborators, including our contract manufacturers, could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with regulatory requirements. Application holders must further notify the FDA, and depending on the nature of the change, obtain FDA pre-approval for product and manufacturing changes. The cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, that the product is less effective than previously thought, problems with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing, distribution, or manufacturing of our product candidates, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- restrictions on the labeling of our product candidates, including required additional warnings, such as black box warnings, contraindications, precautions, and restrictions on the approved indication or use;
- modifications to promotional pieces;
- changes to product labeling or the way the product is administered;
- liability for harm caused to patients or subjects;
- fines, restitution, disgorgement, warning letters, untitled letters, cyber letters, or holds on or termination of clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates;
- injunctions or the imposition of civil or criminal penalties, including imprisonment;
- FDA debarment, debarment from government contracts, and refusal of future orders under existing contracts, exclusion from federal healthcare programs, consent decrees, or corporate integrity agreements;
- regulatory authority issuance of safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings or other safety information about the biologic;
- reputational harm; or
- the product becoming less competitive.

Any of these events could further have other material and adverse effects on our operations and business and could adversely impact our stock price and could significantly harm our business, financial condition, results of operations, and prospects.

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

If we fail to comply with federal and state healthcare and promotional laws, including fraud and abuse and information privacy and security laws, we could face substantial penalties and our business, financial condition, results of operations, and prospects could be adversely affected.

As a pharmaceutical company, we are subject to many federal and state healthcare laws, including the federal Anti-Kickback Statute, the federal civil and criminal False Claims Act, the civil monetary penalties statute, the Medicaid Drug Rebate statute and other price reporting requirements, the Veterans Health Care Act of 1992, the federal Health Insurance Portability and Accountability Act of 1996 (as amended by the Health Information Technology for Economics and Clinical Health Act), the Foreign Corrupt Practices Act of 1977, the Patient Protection and Affordable Care Act of 2010, and similar state laws. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid, or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. If we do not comply with all applicable fraud and abuse laws, we may be subject to healthcare fraud and abuse enforcement by both the federal government and the states in which we conduct our business.

Laws and regulations require calculation and reporting of complex pricing information for prescription drugs, and compliance will require us to invest in significant resources and develop a price reporting infrastructure, or depend on third parties to compute and report our drug pricing. Pricing reported to CMS must be certified. Non-compliant activities expose us to FCA risk if they result in overcharging agencies, underpaying rebates to agencies, or causing agencies to overpay providers.

If we or our operations are found to be in violation of any federal or state healthcare law, or any other governmental regulations that apply to us, we may be subject to penalties, including civil, criminal, and administrative penalties, damages, fines, disgorgement, debarment from government contracts, refusal of orders under existing contracts, exclusion from participation in U.S. federal or state health care programs, corporate integrity agreements, and the curtailment or restructuring of our operations, any of which could materially adversely affect our ability to operate our business and our financial results. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including our collaborators, is found not to be in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including but not limited to, exclusions from participation in government healthcare programs, which could also materially affect our business.

In particular, if we are found to have impermissibly promoted any of our product candidates, we may become subject to significant liability and government fines. We, and any of our collaborators, must comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing approval. Promotional communications with respect to therapeutics are subject to a variety of legal and regulatory restrictions and continuing review by the FDA, Department of Justice, Department of Health and Human Services' Office of Inspector General, state attorneys general, members of Congress, and the public. When the FDA or comparable foreign regulatory authorities issue regulatory approval for a product candidate, the regulatory approval is limited to those specific uses and indications for which a product is approved. If we are not able to obtain FDA approval for desired uses or indications for our products and product candidates, we may not market or promote our products for those indications and uses, referred to as off-label uses, and our business may be adversely affected. We further must be able to sufficiently substantiate any claims that we make for our products including claims comparing our products to other companies' products and must abide by the FDA's strict requirements regarding the content of promotion and advertising.

While physicians may choose to prescribe products for uses that are not described in the product's labeling and for uses that differ from those tested in clinical studies and approved by the regulatory authorities, we are prohibited from marketing and promoting the products for indications and uses that are not specifically approved by the FDA. These off-label uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. Regulatory authorities in the United States generally do not restrict or regulate the behavior of physicians in their choice of treatment within the practice of medicine. Regulatory authorities do, however, restrict communications by biopharmaceutical companies concerning off-label use.

The FDA and other agencies actively enforce the laws and regulations regarding product promotion, particularly those prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted a product may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees of permanent injunctions under which specified promotional conduct is changed or curtailed. Thus, we and any of our collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In the United States, engaging in the impermissible promotion of our products, following approval, for off-label uses can also subject us to false claims and other litigation under federal and state statutes, including fraud and abuse and consumer protection laws, which can lead to civil and criminal penalties and fines, agreements with governmental authorities that materially restrict the manner in which we promote or distribute therapeutic products and do business through, for example, corporate integrity agreements, suspension or exclusion from participation in federal and state healthcare programs, and debarment from government contracts and refusal of future orders under existing contracts. These false claims statutes include the federal civil False Claims Act, which allows any individual to bring a lawsuit against a biopharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims or causing others to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government decides to intervene and prevails in the lawsuit, the individual will share in the proceeds from any fines or settlement funds. If the government declines to intervene, the individual may pursue the case alone. These False Claims Act lawsuits against manufacturers of drugs and biologics have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements, up to \$3.0 billion, pertaining to certain sales practices and promoting off-label uses. In addition, False Claims Act lawsuits may expose manufacturers to follow-on claims by private payors based on fraudulent marketing practices. This growth in litigation has increased the risk that a biopharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, as well as criminal and civil penalties, agree to comply with burdensome reporting and compliance obligations, and be excluded from Medicare, Medicaid, or other federal and state healthcare programs. If we or our future collaborators do not lawfully promote our approved products, if any, we may become subject to such litigation and, if we do not successfully defend against such actions, those actions may have a material adverse effect on our business, financial condition, results of operations and prospects.

Although an effective compliance program can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Moreover, achieving and sustaining compliance with applicable federal and state fraud laws may prove costly. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

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

In both domestic and foreign markets, sales of our product candidates, if approved, depend on the availability of coverage and adequate reimbursement from third-party payors. Such third-party payors include government health programs such as Medicare and Medicaid, managed care providers, private health insurers, and other organizations. In addition, because our product candidates represent new approaches to the treatment of cancer, we cannot accurately estimate the potential revenue from our product candidates.

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

Government authorities and third-party payors decide which drugs and treatments they will cover and the amount of reimbursement. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. If reimbursement is not available, or is available only to limited levels, our product candidates may be competitively disadvantaged, and we, or our collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or our collaborators, to establish or maintain a market share sufficient to realize a sufficient return on our or their investments. Alternatively, securing favorable reimbursement terms may require us to compromise pricing and prevent us from realizing an adequate margin over cost. Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor's determination that use of a product is:

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

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

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

Prices paid for a drug also vary depending on the class of trade. Prices charged to government customers are subject to price controls, including ceilings, and private institutions obtain discounts through group purchasing organizations. Net prices for drugs may be further reduced by mandatory discounts or rebates required by government healthcare programs and demanded by private payors. It is also not uncommon for market conditions to warrant multiple discounts to different customers on the same unit, such as purchase discounts to institutional care providers and rebates to the health plans that pay them, which reduces the net realization on the original sale.

In addition, federal programs impose penalties on manufacturers of drugs marketed under an NDA or BLA, in the form of mandatory additional rebates and/or discounts if commercial prices increase at a rate greater than the Consumer Price Index-Urban, and these rebates and/or discounts, which can be substantial, may impact our ability to raise commercial prices. Regulatory authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of our collaborators to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of our collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost control initiatives could cause us, or our collaborators, to decrease, discount, or rebate a portion of the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If the realized prices for our products, if any, decrease or if governmental and other third-party payors do not provide adequate coverage or reimbursement, our prospects for revenue and profitability will suffer.

Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate. If payors subject our product candidates to maximum payment amounts or impose limitations that make it difficult to obtain reimbursement, providers may choose to use therapies which are less expensive when compared to our product candidates. Additionally, if payors require high copayments, beneficiaries may decline prescriptions and seek alternative therapies. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to the satisfaction of hospitals and other target customers and their third-party payors. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We, and our collaborators, cannot be sure that coverage will be available for any product candidate that we, or they, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any our product candidates for which we obtain marketing approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

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

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

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability. A particular challenge for our product candidates arises from the fact that they will primarily be used in an inpatient setting. Inpatient reimbursement generally relies on stringent packaging rules that may mean that there is no separate payment for our product candidates. Additionally, data used to set the payment rates for inpatient admissions is usually several years old and would not take into account all of the additional therapy costs associated with the administration of our product candidates. If special rules are not created for reimbursement for immunotherapy treatments such as our product candidates, hospitals might not receive enough reimbursement to cover their costs of treatment, which will have a negative effect on their adoption of our product candidates.

We are subject to new legislation, regulatory proposals, and healthcare payor initiatives that may increase our costs of compliance, and adversely affect our ability to market our products, obtain collaborators, and raise capital.

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, or the ability of our collaborators, to profitably sell any products for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or our collaborators, may receive for any approved products.

Since enactment of the ACA in 2010, in both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect on April 1, 2013 and were to remain in effect until 2024. The Bipartisan Budget Act of 2015 extended the 2% sequestration to 2025. In January 2013, the American Taxpayer Relief Act of 2012, or ATRA, was approved which, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. On January 20, 2017, the new administration 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, and, for that reason, some final regulations have yet to take effect. In December 2017, Congress repealed the individual mandate for health insurance required by the ACA and could consider further legislation to repeal other elements of the ACA. At the end of 2017, CMS promulgated regulations that reduce the amount paid to hospitals for outpatient drugs purchased under the 340B program, and some states have enacted transparency laws requiring manufacturers to report information on drug prices and price increases.

Additional federal and state healthcare reform measures may be adopted in the future that may result in more rigorous coverage criteria, increased regulatory burdens and operating costs, decreased net revenue from our pharmaceutical products, decreased potential returns from our development efforts, and additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government healthcare programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Legislative and regulatory proposals may also be made to expand post-approval requirements and restrict sales and promotional activities for drugs. 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 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.

In addition, there have been a number of other legislative and regulatory proposals aimed at changing the pharmaceutical industry. For instance, the enacted Drug Quality and Security Act imposes obligations on manufacturers of pharmaceutical products related to product tracking and tracing. Compliance with the federal track and trace requirements may increase our operational expenses and impose significant administrative burdens. As a result of these and other new proposals, we may determine to change our current manner of operation, provide additional benefits, or change our contract arrangements, any of which could have a material adverse effect on our business, financial condition, and results of operations.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In international markets, reimbursement and health care payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. There can be no assurance that our products will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be available, or that the third-party payors' reimbursement policies will not adversely affect our ability to sell our products profitably. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

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

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to: comply with the laws of the FDA and other similar foreign regulatory bodies, provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws, or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials.

We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our, or our employees', consultants', collaborators', contractors', or vendors' business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, compliance agreements, withdrawal of product approvals, and curtailment of our operations, among other things, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Risks Related to Our Intellectual Property

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

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

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

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights.

The cost to us of any litigation or other proceeding relating to intellectual property rights, even if resolved in our favor, could be substantial. Some of our competitors may be better able to sustain the costs of complex patent litigation because they have substantially greater resources. If there is litigation against us, we may not be able to continue our operations.

Should third parties file patent applications, or be issued patents claiming technology also used or claimed by us, we may be required to participate in interference proceedings in the USPTO to determine priority of invention. We may be required to participate in interference proceedings involving our issued patents and pending applications. We may be required to cease using the technology or to license rights from prevailing third parties as a result of an unfavorable outcome in an interference proceeding. A prevailing party in that case may not offer us a license on commercially acceptable terms.

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

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

If we are unable to protect our proprietary rights, we may not be able to compete effectively or operate profitably.

Our success is dependent in part on maintaining and enforcing the patents and other proprietary rights that we have licensed and may develop, and on our ability to avoid infringing the proprietary rights of others. Certain of our intellectual property rights are licensed from another entity, and as such the preparation and prosecution of these patents and patent applications was not performed by us or under our control. Furthermore, patent law relating to the scope of claims in the biotechnology field in which we operate is still evolving and, consequently, patent positions in our industry may not be as strong as in other more well-established fields. The patent positions of biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date.

The issuance of a patent is not conclusive as to its validity or enforceability and it is uncertain how much protection, if any, will be given to the patents we have licensed from the NIH, Moffitt or M.D. Anderson if any these parties, or we, attempt to enforce the patents and/or if they are challenged in court or in other proceedings, such as oppositions, which may be brought in foreign jurisdictions to challenge the validity of a patent. A third party may challenge the validity or enforceability of a patent after its issuance by the Patent Office. It is possible that a competitor may successfully challenge our patents or that a challenge will result in limiting their coverage. Moreover, the cost of litigation to uphold the validity of patents and to prevent infringement can be substantial. If the outcome of litigation is adverse to us, third parties may be able to use our patented invention without payment to us. Moreover, it is possible that competitors may infringe our patents or successfully avoid the patented technology through design innovation. To stop these activities, we may need to file a lawsuit. These lawsuits are expensive and would consume time and other resources, even if we were successful in stopping the violation of our patent rights. In addition, there is a risk that a court would decide that our patents are not valid and that we do not have the right to stop the other party from using the inventions. There is also the risk that, even if the validity of our patents were upheld, a court would refuse to stop the other party on the grounds that its activities are not covered by, that is, do not infringe, our patents.

Should third parties file patent applications, or be issued patents claiming technology also used or claimed by our licensor(s) or by us in any future patent application, we may be required to participate in interference proceedings in the USPTO to determine priority of invention for those patents or patent applications that are subject to the first-to-invent law in the United States, or may be required to participate in derivation proceedings in the USPTO for those patents or patent applications that are subject to the first-inventor-to-file law in the United States. We may be required to participate in such interference or derivation proceedings involving our issued patents and pending applications. We may be required to cease using the technology or to license rights from prevailing third parties as a result of an unfavorable outcome in an interference proceeding or derivation proceeding. A prevailing party in that case may not offer us a license on commercially acceptable terms.

We cannot prevent other companies from licensing most of the same intellectual properties that we have licensed or from otherwise duplicating our business model and operations.

Certain intellectual properties that we are using to develop TIL-based cancer therapy products were licensed to us by the NIH. The issued or pending patents that the NIH licensed to us are exclusive, and specific with respect to melanoma, breast, HPV-associated, bladder and lung cancers. No assurance can be given that the NIH has not previously licensed, or that the NIH hereafter will not license to other biotechnology companies some or all of the non-exclusive technologies available to us under the NIH License Agreement. In addition, one pending U.S. patent application in the NIH License Agreement is not owned solely by the NIH. No assurance can be given that NIH's co-owner of the certain pending U.S. patent application in the NIH License Agreement has not previously licensed, or that the co-owner thereafter will not license, to other biotechnology companies some or all of the technologies available to us. Co-ownership of these intellectual properties will create issues with respect to our ability to enforce the intellectual property rights in courts, and will create issues with respect to the accountability of one entity with respect to the other.

Since the NCI, Moffitt, M.D. Anderson, and others already use TIL therapy for the treatment of metastatic melanoma and other indications, their methods and data are also available to third parties, who may want to enter into our line of business and compete against us. Other than the Gen 2 manufacturing process, we currently do not own any exclusive rights on our entire product portfolio that could be used to prevent third parties from duplicating our business plan or from otherwise directly competing against us. While additional technologies that may be developed under our CRADA may be licensed to us on an exclusive basis, no assurance can be given that our existing exclusive rights and will be sufficient to prevent others from competing with us and developing substantially similar products.

The use of our technologies could potentially conflict with the rights of others.

Our potential competitors or others may have or acquire patent rights that they could enforce against us. If they do so, then we may be required to alter our products, pay licensing fees or cease activities. If our products conflict with patent rights of others, third parties could bring legal actions against us or our collaborators, licensees, suppliers or customers, claiming damages and seeking to enjoin manufacturing, use and marketing of the affected products. If these legal actions are successful, in addition to any potential liability for damages (including treble damages and attorneys' fees for willful infringement), we could be required to obtain a license to continue manufacturing, promoting the use or marketing the affected products. We may not prevail in any legal action and a required license under the patent may not be available on acceptable terms or at all.

We previously reported that we conducted an extensive freedom-to-operate, or FTO, analysis of the then current patent landscape with respect to our lead product candidate, and based on that analysis, that we believe that we have FTO for our lead TIL product candidate. Because patent applications do not publish for 18 months, and because the claims of patent families can change over time, no FTO analysis can be considered exhaustive. We are undertaking additional FTO analyses of our manufacturing processes, our lead TIL products, and contemplated future processes and products. However, the area of patent and other intellectual property rights in biotechnology remains an evolving area with many risks and uncertainties. As such, we expect our FTO analyses will be ongoing.

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

As is the case with other biopharmaceutical companies, our success is dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. While we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents.

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

We have limited intellectual property rights outside the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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

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

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

Risks Related to Our Securities

Our existing directors and executive officers hold a substantial amount of our common stock and may be able to influence significant corporate decisions.

As of December 31, 2017, our officers and directors beneficially owned approximately 11% of our outstanding common stock. These stockholders, if they act together, may be able to materially affect the outcome of matters presented to our stockholders, including the election of our directors and other corporate actions such as:

- A merger with or into another company;
- A sale of substantially all of our assets; and
- Amendments to our certificate of incorporation.

Additionally, the decisions of these stockholders may conflict with our interests or those of our other stockholders and the market price of our stock may be adversely affected by market volatility.

Our stock price may be volatile, and our stockholders' investment in our stock could decline in value.

The market price of our common stock is likely to be volatile and could fluctuate widely in response to many factors, including but not limited to:

- announcements of the results of clinical trials by us or our competitors;
- developments with respect to patents or proprietary rights;
- announcements of technological innovations by us or our competitors;
- announcements of new products or new contracts by us or our competitors;
- actual or anticipated variations in our operating results due to the level of development expenses and other factors;
- changes in financial estimates by securities analysts and whether our earnings meet or exceed such estimates;
- conditions and trends in the pharmaceutical, biotechnology and other industries;
- receipt, or lack of receipt, of funding in support of conducting our business;
- regulatory developments within, and outside of, the United States;
- litigation or arbitration;
- general volatility in the financial markets;
- general economic, political and market conditions and other factors; and
- the occurrence of any of the risks described in this Annual Report on Form 10-K.

You may experience future dilution as a result of future equity offerings or other equity issuances.

We will have to raise additional capital in the future. To raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may be lower than the current price per share of our common stock. In addition, investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in prior offerings. Any such issuance could result in substantial dilution to our existing stockholders.

Future sales of our common stock in the public market could cause our stock price to fall.

Our stock price could decline as a result of sales of a large number of shares of our common stock or the perception that these sales could occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

As of February 15, 2018, we had 89,016,751 shares of common stock outstanding. In addition, we had 20,736,737 shares of common stock equivalents that would increase the number of common stock outstanding if these instruments were exercised or converted, including stock options and restricted stock units to purchase common stock based on vesting requirements, warrants to purchase common stock and common stock issuable upon the conversion of preferred stock. The issuance and subsequent sale of the shares underlying these common stock equivalents could depress the trading price of our common stock.

In addition, in the future, we may issue additional shares of common stock or other equity or debt securities convertible into common stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. For example, in January 2018, we issued 15,000,000 shares of common stock in connection with an underwritten public offering. Such issuances could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

If securities or industry analysts do not publish research or reports about our company, or if they issue adverse or misleading opinions regarding us or our stock, our stock price and trading volume could decline.

Although we have research coverage by securities and industry analysts, if coverage is not maintained, the market price for our stock may be adversely affected. Our stock price also may decline if any analyst who covers us issues an adverse or erroneous opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet analysts' expectations. If one or more analysts cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline and possibly adversely affect our ability to engage in future financings

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results. As a result, we could become subject to sanctions or investigations by regulatory authorities and/or stockholder litigation, which could harm our business and have an adverse effect on our stock price.

As a public reporting company, we are subject to various regulatory requirements, including the Sarbanes-Oxley Act of 2002, which requires our management to assess and report on our internal controls over financial reporting. Nevertheless, in future years, our testing, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls that we would be required to remediate in a timely manner to be able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act each year. If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act each year, we could be subject to sanctions or investigations by the SEC, Nasdaq or other regulatory authorities which would require additional financial and management resources and could adversely affect the market price of our common stock. In addition, material weaknesses in our internal controls could result in a loss of investor confidence in our financial reports.

Our board could issue one or more additional series of preferred stock without stockholder approval with the effect of diluting existing stockholders and impairing their voting and other rights.

Our certificate of incorporation authorizes the issuance of up to 50,000,000 shares of “blank check” preferred stock (of which only 17,000 have been designated as the Series A Convertible Preferred Stock and 11,500,000 designated as Series B Convertible Preferred Stock) with designations, rights and preferences as may be determined from time to time by our board of directors. Our board is empowered, without stockholder approval, to issue one or more series of preferred stock with dividend, liquidation, conversion, voting or other rights which could dilute the interest of, or impair the voting power of, our common stockholders. The issuance of a series of preferred stock could be used as a method of discouraging, delaying or preventing a change in control. For example, it would be possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to effect a change in control of our company.

We do not anticipate paying cash dividends for the foreseeable future, and therefore investors should not buy our stock if they wish to receive cash dividends.

We have never declared or paid any cash dividends or distributions on our common stock. We currently intend to retain our future earnings to support operations and to finance expansion and, therefore, we do not anticipate paying any cash dividends on our common stock in the foreseeable future.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and amended and restated bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by you and other stockholders. For example, our board of directors will have the authority to issue up to 50,000,000 shares of preferred stock and to fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change in control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Our certificate of incorporation designates the state or federal courts located in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders’ ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our certificate of incorporation provides that, subject to limited exceptions, the state and federal courts located in the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our amended bylaws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our certificate of incorporation described above. This choice of forum provision may limit a stockholder’s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage such lawsuits against us and our directors, officers, and employees. Alternatively, if a court were to find these provisions of our certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

We may be subject to claims for rescission or damages in connection with certain sales of shares of our common stock in the open market.

In January 2014, the SEC declared effective a registration statement that we filed to cover the resale of shares issued and sold (or to be issued and sold) by certain selling stockholders. On March 11, 2016, that registration statement (and the prospectus contained therein) became ineligible for future use, and selling stockholders could no longer sell any shares of our common stock in open market transactions by means of that prospectus. We believe that certain stockholders did sell up to 128,500 shares of our common stock in open market transactions in May 2016 by means of the ineffective registration statement. Accordingly, those sales were not made in accordance with Sections 5 and 10(a)(3) of the Securities Act, and the purchasers of those shares may have rescission rights (if they still own the shares) or claims for damages (if they no longer own the shares). In addition, we also may have indemnification obligations to the selling stockholders. The amount of any such liability is uncertain.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

San Carlos Lease

Since October 2016, our corporate headquarters consisted of 8,733 square feet of space that we lease in San Carlos, California. The corporate headquarters lease is for a term of 54 months and will expire in April 2021. Monthly lease payments are approximately \$38,000.

In April 2017, we entered into a sublease agreement with Teradata US, Inc., pursuant to which we agreed to sublease office space located adjacent to our corporate headquarters in San Carlos, California for approximately \$26,000 per month. The space consists of approximately 11,449 rentable square feet and will expire on October 31, 2018.

New York Lease

We leased office space in New York for a monthly rental of approximately \$18,000 a month from January 2017 through July 2017. In June 2017, we entered into an agreement to lease office space in New York, New York from August 1, 2017 to July 31, 2018 for approximately \$9,000 a month.

Tampa Lease

Our research and development facilities consist of 8,673 square feet in a facility located at the University of South Florida Research Park in Tampa, Florida. The lease expires in November 2019 and rent payments are approximately \$20,000 per month.

We believe that our existing facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

Class Action Lawsuit and Derivative Lawsuit. On April 10, 2017, the SEC announced settlements with us and with other public companies and unrelated parties in the *In the Matter of Certain Stock Promotion* investigation. Our settlement with the SEC is consistent with our previous disclosures (including in our Annual Report on Form 10-K that we filed with the SEC on March 9, 2017). On April 14, 2017, a purported shareholder filed a complaint seeking class action status in the United States District Court, Northern District of California for violations of the federal securities laws (*Leonard DeSilvio v. Lion Biotechnologies, Inc., et al.*, case no. 3:17cv2086) against our company and three of our former officers and directors. On April 19, 2017, a second class action complaint (*Amra Kuc vs. Lion Biotechnologies, Inc., et al.*, case no. 3:17cv2086) was filed in the same court. Both complaints allege, among other things, that the defendants violated the federal securities laws by making materially false and misleading statements, or by failing to make certain disclosures, regarding the actions taken by Manish Singh, our former CEO, and our former investor relations firm that were the subject of the *In the Matter of Certain Stock Promotions* SEC investigation. On July 20, 2017, the plaintiff in the *Kuc* case filed a notice to voluntarily dismiss that case. The court entered an order dismissing the *Kuc* complaint on July 21, 2017. On July 26, 2017, the court appointed a movant as lead plaintiff. On September 8, 2017, the lead plaintiff filed an amended complaint (*Jay Rabkin v. Lion Biotechnologies, Inc., et al.*, case no. 3:17cv0286) seeking class action status that alleges, among other things, that the defendants violated the federal securities laws by making materially false and misleading statements, or by failing to make certain disclosures, regarding the actions taken by Manish Singh and our former investor relations firm that were the subject of the *In the Matter of Certain Stock Promotions* SEC investigation. On October 6, 2017, the court entered an order setting a schedule for the case, which includes a briefing schedule for motions to dismiss and a hearing date of December 22, 2017, which hearing was subsequently rescheduled by the court for January 5, 2018. On January 4, 2018, the court entered an order vacating and deeming the briefing on motions to dismiss submitted without oral argument. On February 5, 2018, court entered an order dismissing two of Plaintiff's six claims with leave to amend.

On December 15, 2017, a purported shareholder derivative complaint, *Kevin Fong v. Manish Singh, et al.* (case no. 17:1806), was filed against us, as nominal defendant, and certain of our current and former officers and directors, and others, as defendants, in the U.S. District Court for the District of Delaware. The complaint alleges breaches of fiduciary duties, unjust enrichment, and violations of Section 14(a) of the Securities Exchange Act of 1934 and Rule 14a-9 promulgated thereunder arising from the Securities and Exchange Commission's investigation in the *In the Matter of Certain Stock Promotions* matter and our April 10, 2017 settlement thereof, and seeks unspecified damages on behalf of our company and injunctive relief.

We intend to vigorously defend against the foregoing complaints. Based on the very early stage of the litigation, it is not possible to estimate the amount or range of possible loss that might result from an adverse judgment or a settlement of these matters.

Solomon Capital, LLC. On April 8, 2016, a lawsuit titled *Solomon Capital, LLC, Solomon Capital 401(K) Trust, Solomon Sharbat and Shelhav Raff v. Lion Biotechnologies, Inc.* was filed by Solomon Capital, LLC, Solomon Capital 401(k) Trust, Solomon Sharbat and Shelhav Raff against us in the Supreme Court of the State of New York, County of New York (index no. 651881/2016). The plaintiffs allege that, between June and November 2012 they provided to us \$0.1 million and that they advanced and paid on our behalf an additional \$0.2 million. The complaint further alleges that we agreed to (i) provide them with promissory notes totaling \$0.2 million, plus interest, (ii) issue a total of 111,425 shares to the plaintiffs (before the 1-for-100 reverse split of our common stock effected in September 2013), and (iii) allow the plaintiffs to convert the foregoing funds into our securities in the next transaction. The plaintiffs allege that they should have been able to convert their advances and payments into shares of our common stock in the restructuring that was effected in May 2013. Based on the foregoing, the plaintiffs allege causes for breach of contract and unjust enrichment and demand judgment against us in an unspecified amount exceeding \$1.5 million, plus interest and attorneys' fees.

On June 3, 2016, we filed an answer and counterclaims in the lawsuit. In its counterclaims, we allege that the plaintiffs misrepresented their qualifications to assist us in fundraising and that they failed to disclose that they were under investigation for securities laws violations. We are seeking damages in an amount exceeding \$0.5 million and an order rescinding any and all agreements that the plaintiffs contend entitled them to obtain stock in our company.

On April 19, 2017, the Court granted plaintiffs' counsel's motion to withdraw from the case. On May 25, 2017, the plaintiffs filed a notice that they had hired new counsel. On June 7, 2017, the judge presiding over the case recused herself because of a conflict of interest arising from her relationship with plaintiffs' new attorneys. The case has been assigned to a new judge, and briefing on a motion to dismiss has occurred, with oral argument on the motion to dismiss scheduled for April 20, 2018.

We intend to vigorously defend the complaint and pursue our counterclaims.

Litigation Involving Dr. Steven Fischkoff. On June 13, 2017, in an action titled *Steven Fischkoff v. Lion Biotechnologies, Inc. and Maria Fardis, Dr. Steven Fischkoff*, our former Vice President and Chief Medical Officer, filed a lawsuit against us in the Supreme Court of the State of New York, County of New York. Dr. Fischkoff was dismissed by us on March 28, 2017. Dr. Fischkoff was terminated "for cause" as that term is defined in his employment agreement. In his complaint, Dr. Fischkoff alleges breaches of his employment agreement and violation of New York Labor Law for failure to pay monies purportedly owed to him, and seeks to recover amounts including severance pay and retention bonus (totaling \$0.3 million), a prorated incentive bonus, and amounts relating to unvested options to 150,000 shares of our common stock, together with prejudgment interest, costs, expenses and attorneys' fees. On July 5, 2017, we filed a removal petition and removed the lawsuit to the United States District Court for the Southern District of New York, where the case has been assigned case no. 17-cv-05041. On July 14, 2017, we filed a partial answer and counterclaims against Dr. Fischkoff, denying his allegations, and alleging breach of contract and related claims, breach of fiduciary duty, and state and federal trade secret misappropriation and related claims, and sought a temporary restraining order and preliminary injunction against Dr. Fischkoff. On July 18, 2017, the court issued a temporary restraining order against Dr. Fischkoff requiring him to return our company materials, prohibiting him from disclosing or using our company materials, and granting expedited discovery, which is currently proceeding.

We intend to vigorously defend against Dr. Fischkoff's lawsuit and pursue our counterclaims. Based on the very early stage of the litigation, it is not possible to estimate the amount or range of (i) a possible loss that might result from an adverse judgment or settlement of this action, or (ii) the potential recovery that might result from a favorable judgment or a settlement of this action.

Other Matters. During the second quarter of 2016, warrants representing 128,500 shares were exercised. The 128,500 shares of common stock had previously been registered for re-sale. However, we believe that these 128,500 warrant shares were sold by the holders in open market transactions in May 2016 at a time when the registration statement was ineffective. Accordingly, those sales were not made in accordance with Sections 5 and 10(a)(3) of the Securities Act, and the purchasers of those shares may have rescission rights (if they still own the shares) or claims for damages (if they no longer own the shares). The amount of any such liability is uncertain and as such, an accrual for any potential loss has not been made. We believe that any claims brought against it would not result in a material impact to our financial position or results of operations. We have not accrued a loss for a potential claim associated with this matter as we are unable to estimate any at this time.

Other

In addition to the items noted above, we may be involved, from time to time, in legal proceedings and claims arising in the ordinary course of our business. Such matters are subject to many uncertainties and outcomes are not predictable with assurance. We accrue amounts, to the extent they can be reasonably estimated, that we believe are adequate to address any liabilities related to legal proceedings and other loss contingencies that we believe will result in a probable loss. While there can be no assurances as to the ultimate outcome of any legal proceeding or other loss contingency involving us, management does not believe any pending matter will be resolved in a manner that would have a material adverse effect on our financial position, results of operations or cash flows. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

Not Applicable.

PART II**Item 5. Market for Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.**

Since June 28, 2017, our common stock has been listed for trading on the Nasdaq Global Market under the symbol "IOVA". From February 26, 2015 through June 27, 2017, our common stock was listed for trading on the Nasdaq Global Market under the symbol "LBIO".

Fiscal Year Ended December 31, 2017	High	Low
First quarter	\$ 8.30	\$ 6.60
Second quarter	7.50	4.90
Third quarter	8.60	4.45
Fourth quarter	9.54	6.60

Fiscal Year Ended December 31, 2016	High	Low
First quarter	\$ 7.54	\$ 4.54
Second quarter	8.65	4.90
Third quarter	9.29	7.78
Fourth quarter	8.07	5.80

Stockholders

As of December 31, 2017, there were approximately 51 holders of record of our common stock. In addition, we had two holders of record who owned shares of our Series A Convertible Preferred Stock and 10 holders of record who owned shares of our Series B Convertible Preferred Stock.

Dividends

We have never declared or paid any cash dividends on our common stock or any other securities. We anticipate that we will retain all available funds and any future earnings, if any, for use in the operation of our business and do not anticipate paying cash dividends in the foreseeable future. Payment of future cash dividends, if any, will be at the discretion of the board of directors after considering various factors, including our financial condition, operating results, current and anticipated cash needs.

Under the terms of our Series A Convertible Preferred Stock, we may not declare, pay or set aside any dividends on shares of any class or series of capital stock (other than dividends on shares of common stock payable in shares of common stock) unless the holders of our Series A Convertible Preferred Stock first receive, or simultaneously receive, an equal dividend on each outstanding share of Series A Convertible Preferred Stock.

Under the terms of our Series B Convertible Preferred Stock, holders shall be entitled to receive dividends on shares equal (on an as-if-converted-to-Common-Stock basis) to and in the same form as dividends (other than dividends in the form of common stock) actually paid on shares of our Series A Convertible Preferred Stock, common stock or other junior securities when, as and if such dividends (other than dividends in the form of common stock) are paid on shares of our Series A Convertible Preferred Stock, common stock or other junior securities. No other dividends shall be paid on shares of Series B Convertible Preferred Stock, and we may not pay dividends (other than dividends in the form of common stock) on shares of our Series A Convertible Preferred Stock, common stock or other junior securities unless it simultaneously complies with the previous sentence.

Unregistered Sales of Equity Securities

None.

Repurchases of Common Stock

There were no share repurchases during the three months ended December 31, 2017.

Stock Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since December 31, 2013, to two indices: the Russell 3000 and the NASDAQ Biotechnology Index. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.



Equity Compensation Plan Information

Information regarding our equity compensation plans is incorporated by reference from the information in our Proxy Statement for our 2018 Annual Meeting of Stockholders, which we will file with the SEC within 120 days after the end of the fiscal year to which this Annual Report on Form 10-K relates.

Item 6. Selected Financial Data (in thousands, except per share information)

The statements of operations data for the years ended December 31, 2017, 2016 and 2015 and the balance sheet data as of December 31, 2017 and 2016 have been derived from our audited financial statements included elsewhere in this Annual Report on Form 10-K. The statements of operations data for the years ended December 31, 2014 and 2013 and the balance sheet data as of December 31, 2015, 2014 and 2013 have been derived from our audited financial statements not included in this Annual Report on Form 10-K. The following selected financial data should be read in conjunction with our "Management's Discussion and Analysis of Financial Condition and Results of Operations" and financial statements and related notes to those statements included elsewhere in this Annual Report on Form 10-K.

	Years Ended December 31,				
	2017	2016	2015	2014	2013
	(in thousands)				
Net revenue	\$ -	\$ -	\$ -	\$ -	\$ -
Operating expenses:					
Research and development	71,615	26,941	15,470	3,849	2,154
General and administrative	21,262	26,698	12,390	8,192	3,831
Cost of Lion transaction - related party	-	-	-	-	16,656
Other income (loss)	813	745	200	6	(2,741)
Net loss	\$ (92,064)	\$ (52,894)	\$ (27,660)	\$ (12,035)	\$ (25,382)
Net loss Per Common Share	\$ (1.41)	\$ (1.85)	\$ (0.62)	\$ (0.48)	\$ (3.47)
	As of December 31,				
	2017	2016	2015	2014	2013
Total assets	\$ 155,373	\$ 171,886	\$ 105,653	\$ 46,507	\$ 19,877
Total liabilities	\$ 9,892	\$ 4,968	\$ 1,630	\$ 1,662	\$ 2,270
Total stockholders' equity	\$ 145,481	\$ 166,918	\$ 104,023	\$ 44,845	\$ 17,604

See "Management's Discussion and Analysis of Financial Condition and Results of Operations" below, and the financial statements and accompanying notes and previously filed Annual Reports on Form 10-K for further information regarding our results and financial position for periods reported herein and for known factors that will impact comparability of future results.

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

The following discussion and analysis of our results of operations and financial condition should be read in conjunction with our financial statements and the notes to those financial statements that are included elsewhere in this report. Our discussion includes forward-looking statements based upon current expectations that involve risks and uncertainties, such as our plans, objectives, expectations and intentions. Actual results and the timing of events could differ materially from those anticipated in these forward-looking statements as a result of a number of factors, including those set forth under the “Business” section and elsewhere in this report. We use words such as “anticipate,” “estimate,” “plan,” “project,” “continuing,” “ongoing,” “expect,” “believe,” “intend,” “may,” “will,” “should,” “could,” and similar expressions to identify forward-looking statements. All forward-looking statements included in this report are based on information available to us on the date hereof and, except as required by law, we assume no obligation to update any such forward-looking statements.

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of novel cancer immunotherapy products designed to harness the power of a patient’s own immune system to eradicate cancer cells. Our lead product candidate, LN-144 for metastatic melanoma, is an autologous adoptive cell therapy utilizing tumor-infiltrating lymphocytes, or TIL, which are T cells derived from patients’ tumors. TIL therapy is a platform technology that has already been studied for the treatment of metastatic melanoma and metastatic cervical cancer by the National Cancer Institute, or NCI. We are investigating the effectiveness and safety of TIL therapy for the treatment of metastatic melanoma, squamous cell carcinoma of the head and neck, cervical carcinoma, and metastatic non-small cell lung cancer, as well as other oncology indications.

We have an on-going Phase 2 clinical trial, C-144-01, of our lead product candidate, LN-144, TIL for the treatment of metastatic melanoma. This multicenter study is enrolling patients with melanoma whose disease has progressed following treatment with at least one systemic therapy, including anti-PD-1 and if BRAF mutated, a BRAF inhibitor. The trial is currently active at fourteen U.S. sites. We anticipate initiating patient dosing in Europe during the first half of 2018. The purpose of the study is to evaluate the efficacy and safety of our autologous LN-144. We have decided to use our Gen 2 manufacturing process for all ongoing Phase 2 trials and in all future TIL clinical development in trials sponsored by us, and as a result, cohort 1 of the C-144-01 melanoma study is closed to enrollment, and new patients are being enrolled in cohort 2.

In addition to our ongoing trial in metastatic melanoma, we have initiated clinical trials of LN-145, TIL therapy in cervical, head and neck cancers, and non-small cell lung cancer, or NSCLC. C-145-03 is a Phase 2, multicenter study that will enroll up to 47 patients and will assess the safety and efficacy of LN-145 for the treatment of patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck. The trial will therefore continue to enroll patients to the full sample size of 47 per protocol. The study is open for enrollment of patients in the United States and we anticipate the start of enrollment of patients in Europe in the first half of 2018. In January 2018, we reported preliminary data from C-145-04 which showed that of the two patients that are currently evaluable, one treated with LN-145 had a confirmed PR and one patient had stable disease. We have amended the protocol so that newly-enrolled patients in both trials can be treated using TIL produced from our Gen 2 manufacturing process.

We are initiating our clinical development around NSCLC, with two studies. One of the studies is an investigator-sponsored Phase 2 study to be conducted at H. Lee Moffitt Cancer Center and Research Institute, or Moffitt, and the other will be sponsored by our company. Patient enrollment has begun in the investigator-sponsored study in collaboration with researchers at Moffitt, Stand Up To Cancer, and others. Patients who are treatment naïve to prior anti-PD-1/ PD-L1 with stage IV or recurrent NSCLC will be enrolled in a study combining TIL and nivolumab. The Iovance-sponsored Phase 2 study in NSCLC patients who are PD-1 and PD-L1 treatment naïve, will initiate in the first half of 2018, in collaboration with MedImmune, the global biologics research and development arm of AstraZeneca. The study with MedImmune will allow for enrollment with LN-145 alone or in combination with durvalumab. In the future, we plan to initiate additional indications alone or through collaborations.

We are also initiating clinical trials as part of our strategic alliance with The University of Texas M.D. Anderson Cancer Center, or M.D. Anderson, in multiple solid tumor cancers using two different TIL manufacturing processes, including our Gen 2 manufacturing process. These multi-arm clinical trials will evaluate the safety and efficacy of TIL therapy in ovarian cancer, various sarcomas, and pancreatic cancer, and are expected to begin enrollment in 2018.

Our current product candidate pipeline is summarized in the graphic below:

INDICATION	REGIMEN	N	PARTNER	PRECLINICAL	PHASE I	PHASE 2
Melanoma	TIL LN-144	60	—			Enrolling
Cervical Cancer	TIL LN-145	47	—			Enrolling
Head & Neck Cancer	TIL LN-145	47	—			Enrolling
Non-Small Cell Lung Cancer	TIL LN-145 vs TIL LN-145 + durvalumab	24	 MedImmune			Phase 2 trials to initiate in 2018

Our current collaboration pipeline is summarized in the graphic below:



For the studies listed in our collaboration pipeline table, the partner listed above is the sponsor of the clinical trial. Such partner may not use our Gen 2 manufacturing process, and/or the therapeutic dosing may differ from our clinical trials. As a result, such partner data may not be representative of our data.

We raised approximately \$53.7 million in net proceeds, after deducting underwriting discounts and offering expenses, through a public offering that closed in September 2017. In January 2018, we closed an underwritten public offering of 15,000,000 shares of our common stock at a public offering price of \$11.50 per share, before underwriting discounts. The shares sold at closing included 1,956,521 shares issued upon the exercise in full by the underwriter of its option to purchase additional shares at the public offering price less the underwriting discount. The gross proceeds from the offering, before deducting the underwriting discounts and commissions and other estimated offering expenses payable by us, are \$172.5 million with estimated net proceeds to us of approximately \$161.7 million.

Financial Overview

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. As a clinical stage company that is currently engaged in the development of novel cancer immunotherapy products, we have not yet generated any revenues from our biotechnology business or otherwise since our formation. Our ability to generate revenues in the future will depend on our ability to complete the development of our product candidates and to obtain regulatory approval for them. Our major sources of funding to date have been proceeds from various public and private offerings of our equity securities (both common stock and preferred stock), option and warrant exercises, and interest income.

Results of Operations for the Years Ended December 31, 2017 and 2016

Revenues

We did not generate any revenues during the years ended December 31, 2017 and 2016, respectively, and we do not anticipate that we will generate any revenues during 2018 from the sale or licensing of our product candidates.

Costs and expenses

Research and Development Expense (in thousands)

	Years Ended December 31,		Increase (Decrease)	
	2017	2016	\$	%
Research and development	\$ 71,615	\$ 26,941	44,674	166%
Stock-based compensation expense included in research and development expense	5,270	3,267	2,003	61%

Research and development expense for the year ended December 31, 2017 increased by \$44.7 million, or 166%, compared to the year ended December 31, 2016, inclusive of stock-based compensation. The increase was primarily attributable to a \$22.1 million increase in drug manufacturing costs due to an increase in the number of manufacturing facilities, development and technology transfer related to the Gen 2 manufacturing process, a \$9.2 million increase in costs related to our clinical trials as a result of the initiation of two new clinical trials in 2017 along with an increase in the number of sites and patients enrolled in both existing and new clinical trials, a \$6.2 million increase in payroll and related expenses primarily due to an increase in headcount, an increase of \$2.3 million related to consultants and outside services contracted with to perform research and development activities on our behalf, an increase of \$1.7 million in lab consumables and tumors, and a \$2.0 million increase in non-cash stock-based compensation expense in the year ended December 31, 2017 as compared to the year ended December 31, 2016.

We expect our research and development expenses to increase over the next several years as we continue to conduct our clinical trial for our products and as we increase our research and development efforts in other cancer indications. However, it is difficult to determine with certainty the duration and completion costs of our current or future preclinical programs and clinical trials of our product candidates.

The duration, costs and timing of our clinical trials and development of our product candidates will depend on a number of factors that include, but are not limited to, the number of patients that enroll in the trial, per patient trial costs, number of sites included in the trial, discontinuation rates of patients, duration of patient follow-up, efficacy and safety profile of the product candidate, and the length of time required to enroll eligible patients. Additionally, the probability of success for our product candidate will depend on a number of factors, including competition, manufacturing capability and cost efficiency, and commercial viability.

General and Administrative Expense (in thousands)

	Years Ended December 31,		Increase (Decrease)	
	2017	2016	\$	%
General and administrative	\$ 21,262	\$ 26,698	(5,436)	-20%
Stock-based compensation expense included in general and administrative	6,698	15,637	(8,939)	-57%

General and administrative expense for the year ended December 31, 2017 decreased by \$5.4 million, or 20%, compared to the year ended December 31, 2016, inclusive of stock-based compensation. The change was primarily attributable to a \$8.9 million decrease in stock-based compensation expense, driven by expense incurred in connection with the separation of our former Chief Executive Officer and Chief Financial Officer from our company in June and August of 2016, respectively, offset by a \$2.4 million increase in legal fees.

General and administrative expenses include personnel costs for our employees engaged in general and administrative activities, legal fees, audit and tax fees, consultants and professional services, and general corporate expenses. We anticipate general and administrative expenses will increase in 2018 as we continue to support our expanded research and development efforts.

Interest Income (in thousands)

	Years Ended December 31,		Increase (Decrease)	
	2017	2016	\$	%
Interest Income	\$ 813	\$ 745	68	9%

Interest income results from our interest-bearing cash and investment balances. Interest income for the year ended December 31, 2017 increased due to the higher average cash balances as a result of the proceeds received from our equity financings in September 2017 and June 2016, and higher interest rates in 2017.

Results of Operations for the Years Ended December 31, 2016 and 2015

Revenues

We did not generate any revenues during the years ended December 31, 2016 and 2015, respectively.

Costs and expenses

Research and Development Expense (in thousands)

	Years Ended December 31,		Increase (Decrease)	
	2016	2015	\$	%
Research and development	\$ 26,941	\$ 15,470	11,471	74%
Stock-based compensation expense included in research and development expense	3,267	2,248	1,019	45%

Research and development expense for the year ended December 31, 2016 increased by \$11.5 million, or 74%, compared to the year ended December 31, 2015, inclusive of stock-based compensation. The increase was primarily attributable to a \$3.2 million increase in drug manufacturing costs, expenses incurred under the PolyBioCept agreement in the amount of \$2.7 million, a \$2.4 million increase in payroll and related expenses primarily due to an increase in headcount, an increase of \$1.3 million related to consultants contracted with to perform research and development activities on our behalf, a \$0.9 million increase in costs related to our clinical trials, and a \$1.0 million increase in non-cash stock-based compensation expense.

General and Administrative Expense (in thousands)

	Years Ended December 31,		Increase (Decrease)	
	2016	2015	\$	%
General and administrative	\$ 26,698	\$ 12,390	14,308	115%
Stock-based compensation expense included in general and administrative	15,637	6,275	9,362	149%

General and administrative expense for the year ended December 31, 2016 increased by \$14.3 million, or 115%, compared to the year ended December 31, 2015, inclusive of stock-based compensation. The increase was primarily attributable to a \$9.4 million increase in stock-based compensation expense primarily due to the accelerated vesting of equity awards upon the termination of employment of our former Chief Executive Officer and our former Chief Financial Officer, and the increase in the number of our employees, a \$1.5 million increase in payroll and related expenses primarily due to the increase in headcount, a \$0.9 million increase due to severance payments to our former Chief Executive Officer and our former Chief Financial Officer, and a \$2.4 million increase in consulting and legal-related expenses.

Interest Income (in thousands)

	Years Ended December 31,		Increase (Decrease)	
	2016	2015	\$	%
Interest Income	\$ 745	\$ 200	545	273%

Interest income for the year ended December 31, 2016 increased by \$0.5 million, or 273%, compared to the year ended December 31, 2015 due to the higher cash balances in 2016 as a result of the proceeds received from our equity financings in 2015 and June 2016.

Net Loss

We had a net loss of \$92.1 million, \$52.9 million and \$27.7 million for the years ended December 31, 2017, 2016 and 2015, respectively. The increase in our net losses in 2017, as compared to 2016, was due to the continued expansion of our research and development activities, increased clinical trials and manufacturing activities, and the overall growth of our corporate infrastructure. We anticipate that we will continue to incur net losses in the future as we further invest in our research and development activities, including our clinical development. The increase in our net loss during 2016, as compared to 2015, was also due to the continued expansion of our research and development activities, increased clinical trials and manufacturing activities, and the overall growth of our corporate infrastructure. In addition, our general and administrative expenses increased in 2016 due to the increase in headcount and the acceleration of stock-based equity awards related to the termination of certain executives.

Liquidity and Capital Resources

We have incurred losses and generated negative cash flows from operations since inception. We expect to continue to incur significant losses in 2018 and may incur significant losses and negative cash flows from operations for the foreseeable future. We have funded our operations primarily through issuance of equity securities.

On December 28, 2017, we filed a shelf registration statement with the Securities and Exchange Commission, or SEC, for the issuance of common stock, preferred stock, warrants, rights, debt securities and units up to an aggregate amount of \$250 million, of which \$42.5 million consists of unsold securities previously registered under the 2016 Shelf Registration Statement (see below), and which we refer to as the 2017 Shelf Registration Statement. The 2017 Registration Statement was declared effective on January 19, 2018. We completed an offering of common stock in January 2018 utilizing the 2017 Shelf Registration Statement (see below). In the future, we may periodically offer one or more of these securities in amounts, prices and terms to be announced when and if the securities are offered. At the time, any of the securities covered by the 2017 Shelf Registration Statement are offered for sale, a prospectus supplement will be prepared and filed with the SEC containing specific information about the terms of any such offering.

On December 23, 2016, we filed a shelf registration statement with the SEC for the issuance of common stock, preferred stock, warrants, rights, debt securities and units up to an aggregate amount of \$100 million, which we refer to as the 2016 Shelf Registration Statement. On January 11, 2017, the 2016 Shelf Registration Statement was declared effective by the SEC. We completed an offering of common stock in September 2017 utilizing the 2016 Shelf Registration Statement (see below).

In September 2017, we sold 8,846,154 shares of our common stock in an underwritten public offering at a public offering price of \$6.50 per share, under the 2016 Shelf Registration Statement. We received gross proceeds of approximately \$57.5 million and net proceeds of approximately \$53.7 million, after deducting underwriting discounts and offering expenses.

In January 2018, we announced the closing of our public offering of 15,000,000 shares of our common stock at a public offering price of \$11.50 per share, before underwriting discounts, which included 1,956,521 shares issued upon the exercise in full by the underwriter of its option to purchase additional shares at the public offering price less the underwriting discount, under the 2017 Shelf Registration Statement. The gross proceeds from the offering, before deducting the underwriting discounts and commissions and other estimated offering expenses payable by us, are \$172.5 million with estimated net proceeds to us of approximately \$161.7 million.

We are currently engaged in the development of therapeutics to fight cancer. We do not have any commercial products and have not yet generated any revenues from our biopharmaceutical business. We currently do not anticipate that we will generate any revenues during 2018 from the sale or licensing of any products. We have incurred a net loss of \$92.1 million for the year ended December 31, 2017 and used \$78.7 million of cash in our operating activities for the year ended December 31, 2017. As of December 31, 2017, we had \$145.4 million of cash and cash equivalents, stockholders' equity of \$145.5 million and had working capital of \$139.4 million.

We expect to further increase our research and development activities, which will increase the amount of cash we will use during 2018 and beyond. Specifically, we expect increased spending on clinical trials, research and development activities, higher payroll expenses as we increase our professional and scientific staff and continue our expansion of manufacturing activities. Based on the funds we have available as of the date of the filing of this Annual Report on Form 10-K, which includes the net proceeds of approximately \$161.7 million raised in connection with our January 2018 public offering, we believe that we have sufficient capital to fund our anticipated operating expenses for at least 24 months from the date of filing this report.

Cash Flows

Cash Flows from Operating, Investing and Financing Activities (in thousands):

	Years Ended December 31,		
	2017	2016	2015
Net cash (used in) provided by :			
Operating activities	\$ (78,709)	\$ (32,668)	\$ (18,381)
Investing activities	58,677	8,894	(71,208)
Financing activities	58,688	96,904	78,267
Net increase (decrease) in cash and cash equivalents	<u>\$ 38,656</u>	<u>\$ 73,130</u>	<u>\$ (11,322)</u>

Operating Activities

Net cash used in operating activities of \$78.7 million for the year ended December 31, 2017, resulted primarily from our net loss of \$92.1 million, adjusted by a non-cash charge of \$12.0 million for stock-based compensation expense, a \$4.6 million increase in accrued liabilities primarily due to increases in activities by our company, a \$3.6 million increase in long-term assets and a \$0.9 million increase in prepaids, both due to timing of certain upfront payments associated with our research agreements, and \$1.0 million in non-cash depreciation expense.

Net cash used in operating activities of \$32.7 million for the year ended December 31, 2016, resulted primarily from our net loss of \$52.9 million, adjusted by \$18.9 million for stock-based compensation expense, a \$2.8 million increase in prepaids due to timing of certain upfront payments associated with our research agreements, and a \$3.4 million increase in accrued liabilities primarily due to increases in activities by our company.

Net cash used in operating activities of \$18.4 million for the year ended December 31, 2015, resulted primarily from our net loss of \$27.7 million, adjusted by \$8.5 million for stock-based compensation expense.

Investing Activities

Net cash provided by investing activities of \$58.7 million for the year ended December 31, 2017, consisted primarily of \$59.7 million of proceeds from the maturities of short-term investments, offset by \$1.0 million used for the purchase of property and equipment.

Net cash provided by investing activities of \$8.9 million for the year ended December 31, 2016, consisted primarily of \$1.5 million used for the purchase of property and equipment, and \$110.2 million used for purchases of short-term investments, offset by \$120.7 million of proceeds from the maturities of short-term investments.

Net cash used in investing activities of \$71.2 million for the year ended December 31, 2015, consisted primarily of \$1.1 million used for the purchase of property and equipment, and \$140.7 million used for purchases of short-term investments, offset by \$70.6 million of proceeds from the maturities of short-term investments.

Financing Activities

Net cash provided by financing activities of \$58.7 million for the year ended December 31, 2017, consisted primarily of net proceeds of \$53.7 million from the issuance of shares in a private offering at \$6.50 per share after deducting expenses of the offering, \$5.6 million from the exercise of options, \$0.7 million of proceeds exercise of warrants, offset by \$1.3 million in connection with tax payments made by our company in connection with vested restricted stock.

Net cash provided by financing activities of \$96.9 million for the year ended December 31, 2016, consisted primarily of net proceeds of \$95.7 million from the issuance of shares in a private offering at \$4.75 per share after deducting expenses of the offering, \$1.2 million of proceeds exercise of warrants, \$0.6 million from the exercise of options offset by \$0.6 million in connection with tax payments made by our company in connection with vested restricted stock awards.

Net cash provided by financing activities of \$78.3 million for the year ended December 31, 2015, consisted primarily of net proceeds of \$68.3 million from the issuance of shares in a private offering at \$8.00 per share after deducting expenses of the offering, \$9.7 million of proceeds exercise of warrants and \$0.3 million from the exercise of options.

Significant Accounting Policies and Recent Accounting Standards

See Note 2 of the financial statements for a discussion of our significant accounting policies, including the discussion of recently issued and adopted accounting standards.

Contractual Obligations

We acquire assets still in development and enter into research and development arrangements with third parties that often require milestone and royalty payments to the third-party contingent upon the occurrence of certain future events linked to the success of the asset in development. Milestone payments may be required, contingent upon the successful achievement of an important point in the development life-cycle of the pharmaceutical product (e.g., approval of the product for marketing by a regulatory agency). If required by the arrangement, we may have to make royalty payments based upon a percentage of the sales of the pharmaceutical product in the event that regulatory approval for marketing is obtained. Because of the contingent nature of these milestone payments, they are not included in the table of contractual obligations.

These arrangements may be material individually, and in the event that milestones for multiple products covered by these arrangements were reached in the same period, the aggregate charge to expense could be material to the results of operations in any one period. In addition, these arrangements often give us the discretion to unilaterally terminate development of the product, which would allow us to avoid making the contingent payments.

Our current non-cancelable contractual obligations as of December 31, 2017 that will require future cash payments are as follows (in thousands):

Contractual Obligations	Payments due by period						
	Total	2018	2019	2020	2021	2022	Thereafter
Operating lease obligations	\$ 2,387	\$ 1,023	\$ 700	\$ 495	\$ 169	\$ -	\$ -
Total	\$ 2,387	\$ 1,023	\$ 700	\$ 495	\$ 169	\$ -	\$ -

Off-Balance Sheet Arrangements

At December 31, 2017, we had no obligations that would require disclosure as off-balance sheet arrangements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

Our exposure to interest rate risk relates primarily to our investment portfolio. The fair market value of fixed rate securities may be adversely impacted due to fluctuations in interest rates, while floating rate securities may produce less income than expected if interest rates fall. Due in part to these factors, our future investment income may fall short of expectations due to changes in interest rates or we may suffer losses in principal if forced to sell securities which have declined in market value due to changes in interest rates. The primary objective of our investment activities is to preserve principal while at the same time improving yields without significantly increasing risk. To achieve this objective, our cash and cash equivalents are primarily held in cash deposits and money market funds. As of December 31, 2017, we did not hold any short-term investments and we believe we do not have any material exposure to changes in the fair value of our investment portfolio as a result of changes in interest rates. Assuming a hypothetical change in interest rates of one percentage point, change in the fair value of our total investment portfolio as of December 31, 2017 would not have had a material effect on our results of operations or cash flows for that period.

Inflation Risk

Inflation has not had a material effect on our business, financial condition or results of operations during the years ended December 31, 2017, 2016 or 2015.

Item 8. Financial Statements and Supplementary Data

Financial Statements are referred to in Item 15, listed in the Index to Financial Statements as a part of this Annual Report on Form 10-K, and are incorporated herein by this reference.

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

None.

Item 9A. Controls and Procedures

(a) Evaluation of Disclosure Controls and Procedures:

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As of the end of the period covered by this Annual Report on Form 10-K, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

(b) Management's Annual Report on Internal Control Over Financial Reporting:

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2017 based on the framework in *Internal Control—Integrated Framework 2013* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on that evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2017.

The independent registered public accounting firm, Marcum LLP, has issued an attestation report on our internal control over financial reporting. The report on the audit of internal control over financial reporting is included in this Annual Report on Form 10-K.

(c) Changes in Internal Control Over Financial Reporting:

There has been no change in our internal control over financial reporting during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K because we will file a definitive Proxy Statement for the Annual Meeting of Stockholders pursuant to Regulation 14A of the Securities Exchange Act of 1934 (the Proxy Statement), not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and the applicable information included in the Proxy Statement is incorporated herein by reference.

Item 10. Directors, Executive Officers, and Corporate Governance

Information required by this Item 10 will be presented in the Proxy Statement “Election of Directors,” “Management Executive Officers,” “Section 16(a) Beneficial Ownership Reporting Compliance” and “Board of Directors and Corporate Governance,” and is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this Item is incorporated herein by reference to the sections entitled “Executive Compensation,” “Executive Compensation—Compensation Discussion and Analysis” and “Directors’ Compensation” in the Proxy Statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item is incorporated herein by reference to the sections entitled “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in the Proxy Statement.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item is incorporated herein by reference to the section entitled “Certain Relationships and Related Transactions” in the Proxy Statement.

Item 14. Principal Accountant’s Fees and Services

Information required by this Item is incorporated herein by reference to the section of the Proxy Statement entitled “Principal Accountant Fees and Services.”

PART IV

Item 15. Exhibits, Financial Statements Schedules

The Company’s financial statements and related notes thereto are listed and included in this Annual Report on Form 10-K beginning on page F-1. The following exhibits are filed with, or are incorporated by reference into, this Annual Report on Form 10-K.

Item 16. Form 10-K Summary

We may voluntarily include a summary of information required by Form 10-K under this Item 16. We have elected not to include such summary information.

EXHIBIT INDEX

Exhibit	Description
2.1	Plan of Conversion (incorporated herein by reference to Exhibit 2.1 to Registrant’s Current Report on Form 8-K filed with the Commission on June 2, 2017).
3.1	Articles of Conversion (incorporated herein by reference to Exhibit 3.1 to Registrant’s Current Report on Form 8-K filed with the Commission on June 2, 2017).
3.2	Certificate of Conversion (incorporated herein by reference to Exhibit 3.2 of Registrant’s Current Report on Form 8-K filed with the Commission on June 2, 2017).
3.3	Certificate of Incorporation of Registrant (incorporated herein by reference to Exhibit 3.3 of Registrant’s Current Report on Form 8-K filed with the Commission on June 2, 2017).
3.4	Certificate of Designations of Rights, Preferences and Privileges of Series A Convertible Preferred Stock (incorporated herein by reference to Exhibit 3.4 of Registrant’s Registration Statement on Form S-3 filed with the Commission on July 31, 2017).
3.5	Certificate of Designations of Rights, Preferences and Privileges of Series B Preferred Stock (incorporated herein by reference to Exhibit 3.5 of Registrant’s Registration Statement on Form S-3 filed with the Commission on July 31, 2017).
3.6	Certificate of Amendment of Certificate of Incorporation of Registrant (incorporated herein by reference to Exhibit 3.1 of Registrant’s Current Report on Form 8-K filed with the Commission on June 27, 2017).
3.7	Bylaws of Registrant (incorporated herein by reference to the Exhibit 3.4 to Registrant’s Current Report on Form 8-K filed with the Commission on June 2, 2017).
3.8	Amendment to the Bylaws of Registrant (incorporated herein by reference to the Exhibit 3.2 to Registrant’s Current Report on Form 8-K filed with the Commission on June 27, 2017).
4.1	Form of Warrant (incorporated herein by reference to Registrant’s Form 8-K filed with the Commission on October 31, 2013).
4.2	Specimen of Stock Certificate.
10.1	Genesis Biopharma, Inc. 2010 Equity Compensation Plan (incorporated herein by reference to the Registrant’s Annual Report on Form 10-K filed with the Commission on March 31, 2010).
10.2	Form of Stock Option Agreement for grants under the Genesis Biopharma Inc. 2010 Equity Incentive Plan (incorporated herein by reference to the Registrant’s Annual Report on Form 10-K filed with the Commission on March 31, 2010).
10.3	Genesis Biopharma, Inc. 2011 Equity Compensation Plan (incorporated herein by reference to Registrant’s Form 8-K filed with the Commission on October 20, 2011).

- [10.4](#) [Form of ISO Stock Option Agreement for grants under the Genesis Biopharma Inc. 2011 Equity Incentive Plan \(incorporated herein by reference to Exhibit 10.4 of the Registrant's Form 8-K filed with the Commission on October 20, 2011\).](#)
- [10.5](#) [Form of NQSO Stock Option Agreement for grants under the Genesis Biopharma Inc. 2011 Equity Incentive Plan \(incorporated herein by reference to the Registrant's Form 8-K filed with the Commission on October 20, 2011\).](#)
- [10.6](#) [Lion Biotechnologies, Inc. 2014 Equity Incentive Plan, as amended \(incorporated herein by reference to Appendix A to Registrant's definitive Proxy Statement on Schedule 14C filed with the Commission on July 7, 2016\).](#)
- [10.7](#) [Form of ISO Stock Option Agreement under 2014 Equity Incentive Plan \(incorporated herein by reference to the Registrant's Form S-8 filed with the Commission on June 18, 2015\).](#)
- [10.8](#) [Form of NQSO Stock Option Agreement under 2014 Equity Incentive Plan \(incorporated herein by reference to the Registrant's Form S-8 filed with the Commission on June 18, 2015\).](#)
- [10.9](#) [Patent License Agreement between the Company and the National Institutes of Health effective October 5, 2011 \(incorporated herein by reference to the Registrant's Form 8-K/A filed with the Commission on December 13, 2011\).*](#)
- [10.10](#) [Cooperative Research and Development Agreement for Intramural-PHS Clinical Research, dated August 5, 2011, between the U.S. Department of Health and Human Services, as represented by the National Cancer Institute and the Company \(incorporated herein by reference to the Registrant's Form 8-K/A \(No.2\) filed with the Commission on November 29, 2011\).](#)
- [10.11](#) [Form of Director Stock Award Agreement \(incorporated herein by reference to the Registrant's Form 8-K filed with the Commission on July 25, 2013\).](#)
- [10.12](#) [Form of Registration Rights Agreement by and among Lion Biotechnologies, Inc. and the Investors thereunder \(incorporated herein by reference to the Registrant's Form 8-K filed with the Commission on October 31, 2013\).](#)
- [10.13](#) [Cooperative Research and Development Agreement for the Development and Evaluation of the NCI Proprietary Adoptive Cell Transfer Immunotherapy Using Tumor Infiltrating Lymphocytes in Patients with Metastatic Melanoma, Bladder, Lung, Triple-negative Breast, and HPV-associated Cancers, Utilizing Lion Biotechnologies, Inc.'s Business Development Expertise in Adoptive Cell Transfer Immunotherapy, executed by Lion Biotechnologies, Inc. on January 22, 2015 \(incorporated herein by reference to the Registrant's Form 8-K filed with the Commission on January 26, 2015\).*](#)
- [10.14](#) [Patent License Agreement, dated February 9, 2015, by and between the Company and the National Institutes of Health. \(incorporated herein by reference to the Registrant's Form 10-K filed with the Commission on March 16, 2015\).*](#)
- [10.15](#) [Patent License Agreement, dated February 10, 2015, by and between the Company and the National Institutes of Health. \(incorporated herein by reference to the Registrant's Form 10-K filed with the Commission on March 16, 2015\).*](#)
- [10.16](#) [First Amendment to Patent License Agreement-Exclusive, effective October 2, 2015, between the Company and the National Institutes of Health \(incorporated herein by reference to the Registrant's Form 10-Q filed with the Commission on November 6, 2015\).*](#)
- [10.17](#) [Form of Securities Purchase Agreement, dated June 2, 2016, among Lion Biotechnologies, Inc. and the Investors thereunder \(incorporated herein by reference to the Registrant's Form 8-K filed with the Commission on June 3, 2016\).](#)
- [10.18](#) [Form of Registration Rights Agreement, dated June 2, 2016, by and among Lion Biotechnologies, Inc. and the Investors thereunder. \(incorporated herein by reference to the Registrant's Form 8-K filed with the Commission on June 3, 2016\).](#)
- [10.19](#) [Severance Agreement and General Release, dated June 1, 2016, between Lion Biotechnologies, Inc. and Dr. Elma Hawkins \(incorporated herein by reference to the Registrant's Form 8-K filed with the Commission on June 3, 2016\).#](#)
- [10.20](#) [Board Adviser Agreement, dated June 1, 2016, between Lion Biotechnologies, Inc. and Dr. Elma Hawkins \(incorporated herein by reference to the Registrant's Form 8-K filed with the Commission on June 3, 2016\).#](#)
- [10.21](#) [Form of Retention Bonus Agreement \(incorporated herein by reference to the Registrant's Form 8-K filed with the Commission on June 3, 2016\).#](#)
- [10.22](#) [Office Lease between Lion Biotechnologies, Inc. and Hudson Skyway Landing, LLC \(incorporated herein by reference to the Registrant's Form 8-K filed with the Commission on August 8, 2016\).](#)
- [10.23](#) [Amendment #2 Cooperative Research and Development Agreement # 02734, dated August 18, 2016, between the National Cancer Institute, and Registrant \(incorporated herein by reference to the Registrant's Form 10-Q filed with the Commission on November 4, 2016\).](#)
- [10.24](#) [Exclusive and Co-Exclusive License Agreement, dated September 14, 2016, between Lion Biotechnologies, Inc. and PolyBioCept AB \(incorporated herein by reference to the Registrant's Form 10-Q filed with the Commission on November 4, 2016\).*](#)
- [10.25](#) [Executive Employment Agreement, dated January 27, 2017, by and among Lion Biotechnologies, Inc. and Michael T. Lotze \(incorporated herein by reference to the Registrant's Form 10-Q filed with the Commission on May 9, 2016\).#](#)
- [10.26](#) [Amended and Restated Manufacturing Services Agreement, dated December 18, 2017, between WuXi AppTec, Inc. and Iovance Biotherapeutics, Inc.*](#)
- [10.27](#) [2018 Corporate Goals and Cash Bonus Plan \(incorporated herein by reference to the Registrant's Form 8-K filed with the Commission on February 12, 2018\).](#)
- [10.28](#) [Strategic Alliance Agreement, between Lion Biotechnologies, Inc. and The University of Texas M.D. Anderson Cancer Center, effective April 17, 2017 \(incorporated herein by reference to the Registrant's Form 10-Q filed with the Commission on August 3, 2017\).*](#)
- [10.29](#) [Sublease Agreement, entered into as of April 28, 2017, between Lion Biotechnologies, Inc. and Teradata US, Inc. \(incorporated herein by reference to the Registrant's Current Report on Form 8-K filed with the Commission on May 1, 2017\).](#)
- [10.30](#) [Executive Employment Agreement, effective August 14, 2017, between Timothy E. Morris and Iovance Biotherapeutics, Inc. \(incorporated herein by reference to the Registrant's Form 10-Q filed with the Commission on November 2, 2017\).#](#)
- [10.31](#) [Consulting Agreement, dated as of September 8, 2017, between Iovance Biotherapeutics, Inc. and Iain Dukes, D. Phil. \(incorporated herein by reference to the Registrant's Current Report on Form 8-K filed with the Commission on September 15, 2017\).#](#)
- [10.32](#) [Executive Employment Agreement, effective September 30, 2016, between Frederick G. Vogt and Lion Biotechnologies, Inc.#](#)
- [10.33](#) [Executive Employment Agreement, dated January 22, 2016, between Lion Biotechnologies, Inc. and Steven A. Fischkoff \(incorporated herein by reference to the Registrant's Form 10-Q filed with the Commission on May 9, 2016\).#](#)

10.34	First Amendment to the Strategic Alliance Agreement between Lion Biotechnologies, Inc., and The University of Texas M.D. Anderson Cancer Center, effective August 2, 2017.
10.35	Second Amendment to the Strategic Alliance Agreement between Iovance Biotherapeutics, Inc., and The University of Texas M.D. Anderson Cancer Center, effective February 16, 2018.
21.1	Subsidiaries of the Company (incorporated herein by reference to the Registrant's Form 10-K filed with the Commission on March 9, 2017).
23.1	Consent of Independent Registered Public Accounting Firm.
23.2	Consent of Independent Registered Public Accounting Firm.
31.1	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer.
31.2	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer.
32.1	Section 1350 Certification of Chief Executive Officer (furnished herewith).
32.2	Section 1350 Certification of Chief Financial Officer (furnished herewith).
101	The following financial information from the Annual Report on Form 10-K of Iovance Biotherapeutics, Inc. for the year ended December 31, 2017, formatted in XBRL (eXtensible Business Reporting Language): (1) Balance Sheets as of December 31, 2017 and 2016; (2) Statements of Income for the years ended December 31, 2017 and 2016; (3) Statements of Shareholders' Equity for the years ended December 31, 2017 and 2016; (4) Statements of Cash Flows for the years ended December 31, 2017 and 2016; and (5) Notes to Financial Statements.

* Certain portions of the Exhibit have been omitted based upon a request for confidential treatment filed by us with the Commission. The omitted portions of the Exhibit have been separately filed by us with the Commission.

Indicates a management contract or compensatory plan or arrangement.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

IOVANCE BIOTHERAPEUTICS, INC.

Date: March 12, 2018

By: /s/ Maria Fardis
Name: Maria Fardis
Title: Chief Executive Officer

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 and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Maria Fardis</u> Maria Fardis	Chief Executive Officer (Principal Executive Officer) and Director	March 12, 2018
<u>/s/ Timothy E. Morris</u> Timothy E. Morris	Chief Financial Officer and Treasurer (Principal Financial Officer and Accounting Officer)	March 12, 2018
<u>/s/ Merrill A. McPeak</u> Merrill A. McPeak	Director	March 12, 2018
<u>/s/ Sanford J. Hillsberg</u> Sanford J. Hillsberg	Director	March 12, 2018
<u>/s/ Ryan D. Maynard</u> Ryan D. Maynard	Director	March 12, 2018
<u>/s/ Iain Dukes</u> Iain Dukes	Director	March 12, 2018
<u>/s/ Wayne Rothbaum</u> Wayne Rothbaum	Director	March 12, 2018

IOVANCE BIOTHERAPEUTICS, INC.
Index to Financial Statements

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Audit Committee of the
Board of Directors and Shareholders of
Iovance Biotherapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Iovance Biotherapeutics, Inc. (the "Company") as of December 31, 2017 and 2016, and the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the two years in the period ended December 31, 2017, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2017, in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2017, based on the criteria established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in 2013 and our report dated March 12, 2018, expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Marcum LLP

We have served as the Company's auditor since 2016.

Marcum LLP
New York, NY
March 12, 2018

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of
Iovance Biotherapeutics (formerly Lion Biotechnologies, Inc.)

We have audited the accompanying consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows of Iovance Biotherapeutics, Inc. (formerly Lion Biotechnologies, Inc.) for the year ended December 31, 2015. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the results of operations and cash flows of Iovance Biotherapeutics, Inc. (formerly Lion Biotechnologies, Inc.) for the year ended December 31, 2015, in conformity with accounting principles generally accepted in the United States of America.

/s/ Weinberg & Company, P.A.

Weinberg & Company, P.A.
Los Angeles, California
March 11, 2016

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM ON INTERNAL CONTROL OVER FINANCIAL REPORTING

To the Audit Committee of the
Board of Directors and Shareholders
of Iovance Biotherapeutics, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Iovance Biotherapeutics, Inc.'s (the "Company") internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control—Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control—Integrated Framework (2013)* issued by COSO.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets as of December 31, 2017 and 2016 and the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2017 and the related notes of the Company, and our report dated March 12, 2018, expressed an unqualified opinion on those financial statements.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying "Management's Annual Report on Internal Control over Financial Reporting". Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Marcum LLP

Marcum LLP
New York, NY
March 12, 2018

IOVANCE BIOTHERAPEUTICS, INC.
Consolidated Balance Sheets
(In thousands, except share and per share information)

	<u>December 31,</u> <u>2017</u>	<u>December 31,</u> <u>2016</u>
ASSETS		
Current Assets		
Cash and cash equivalents	\$ 145,373	\$ 106,717
Short-term investments	-	59,753
Prepaid expenses and other current assets	3,917	3,042
Total Current Assets	<u>149,290</u>	<u>169,512</u>
Property and equipment, net	2,450	2,374
Long-term assets	3,633	-
Total Assets	<u>\$ 155,373</u>	<u>\$ 171,886</u>
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities		
Accounts payable	\$ 1,232	\$ 863
Accrued expenses	8,660	4,105
Total Current Liabilities	<u>9,892</u>	<u>4,968</u>
Commitments and contingencies (Note 11)		
Stockholders' Equity		
Series A Convertible Preferred stock, \$0.001 par value; 17,000 shares authorized, 1,694 shares issued and outstanding, as of December 31, 2017 and December 31, 2016, respectively (aggregate liquidation value of \$1,694)	-	-
Series B Convertible Preferred stock, \$0.001 par value; 11,500,000 shares authorized, 7,378,241 and 7,946,673 shares issued and outstanding as of December 31, 2017 and December 31, 2016, respectively (aggregate liquidation value of \$35,047)	7	8
Common stock, \$0.000041666 par value; 150,000,000 shares authorized, 73,164,914 and 62,248,074 shares issued and outstanding as of December 31, 2017 and December 31, 2016, respectively	3	3
Additional paid-in capital	394,651	323,994
Accumulated other comprehensive income	-	29
Accumulated deficit	(249,180)	(157,116)
Total Stockholders' Equity	<u>145,481</u>	<u>166,918</u>
Total Liabilities and Stockholders' Equity	<u>\$ 155,373</u>	<u>\$ 171,886</u>

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

IOVANCE BIOTHERAPEUTICS, INC.
Consolidated Statements of Operations
(In thousands, except per share information)

	Years ended December 31,		
	2017	2016	2015
Revenues	\$ -	\$ -	\$ -
Costs and expenses			
Research and development	71,615	26,941	15,470
General and administrative	21,262	26,698	12,390
Total costs and expenses	<u>92,877</u>	<u>53,639</u>	<u>27,860</u>
Loss from operations	(92,877)	(53,639)	(27,860)
Other income			
Interest income	813	745	200
Net Loss	\$ (92,064)	\$ (52,894)	\$ (27,660)
Deemed dividend related to beneficial conversion feature of convertible preferred stock	-	(49,454)	-
Net Loss Attributable to Common Stockholders	<u>(92,064)</u>	<u>(102,348)</u>	<u>(27,660)</u>
Net Loss Per Common Share, Basic and Diluted	<u>\$ (1.41)</u>	<u>\$ (1.85)</u>	<u>\$ (0.62)</u>
Weighted-Average Common Shares Outstanding, Basic and Diluted	<u>65,242</u>	<u>55,268</u>	<u>44,410</u>

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

IOVANCE BIOTHERAPEUTICS, INC.
Consolidated Statements of Comprehensive Loss
(in thousands)

	Years ended December 31,		
	2017	2016	2015
Net Loss	\$ (92,064)	\$ (52,894)	\$ (27,660)
Other comprehensive income:			
Unrealized (loss) gain on short-term investments	(29)	(19)	48
Comprehensive Loss	<u>\$ (92,093)</u>	<u>\$ (52,913)</u>	<u>\$ (27,612)</u>

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

IOVANCE BIOTHERAPEUTICS, INC.
Consolidated Statements of Stockholders' Equity
(In thousands, except share information)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance - January 1, 2015	5,694	\$ -	-	\$ -	33,750,188	\$ 2	\$ 121,405	\$ -	\$ (76,562)	\$ 44,845
Stock-based compensation expense							6,752			6,752
Common stock issued upon exercise of warrants					3,880,210		9,705			9,705
Common stock issued upon exercise of stock options					42,387		255			255
Conversion of convertible preferred stock into common stock	(4,000)				2,000,000					-
Common stock issued for services					15,000		1,771			1,771
Common stock sold in public offering, net of offering costs					9,200,000		68,307			68,307
Cancellation of restricted shares					(340,065)	-				-
Unrealized gain on short-term investments								48		48
Net loss									(27,660)	(27,660)
Balance - December 31, 2015	1,694	-	-	-	48,547,720	2	208,195	48	(104,222)	104,023
Stock-based compensation expense							18,904			18,904
Tax payments related to shares withheld for vested restricted stock awards							(642)			(642)
Common stock issued upon exercise of warrants					592,132	-	1,235			1,235
Common stock issued upon exercise of stock options					100,480		626			626
Common stock sold in private placement, net of offering costs					9,684,000	1	44,008			44,009
Preferred stock sold in private placement, net of offering costs			11,368,633	11			51,665			51,676
Conversion of convertible preferred stock into common stock			(3,421,960)	(3)	3,421,960		3			-
Cancellation of restricted shares, net					(98,218)	-				-
Beneficial conversion feature of preferred stock							(49,454)			(49,454)
Deemed dividend on beneficial conversion feature of preferred stock							49,454			49,454
Unrealized loss on short-term investments								(19)		(19)
Net loss									(52,894)	(52,894)
Balance - December 31, 2016	1,694	-	7,946,673	8	62,248,074	3	323,994	29	(157,116)	166,918
Stock-based compensation expense							11,968			11,968
Tax payments related to shares withheld for vested restricted stock awards							(1,252)			(1,252)
Common stock issued upon exercise of warrants					265,000	-	662			662
Common stock issued upon exercise of stock options					1,011,284	-	5,616			5,616
Conversion of convertible preferred stock into common stock			(568,432)	(1)	568,432		1			-
Common stock sold in public offering, net of offering costs					8,846,154	-	53,662			53,662
Vesting of restricted shares issued for services					225,970	-	0			-

Unrealized loss on short-term investments									(29)	(29)
Net loss									(92,064)	(92,064)
Balance - December 31, 2017	<u>1,694</u>	<u>\$ -</u>	<u>7,378,241</u>	<u>\$ 7</u>	<u>73,164,914</u>	<u>\$ 3</u>	<u>\$ 394,651</u>	<u>\$ -</u>	<u>\$ (249,180)</u>	<u>\$ 145,481</u>

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

IOVANCE BIOTHERAPEUTICS, INC.
Consolidated Statements of Cash Flows
(In thousands)

	Years Ended December 31,		
	2017	2016	2015
Cash Flows From Operating Activities			
Net loss	\$ (92,064)	\$ (52,894)	\$ (27,660)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	952	978	999
Amortization of discount (premium) on investments	19	(74)	0
Stock-based compensation expense	11,968	18,904	8,523
Changes in assets and liabilities:			
Prepaid expenses and other assets	(875)	(2,765)	(211)
Accounts payable	369	(250)	(290)
Accrued expenses	4,555	3,433	258
Other assets	(3,633)	-	-
Net cash used in operating activities	<u>(78,709)</u>	<u>(32,668)</u>	<u>(18,381)</u>
Cash Flows From Investing Activities			
Purchase of short- term investments	-	(110,249)	(140,665)
Maturities of short- term investments	59,705	120,664	70,600
Purchase of property and equipment	(1,028)	(1,521)	(1,143)
Net cash provided by (used in) investing activities	<u>58,677</u>	<u>8,894</u>	<u>(71,208)</u>
Cash Flows From Financing Activities			
Tax payments related to shares withheld for vested restricted stock	(1,252)	(642)	0
Proceeds from the issuance of common stock upon exercise of warrants	662	1,235	9,705
Proceeds from the issuance of common stock upon exercise of options	5,616	626	255
Proceeds from the issuance of preferred stock and common stock, net	53,662	95,685	68,307
Net cash provided by financing activities	<u>58,688</u>	<u>96,904</u>	<u>78,267</u>
Net increase (decrease) in cash and cash equivalents	<u>38,656</u>	<u>73,130</u>	<u>(11,322)</u>
Cash and Cash Equivalents, Beginning of Period	<u>106,717</u>	<u>33,587</u>	<u>44,909</u>
Cash and Cash Equivalents, End of Period	<u>\$ 145,373</u>	<u>\$ 106,717</u>	<u>\$ 33,587</u>
Supplemental Disclosures of Cash Flow Information:			
Cash paid for income taxes	\$ -	\$ -	\$ -
Interest paid	-	-	-
Supplemental disclosure of non-cash investing and financing activities:			
Unrealized (loss) gain on short-term investments	\$ (29)	\$ (19)	\$ 48
Acquisitions of property and equipment under accounts payable	-	155	-
Deemed dividend related to a beneficial conversion feature	-	49,454	-
Conversion of convertible preferred stock to common stock	1	3	-

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

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 1. GENERAL ORGANIZATION, BUSINESS AND LIQUIDITY

General Organization and Business

Iovance Biotherapeutics, Inc. (the “Company”) is a biopharmaceutical company focused on the development and commercialization of novel cancer immunotherapy products designed to harness the power of a patient’s own immune system to eradicate cancer cells. The Company’s lead program is an adoptive cell therapy (“ACT”) utilizing tumor-infiltrating lymphocytes (“TIL”), which are T cells derived from patients’ tumors, for the treatment of metastatic melanoma. The TIL are extracted from the tumor tissue, expanded in the Company’s manufacturing suites and then infused back into the patient to fight their cancer. On June 1, 2017, the Company reincorporated from Nevada to Delaware. On June 27, 2017, the Company changed its corporate name from Lion Biotechnologies, Inc. to Iovance Biotherapeutics, Inc.

Liquidity

The Company is currently engaged in the development of therapeutics to fight cancer, specifically solid tumors. The Company does not have any commercial products and has not yet generated any revenues from its business. The Company currently does not anticipate that it will generate any revenues during the 12 months from the date these financial statements are issued, from the sale or licensing of any of its product candidates. The Company has incurred a net loss of \$92.1 million for the year ended December 31, 2017 and used \$78.7 million of cash in its operating activities during the year ended December 31, 2017. As of December 31, 2017, the Company had \$145.4 million of cash and cash equivalents. In January 2018, the Company announced the closing of its underwritten public offering of 15,000,000 shares of the Company’s common stock at a public offering price of \$11.50 per share, before underwriting discounts, which included 1,956,521 shares issued upon the exercise in full by the underwriter of its option to purchase additional shares at the public offering price less the underwriting discount. The gross proceeds from the offering, before deducting the underwriting discounts and commissions and other estimated offering expenses payable by the Company, are \$172.5 million, with estimated net proceeds to the Company of approximately \$161.7 million.

The Company expects to further increase its research and development activities, which will increase the amount of cash used during 2018 and beyond. Specifically, the Company expects continued spending on clinical trials, continued and expansion of manufacturing activities, higher payroll expenses as the Company increases its professional and scientific staff and research and development activities. Based on the funds the Company has available as of the date these financial statements are issued, which includes the net proceeds of approximately \$161.7 million raised in connection with the Company’s January 2018 public offering, the Company believes that it has sufficient capital to fund its anticipated operating expenses for at least 24 months from the date these financial statements are issued.

NOTE 2. SUMMARY OF SIGNIFICANT ACCOUNTING PRACTICES

Cash and Cash Equivalents

All highly liquid investments with an original maturity date of three months or less when purchased that are readily convertible into cash and have an insignificant interest rate risk are considered to be cash equivalents.

Short-term Investments

The Company’s short-term investments are classified as “available-for-sale”. The Company includes these investments in current assets and carries them at fair value. Unrealized gains and losses on available-for-sale securities are included in accumulated other comprehensive income (loss). The amortized cost of debt securities is adjusted for the amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income. Gains and losses on securities sold are recorded based on the specific identification method and are included in interest income in the statement of operations. The Company has not incurred any realized gains or losses from sales of securities to date.

Management assesses whether declines in the fair value of short-term investments are other than temporary. If the decline is judged to be other than temporary, the cost basis of the individual security is written down to fair value and the amount of the write down is included in the statement of operations within other expense, net. In determining whether a decline is other than temporary, management considers various factors including the length of time and the extent to which the market value has been less than cost, the financial condition and near-term prospects of the issuer and the Company’s intent and ability to retain its investment in the issuer for a period of time sufficient to allow for any anticipated recovery in market value. To date, the Company has not recorded any impairment charges on short-term investments related to other-than-temporary declines in market value.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

At December 31, 2017, the Company did not have any short-term investments. At December 31, 2016, the Company's short-term investments were invested in short-term fixed income debt securities and notes of domestic and foreign high credit issuers and in money market funds. The Company's investment policy limits investments to certain types of instruments such as certificates of deposit, money market instruments, obligations issued by the U.S. government and U.S. government agencies as well as corporate debt securities, and places restrictions on maturities and concentration by type and issuer.

Property and Equipment, net

Property and equipment is stated at cost, net of accumulated depreciation and amortization. The cost of property and equipment is depreciated or amortized on the straight-line method over the following estimated useful lives:

Computer equipment	2 years
Office furniture and equipment	5 years
Lab equipment	2-5 years
Leasehold improvements	Lesser of the remaining life of the asset or the lease-term

Expenditures for maintenance and repairs are charged to operations as incurred while renewals and betterments are capitalized. Gains and losses on disposals are included within operating expenses in the statements of operations.

Management assesses the carrying value of property and equipment whenever events or changes in circumstances indicate that the carrying value may not be recoverable. If there is indication of impairment, management prepares an estimate of future cash flows expected to result from the use of the asset and its eventual disposition. If these cash flows are less than the carrying amount of the asset, an impairment loss is recognized to write down the asset to its estimated fair value. For the years ended December 31, 2017, 2016 and 2015, the Company did not recognize any impairments for its property and equipment.

Fair value of financial instruments

Cash and cash equivalents and short-term investments are carried at fair value. As of December 31, 2017 and 2016, the Company had no liabilities measured at fair value.

Loss per Share

Basic net loss per share is computed using the weighted average number of common shares outstanding during the period. Diluted net loss per share is computed using the weighted average number of shares of common stock outstanding during the period increased to include the number of additional shares of common stock that would have been outstanding if the potentially dilutive securities had been issued.

At December 31, 2017, 2016 and 2015, the following outstanding common stock equivalents have been excluded from the calculation of net loss per share because their impact would be anti-dilutive.

	As of December 31,		
	2017	2016	2015
Stock options	6,072,368	6,233,150	2,693,237
Warrants	6,301,216	6,566,216	7,202,216
Series A Convertible Preferred*	847,000	847,000	847,000
Series B Convertible Preferred*	7,378,241	7,946,673	-
Restricted stock awards	-	7,084	321,252
Restricted stock units	114,582	550,000	-
	<u>20,713,407</u>	<u>22,150,123</u>	<u>11,063,705</u>

* on an as-converted basis

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Fair Value Measurements

Under Financial Accounting Standards Board (“FASB”) Accounting Standards Codification (“ASC”) 820, Fair Value Measurements and Disclosures, fair value is defined as the price at which an asset could be exchanged, or a liability transferred in a transaction between knowledgeable, willing parties in the principal or most advantageous market for the asset or liability. Where available, fair value is based on observable market prices or parameters or derived from such prices or parameters. Where observable prices or parameters are not available, valuation models are applied.

Assets and liabilities recorded at fair value in the Company’s financial statements are categorized based upon the level of judgment associated with the inputs used to measure their fair value. Hierarchical levels directly related to the amount of subjectivity associated with the inputs to fair valuation of these assets and liabilities, are as follows:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets at the reporting date. Active markets are those in which transactions for the asset or liability occur in sufficient frequency and volume to provide pricing information on an ongoing basis.

Level 2—Are inputs, other than quoted prices included in Level 1, that are either directly or indirectly observable for the asset or liability through correlation with market data at the reporting date and for the duration of the instrument’s anticipated life.

The fair valued assets the Company holds that are generally assessed under Level 2 are corporate bonds and commercial paper. The Company utilizes third party pricing services in developing fair value measurements where fair value is based on valuation methodologies such as models using observable market inputs, including benchmark yields, reported trades, broker/dealer quotes, bids, offers and other reference data. The Company uses quotes from external pricing service providers and other on-line quotation systems to verify the fair value of investments provided by its third-party pricing service providers. The Company reviews independent auditor’s reports from its third-party pricing service providers particularly regarding the controls over pricing and valuation of financial instruments and ensure that its internal controls address certain control deficiencies, if any, and complementary user entity controls are in place.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities and which reflect management’s best estimate of what market participants would use in pricing the asset or liability at the reporting date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

The Company does not have fair valued assets classified under Level 3.

As of December 31, 2017, the Company had no financial assets measured at fair value on a recurring basis.

As of December 31, 2016, financial assets measured at fair value on a recurring basis are categorized in the table below based upon the lowest level of significant input to the valuations (in thousands):

	Assets at Fair Value as of December 31, 2016			
	Level 1	Level 2	Level 3	Total
Commercial paper	\$ -	\$ 29,178	\$ -	\$ 29,178
Corporate debt securities	-	26,578	-	26,578
US Government agency securities	-	3,997	-	3,997
Total	\$ -	\$ 59,753	\$ -	\$ 59,753

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America (“GAAP”) requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. Actual results could differ from those estimates. Significant estimates include valuation of short-term investments, the useful lives of property and equipment, accounting for potential liabilities, the valuation allowance associated with the Company’s deferred tax assets, and the assumptions made in valuing stock instruments issued for services.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Iovance Biotherapeutics, Inc. and its wholly-owned subsidiary, Iovance Biotherapeutics GmbH (formerly Lion Biotechnologies GmbH). All intercompany accounts and transactions have been eliminated. The U.S. dollar is the functional currency for all the Company's consolidated operations.

Stock-Based Compensation

The Company periodically grants stock options and warrants to employees and non-employees in non-capital raising transactions as compensation for services rendered. The Company accounts for stock option grants to employees based on the authoritative guidance provided by the FASB where the value of the award is measured on the date of grant and recognized over the vesting period. The Company accounts for stock option grants to non-employees in accordance with the authoritative guidance of the FASB where the value of the stock compensation is determined based upon the measurement date at either a) the date at which a performance commitment is reached, or b) at the date at which the necessary performance to earn the equity instruments is complete. Non-employee stock-based compensation charges generally are amortized over the vesting period on a straight-line basis. In certain circumstances where there are no future performance requirements by the non-employee, option grants are immediately vested, and the total stock-based compensation charge is recorded in the period of the measurement date.

The fair value of the Company's common stock option grants is estimated using a Black-Scholes option pricing model, which uses certain assumptions related to risk-free interest rates, expected volatility, expected life of the common stock options, and future dividends. Compensation expense is recorded based upon the value derived from the Black-Scholes option pricing model, and based on actual experience. The assumptions used in the Black-Scholes option pricing model could materially affect compensation expense recorded in future periods. During the years ended December 31, 2016 and 2015, the Company estimated forfeitures at the time of grant and revised those estimates in subsequent periods if actual forfeitures differed from those estimates. Effective January 1, 2017, the Company adopted ASU 2016-09 and elected to recognize forfeitures when they occur using a modified retrospective approach, which did not have a material impact on its consolidated financial statements.

The Company has in the past issued restricted shares of its common stock for share-based compensation programs. The Company measures the compensation cost with respect to restricted shares issued to employees based upon the estimated fair value of the equity instruments at the date of the grant, which is recognized as an expense over the period during which an employee is required to provide services in exchange for the award.

The fair value of restricted stock units is based on the closing price of the Company's common stock on the grant date.

Total stock-based compensation expense related to all of the Company's stock-based awards was recorded on the statements of operations as follows (in thousands):

	Years Ended December 31,		
	2017	2016	2015
Research and development	\$ 5,270	\$ 3,267	\$ 2,248
General and administrative	6,698	15,637	6,275
Total stock-based compensation expense	\$ 11,968	\$ 18,904	\$ 8,523

Total stock-based compensation broken down based on each individual instrument was as follows (in thousands):

	Years Ended December 31,		
	2017	2016	2015
Stock option expense	\$ 10,862	\$ 16,453	\$ 6,752
Restricted stock award expense	34	989	1,771
Restricted stock unit expense	1,072	1,462	-
Total stock-based compensation expense	\$ 11,968	\$ 18,904	\$ 8,523

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Research and Development Expenses

Research and development expenses include personnel and facility-related expenses, outside contracted services including clinical trial costs, manufacturing and process development costs, research costs and other consulting services. Research and development costs are expensed as incurred. Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and amortized over the period that the goods are delivered, or the related services are performed, subject to an assessment of recoverability.

Clinical development costs are a significant component of research and development expenses. The Company has a history of contracting with third parties that perform various clinical trial activities on its behalf in connection with the ongoing development of its product candidates. The financial terms of these contracts are subject to negotiations and may vary from contract to contract and may result in uneven payment flow. The Company accrues and expenses costs for clinical trial activities performed by third parties based upon estimates of the percentage of work completed over the life of the individual study in accordance with agreements established with contract research organizations and clinical trial sites. The Company determines its estimates through discussions with internal clinical personnel and outside service providers as to the progress or stage of completion of trials or services and the agreed upon fee to be paid for such services.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, legal, investor relations, facilities, business development and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, sublicense royalty expenses, legal fees relating to corporate matters, insurance, public company expenses relating to maintaining compliance with Nasdaq listing rules and Securities and Exchange Commission ("SEC") requirements, insurance and investor relations costs, and fees for accounting and consulting services. General and administrative costs are expensed as incurred, and the Company accrues for services provided by third parties related to the above expenses by monitoring the status of services provided and receiving estimates from its service providers, and adjusting its accruals as actual costs become known.

Income taxes

The Company accounts for income taxes using the asset and liability method whereby deferred tax assets are recognized for deductible temporary differences, and deferred tax liabilities are recognized for taxable temporary differences. Temporary differences are the differences between the reported amounts of assets and liabilities and their tax bases. Deferred tax assets are reduced by a valuation allowance when, in the opinion of management, it is more likely than not that some portion or all of the deferred tax assets will be realized. Deferred tax assets and liabilities are adjusted for the effects of changes in tax laws and rates on the date of enactment.

ASC Topic 740-10-30 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements and prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. ASC Topic 740-10-40 provides guidance on de-recognition, classification, interest and penalties, accounting in interim periods, disclosure, and transition. The Company will classify as income tax expense any interest and penalties. The Company has no material uncertain tax positions for any of the reporting periods presented.

Concentrations

Financial instruments, which potentially subject the Company to concentrations of credit risk, consist principally of cash and cash equivalents.

The Company maintains cash balances at two financial institutions. At times, the amounts on deposit exceed the federally insured limits. Management believes that the financial institutions which hold the Company's cash are financially sound and, accordingly, minimal credit risk exists. As of December 31, 2017 and 2016, respectively, the Company's cash balances were in excess of insured limits maintained at the financial institutions.

Preferred Stock

The Company applies the accounting standards for distinguishing liabilities from equity when determining the classification and measurement of its preferred stock. Preferred shares subject to mandatory redemption are classified as liability instruments and are measured at fair value. Conditionally redeemable preferred shares (including preferred shares that feature redemption rights that are either within the control of the holder or subject to redemption upon the occurrence of uncertain events not solely within the Company's control) are classified as temporary equity. At all other times, preferred shares are classified as stockholders' equity.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Convertible Instruments

The Company applies the accounting standards for derivatives and hedging and for distinguishing liabilities from equity when accounting for hybrid contracts that feature conversion options. The accounting standards require companies to bifurcate conversion options from their host instruments and account for them as free-standing derivative financial instruments according to certain criteria. The criteria include circumstances in which (i) the economic characteristics and risks of the embedded derivative instrument are not clearly and closely related to the economic characteristics and risks of the host contract, (ii) the hybrid instrument that embodies both the embedded derivative instrument and the host contract is not re-measured at fair value under otherwise applicable generally accepted accounting principles with changes in fair value reported in earnings as they occur and (iii) a separate instrument with the same terms as the embedded derivative instrument would be considered a derivative instrument. The derivative is subsequently marked to market at each reporting date based on current fair value, with the changes in fair value reported in results of operations.

Conversion options that contain variable settlement features such as provisions to adjust the conversion price upon subsequent issuances of equity or equity linked securities at exercise prices more favorable than that featured in the hybrid contract generally result in their bifurcation from the host instrument.

The Company also records, when necessary, deemed dividends for the intrinsic value of the conversion options embedded in preferred stock based upon the difference between the fair value of the underlying common stock at the commitment date of the transaction and the effective conversion price embedded in the preferred stock.

Recent Accounting Standards

In March 2016, the FASB issued ASU 2016-09, Compensation - Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting. This ASU identifies areas for simplification involving several aspects of accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, an option to recognize gross stock compensation expense with actual forfeitures recognized as they occur, as well as certain classifications on the statement of cash flows. This ASU will be effective for fiscal years beginning after December 15, 2016, and interim periods within those annual periods. The Company adopted this ASU in the beginning of fiscal year 2017. Upon adoption, the Company elected to recognize forfeitures when they occur using a modified retrospective approach, which did not have a material impact on its consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which establishes a new lease accounting model for lessees. The updated guidance requires an entity to recognize assets and liabilities arising from a lease for both financing and operating leases, along with additional qualitative and quantitative disclosures. The amended guidance is effective for fiscal years, and interim periods within those years, beginning after December 15, 2018, with early adoption permitted. The Company has not yet selected a transition date and is currently evaluating the impact of the adoption of this standard on its consolidated financial statements.

Segment reporting

The Company operates in one segment, focused on developing and commercializing ACT using autologous TIL for the treatment of metastatic melanoma and other solid cancers.

Subsequent Events

Management evaluates events that have occurred after the balance sheet date but before the financial statements are issued. Based upon the review, management did not identify any recognized or non-recognized subsequent events which would have required an adjustment or disclosure in the financial statements, except as described in Note 15.

Reclassifications

Certain amounts within the balance sheets and statements of operations and stockholders' equity for the prior periods have been reclassified to conform with the current period presentation. These reclassifications had no impact on the Company's previously reported financial position or cash flows for any of the periods presented.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 3. CASH AND CASH EQUIVALENTS, AND SHORT-TERM INVESTMENTS

Cash and cash equivalents, and short-term investments consist of the following (in thousands):

	December 31, 2017	December 31, 2016
Cash - Demand deposits	\$ 54,092	\$ 76,071
Cash equivalents - Money market funds	91,281	30,646
Cash and cash equivalents total	<u>\$ 145,373</u>	<u>\$ 106,717</u>

	December 31, 2017	December 31, 2016
Commercial paper	\$ -	\$ 29,178
Corporate debt securities	-	26,578
US Government agency securities	-	3,997
Short-term investments total	<u>\$ -</u>	<u>\$ 59,753</u>

Money market funds and short-term investments include the following securities with gross unrealized gains and losses (in thousands):

As of December 31, 2017	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	<u>\$ 91,281</u>	<u>\$ -</u>	<u>\$ -</u>	<u>\$ 91,281</u>

As of December 31, 2016	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	\$ 30,646	\$ -	\$ -	\$ 30,646
Commercial paper	29,118	60	-	29,178
Corporate debt securities	26,606	1	(29)	26,578
US Government agency securities	4,000	-	(3)	3,997
Total	<u>\$ 90,370</u>	<u>\$ 61</u>	<u>\$ (32)</u>	<u>\$ 90,399</u>

Unrealized gains and losses are included in accumulated other comprehensive income.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 4. BALANCE SHEET COMPONENTS

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

	December 31,	December 31,
	2017	2016
Lab equipment	\$ 3,207	\$ 2,405
Leasehold improvements	1,726	1,381
Computer equipment	349	245
Office furniture and equipment	188	148
Construction in progress	13	276
Total Property and equipment, cost	5,483	4,455
Less: Accumulated depreciation and amortization	(3,033)	(2,081)
Property and equipment, net	<u>\$ 2,450</u>	<u>\$ 2,374</u>

Depreciation expense for the years ended December 31, 2017, 2016 and 2015 was \$1.0 million, \$1.0 million and \$1.0 million, respectively.

Accrued liabilities consist of the following (in thousands):

	December 31,	December 31,
	2017	2016
Accrued payroll and employee related expenses	\$ 2,613	\$ 1,581
Legal and related services	935	927
Clinical related	3,310	614
Manufacturing related	876	437
Deferred rent	430	422
Accrued other	496	124
	<u>\$ 8,660</u>	<u>\$ 4,105</u>

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 5. STOCKHOLDERS' EQUITY

Preferred stock

The Company's certificate of incorporation authorizes the issuance of up to 50,000,000 shares of "blank check" preferred stock. At December 31, 2017, 17,000 shares were designated as Series A Convertible Preferred Stock ("Series A Preferred Stock") and 11,500,000 shares were designated as Series B Preferred Stock ("Series B Preferred Stock").

Series A Convertible Preferred Stock

A total of 17,000 shares of Series A Preferred Stock have been authorized for issuance under the Company's Certificate of Designation of Preferences and Rights of Series A Convertible Preferred Stock. The shares of Series A Preferred Stock have a stated value of \$1,000 per share and are initially convertible into shares of common stock at a price of \$2.00 per share, subject to adjustment.

The Series A Preferred Stock may, at the option of each investor, be converted into fully paid and non-assessable shares of the Company's common stock. The holders of shares of Series A Preferred Stock do not have the right to vote on matters that come before the Company's stockholders. In the event of any dissolution or winding up of the Company, proceeds shall be paid pari passu among the holders of the Company's common stock and preferred stock, pro rata based on the number of shares held by each holder. The Company may not declare, pay or set aside any dividends on shares of capital stock of the Company (other than dividends on shares of common stock payable in shares of common stock) unless the holders of the Series A Preferred Stock shall first receive an equal dividend on each outstanding share of Series A Preferred Stock.

During the year ended December 31, 2017, no shares of Series A Preferred Stock were converted into shares of common stock. During the years ended December 31, 2016 and 2015, 4,000 and 11,306 shares, respectively, of Series A Preferred Stock were converted into 2,000,000 and 5,653,000 shares of common stock, respectively. The common shares issued were determined on a formula basis of 500 common shares for each share of Series A Preferred Stock converted.

Series B Preferred Stock

A total of 11,500,000 shares of Series B Preferred Stock are authorized for issuance under the Company's Series B Certificate of Designation of Rights, Preferences and Privileges of Series B Preferred Stock. The shares of Series B Preferred Stock have a stated value of \$4.75 per share and are convertible into shares of the Company's common stock at an initial conversion price of \$4.75 per share.

Holders of Series B Preferred Stock are entitled to dividends on an as-if-converted basis in the same form as any dividends actually paid on shares of the Series A Preferred Stock or the Company's common stock. So long as any Series B Preferred Stock remains outstanding, the Company may not redeem, purchase or otherwise acquire any material amount of the Series A Preferred Stock or any securities junior to the Series B Preferred Stock.

During the year ended December 31, 2017 568,432 shares of Series B Preferred Stock were converted into 568,432 shares of common stock, and during the year ended December 31, 2016, 3,421,960 shares of Series B Preferred Stock were converted into 3,421,960 shares of common stock. 7,378,241 shares of Series B Preferred Stock remained outstanding at December 31, 2017.

2016 Private Placement

On June 2, 2016, the Company entered into a securities purchase agreement with various institutional and individual accredited investors to raise gross proceeds of \$100 million in a private placement (the "2016 Private Placement"). On June 7, 2016, the Company completed the 2016 Private Placement. In the 2016 Private Placement, the Company issued (i) 9,684,000 shares of its common stock and (ii) 11,368,633 shares of its newly created Series B Preferred Stock. The shares of common stock and Series B Preferred Stock were sold for \$4.75 per share. The shares of Series B Preferred initially were not convertible into common stock and, except as required by law, are non-voting. On July 7, 2016, the Company filed a proxy statement with the SEC with respect to a stockholders meeting that was held on August 16, 2016 at which the stockholders were asked to vote on a proposal to permit the Series B Preferred Stock to become convertible into shares of the Company's common stock and to permit the issuance of shares of common stock upon such conversion. The requisite stockholder approval was obtained and, as a result, on August 16, 2016 the Series B Preferred Stock became convertible into shares of common stock at an initial conversion price of \$4.75 per share.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The Company has also evaluated its convertible preferred stock in accordance with the provisions of ASC 815, Derivatives and Hedging, including consideration of embedded derivatives requiring bifurcation. The issuance of the convertible preferred stock could generate a beneficial conversion feature (“BCF”), which arises when a debt or equity security is issued with an embedded conversion option that is beneficial to the investor or in the money at inception because the conversion option has an effective strike price that is less than the market price of the underlying stock at the commitment date. The Company recognized the BCF by allocating the intrinsic value of the conversion option, which is the number of shares of common stock available upon conversion multiplied by the difference between the effective conversion price per share and the fair value of common stock per share on the commitment date, to additional paid-in capital, resulting in a discount on the convertible preferred stock. As the convertible preferred stock may be converted immediately, the Company recognized a BCF of \$49.5 million as a deemed dividend in the statements of operations. This one-time, non-cash charge impacted net loss attributable to common stockholders and loss per share for the year ended December 31, 2016.

The Company received net proceeds of approximately \$95.7 million from the 2016 Private Placement, after paying placement agent fees and estimated offering expenses.

Public Offering

On September 25, 2017, the Company sold 8,846,154 shares of its common stock in an underwritten public offering at \$6.50 per share for net proceeds of \$53.7 million after deducting underwriting discounts and expenses of the offering.

Warrants

A summary of the status of stock warrants at December 31, 2017, and the changes during the three years then ended, is presented in the following table:

	Shares Under Warrants	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life	Aggregate Intrinsic Value (in thousands)
Outstanding at January 1, 2015	11,084,426	\$ 2.51		
Issued	-	-		
Exercised	(3,882,210)	2.50		
Expired/Cancelled	-	-		
Outstanding at December 31, 2015	7,202,216	\$ 2.51		
Issued	-	-		
Exercised	(592,132)	2.50		
Expired/Cancelled	(43,868)	2.50		
Outstanding at December 31, 2016	6,566,216	\$ 2.51		
Issued	-	-		
Exercised	(265,000)	2.50		
Expired/Cancelled	-	-		
Outstanding at December 31, 2017	6,301,216	\$ 2.51	0.8 years	\$ 34,651

NOTE 6. STOCK BASED COMPENSATION

Stock Plans

As of October 14, 2011, the Company adopted the 2011 Equity Incentive Plan (the “2011 Plan”). Employees, directors, consultants and advisors of the Company are eligible to participate in the 2011 Plan. The 2011 Plan initially had 180,000 shares of common stock reserved for issuance in the form of incentive stock options, non-qualified options, common stock, and grant appreciation rights. The 2011 Plan was not approved by the Company’s stockholders within the required one-year period following its adoption and, accordingly, no incentive stock options can be granted under that plan. In August 2013, the Company’s Board of Directors and a majority of the Company’s stockholders approved an amendment to increase the number of shares available under the 2011 Plan from 180,000 shares to 1,700,000 shares, and an amendment to increase the number options or other awards that can be granted to any one person during a twelve (12) month period from 50,000 shares to 300,000 shares. The foregoing amendment to the 2011 Plan became effective in September 2013. On August 20, 2014, the Company’s Board of Directors amended the 2011 Plan to increase the number of shares available for issuance upon the exercise of stock options under the 2011 Plan from 1,700,000 to 1,900,000 shares, effective immediately. As of December 31, 2017, 725,267 shares were available for future grant under the 2011 Plan.

On September 19, 2014, the Company’s Board of Directors (the “Board”) adopted the Iovance Biotherapeutics, Inc. 2014 Equity Incentive Plan (the “2014 Plan”). The 2014 Plan was approved by the Company’s stockholders at the Company’s 2014 Annual Meeting of Stockholders held in November 2014. The 2014 Plan, as approved by the stockholders, authorized the issuance up to an aggregate of 2,350,000 shares of the Company’s common stock. On April 10, 2015, the Board amended the 2014 Plan to increase the total number of shares that can be issued under the 2014 Plan to 4,000,000 shares of the Company’s common stock. The increase in shares available for issuance under the 2014 Plan was approved by the Company’s stockholders at the Company’s 2015 Annual Meeting of Stockholders in June 2015.

On August 16, 2016, the Company’s stockholders approved an increase in the total number of shares that can be issued under the 2014 Plan to 9,000,000 shares of the Company’s common stock. At December 31, 2017, 2,516,992 shares were available for grant under the Company’s 2014 Plan.

Restricted Stock Units

On June 1, 2016, the Company entered into a restricted stock unit agreement with the Company’s new Chief Executive Officer, Maria Fardis, Ph.D., pursuant to which the Company granted Dr. Fardis 550,000 non-transferrable restricted stock units at fair market value of \$5.87 per share as an inducement of employment pursuant to the exception to The Nasdaq Global Market rules that generally require stockholder approval of equity incentive plans. The 550,000 restricted stock units vest in installments as follows: (i) 137,500 restricted stock units vested upon the first anniversary of the effective date of Dr. Fardis’ employment agreement; (ii) 275,000 restricted stock units vest upon the satisfaction of certain clinical trial milestones; and (iii) 137,500 restricted stock units vest in equal monthly installments over the 36-month period following the first anniversary of the effective date of Dr. Fardis’ employment, provided that Dr. Fardis has been continuously employed with the Company as of such vesting dates.

Stock-based compensation expense for restricted stock units (“RSUs”) is measured based on the closing fair market value of the Company’s common stock on the date of grant. As of December 31, 2017, \$0.7 million of total unrecognized compensation costs related to non-vested RSUs are scheduled to be recognized over a weighted average period of 2.5 years.

During the years ended December 31, 2017 and 2016, the Company recognized \$1.1 million and \$1.5 million, respectively, in stock-based compensation expense related to RSUs.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Stock Options

A summary of the status of stock options at December 31, 2017, and the changes during the three years then ended, is presented in the following table:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life	Aggregate Intrinsic Value (in thousands)
Outstanding at January 1, 2015	1,857,877	\$ 7.31		
Granted	1,171,984	8.12		
Exercised	(42,387)	-		
Expired/Forfeited	(294,237)	2.88		
Outstanding at December 31, 2015	2,693,237	\$ 8.12		
Granted	4,407,983	6.86		
Exercised	(100,480)	6.23		
Expired/Forfeited	(767,590)	8.12		
Outstanding at December 31, 2016	6,233,150	\$ 7.24		
Granted	2,188,800	6.68		
Exercised	(1,011,284)	5.55		
Expired/Forfeited	(1,338,298)	6.79		
Outstanding at December 31, 2017	6,072,368	\$ 7.42	7.9 years	\$ 6,199
Exercisable at December 31, 2017	2,769,205	\$ 7.96	6.4 years	\$ 2,457
Exercisable at December 31, 2016	2,496,695	\$ 7.35	4.1 years	\$ 1,839

The total pre-tax intrinsic value of stock options exercised during the year ended December 31, 2017, 2016 and 2015 was \$2.6 million, \$0.2 million and \$0.0 million, respectively.

The weighted average grant date fair value for employee options granted under the Company's stock option plans during the year ended December 31, 2017, 2016 and 2015 was \$6.58, \$6.78 and \$8.77, per option respectively.

As of December 31, 2017, \$19.5 million of total unrecognized compensation costs related to non-vested employee options are scheduled to be recognized over a weighted average period of 1.9 years.

The following table summarizes the assumptions relating to options granted pursuant to the Company's equity incentive plans for the years ended December 31, 2017, 2016 and 2015:

	Years Ended December 31,		
	2017	2016	2015
Expected dividend yield	0%	0%	0%
Risk-free interest rate	2.34 % - 1.72%	2.16 % - 1.18%	1.56%
Expected term (in years)	6.50 - 5.13	6.50 - 5.07	6.00
Expected volatility	209.69% - 190.46%	213.60% - 189.40%	218.00% - 207.00%

Expected Dividend Yield —The Company has never paid dividends and does not expect to pay dividends in the foreseeable future.

Risk-Free Interest Rate —The risk-free interest rate was based on the market yield currently available on United States Treasury securities with maturities approximately equal to the option's expected term.

Expected Term —The expected term of the stock option grants was calculated using the "simplified" method in accordance with the SEC Staff Accounting Bulletin 107. The "simplified" method was used since the Company believes its historical data does not provide a reasonable basis upon which to estimate expected term and the Company does not have enough option exercise data from its grants issued to support its own estimate as a result of vesting terms and changes in the stock price. The "simplified" method, as permitted by the SEC, is calculated as the average of the time-to-vesting and the contractual life of the options.

IOVANCE BIOTHERAPEUTICS, INC.
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Expected Volatility —The expected volatility is based on the historical volatility for the Company's stock over a period equal to the expected terms of the options.

Forfeiture Rate —The Company recognizes forfeitures as they occur.

Each of the inputs discussed above is subjective and generally requires significant management judgment.

During the years ended December 31, 2017, 2016 and 2015, the Company recorded compensation costs of \$10.9 million, \$16.5 million and \$6.8 million, respectively, relating to the vesting of stock options.

A summary of outstanding, exercisable and vested stock options as of December 31, 2017 is as follows (in thousands, except per share amounts):

Range of Exercise Prices	Options Outstanding			Exercisable				
	Number of Shares	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price Per Share	Aggregate Intrinsic Value	Number of Shares	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price Per Share	Aggregate Intrinsic Value
\$5.05 - \$5.86	959,200	8.16	\$ 5.32	\$	390,000	6.31	\$ 5.43	
\$5.87 - \$6.58	932,550	7.90	6.02		421,712	6.77	6.08	
\$6.59 - \$7.43	897,500	7.51	6.99		323,790	4.25	6.94	
\$7.44 - \$7.57	1,358,166	8.91	7.52		434,370	8.67	7.54	
\$7.58 - \$9.00	864,286	7.37	7.83		401,273	5.50	7.81	
\$9.01 - \$117	1,060,666	6.90	10.46		798,060	6.33	10.90	
	<u>6,072,368</u>	7.86	\$ 7.42	\$ 6,199	<u>2,769,205</u>	6.40	\$ 7.96	\$ 2,457

Restricted Common Stock Awards

The following table summarizes restricted common stock awards activity:

	Number of Shares	Weighted Average Grant Date Fair Value
Non-vested shares, January 1, 2015	782,500	\$ 7.04
Granted	15,000	8.44
Vested	(284,748)	4.31
Forfeited	(191,500)	6.81
Non-vested shares, December 31, 2015	321,252	\$ 6.96
Granted	-	-
Vested	(274,167)	6.90
Forfeited	(40,001)	7.02
Non-vested shares, December 31, 2016	7,084	\$ 6.48
Granted	-	-
Vested	(7,084)	(6.48)
Forfeited	-	-
Non-vested shares, December 31, 2017	-	\$ -

During the years ended December 31, 2017, 2016 and 2015, the Company recorded compensation costs of \$0.0 million, \$1.0 million and \$1.8 million, respectively, in connection with these awards and is recognized as expense in the accompanying statements of operations. As of December 31, 2017, there were no outstanding unvested restricted common stock awards.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 7. EMPLOYEE BENEFIT PLAN

The Company maintains a defined contribution plan covering substantially all U.S. employees under Section 401(k) of the Internal Revenue Code of 1986, as amended (the "IRC"). The Company's matching contribution to the plan was \$0.3 million, \$0.1 million and \$0.0 million for the years ended December 31, 2017, 2016 and 2015, respectively.

NOTE 8. SEPARATION AGREEMENTS

In June 2016, the Company entered into a separation agreement with Dr. Elma Hawkins, its former Chief Executive Officer. Under the terms of the agreement, Dr. Hawkins vesting was accelerated on certain outstanding options and she was entitled to receive a severance payment of approximately \$0.5 million. The Company recorded approximately \$5.0 million in additional share-based compensation expense related to this acceleration of the equity awards during the year ended December 31, 2016.

In July 2016, Molly Henderson, the former Chief Financial Officer provided the Board with written notice under her Employment Agreement, dated June 5, 2015, that she would terminate her employment with the Company for "good reason" effective August 16, 2016. In connection with this event all unvested options were accelerated and she received a severance payment of approximately \$0.4 million, representing one year's salary. The Company recorded approximately \$4.5 million in additional share-based compensation expense related to the acceleration of the equity awards during the year ended December 31, 2016.

NOTE 9. INCOME TAXES

Net deferred tax assets (liabilities) are summarized as follows (in thousands):

	As of December 31,	
	2017	2016
Deferred income tax asset:		
Net operating loss carry forward	\$ 33,300	\$ 23,912
Stock-based compensation	4,568	9,562
Tax credit carryforwards	9,323	8,167
Reserves and accruals	733	139
Deferred tax assets before valuation allowance	47,924	41,780
Less: valuation allowance	(47,849)	(41,402)
Net deferred income tax assets	75	378
Deferred tax liabilities:		
Depreciation and amortization	(75)	(378)
Net deferred tax assets (liabilities)	<u>\$ -</u>	<u>\$ -</u>

Reconciliation of the effective income tax rate to the U.S. statutory rate is as follows:

	Years ended December 31,		
	2017	2016	2015
Federal statutory tax rate	(34)%	(34)%	(34)%
Orphan Drug & Research credits	0	(8)	(12)
Permanent and other differences	4	4	10
Tax rate change	23	-	-
State tax, net of federal benefit	-	(4)	(5)
	<u>(7)%</u>	<u>(42)%</u>	<u>(41)%</u>
Valuation allowance	7%	42%	41%
Effective tax rate	<u>-%</u>	<u>-%</u>	<u>-%</u>

IOVANCE BIOTHERAPEUTICS, INC.
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The components of income tax expense (benefit) are as follows (in thousands):

	Years ended December 31,		
	2017	2016	2015
Federal:			
Current	\$ -	\$ -	\$ -
Deferred	(7,391)	(19,050)	(9,724)
State and Local			
Current	-	-	-
Deferred	944	(3,007)	(1,887)
Change in Valuation Allowance	6,447	22,057	11,611
Total income tax expense (benefit)	\$ -	\$ -	\$ -

The Company had net operating loss carryovers (“NOLs”) for federal and state income tax purposes of approximately \$143.3 million and \$66.3 million, respectively, as of December 31, 2017. The federal NOLs will expire beginning in 2027 through 2037. The state NOLs will expire if unused in years 2030 through 2037.

The Company’s utilization of NOLs is subject to an annual limitation due to ownership changes that have occurred previously or that could occur in the future as provided in Section 382 of the IRC (“Section 382”), as well as similar state provisions. Section 382 limits the utilization of NOLs when there is a greater than 50% change of ownership as determined under the regulations. Since its formation, the Company has raised capital through the issuance of capital stock and various convertible instruments which, combined with the purchasing shareholders’ subsequent disposition of these shares, has resulted in an ownership change as defined by Section 382, and could result in an ownership change in the future upon subsequent disposition.

On December 22, 2017, the Tax Cuts and Jobs Act of 2017 (“Tax Act”) was signed into law making significant changes to the Internal Revenue Code. Changes include, but are not limited to, a corporate tax rate decrease from 35% to 21% effective for tax years beginning after December 31, 2017, the transition of U.S international taxation from a worldwide tax system to a territorial system, and a one-time transition tax on the mandatory deemed repatriation of cumulative foreign earnings as of December 31, 2017. The Company has calculated its 2017 year-end income tax provision with its best estimate of the impact of the Act in accordance with its understanding of the Act and guidance available as of the date of this filing. The tax rate decrease resulted in a reduction of \$20.8 million in the Company’s deferred tax assets, and a corresponding decrease of the same amount in the valuation allowance against these deferred tax assets.

In assessing the realization of deferred tax assets, management considers whether it is more likely than not that some portion or all the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon future generation for taxable income during the periods in which temporary differences representing net future deductible amounts become deductible. Management considers the scheduled reversal of deferred tax liabilities, projected future taxable income and tax planning strategies in making this assessment. After consideration of all the information available, management believes that significant uncertainty exists with respect to future realization of the deferred tax assets and has therefore established a full valuation allowance. For the years ended December 31, 2017, 2016 and 2015, the change in the valuation allowance was approximately \$6.4 million, \$22.1 million and \$11.6 million, respectively.

The Company evaluated the provisions of ASC 740 related to the accounting for uncertainty in income taxes recognized in an enterprise’s financial statements. ASC 740 prescribes a comprehensive model for how a company should recognize, present, and disclose uncertain positions that the company has taken or expects to take in its tax return. For those benefits to be recognized, a tax position must be more-likely-than-not to be sustained upon examination by taxing authorities. Differences between tax positions taken or expected to be taken in a tax return and the net benefit recognized and measured pursuant to the interpretation are referred to as “unrecognized benefits.” A liability is recognized (or amount of net operating loss carry forward or amount of tax refundable is reduced) for unrecognized tax benefit because it represents an enterprise’s potential future obligation to the taxing authority for a tax position that was not recognized as a result of applying the provisions of ASC 740.

If applicable, interest costs related to the unrecognized tax benefits are required to be calculated and would be classified as “Other Income (Expense)” in the consolidated statement of operations. Penalties would be recognized as a component of “General and Administrative Expenses” in the consolidated statement of operations.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

A reconciliation of the beginning and ending balances of the unrecognized tax benefits during the years ended December 31, 2017, 2016 and 2015 is as follows (in thousands):

	Years ended December 31,		
	2017	2016	2015
Unrecognized benefit—beginning of period	\$ -	\$ -	\$ -
Gross decreases—prior period tax positions	2,780	-	-
Gross increases—current period tax positions	1,331	-	-
Unrecognized benefit—end of period	<u>\$ 4,111</u>	<u>\$ -</u>	<u>\$ -</u>

No interest or penalties on unpaid tax were recorded during the years ended December 31, 2017, 2016 and 2015, respectively. The Company does not anticipate any significant changes within 12 months of this reporting date of its uncertain tax positions.

The Company files tax returns in the U.S. federal and state jurisdictions. The tax years beginning with the year ended December 31, 2007 remain open to examination by tax authorities to the extent of the utilization of net operating losses and credit carryovers. The Company is not currently under examination by income tax authorities in federal, state or other foreign jurisdictions.

NOTE 10. LICENSES AND AGREEMENTS

National Institutes of Health (NIH) and the National Cancer Institute (NCI)

Cooperative Research and Development Agreement (CRADA)

In August 2011, the Company signed a five-year Cooperative Research and Development Agreement (“CRADA”) with the National Cancer Institute (NCI”) to work with Dr. Steven Rosenberg on developing adoptive cell immunotherapies that are designed to destroy metastatic melanoma cells using a patient’s tumor infiltrating lymphocytes.

In January 2015, the Company executed an amendment to the CRADA (the “Amendment”) to include four new indications. As amended, in addition to metastatic melanoma, the CRADA included the development of TIL therapy for the treatment of patients with bladder, lung, triple-negative breast, and Human Papilloma Virus (“HPV”)-associated cancers.

In August 2016, the NCI and the Company entered into a second amendment to the CRADA (the “Second Amendment”). The principal changes effected by the Second Amendment included (i) extending the term of the CRADA by another five years to August 2021, and (ii) modifying the focus on the development of unmodified TIL as a stand-alone therapy or in combination with U.S. Food and Drug Administration (“FDA”) licensed products and commercially available reagents routinely used for adoptive cell therapy. The parties will continue the development of improved methods for the generation and selection of TIL with anti-tumor reactivity in metastatic melanoma, bladder, lung, breast, and HPV-associated cancers.

Pursuant to the terms of the CRADA, the Company is currently required to make quarterly payments of \$0.5 million to the NCI for support of research activities. To the extent the Company licenses patent rights relating to a TIL-based product candidate, the Company will be responsible for all patent-related expenses and fees, past and future, relating to the TIL-based product candidate. In addition, the Company may be required to supply certain test articles, including TIL, grown and processed under cGMP conditions, suitable for use in clinical trials, where the Company holds the investigational new drug application for such clinical trial. The extended CRADA has a five-year term expiring in August 2021. The Company or the NCI may unilaterally terminate the CRADA for any reason or for no reason at any time by providing written notice at least 60 days before the desired termination date. During the years ended December 31, 2017, 2016 and 2015, the Company recorded costs associated with the CRADA of \$2.0 million, \$1.8 million and \$2.0 million, respectively, as research and development expenses.

Patent License Agreement Related to the Development and Manufacture of TIL

Effective October 5, 2011, the Company entered into a patent license agreement (the “Patent License Agreement”) with the National Institutes of Health, an agency of the United States Public Health Service within the Department of Health and Human Services (“NIH”), which was subsequently amended on February 9, 2015 and October 2, 2015. Pursuant to the Patent License Agreement, as amended, the NIH granted the Company licenses, including exclusive, co-exclusive, and non-exclusive licenses, to certain technologies relating to autologous tumor infiltrating lymphocyte adoptive cell therapy products for the treatment of metastatic melanoma, lung, breast, bladder and HPV-positive cancers. The Patent License Agreement requires the Company to pay royalties based on a percentage of net sales (which percentage is in the mid-single digits), a percentage of revenues from sublicensing arrangements, and lump sum benchmark royalty payments on the achievement of certain clinical and regulatory milestones for each of the various indications and other direct costs incurred by the NIH pursuant to the agreement.

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Exclusive Patent License Agreement Related to TIL Selection

On February 10, 2015, the Company entered into an exclusive patent license agreement (the “Exclusive Patent License Agreement”) with the NIH under which the Company received an exclusive license to the NIH’s rights to patent-pending technologies related to methods for improving adoptive cell therapy through more potent and efficient production of TIL from melanoma tumors by selecting for T-cell populations that express various inhibitory receptors. Unless terminated sooner, the license shall remain in effect until the last licensed patent right expires.

In consideration for the exclusive rights granted under the Exclusive Patent License Agreement, the Company paid the NIH a non-refundable upfront licensing fee in the amount of \$0.8 million. The Company also agreed to pay customary royalties based on a percentage of net sales of a licensed product (which percentage is in the mid-single digits), a percentage of revenues from sublicensing arrangements, and lump sum benchmark payments upon the successful completion of clinical studies involving licensed technologies, the receipt of the first FDA approval or foreign equivalent for a licensed product or process resulting from the licensed technologies, the first commercial sale of a licensed product or process in the United States, and the first commercial sale of a licensed product or process in any foreign country. The Company will also be responsible for all costs associated with the preparation, filing, maintenance and prosecution of the patent applications and patents covered by the Exclusive Patent License Agreement.

During the year ended December 31, 2017, the costs associated with the NIH patent licenses were immaterial. During the years ended December 31, 2016 and 2015, the Company recorded \$0.4 million and \$0.4 million, respectively, as research and development expenses associated with the NIH patent licenses.

H. Lee Moffitt Cancer Center

Research Collaboration and Clinical Grant Agreements with Moffitt

In September 2014, the Company entered into a research collaboration agreement with the H. Lee Moffitt Cancer Center (“Moffitt”) to jointly engage in translational research and development of adoptive tumor-infiltrating lymphocyte cell therapy with improved anti-tumor properties and process.

In December 2016, the Company entered into a new three-year Sponsored Research Agreement with Moffitt (the “Moffitt SRA”). At the same time, the Company entered into a clinical grant agreement with Moffitt to support an ongoing clinical trial at Moffitt that combines TIL therapy with nivolumab for the treatment of patients with metastatic melanoma. In June 2017, the Company entered into a second clinical grant agreement with Moffitt to support a new clinical trial at Moffitt that combines TIL therapy with nivolumab for the treatment of patients with non-small cell lung cancer. In the years ended December 31, 2017, 2016 and 2015, the Company recorded research and development costs of \$1.2 million, \$0.7 million, and \$0.7 million, respectively, in connection with the research collaboration and clinical grant agreements with Moffitt.

Exclusive License Agreement with Moffitt

The Company entered into a license agreement with Moffitt (the “Moffitt License”), effective as of June 28, 2014, under which the Company received a world-wide license to Moffitt’s rights to patent-pending technologies related to methods for improving TIL for adoptive cell therapy. Unless earlier terminated, the term of the license extends until the earlier of the expiration of the last issued patent related to the licensed technology or 20 years after the effective date of the license agreement.

Pursuant to the Moffitt License, the Company paid an upfront licensing fee in the amount of \$0.1 million. A patent issuance fee will also be payable under the Moffitt License, upon the issuance of the first U.S. patent covering the subject technology. In addition, the Company agreed to pay milestone license fees upon completion of specified milestones, customary royalties based on a specified percentage of net sales (which percentage is in the low single digits) and sublicensing payments, as applicable, and annual minimum royalties beginning with the first sale of products based on the licensed technologies, which minimum royalties will be credited against the percentage royalty payments otherwise payable in that year. The Company will also be responsible for all costs associated with the preparation, filing, maintenance and prosecution of the patent applications and patents covered by the Moffitt License related to the treatment of any cancers in the United States, Europe and Japan and in other countries designated by the Company in agreement with Moffitt. During the years ended December 31, 2017, 2016 and 2015, the Company did not record any costs associated with Moffitt License.

IOVANCE BIOTHERAPEUTICS, INC.
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PolyBioCept and Karolinska University Hospital

PolyBioCept Exclusive and Co-Exclusive License Agreement

On September 14, 2016, the Company entered into an exclusive and co-exclusive license agreement (the “PolyBioCept Agreement”) with PolyBioCept AB, a corporation organized under the laws of Sweden (“PolyBioCept”). PolyBioCept has filed two patent applications with claims related to a cytokine cocktail for use in expansion of lymphocytes, one of which has been abandoned. Under the PolyBioCept Agreement, the Company received the exclusive right and license to PolyBioCept’s intellectual property to develop, manufacture, market and genetically engineer TIL produced by expansion, selection and enrichment using a proprietary cytokine cocktail. The Company also received a co-exclusive license (with PolyBioCept) to develop, manufacture and market genetically engineered TIL under the same intellectual property. The licenses are for the use in all cancers and are worldwide in scope, with the exception that the uses in melanoma are not included for certain countries of the former Soviet Union.

The Company paid PolyBioCept a total of \$2.5 million as an upfront exclusive license payment. The Company will also have to make additional milestone payments to PolyBioCept under the PolyBioCept Agreement if, and when, (i) certain product development milestones are achieved, (ii) certain regulatory approvals have been obtained from the FDA and/or the European Medicines Agency, and (iii) certain product sales targets are achieved. The milestone payments will be payable both in cash (U.S. dollars) and in shares of the Company’s common stock.

If all of the foregoing product development, regulatory approval and sales milestone payments are met, the Company will have to pay PolyBioCept an additional \$8.7 million and will have to issue to PolyBioCept a total 2,219,376 shares of unregistered common stock. In addition to these potential payments, the Company reimbursed PolyBioCept \$0.2 million in expenses related to the transfer of know-how and paid PolyBioCept \$0.1 million as a clinical trials management fee. The Company also separately engaged PolyBioCept as a consultant to provide certain product development and research related services in a one-year agreement for up to \$0.2 million, subject to the consent of the Karolinska Institute to the services to be performed by its employees thereunder. The PolyBioCept Agreement has an initial term of 30 years and may be extended for additional five-year periods. The Company recognized \$0.2 million in connection with this agreement in the year ended December 31, 2017. The Company recognized \$2.7 million in connection with this agreement in the year ended December 31, 2016, as research and development expense, which amount included the \$2.5 million upfront exclusive license payment.

Karolinska University Hospital and Karolinska Institute Agreements

In connection with the execution of the PolyBioCept Agreement, the Company also (i) entered into a clinical trials agreement with the Karolinska University Hospital to conduct clinical trials in glioblastoma and pancreatic cancer at the Karolinska University Hospital, and (ii) agreed to enter into a sponsored research agreement with the Karolinska Institute for the research of the cytokine cocktail in additional indications. The Company agreed to enter into the sponsored research agreement within 90 days after the date of the PolyBioCept Agreement, which date has been extended by amendments to the PolyBioCept Agreement. Failure to enter into the sponsored research agreement or further amend the PolyBioCept Agreement will give PolyBioCept the right to terminate the PolyBioCept Agreement, while the Company will have the right to recoup \$2.2 million of the payments it made under the PolyBioCept Agreement. The Company will pay the Karolinska Institute an additional \$2.6 million in connection with these other related agreements. In the years ended December 31, 2016, the Company paid Karolinska University Hospital \$1.6 million under the clinical trials agreement to conduct the clinical trials. The \$1.6 million payment was classified as a prepaid expense and is being expensed in accordance with the Company’s research and development expense accounting policy (see Note 1). Accordingly, the Company recognized \$0.3 million and \$0.1 million in connection with this agreement as research and development expense in the years ended December 31, 2017 and 2016, respectively.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

M.D. Anderson Cancer Center

Strategic Alliance Agreement

On April 17, 2017, the Company entered into a Strategic Alliance Agreement (the “SAA”) with M.D. Anderson Cancer Center (“M.D. Anderson”) under which the Company and M.D. Anderson agreed to conduct clinical and preclinical research studies. The Company agreed in the SAA to provide total funding not to exceed approximately \$14.2 million for the performance of the multi-year studies under the SAA. In return, the Company will acquire all rights to inventions resulting from the studies and has been granted a non-exclusive, sub-licensable, royalty-free, and perpetual license to specified background intellectual property of M.D. Anderson reasonably necessary to exploit any invention, including the commercialization thereof. The Company has also been granted certain rights to clinical data generated by M.D. Anderson outside of the clinical trials to be performed under the SAA. The SAA’s term shall continue in effect until the later of the fourth anniversary of the SAA or the completion or termination of the research and receipt by the Company of all deliverables due from M.D. Anderson thereunder. As of December 31, 2017, the Company had paid \$1.4 million under the SAA. This amount has been recorded under long-term assets on the Company’s consolidated balance sheets and will be amortized to research and development expenses in accordance with the Company’s research and development accounting policy, based on enrollment and other factors. The Company did not recognize any research and development expense associated with the M.D. Anderson SAA for the year ended December 31, 2017.

MedImmune

In December 2015, the Company entered into a collaboration agreement (the “MedImmune Agreement”) with MedImmune, the global biologics research and development arm of AstraZeneca (“MedImmune”), to conduct clinical and preclinical research immuno-oncology. Under the MedImmune Agreement, the Company will fund and conduct at least one clinical trial combining MedImmune’s PD-L1 inhibitor, durvalumab, with TIL for the treatment of patients. MedImmune will supply durvalumab for the clinical trials. The purpose of the studies is to establish a dosing regimen for this combination therapy and assess its safety and efficacy.

WuXi Apptech, Inc. (“WuXi”)

In November 2016, the Company entered into that a three-year manufacturing and services agreement with WuXi pursuant to which WuXi agreed to provide manufacturing and other services. Under the agreement, the Company entered into two statements of work for two cGMP manufacturing suites to be established and operated by WuXi for Lion, one of which is expected to be capable of being used for the commercial manufacture of our products. The fee payable under the first statement of work for the use of one of the manufacturing suites during the first year of the agreement, including the fees for the necessary personnel, is \$2.5 million. The second statement of work, under which WuXi agreed to establish and operate a second, dedicated facility for a late stage/commercial manufacturing cGMP suite requires the Company to pay approximately \$5.85 million during the first year of the agreement. The Company and WuXi have extended the term of the related statements of work until May 2020. During the years ended December 31, 2017 and 2016, the Company recorded costs associated with agreements with WuXi of \$13.9 million and \$2.4 million, respectively, as research and development expenses.

NOTE 11. COMMITMENTS AND CONTINGENCIES

Facilities Leases

Tampa Lease

In December 2014, the Company commenced a five-year non-cancellable operating lease with the University of South Florida Research Foundation for a 5,115 square foot facility located in Tampa, Florida. The facility is part of the University of South Florida research park and is used as the Company’s research and development facilities. The Company has the option to extend the lease term of this facility for an additional five-year period on the same terms and conditions, except that the base rent for the renewal term will be increased in accordance with the applicable consumer price index.

In April 2015, the Company amended the original lease agreement to increase the rentable space to 6,043 square feet. In September 2016, the Company further increased the rentable space to 8,673 square feet. The per square foot cost and term of the lease were unchanged, and rent payments are approximately \$20,000 per month. The lease expires in November 2019.

San Carlos Lease

On August 4, 2016, the Company entered into an agreement to lease 8,733 square feet in San Carlos, California. The term of the lease is 54 months subsequent to the commencement date and will expire in April 2021. Monthly lease payments are approximately \$38,000.

On April 28, 2017, the Company entered into a sublease agreement with Teradata US, Inc., pursuant to which the Company agreed to sublease certain office space located adjacent to the Company’s headquarters for approximately \$26,000 per month. The space consists of approximately 11,449 rentable square feet in the building located in San Carlos, California and will expire on October 31, 2018.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

New York Lease

The Company leased office space in New York for a monthly rental of approximately \$18,000 a month from January 2017 through July 2017. On June 5, 2017, the Company entered into an agreement whereby the Company will lease office space from August 1, 2017 to July 31, 2018, for approximately \$9,000 a month.

The Company recognizes rental expense on the facilities on a straight-line basis over the lease term. Differences between the straight-line rent expense and rent payments are classified as deferred rent liability on the balance sheet.

As of December 31, 2017, the Company's future minimum lease payments under non-cancelable operating leases are as follows (in thousands):

Year	Operating Lease Commitments
2018	\$ 1023
2019	700
2020	495
2021	169
	<u>\$ 2,387</u>

Rent expense for the years ended December 31, 2017, 2016 and 2015 was \$1.0 million, \$0.7 million and \$0.3 million, respectively.

NOTE 12. LEGAL PROCEEDINGS

Class Action Lawsuit and Derivative Lawsuit. On April 10, 2017, the SEC announced settlements with us and with other public companies and unrelated parties in the *In the Matter of Certain Stock Promotion* investigation. The Company's settlement with the SEC is consistent with its previous disclosures (including in the Company's Annual Report on Form 10-K that it filed with the SEC on March 9, 2017). On April 14, 2017, a purported shareholder filed a complaint seeking class action in the United States District Court, Northern District of California for violations of the federal securities laws (*Leonard DeSilvio v. Lion Biotechnologies, Inc., et al., case no: 3:17cv2086*) against the Company and three of its former officers and directors. On April 19, 2017, a second class action complaint (*Amra Kuc vs. Lion Biotechnologies, Inc., et al., case no: 3:17cv2086*) was filed in the same court. Both complaints allege, among other things, that the defendants violated the federal securities laws by making materially false and misleading statements, or by failing to make certain disclosures, regarding the actions taken by Manish Singh, the Company's former CEO, and the Company's former investor relations firm that were the subject of the *In the Matter of Certain Stock Promotions* SEC investigation. On July 20, 2017, the plaintiff in the *Kuc* case filed a notice to voluntarily dismiss that case. The court entered an order dismissing the *Kuc* complaint on July 21, 2017. On July 26, 2017, the court appointed a movant as lead plaintiff. On September 8, 2017, the lead plaintiff filed an amended complaint (*Jay Rabkin v. Lion Biotechnologies, Inc., et al., case no. 3:17cv0286*) seeking class action status that alleges, among other things, that the defendants violated the federal securities laws by making materially false and misleading statements, or by failing to make certain disclosures, regarding the actions taken by Manish Singh and the Company's former investor relations firm that were the subject of the *In the Matter of Certain Stock Promotions* SEC investigation. On October 6, 2017, the court entered an order setting a schedule for the case, which includes a briefing schedule for motions to dismiss and a hearing date of December 22, 2017, which hearing was subsequently rescheduled by the court for January 5, 2018. On January 4, 2018, the court entered an order vacating and deeming the briefing on motions to dismiss submitted without oral argument. On February 5, 2018, court entered an order dismissing two of Plaintiff's six claims with leave to amend.

On December 15, 2017, a purported shareholder derivative complaint, *Kevin Fong v. Manish Singh, et al.* (case no. 17:1806), was filed against the Company, as nominal defendant, and certain of its current and former officers and directors, and others, as defendants, in the U.S. District Court for the District of Delaware. The complaint alleges breaches of fiduciary duties, unjust enrichment, and violations of Section 14(a) of the Securities Exchange Act of 1934 and Rule 14a-9 promulgated thereunder arising from the Securities and Exchange Commission's investigation in the *In the Matter of Certain Stock Promotions* matter and the Company's April 10, 2017 settlement thereof, and seeks unspecified damages on behalf of the Company and injunctive relief.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The Company intends to vigorously defend against the foregoing complaints. Based on the very early stage of the litigation, it is not possible to estimate the amount or range of possible loss that might result from an adverse judgment or a settlement of these matters.

Solomon Capital, LLC. On April 8, 2016, a lawsuit titled *Solomon Capital, LLC, Solomon Capital 401(K) Trust, Solomon Sharbat and Shelhav Raff v. Lion Biotechnologies, Inc.* was filed by Solomon Capital, LLC, Solomon Capital 401(k) Trust, Solomon Sharbat and Shelhav Raff against the Company in the Supreme Court of the State of New York, County of New York (index no. 651881/2016). The plaintiffs allege that, between June and November 2012 they provided to the Company \$0.1 million and that they advanced and paid on the Company's behalf an additional \$0.2 million. The complaint further alleges that the Company agreed to (i) provide them with promissory notes totaling \$0.2 million, plus interest, (ii) issue a total of 111,425 shares to the plaintiffs (before the 1-for-100 reverse split of the Company's common stock effected in September 2013), and (iii) allow the plaintiffs to convert the foregoing funds into the Company's securities in the next transaction. The plaintiffs allege that they should have been able to convert their advances and payments into shares of the Company's common stock in the restructuring that was effected in May 2013. Based on the foregoing, the plaintiffs allege causes for breach of contract and unjust enrichment and demand judgment against the Company in an unspecified amount exceeding \$1.5 million, plus interest and attorneys' fees.

On June 3, 2016, the Company filed an answer and counterclaims in the lawsuit. In its counterclaims, the Company alleges that the plaintiffs misrepresented their qualifications to assist it in fundraising and that they failed to disclose that they were under investigation for securities laws violations. The Company is seeking damages in an amount exceeding \$0.5 million and an order rescinding any and all agreements that the plaintiffs contend entitled them to obtain stock in the Company.

On April 19, 2017, the Court granted plaintiffs' counsel's motion to withdraw from the case. On May 25, 2017, the plaintiffs filed a notice that they had hired new counsel. On June 7, 2017, the judge presiding over the case recused herself because of a conflict of interest arising from her relationship with plaintiffs' new attorneys. The case has been assigned to a new judge, and briefing on a motion to dismiss has occurred, with oral argument on the motion to dismiss scheduled for April 20, 2018.

The Company intends to vigorously defend the complaint and pursue its counterclaims.

Litigation Involving Dr. Steven Fischkoff. On June 13, 2017, in an action titled *Steven Fischkoff v. Lion Biotechnologies, Inc. and Maria Fardis*, Dr. Steven Fischkoff, the Company's former Vice President and Chief Medical Officer, filed a lawsuit against the Company in the Supreme Court of the State of New York, County of New York. Dr. Fischkoff was dismissed by the Company on March 28, 2017. Dr. Fischkoff was terminated "for cause" as that term is defined in his employment agreement. In his complaint, Dr. Fischkoff alleges breaches of his employment agreement and violation of New York labor law for failure to pay monies purportedly owed to him, and seeks to recover amounts including severance pay and retention bonus (totaling \$0.3 million), a prorated incentive bonus, and amounts relating to unvested options to 150,000 shares of the Company's common stock, together with prejudgment interest, costs, expenses and attorneys' fees. On July 5, 2017, the Company filed a removal petition and removed the lawsuit to the United States District Court for the Southern District of New York, where the case has been assigned case no. 17-cv-05041. On July 14, 2017, the Company filed a partial answer and counterclaims against Dr. Fischkoff, denying his allegations, and alleging breach of contract and related claims, breach of fiduciary duty, and state and federal trade secret misappropriation and related claims, and sought a temporary restraining order and preliminary injunction against Dr. Fischkoff. On July 18, 2017, the court issued a temporary restraining order against Dr. Fischkoff requiring him to return Company materials, prohibiting him from disclosing or using Company materials, and granting expedited discovery, which is currently proceeding.

The Company intends to vigorously defend against Dr. Fischkoff's lawsuit and pursue the Company's counterclaims. Based on the very early stage of the litigation, it is not possible to estimate the amount or range of (i) a possible loss that might result from an adverse judgment or settlement of this action, or (ii) the potential recovery that might result from a favorable judgment or a settlement of this action.

Other Matters. During the second quarter of 2016, warrants representing 128,500 shares were exercised. The 128,500 shares of common stock had previously been registered for re-sale. However, the Company believes that these 128,500 warrant shares were sold by the holders in open market transactions in May 2016 at a time when the registration statement was ineffective. Accordingly, those sales were not made in accordance with Sections 5 and 10(a)(3) of the Securities Act, and the purchasers of those shares may have rescission rights (if they still own the shares) or claims for damages (if they no longer own the shares). The amount of any such liability is uncertain and as such, an accrual for any potential loss has not been made. The Company believes that any claims brought against it would not result in a material impact to the Company's financial position or results of operations. The Company has not accrued a loss for a potential claim associated with this matter as it is unable to estimate any at this time.

The Company may be involved, from time to time, in legal proceedings and claims arising in the ordinary course of its business. Such matters are subject to many uncertainties and outcomes are not predictable with assurance. The Company accrues amounts, to the extent they can be reasonably estimated, that it believes are adequate to address any liabilities related to legal proceedings and other loss contingencies that the Company believes will result in a probable loss. While there can be no assurances as to the ultimate outcome of any legal proceeding or other loss contingency involving the Company, management does not believe any pending matter will be resolved in a manner that would have a material adverse effect on the Company's financial position, results of operations or cash flows. Regardless of outcome, litigation can have an adverse impact on the Company because of defense and settlement costs, diversion of management resources and other factors.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 13. QUARTERLY UNAUDITED RESULTS

The results of operations by quarter for the years ended December 31, 2017 and 2016 are as follow:

	2017				2016			
	(in thousands, except per share information)							
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Revenue	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Net loss attributable to common stockholders	\$ (20,684)	\$ (23,377)	\$ (22,149)	\$ (25,854)	\$ (6,884)	\$ (11,563)	\$ (68,212)	\$ (15,689)
Net loss per share, basic and diluted	\$ (0.33)	\$ (0.37)	\$ (0.35)	\$ (0.36)	\$ (0.14)	\$ (0.23)	\$ (1.15)	\$ (0.25)
Weighted average shares used in computing net loss per share, basic and diluted	62,286	62,457	63,332	72,794	48,548	51,082	59,113	62,130

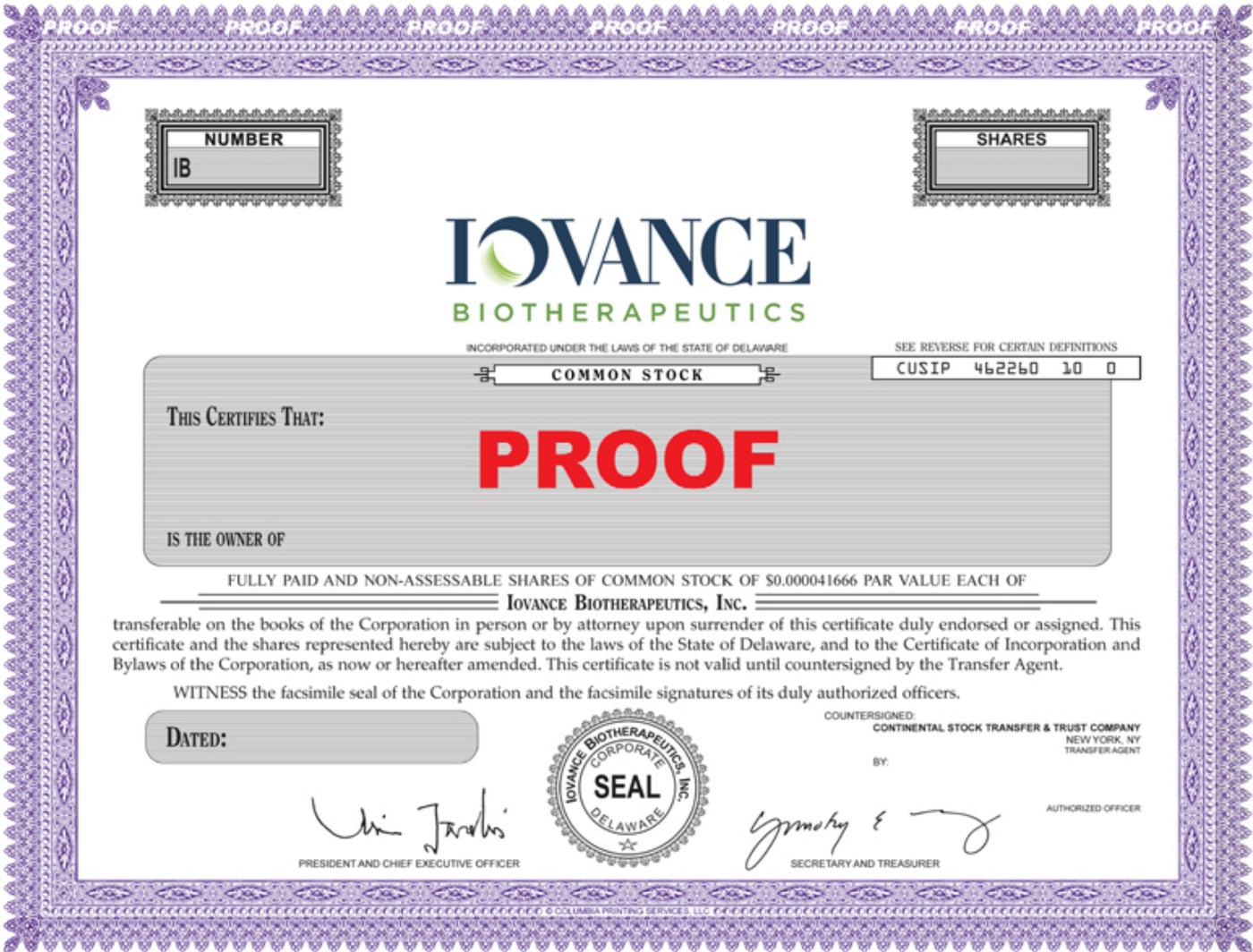
NOTE 14. RELATED PARTY TRANSACTIONS

Sanford J. Hillsberg, one of the Company's directors, is an attorney at TroyGould PC. TroyGould PC rendered and continues to render legal services to the Company. The Company paid TroyGould PC \$0.7 million, \$0.8 million and \$0.7 million, during the years ended December 31, 2017, 2016 and 2015, respectively. Mr. Hillsberg did not directly provide any legal services to the Company during the periods noted. As of December 31, 2017 and 2016, the Company had \$0.1 million and \$0.1 million in liabilities owing to TroyGould PC related to legal services, respectively.

On September 14, 2017, the Company entered into a three-year consulting agreement with Iain Dukes, D. Phil, the Chairman of the Board. As compensation for his consulting services, the Company granted Dr. Dukes a stock option to purchase up to 150,000 shares of the Company's common stock, at an exercise price of \$7.30 per share. Under the consulting agreement, Dr. Dukes agreed to provide the Company with services regarding business development opportunities, licensing transactions and technology acquisitions by the Company, and any such strategic initiatives appropriate for the Company that Dr. Dukes may identify. The granted stock options vest in 12 quarterly installments (with 1/12th of the option shares having vested on the date of grant). The vesting of the granted stock options will accelerate, and the entire award will become fully vested upon the closing of a significant licensing transaction, a material product acquisition, a material strategic transaction, or upon a change of control transaction. The Company recognized \$0.2 million in stock-based compensation expense related to this consulting agreement during the year ended December 31, 2017.

NOTE 15. SUBSEQUENT EVENT

In January 2018, the Company announced the closing of its underwritten public offering of 15,000,000 shares of the Company's common stock at a public offering price of \$11.50 per share, before underwriting discounts, which included 1,956,521 shares issued upon the exercise in full by the underwriter of its option to purchase additional shares at the public offering price less the underwriting discount. The gross proceeds from the offering, before deducting the underwriting discounts and commissions and other estimated offering expenses payable by the Company, are \$172.5 million, with estimated net proceeds to the Company of approximately \$161.7 million.



NUMBER
1B

SHARES

IOVANCE
BIOTHERAPEUTICS

INCORPORATED UNDER THE LAWS OF THE STATE OF DELAWARE

SEE REVERSE FOR CERTAIN DEFINITIONS

COMMON STOCK

CUSIP 462260 10 0

THIS CERTIFIES THAT:

PROOF

IS THE OWNER OF

FULLY PAID AND NON-ASSESSABLE SHARES OF COMMON STOCK OF \$0.000041666 PAR VALUE EACH OF

IOVANCE BIOTHERAPEUTICS, Inc.

transferable on the books of the Corporation in person or by attorney upon surrender of this certificate duly endorsed or assigned. This certificate and the shares represented hereby are subject to the laws of the State of Delaware, and to the Certificate of Incorporation and Bylaws of the Corporation, as now or hereafter amended. This certificate is not valid until countersigned by the Transfer Agent.

WITNESS the facsimile seal of the Corporation and the facsimile signatures of its duly authorized officers.

DATED:

Umi Jankovic
PRESIDENT AND CHIEF EXECUTIVE OFFICER



Gymothy E. [Signature]
SECRETARY AND TREASURER

COUNTERSIGNED:
CONTINENTAL STOCK TRANSFER & TRUST COMPANY
NEW YORK, NY
TRANSFER AGENT

BY:

AUTHORIZED OFFICER

IOVANCE BIOTHERAPEUTICS, INC.

The Corporation is authorized to issue 200,000,000 shares, consisting of 150,000,000 shares of Common Stock, \$0.000041666 par value per share, and 50,000,000 shares of Preferred Stock, \$0.001 par value per share.

The Corporation will furnish without charge to each stockholder requesting the same a statement of the designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof, and of the qualifications, limitations or restrictions of such preferences and/or rights.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM - as tenants in common
TEN ENT - as tenants by the entireties
JT TEN - as joint tenants with right of survivorship and not as tenants in common

UNIF GIFT MIN ACT -Custodian.....
(Cust) (Minor)
under Uniform Gifts to Minors Act
(State)

Additional abbreviations may also be used though not in the above list.

For Value Received, _____ hereby sell, assign and transfer unto

PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

(PLEASE PRINT OR TYPE NAME AND ADDRESS, INCLUDING ZIP CODE, OF ASSIGNEE)

of the stock represented by the within Certificate, and do hereby irrevocably constitute and appoint

to transfer the said stock on the books of the within named Corporation with full power of substitution in the premises.

Dated _____

NOTICE: THE SIGNATURE TO THIS ASSIGNMENT MUST CORRESPOND WITH THE NAME AS WRITTEN UPON THE FACE OF THE CERTIFICATE IN EVERY PARTICULAR, WITHOUT ALTERATION OR ENLARGEMENT OR ANY CHANGE WHATSOEVER.

Signature(s) Guaranteed

By _____
The Signature(s) must be guaranteed by an eligible guarantor institution (Banks, Stockbrokers, Savings and Loan Associations and Credit Unions with membership in an approved Signature Guarantee Medallion Program), pursuant to SEC Rule 17Ad-15.

TEXT MARKED BY [***] HAS BEEN OMITTED PURSUANT TO A REQUEST FOR CONFIDENTIAL TREATMENT AND WAS FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

AMENDED AND RESTATED MANUFACTURING SERVICES AGREEMENT

This Amended and Restated Manufacturing Services Agreement (this "Agreement") is made as of December 18, 2017 (the "Effective Date") by and between WuXi AppTec, Inc., a corporation organized under the laws of Delaware having a place of business at 4751 League Island Blvd., Philadelphia, PA 19112 ("Company"), and Iovance Biotherapeutics, Inc. (f.d.b.a. Lion Biotechnologies, Inc.), a Delaware corporation having its principal place of business at 999 Skyway Road, Suite 150, San Carlos, CA 94070 ("Iovance") (each of Company and Iovance, a "Party" and, collectively, the "Parties").

RECITALS

WHEREAS, Company has experience in the development, manufacture and supply of biopharmaceutical products;

WHEREAS, Iovance is developing various novel cancer immunotherapies, including autologous cell therapy products based on its tumor infiltrating lymphocytes ("TILs") technology;

WHEREAS, Iovance has developed a proprietary process that utilizes a patient's own TILs, whereby a patient's TILs are expanded in vitro and then infused back into the patient;

WHEREAS, from time to time, Iovance may engage Company to manufacture and perform services related to the manufacture of Iovance's autologous cell therapy products for use in clinical trials, all on the terms set out in this Agreement and the applicable Statements of Work between the Parties;

WHEREAS, the Parties previously executed that certain Manufacturing Services Agreement (the "Original Agreement"), with an effective date of November 23, 2016 (the "Original Effective Date"); and

WHEREAS, the Parties desire to amend and restate the Original Agreement in its entirety on the terms and subject to the conditions set forth in this Agreement to modify the terms applicable to equipment provided by Iovance and augment the scope of the relationship to permit the manufacturing of Product for patients based in the European Union and certain other countries as described herein and the Parties acknowledge and agree that this Agreement satisfies the requirement of Section 18.5.1 of the Original Agreement that any amendment of the Original Agreement be in writing.

NOW, THEREFORE, in consideration of the foregoing and the mutual promises and covenants hereinafter set forth, Company and Iovance, intending to be legally bound, hereby agree as follows:

AGREEMENT

1. DEFINITIONS

When used in this Agreement, capitalized terms will have the meanings as defined below and throughout this Agreement. Unless the context indicates otherwise, the singular will include the plural and the plural will include the singular.

1.1 “AAA” has the meaning set forth in Section 18.15.3.

1.2 “Affiliate” means, with respect to either Party, any other corporation or business entity that directly, or indirectly through one (1) or more intermediaries, controls, is controlled by or is under common control with such Party. For purposes of this definition, the term “control” and, with correlative meanings, the terms “controlled by” and “under common control with” means direct or indirect ownership of more than fifty percent (50%) of the securities or other ownership interests representing the equity voting stock or general partnership or membership interest of such entity or the power to direct or cause the direction of the management or policies of such entity, whether through the ownership of voting securities, by contract, or otherwise.

1.3 “Agreement” has the meaning set forth in the preamble, and, for clarity, includes the Appendices, the Statements of Work and the Quality Agreement, all of which are incorporated herein by this reference, as amended from time to time in accordance with this Agreement or otherwise by written agreement of the Parties.

1.4 “Background Intellectual Property” has the meaning set forth in Section 13.1.

1.5 “Batch” means a specific quantity of Product that is intended to have uniform character and quality, within specified limits, and is produced from one manufacturing run using the Process.

1.6 “Batch Record” means the production record pertaining to a Batch.

1.7 “cGMP” means the then current good manufacturing practices, standards, guidelines and regulations promulgated and published by the FDA, European Commission and/or the European Medicines Agency relating to the testing, manufacturing, processing, packaging, labelling, holding or distribution of biologics, drug substances, human cells, tissues, and cellular or tissue-based products, and/or finished drugs, to the extent applicable to the Services, including any standards, guidelines and regulations as promulgated by: (i) the FDA under and in accordance with the U.S. Federal Food, Drug and Cosmetic Act, Title 21, Parts 210, 211, 600, 610, and 1271 of the U.S. Code of Federal Regulations and the Public Health Service Act, to the extent applicable; and/or (ii) the European Medicines Agency, EU Commission and EU member state governmental authorities under and in accordance with European Directive 2003/94/EC, including, in each case of (i) and (ii), the ICH Harmonised Tripartite Good Manufacturing Practice Guide to the extent it, or components thereof, are adopted by the FDA and/or the European Medicines Agency.

1.8 “Change Order” has the meaning set forth in Section 2.2.

1.9 “COA” means a certificate of analysis, which, with respect to a Batch of Product or Product components, including packaging and labelling, shall include, at a minimum: (i) name, address, and contact phone number of each of the facilities where such Product or component was manufactured; (ii) Product or component name and details; (iii) Product or component batch number and other identification; (iv) date of manufacture; (v) date of expiry, to the extent applicable; (vi) a list of each test performed, the location of the test facility, the acceptance limits as indicated in the Product Specifications or material specifications, and the results obtained (and the COA should document actual values, where Product Specifications or component specifications are quantitative, and maintain the significant figures and rounding of numbers defined in the Product Specifications or component specifications); and (vii) such other information or statements as may reasonably be requested by Iovance.

1.10 “Company” has the meaning set forth in the preamble.

1.11 “Company Confidential Information” means the Confidential Information of Company.

1.12 “Company Operating Documents” means the standard operating procedures, standard manufacturing procedures, standard testing procedures, control specifications, raw material specifications, protocols, validation documentation, and supporting documentation used by Company in the performance of Services and for operation and maintenance of a Facility and Company equipment used in the performance of Services, excluding any of the foregoing that are unique to the Product or Services or provided by Iovance.

1.13 “Company Parties” has the meaning set forth in Section 17.2.

1.14 “Condemnation” has the meaning set forth in Section 18.3.

1.15 “Confidential Information” has the meaning set forth in Section 12.1.

1.16 “CPA” has the meaning set forth in Section 11.2.

1.17 “Effective Date” has the meaning set forth in the preamble.

1.18 “Facility(ies)” means the facility(ies) designated within the applicable Statement of Work where all development work, processing and manufacturing and other Services shall be conducted. Such term includes all of the equipment, machinery and facilities of Company at such location that are used in the performance of the Services.

1.19 “FDA” means the U.S. Food and Drug Administration, and any successor agency thereof.

1.20 “Force Majeure Event” has the meaning set forth in Section 18.2.

1.21 “Forecast” has the meaning set forth in Section 2.7.

1.22 “Improvements” has the meaning set forth in Section 13.2.1.

- 1.23 “Indemnitee” has the meaning set forth in Section 17.4.1.
- 1.24 “Indemnitor” has the meaning set forth in Section 17.4.1.
- 1.25 “Initial Agreement” has the meaning set forth in Section 18.5.2.
- 1.26 “Institutional Review Board” means an institutional review board, independent ethics committee or equivalent entity that approves, monitors and reviews medical research.
- 1.27 “Insurance Policy” has the meaning set forth in Section 17.5.
- 1.28 “Intellectual Property” has the meaning set forth in Section 13.1.
- 1.29 “Iovance” has the meaning set forth in the preamble.
- 1.30 “Iovance Confidential Information” means the Confidential Information of Iovance.
- 1.31 “Iovance Intellectual Property” means Background Intellectual Property of Iovance and New Iovance Intellectual Property.
- 1.32 “Iovance Materials” has the meaning set forth in Section 5.1.
- 1.33 “Iovance Parties” has the meaning set forth in Section 17.1.
- 1.34 “Joint Steering Committee” or “JSC” has the meaning set forth in Section 3.3.
- 1.35 “Law” or “Laws” means (a) all applicable constitutional provisions, laws, statutes, codes, rules, regulations, guidances, orders, treaties, judgments, decrees, directives, injunctions and/or ordinances of any United States or European Union (as it exists on the Effective Date) governmental entity or authority, which are applicable to the Parties, their respective obligations under this Agreement, or otherwise to the Patient Materials, Process and/or Product (any component thereof and/or the manufacture or processing thereof), including Directive 2001/83/EC, Directive 2004/23/EC and Directive 95/374/EC and the General Data Protection Regulation 2016 (when in force), and (b) cGMPs. Any reference to a particular law or regulation will be interpreted to include any revision of or successor to such statute, law, rule or regulation regardless of how it is numbered or classified.
- 1.36 “Losses” has the meaning set forth in Section 17.1.
- 1.37 “Master Batch Record” or “MBR” means the documentation that contains a detailed description of the Process and any other instructions to be followed by Company in the production of Product.
- 1.38 “Materials” has the meaning set forth in Section 5.2.
- 1.39 “New Iovance Intellectual Property” has the meaning set forth in Section 13.2.1.
- 1.40 “Original Agreement” has the meaning set forth in the Recitals.

1.41 “Original Effective Date” has the meaning set forth in the Recitals.

1.42 “Party” or “Parties” has the meaning set forth in the preamble.

1.43 “Patient Material” means (a) the Patient Tumor, and (b) all biological materials derived therefrom.

1.44 “Patient Tumor” means the patient’s primary or metastatic tumor provided by or on behalf of Iovance to Company hereunder for Company to apply the Process to and from which the TILs will be isolated and expanded to produce a Product.

1.45 “Personal Information” means any data about an identified or identifiable individual, including data that identifies an individual or that could be reasonably used to identify, locate, track, or contact an individual, in any media or format, including computerized or electronic records and paper-based files. Personal Information includes both (i) directly identifiable information, such as a name, identification number or unique job title, Social Security number or other government-issued identifier, or credit card information, and (ii) indirectly identifiable information, such as date of birth, unique mobile or wearable device identifier, telephone number and Internet Protocol address, as well as key-coded data.

1.46 “Process” means Iovance’s proprietary process for expanding TILs from a Patient Tumor in vitro to produce a Product and provided by Iovance to Company pursuant to this Agreement, as such process may be further developed under this Agreement.

1.47 “Process Specifications” means robust, data-driven specifications developed by or for Iovance with respect to the implementation of the Process as set forth in the Quality Agreement, as such specifications may be amended from time to time in accordance with the Quality Agreement.

1.48 “Product” means the finalized TIL cell therapy product that is produced from Patient Material by the application of the Process.

1.49 “Product Specifications” means the testing methods and associated robust, data-driven acceptance criteria used to assess the Product manufactured under this Agreement, as such methods and/or acceptance criteria may be amended from time to time in accordance with the Quality Agreement.

1.50 “Product Warranties” means those warranties as specifically stated in Section 9.1.

1.51 “Project Team” has the meaning set forth in Section 3.1.

1.52 “Purchased Equipment” has the meaning set forth in Section 2.3.5.

1.53 “Quality Agreement” means the Quality Agreement entered into by the Parties on November 3, 2016, as may be amended or restated from time to time by the Parties.

1.54 “Regulatory Approval” means the approvals, licenses, registrations or authorizations (including marketing authorizations) of any regulatory authority that may be necessary for the development, marketing, sale and commercialization of the Product (including such approvals as are necessary to distribute investigational product).

1.55 “Remedial Event” means an event whereby Product is subject to a recall, field corrective action, or other regulatory action, including a clinical hold.

1.56 “Report” has the meaning set forth in Section 3.2.

1.57 “Representatives” means, with respect to a Party, (a) its employees, contractors, subcontractors, consultants, agents, Affiliates or persons otherwise associated with such Party as a result of the performance of this Agreement or a Statement of Work and (b) the employees, contractors, subcontractors, consultants, agents of such Party’s Affiliates or persons otherwise associated with such Party’s Affiliates as a result of the performance of this Agreement or a Statement of Work.

1.58 “Security Incident” has the meaning set forth in Section 6.2.7.

1.59 “Services” means the activities performed by Company under a Statement of Work.

1.60 “SOP” means a standard operating procedure.

1.61 “Specifications” means the Product Specifications and the Process Specifications.

1.62 “Statement of Work” means a statement of work that is signed by the Parties and attached hereto as Appendix A or later becomes attached through an amendment by the Parties as further detailed in Article 2. As each subsequent Statement of Work is agreed to and signed by the Parties, each shall state that it is to be incorporated and made a part of this Agreement and shall be consecutively numbered (for example as A-1, A-2, A-3, etc.). For clarity, the plural of “Statement of Work” is “Statements of Work”.

1.63 “Suite” means one (1) Company cGMP compliant unit space suitable for the performance of Services under a Statement of Work.

1.64 “Taxes” has the meaning set forth in Section 11.3.

1.65 “Term” has the meaning set forth in Section 16.1.

1.66 “Third Party” means any party other than Company, Iovance or their respective Affiliates.

1.67 “TILs” has the meaning set forth in the recitals.

1.68 “Use” means to perform any operation or set of operations on Patient Materials or Personal Information, whether or not by automatic means, including collecting, recording, organization, storage, access, adaptation, alteration, retrieval, consultation, use, evaluation, analysis, reporting, sharing, disclosure, dissemination, transmission, making available, alignment, combination, blocking, deleting, erasure or destruction.

1.69 “WO A-4” has the meaning set forth in Section 18.5.2.

1.70 “Work” has the meaning set forth in Section 13.2.1.

2. STATEMENTS OF WORK; PERFORMANCE

2.1 **Statement of Work.** From time to time, the Parties will enter into individual Statements of Work, which shall describe the Services to be performed by Company thereunder and other details related thereto. Statements of Work shall be in a form to be agreed by the Parties and may include the following as applicable to the Services: Process transfer, Process development, Specifications, nature (e.g., expected tumor types) of applicable Patient Tumors, number of Product lots required to be produced per month and in the aggregate during the term of the Statement of Work, timelines for receipt, delivery and dispatch of applicable Patient Tumors and Products, required Suite availability, required delivery terms for Product, financial consideration, and such other terms as the Parties mutually determine. Once agreed to by the Parties, each such Statement of Work shall be executed by each of the Parties and appended hereto as part of Appendix A. In the event of a conflict between the terms and conditions of this Agreement and any Statement of Work, the terms and conditions of this Agreement shall control unless the Parties expressly agree in a Statement of Work that a particular clause in such Statement of Work will control.

2.2 **Modification of Statement of Work.** Should Iovance want to modify a Statement of Work, including a change or revision to the method or manner of performance of Company’s obligations under such Statement of Work, or the facilities, equipment, or materials to be used in performing the Services subject to such Statement of Work, Iovance may propose to Company an amendment to the Statement of Work with the desired modifications (“Change Order”). Upon receipt of such Change Order, Company will evaluate the Change Order and discuss with Iovance those Change Order elements that Company may reasonably accommodate. Based on such discussions, Company will prepare a modified version of the Statement of Work reflecting the elements of such Change Order (including any changes to the estimated timing, estimated charges or scope of Services) and will submit such modified version of the Statement of Work to Iovance for review and comment. Additionally, if Company reasonably determines that a change or addition to the information provided by Iovance hereunder, or gained under an applicable Statement of Work necessitates a change to (i) the method or manner of performance of Company’s obligations hereunder including an acceleration of such obligations, (ii) production or assay batch records, or (iii) the facilities, equipment, materials, Services or site, which may cause an activity start date to be rescheduled, Company may propose a Change Order to Iovance, which Iovance will consider in good faith, but which will otherwise be subject to this Section 2.2. If the Parties agree on terms, they will execute such modified Statement of Work and such modified Statement of Work shall be appended and become part of the original (or prior) Statement of Work and this Agreement. Thereafter such modified version of the Statement of Work will be deemed to have replaced the prior version of the Statement of Work and to be binding on the Parties. Notwithstanding the foregoing, if a modified version of the Statement of Work is not agreed to and executed by both Parties, the then-current Statement of Work shall remain in effect.

2.3 Performance by Company.

2.3.1 Company will perform the Services in a professional and workmanlike manner and in accordance with generally accepted industry practices and the standards and the terms of this Agreement, the applicable Statement of Work, the Quality Agreement, and all Laws, and will ensure the same of any Affiliates and Third Parties performing Services on behalf of Company.

2.3.2 Company shall not amend, modify, change or supplement a Statement of Work, or any part thereof, without the prior written consent of Iovance.

2.3.3 Company shall assign such qualified scientific, technical, and other personnel and allocate such Suite capacity to perform the Services as set forth in the applicable Statement of Work. To the extent such Statement of Work does not specify scientific, technical or other personnel or Suite capacity, Company shall assign such scientific, technical and other personnel, and shall allocate such Suite capacity, as is reasonably and customarily necessary for performing the Services as set forth in the applicable Statement of Work, and consistent with all Laws, this Agreement and the Quality Agreement. Company shall ensure that Company personnel, and any Affiliates or Third Parties, assigned to perform activities under this Agreement shall be capable of professionally and competently performing the applicable Services. All persons and entities providing Services shall be appropriately trained and qualified to perform their assigned responsibilities.

2.3.4 Company will promptly notify Iovance of any delays that arise during the performance of a Statement of Work.

2.3.5 Unless authorized by Iovance in writing, Company shall perform the Services only at the Facility(ies) designated in the applicable Statement of Work. Unless authorized by Iovance in writing, Company may not utilize any facility, other than the Facility(ies), in connection with the Services and/or Products. Unless otherwise provided by or authorized by Iovance in writing, Company will use Company's equipment for the performance of the Services. Without limiting the foregoing, Iovance will purchase and lease to Company, for no additional consideration other than Company's performance under this Agreement and the Statements of Work, such equipment as is identified in the applicable Statement of Work to be provided by Iovance to Company (the "Purchased Equipment"). All Purchased Equipment will be delivered to Company free and clear of all liens and encumbrances other than those securing obligations being serviced by Iovance, and Company will not permit or cause to be suffered any liens or encumbrance on any Purchased Equipment. Company will be responsible for the maintenance of the Purchased Equipment for so long as the Purchased Equipment is used in performance of the Services, including furnishing all necessary and appropriate utilities for its operation and maintenance.

2.3.6 Company shall ensure that all Purchased Equipment is properly maintained in accordance with cGMP, is protected from deterioration other than normal wear and tear, is only used for the Services, and is returned to Iovance upon the expiration or termination of this Agreement at Iovance's reasonable and pre-approved cost and expense. Except for the use of accessories required for the operation of the Purchased Equipment, Company shall not make any alterations, modifications, or additions to the Purchased Equipment and shall not remove anything from the Purchased Equipment, without the prior written consent of Iovance. Company shall provide Iovance and its Representatives with full and free access to the Purchased Equipment during normal business hours. All Purchased Equipment is and shall remain the property of Iovance and shall be and remain tagged accordingly. In no event shall Company have any interest in the Purchased Equipment other than Company's leasehold interest consisting of Company's right to possess and use the Purchased Equipment as provided in this Agreement. Company will not claim or identify the Purchased Equipment as being owned by Company. The Purchased Equipment will be located solely at the Facilities until so notified by Iovance. Iovance may file at Iovance's expense any document or other information necessary to demonstrate and secure its ownership in the Purchased Equipment, including a Uniform Commercial Code financing statement providing the name of Iovance as lessor and of Company as lessee and indicating the collateral as the Purchased Equipment. Iovance may also notify any person who has filed a Uniform Commercial Code financing statement against Company covering equipment, or who otherwise might claim an interest in Company's equipment, as to Iovance's interest in the Purchased Equipment. Company shall cooperate with Iovance in completing and filing, and shall execute or join with Iovance in executing, any such documents, information or notifications. Iovance shall not be liable or otherwise responsible for any loss, damage or other consequence suffered by Company, its Affiliates or any Third Party as a direct or indirect result of the Purchased Equipment or the use of the Purchased Equipment by Company, its Representatives or any unauthorized person while the Purchased Equipment is in the possession or under the control of Company, except to the extent such loss, damage or consequence is the direct or indirect result of the actions or omissions of Iovance's or any of its Representatives' (for clarity, excluding Company) use of or physical contact with the Purchased Equipment.

2.3.7 All Facilities, equipment, including Purchased Equipment, and processes shall be appropriately qualified, monitored, verified, and validated, as applicable, commensurate with the Services to be performed as may be required under Law, prior to the commencement of the Services utilizing such Facilities, equipment and processes, including Purchased Equipment, by Company. Company shall maintain the Facility(ies), equipment, including Purchased Equipment and contract rights in use at the Facility(ies) in conditions adequate to perform the Services in accordance with all Laws, this Agreement, the Quality Agreement, and the applicable Statement of Work.

2.3.8 Company shall timely procure and store all materials (other than the Patient Materials and Iovance Materials) that are required for the performance of the Services as such Services are described in applicable Statements of Work.

2.4 Compliance with Safety, Health and Environmental Laws. Company shall be responsible for compliance with all Laws related to health, safety and the environment where Services are performed, including providing its employees and consultants engaged in the performance of Services or Iovance representatives engaged in the review of Services with all required information and training concerning any potential hazards involved in the performance or review of the Services and any precautionary measures to protect such Iovance representatives, and Company's employees and consultants from any such hazards. Except to the extent caused by the negligent act or omission of Iovance or any Iovance representative, Iovance shall not be responsible for any injuries that Company's employees or consultants or Iovance's representatives may suffer in the performance or review of Services.

2.5 Outsourcing to Third Parties. Company shall, only after receiving prior written approval by Iovance (which such approval may be withheld in Iovance's sole discretion), be entitled to outsource discrete portions of the Services to Third Parties, which such approval shall be received in the form of an executed Statement of Work that specifically identifies such Third Parties, the Services to be so outsourced, and the location(s) at which such outsourced Services will be performed; provided that (i) the terms of any such arrangement between such Third Party and Company are substantially identical in their effect to those set forth in this Agreement, especially in terms of confidentiality, Intellectual Property rights, and compliance with Laws, (ii) Company shall be responsible for the initial and ongoing Third Party qualification (including any appropriate validation or verification of the Services to be performed by such Third Party, including, to the extent applicable, equipment to be used by any such Third Party), to the extent required by Law, and for Company's obligations for Services provided by any Third Party under this Agreement or any Statement of Work, and (iii) Company shall remain liable for Company's obligations under this Agreement or any applicable Statement of Work regardless of the failure of any such Third Party to perform the subcontracted Services in accordance with this Agreement. Company hereby expressly waives any requirement that Iovance exhaust any right, power or remedy, or proceed against any such Third Party, for a breach of any of Company's obligation or performance hereunder due to such Third Party's failure prior to proceeding directly against Company. Subject to Section 10.4.2, Iovance shall have the right to review Company's qualification of all Third Parties and Third Party activities under this Agreement or any Statement of Work and shall have the right to inspect or audit, itself or through a Representative, or attend any Company inspection or audit of such Third Party before providing written approval of such Third Party. Iovance's review, audit and inspection, and attendance rights hereunder shall continue following Iovance's written approval of the Third Party and shall further extend to any Third Party re-qualification (including any appropriate re-validation or re-verification of Services, including, to the extent applicable, equipment to be used by any such Third Party), to the extent such re-qualification is required by Law, and re-qualification of Third Party activities under this Agreement or any Statement of Work conducted by Company of any such Third Party.

2.6 Use of Affiliates. Company may exercise its rights and perform its obligations under this Agreement through one (1) or more of its Affiliates with Iovance's prior written consent; provided, that, Company (i) shall be responsible for ensuring that all of its Affiliates comply with the terms and conditions of this Agreement (including all obligations with respect to the confidential treatment of Iovance Confidential Information and assignment of any New Iovance Intellectual Property), each Statement of Work, the Quality Agreement and all Laws, (ii) shall be responsible for the initial and ongoing Affiliate qualification, to the extent required by Law, and for its obligations with respect to the Services that are provided by any Affiliates on behalf of Company under this Agreement or any Statement of Work, (iii) shall remain directly responsible for the performance of its Affiliates under this Agreement (including performance under any applicable Statement of Work), and (iv) hereby expressly waives any requirement that Iovance exhaust any right, power or remedy, or proceed against any such Affiliate for any obligation or performance hereunder (including performance under any applicable Statement of Work), prior to proceeding directly against Company. Subject to Section 10.4.2, Iovance shall have the right to review Company's Affiliate qualification and qualification of such Affiliate's activities under this Agreement or any Statement of Work and shall have the right to inspect or audit, itself or through a Representative, or attend any Company inspection or audit of such Affiliate before providing written approval of such Affiliate. Iovance's review, audit and inspection, and attendance rights hereunder shall continue following Iovance's written approval of any such Affiliate of Company and shall further extend to any Affiliate re-qualification, to the extent such re-qualification is required by Law, and re-qualification of such Affiliate's activities under this Agreement or any Statement of Work conducted by Company.

2.7 Forecast and Suspended Services. From time-to-time during the Term, Iovance will provide to Company a rolling twelve (12)-month forecast specifying Iovance's anticipated requirements for the number of Batches to be Processed by calendar quarter for the succeeding four (4) calendar quarters, including anticipated tumor type (the "Forecast"). The number of Batches set forth in the Forecast shall constitute Iovance's good faith estimate of Iovance's requirements for Company's manufacturing capacity for such periods. Additionally, the Parties shall meet once per month, either in person or via teleconference or videoconference, to discuss Iovance's anticipated manufacturing needs. In the event of a Remedial Event the Parties agree that Company's obligation to supply and Iovance's obligation to purchase any Batches included in the Forecast that would be affected by such Remedial Event, shall be suspended commencing upon receipt by Company of written notice from Iovance of the Remedial Event and continuing until such time as such Remedial Event is resolved. Iovance shall promptly notify Company when any such Remedial Event is resolved and the Parties obligations which were suspended shall resume. Regardless of any such suspension, Iovance shall remain obligated to pay for the manufacturing suite fees as specified in an applicable Statement of Work; provided, that, if an investigation conducted under the Quality Agreement determines that such Remedial Event was caused by the negligence or willful misconduct of Company, Iovance shall have no obligation to pay such fees during the period of suspension. If the Remedial Event lasts longer than three (3) months then Iovance may (i) elect to resume the affected manufacturing activities in accordance with the Forecast, or (ii) pay Company for the agreed suite fees plus other fixed costs for the Batches contained in the Forecast for the duration of the Remedial Event, or (iii) allow Company to use the suite(s) and manufacturing capacity for Third Party projects for the duration of the Remedial Event plus six (6) months, in which case during such time Iovance shall have no obligation to pay to Company any amounts for such manufacturing suite fees or Batches included in the Forecast; provided, that, if an investigation conducted under the Quality Agreement determines that such Remedial Event is caused by the negligence or willful misconduct of Company, Iovance shall have no obligation to pay suite fees or other fixed costs during the period of suspension and may elect to maintain the suspension of manufacturing activities until the resolution of the Remedial Event. With regard to Iovance's election under the previous sentence, Iovance shall give Company at least thirty (30) days' notice of its intent.

2.8 Timing of Services. Each Party understands that once the timing for manufacturing Batches is established that it is of the utmost importance that the execution of each Party's obligations is consistent with meeting the timing required for Batch production. Accordingly, both Parties shall perform their respective obligations in order to meet the timing guidelines for Batch production provided in the applicable Statement of Work.

2.9 Commercial Manufacturing Agreement. Upon Iovance's request (and at Iovance's sole discretion), Company and Iovance shall enter into a mutually agreeable commercial manufacturing agreement whereby Company will provide Product to Iovance for commercial purposes.

3. GOVERNANCE

3.1 Project Team.

3.1.1 In accordance with the Original Agreement, the Parties have established a project team (“Project Team”), which consists of personnel from each Party who are appropriately skilled and knowledgeable in relation to the Services. The Project Team is comprised of equal numbers of representatives from Iovance and Company. A representative from Iovance shall chair the Project Team.

3.1.2 The Project Team shall be responsible for the following:

- (a) coordinating transfer of technology and knowledge related to the Services;
- (b) amending and updating Statements of Work;
- (c) implementation of the Services through each Statement of Work;
- (d) monitoring of the Services under each Statement of Work;
- (e) reporting to the JSC on the progress of the Services; and
- (f) establishing Project Team subgroups as reasonably necessary.

3.1.3 Decisions of the Project Team shall be made by unanimous agreement of the Parties, with each Party’s representatives having one (1) vote in the aggregate. For purposes of clarity, decisions by the Project Team may be made by as few as one (1) representative from each Party and in any forum (face-to-face, videoconference, teleconference, etc.). In the event that unanimity is not achieved within the Project Team, either Party may, within thirty (30) days, refer such matter to the JSC and the JSC shall promptly discuss the matter and attempt in good faith to resolve the matter.

3.1.4 Unless otherwise agreed to by the Parties in writing;

- (a) the Project Team shall meet at least bi-weekly, in person, or by teleconference or videoconference;
- (b) the Project Team members from Company shall keep the Project Team members from Iovance fully and regularly informed as to its progress with its obligations under each Statement of Work, including written Project reports, and progress with respect to general obligations under this Agreement as Iovance may reasonably request; and
- (c) Project Team subgroups shall communicate and meet as necessary in order for the activities allocated to them to be conducted in accordance with the timelines mandated by the Project Team.

3.2 Reports. Company shall (a) be available for conference calls discussing progress, problems and plans associated with the Services and (b) upon the request of Iovance provide written reports to the Project Team setting forth the results of the Services (each a "Report"). Company shall also provide other reports, data, and information to the Project Team as agreed to by the Project Team, or as set forth in an applicable Statement of Work, from time-to-time. Company shall further provide other reports, data, and information that (i) Company is required to provide to Iovance under Laws within the timeframes specified by such Laws, and/or (ii) Iovance is required to report to the applicable regulatory authorities with sufficient time to allow Iovance to evaluate the relevant reports, data, and/or information and provide its report to the applicable regulatory authorities within the timeframes required by Law.

3.3 Joint Steering Committee.

3.3.1 In accordance with the Original Agreement, the Parties have established a joint steering committee (the "Joint Steering Committee" or "JSC"), which consists of personnel from each Party who are appropriately skilled and knowledgeable in relation to the Services. The JSC is comprised of equal numbers of representatives from Iovance and Company. A representative from Iovance shall chair the JSC.

3.3.2 The JSC shall be responsible for the following:

- (a) managing the overall relationship between the Parties;
- (b) providing strategic guidance and management regarding clinical and commercial development, key contractual responsibilities and alignment across all functional activities;
- (c) establishing and monitoring the goals and prioritization of the Services, and overseeing the Services generally;
- (d) providing resources and budget guidance for the Services;
- (e) establishing performance metrics focusing on adherence to milestones, budgets and the objectives of the Services;
- (f) resolving disputes referred to the JSC by the Project Team; and
- (g) discussing reports provided by the Project Team.

3.3.3 Decisions of the JSC shall be made by unanimous agreement of the Parties, with each Party's representatives having one (1) vote in the aggregate. For purposes of clarity, decisions by the JSC may be made by as few as one (1) representative from each Party and in any forum (face-to-face, videoconference, teleconference, etc.). In the event that unanimity is not achieved within the JSC, either Party may, within thirty (30) days, refer such matter for resolution pursuant to Section 18.15.1.

3.3.4 Unless otherwise agreed to by the Parties in writing, the JSC shall meet once per calendar quarter, in person, or by teleconference or videoconference.

3.4 Committee Minutes. The Party hosting a given Project Team or JSC meeting will be responsible for preparing reasonably detailed written minutes that reflect, without limitation, material decisions made, action items identified and unresolved matters discussed at such meetings. The initial draft of the meeting minutes for a given meeting, reflecting key decisions, action items and unresolved matter, among other details, shall be completed by the end of such meeting and circulated to the other Party for subsequent review and approval.

4. TECHNOLOGY TRANSFER

4.1 Process Specifications. From time to time, Iovance shall provide the Process Specifications to Company and such Background Intellectual Property of Iovance as may be reasonably required by Company to perform the Services hereunder pursuant to a Statement of Work. For clarity, all right and title to and in such Process Specifications and Iovance's Background Intellectual Property shall remain solely vested in Iovance.

4.2 Master Batch Record.

4.2.1 Company will prepare Master Batch Records as required to execute the Process in accordance with the Process Specifications, this Agreement, any applicable Statement of Work, all Laws, and the Quality Agreement. Iovance will inform Company of any specific requirements Iovance may have relating to the Master Batch Records, including any information or procedures, including testing procedures, Iovance wishes to have incorporated therein and Company will reflect any such instructions provided by Iovance in the Master Batch Record. If Company intends to include in the Master Batch Record the use of any assay, medium, or other technology that either is not commercially available or is subject to a separate licensing or royalty payment, Company will inform Iovance of such intention in advance and the Parties will meet to discuss and attempt to agree in good faith on the terms of use of such non-commercially available materials or technology in the Process. Company will not incorporate any of Company's Background Intellectual Property, or that of any Affiliate or Third Party, into the Process or the Master Batch Records without the prior written consent of Iovance.

4.2.2 Company will deliver iterative versions of the Master Batch Record to Iovance on timing set forth in each Statement of Work that calls for the preparation of a new Master Batch Record. Iovance will notify Company in writing of any objections or comments it has to the draft Master Batch Record, and upon such notification, representatives of Company and Iovance will meet promptly to resolve such objections. The Master Batch Record will be final when approved by Iovance and shall be deemed Iovance Confidential Information.

5. IOVANCE MATERIALS

5.1 Iovance Materials. Iovance will provide Company with the materials, and rights with respect to associated intellectual property, set forth in Appendix B or as expressly stated in a Statement of Work ("Iovance Materials"). All Iovance Materials supplied to Company shall remain the exclusive property of Iovance. Iovance Materials shall only be used as described in the applicable Statement of Work, this Agreement, the Quality Agreement and in compliance with all Laws. Under no circumstances shall Iovance Materials be used in humans without the prior written consent of Iovance.

5.2 Limitation on Liability. Company shall not be liable for (i) the accuracy or inherent characteristic, or defect of Iovance Materials, Iovance Confidential Information, Patient Materials, or other information or material provided by Iovance as such are first provided or made available by or on behalf of Iovance (collectively, “Materials”) or for any error or defect in the Services to the extent directly arising out of or related to any such inaccuracies, inherent characteristic or defect in such Materials at the time first provided or made available nor for (ii) any consequences of such inaccuracies, inherent characteristics or defects that could not reasonably be avoided by Company, including any delay in Company’s performance of the Services in accordance with any Statement of Work to the extent directly resulting from such inaccuracies, inherent characteristic or defects in Materials at the time first provided or made available.

5.3 Disclaimer. ANY MATERIALS PROVIDED BY IOVANCE HEREUNDER (INCLUDING “MATERIALS”) ARE PROVIDED WITHOUT REPRESENTATION OR WARRANTY OF ANY SORT, WHETHER WRITTEN OR ORAL, EXPRESS OR IMPLIED, INCLUDING ANY REPRESENTATION OR WARRANTY OF QUALITY, PERFORMANCE, MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, AND IOVANCE MAKES NO REPRESENTATION THAT THE USE OF SUCH MATERIALS WILL NOT INFRINGE ANY PATENT OR OTHER PROPRIETARY RIGHT OF ANY THIRD PARTY.

5.4 Transfer, Records and Return. Company shall not transfer any portion of the Iovance Materials to any Third Party or use the Iovance Materials for any purpose other than the purposes of performing its obligations under, and in accordance with, this Agreement, the Quality Agreement, the applicable Statement of Work, and all Laws. Company shall hold, store and transport all supplies of the Iovance Materials in compliance with all Laws, this Agreement, the Quality Agreement, and the applicable Statement of Work. Company shall maintain complete and accurate records relating to the disposition of all Iovance Materials. Within thirty (30) days of the expiration or termination of any Statement of Work or this Agreement, or Iovance’s request, Company shall return to Iovance, or destroy, at Iovance’s option, all unused supplies of Iovance Materials.

6. **PATIENT MATERIALS**

6.1 Handling, Storage and Use of Patient Materials. As Patient Materials will include biological materials received from individual patients, as well as intermediates and Product manufactured from Patient Tumors, Company shall handle, use and store Patient Materials strictly in accordance with this Agreement, the applicable Statement of Work, the Quality Agreement, and all Laws, and, unless otherwise requested by Iovance in writing, exclusively at the Facility(ies). All Patient Materials shall remain the sole property of Iovance and shall not be used for any other purpose other than for the performance of obligations under the applicable Statement of Work.

6.2 Privacy and Data Protection. Throughout the Term, Company shall:

6.2.1 promptly inform Iovance of all subcontractors and other Third Parties involved in and the geographic location of all Patient Material data and any such data flows across country borders that are undertaken by or on behalf of Company in performing the Services;

6.2.2 use its material tracking system to ensure that Patient Materials can be traced and identified through the production stream and ultimately matched with the correct subject. Company shall work with Iovance to incorporate Iovance's existing clinical coding system into Company's Patient Material tracking system, the incorporation of which shall be subject to Iovance's prior written approval;

6.2.3 Use Patient Materials only in accordance with Iovance's instructions, this Agreement, the Quality Agreement, each Statement of Work, and all Laws, and in good faith performance of its obligations on behalf of Iovance under this Agreement. Where disclosure is required by Law, Company shall immediately notify Iovance, work with Iovance to take actions Iovance deems necessary with regard to the disclosure, use its best efforts to limit the disclosure, cooperate with Iovance should Iovance wish to pursue an order limiting the disclosure, and only disclose the minimum amount of Patient Materials needed to comply with such Law. For the avoidance of doubt, Company shall not Use any Patient Materials that it may access or otherwise receive under this Agreement for its own marketing, analytics or other purposes, Company shall not license, sell or otherwise provide Patient Materials to any Third Party that has not been approved in writing by Iovance and that has not entered into a written agreement obligating it to protect Patient Materials in accordance with the standards set forth in this Article 6;

6.2.4 without limiting Section 6.1, Use all Personal Information and Patient Materials only in accordance with

- (a) all applicable privacy, security and data protection Laws (including the United States Health Insurance Portability and Accountability Act of 1996, as amended by the HITECH Act, including the Standards for Privacy of Individually Identifiable Health Information, and the EU Data Protection Directive 95/46/EC and the General Data Protection Regulation 2016 (when in force)), rules, regulations, codes of conduct, certifications, bilateral and multilateral privacy and data protection frameworks and enforceable forms of self-regulation, including those restricting cross border transfer of data,
- (b) all Laws governing biosamples and their use (such as EU Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorization of the manufacturing or importation of such products) and its various implementation laws in the EU Member States,
- (c) all similar laws in Switzerland as are referenced in the foregoing subsections (a) and (b), such as the Swiss Human Research Act (as amended in 2014) and the Swiss Federal Data Protection Act, and

- (d) all Laws governing outbound telephone calls, transmission of electronic mail, transmission of facsimile messages and any other communications-related privacy or data protection laws and regulations (including the EU ePrivacy Regulation once it has entered into force);

6.2.5 maintain control over Patient Materials received by it hereunder and not release Patient Materials, without Iovance's written consent, to any person or entity other than the Representatives of Company who (a) are under Company's direct supervision and control and (b) have a need to access Patient Materials in connection with this Agreement. Any Representative of Company that is a Third Party shall first be approved by Iovance prior to receipt of or access to Patient Materials. Company shall further not allow anyone to take or send Patient Materials to any location other than the Facility(ies), unless written permission is obtained by Company from Iovance prior to such transfer. Notwithstanding the foregoing, the restrictions in this Section 6.2.4 shall not apply to the extent specifically requested by Iovance, in which case, Company shall take all Iovance requested action;

6.2.6 implement reasonable physical, technical and administrative safeguards, which shall be in accordance with all Laws, as appropriate for the sensitivity of the information and Patient Materials, to protect Patient Materials and Iovance Confidential Information received by Company pursuant to this Agreement from loss, misuse, and unauthorized access, disclosure, alteration or destruction, including implementation and enforcement of administrative, technical and physical security policies and procedures, and training of all staff responsible for handling Patient Materials in accordance with the requirements set forth in this Article 6;

6.2.7 notify Iovance within a reasonable period, in no event to exceed seventy-two (72) hours after discovery, or shorter if required by Law of any unauthorized uses or disclosures of Patient Materials or any Security Incident involving Patient Materials, including any incident that Company reasonably believes to involve unauthorized access to or disclosure of Patient Materials, of which it becomes aware; provided, further, that if Company (or any of its Representatives, or their personnel) is responsible for the Security Incident, Company shall promptly take all necessary and appropriate corrective action. All corrective actions shall be subject to Iovance's prior written approval. Company shall reasonably cooperate with Iovance in its investigation of a Security Incident, whether discovered by Company, Iovance or a Third Party, which shall include providing Iovance a detailed description of the Security Incident, the identity of the Patient Materials affected, and any other information Iovance reasonably may request concerning such Security Incident, as soon as such information can be collected or otherwise becomes available. Company shall pay for or reimburse Iovance for all costs, losses and expenses relating to any Security Incident arising from Company's gross negligence or willful misconduct, including costs of forensic assessments and breach notifications, as applicable, and all other remedies required by Law. "Security Incident" shall mean any actual or suspected event in which Patient Materials is or may have been lost, stolen, improperly altered or destroyed, improperly accessed, or used for a purpose not permitted under this Agreement;

6.2.8 cooperate with Iovance to respond to any inquiries regarding practices related to the Use of Patient Materials in connection with this Agreement; and

6.2.9 obligate its Representatives, or any personnel thereof, to adhere to the standards as described in this Article 6.

6.3 Personal Information. Iovance shall use commercially reasonable efforts to not provide, and Company shall not receive, any patient identifying information, including Personal Information. In the event that Company receives any patient identifying information, including Personal Information, Company shall (a) immediately notify Iovance, and (b) take tangible actions, including implementing any necessary security and/or protection precautions, as may be directed by Iovance.

6.4 Return or Destruction. Company shall return or destroy all unused or leftover Patient Materials received from, or on behalf of, Iovance, or otherwise received by Company on behalf of Iovance upon the earlier of (a) thirty (30) days after completion or termination of the Services utilizing such Patient Materials or (b) Iovance's request, and in accordance with all Iovance written instructions, including confirmation of destruction. Company shall not retain such Patient Materials, except as set forth in the Quality Agreement.

6.5 Breach. Company shall be responsible for any and all breaches of this Article 6 by its Representatives.

7. **MANUFACTURE OF PRODUCT; ORDER PROCESS; DELIVERIES**

7.1 Manufacture by Company. Iovance shall provide the requisite Iovance Materials (including, to the extent applicable, Patient Materials), and information related to such Iovance Materials, as is required for Processing by Company into Product in accordance with the timing set forth in the applicable Statement of Work. Company will perform such Services as set forth in this Agreement, the Quality Agreement and the applicable Statement of Work. Company shall handle and store all quantities of Product, Patient Materials and any other materials used in the Services in accordance with the terms and conditions of this Agreement (including the applicable Specifications), the Quality Agreement, the applicable Statement of Work, and all Laws.

7.2 Quality Agreement. The Parties have entered into the Quality Agreement, which sets forth the respective quality assurance and regulatory responsibilities of the Parties.

7.3 Delivery. Product shall be delivered FCA (Incoterms 2010) Company Facility. Transportation of Product or Materials, whether or not under any arrangements made by Company, will be at the sole risk and expense of Iovance. Product shall be made available for shipment in accordance with the Quality Agreement.

7.4 Shipment. Company will package and label Product for shipment in accordance with the Master Batch Record, Specifications, any written instructions provided by Iovance, the applicable Statement of Work, this Agreement, the Quality Agreement, and all Laws. Such packaging and labelling shall further comply with Company's SOPs to the extent they do not conflict with the foregoing. At its sole discretion, Iovance will arrange or Iovance will instruct Company to arrange the transportation of Product or Iovance Materials from Company's Facility to the destination indicated by Iovance in accordance with the applicable Statement of Work and the Quality Agreement, and, if applicable, Iovance's written requests, instructions, and directions. All reasonable, pre-approved costs and expenses incurred by Company in complying with this Section 7.4 will be charged to Iovance in accordance with the applicable Statement of Work.

7.5 Inspection. Iovance shall arrange for the examination of the Product or Iovance Materials by recipient as soon as practicable after receipt. Notice of all claims arising out of: (1) visible damage to or total or partial loss of Product in transit or (2) non-delivery shall be given in writing to Company and the carrier as soon as possible by Iovance or Iovance's designee.

7.6 Damaged Product or Iovance Materials. To the extent possible, Iovance or Iovance's designee shall make damaged Product or Iovance Materials and associated packaging materials available for inspection and shall reasonably comply with the requirements of any insurance policy covering the Product or Iovance Materials. Company shall provide reasonable assistance to Iovance in pursuing any claims arising out of the transportation of Product or Materials.

7.7 Low Yield. Company shall notify Iovance in writing as soon as Company becomes aware of an anticipated low yield of Product (e.g., a Batch is not expected to yield the number of cells anticipated for the particular Patient Material type as set forth in the Statement of Work or Specifications or any other circumstances that may lead to a low yield or inadequate Product volume) and such notification shall include the relevant circumstances, including the underlying reasons (if known at the time of notification) for such low yield (e.g., available quantities of materials, equipment problem, manufacturing capacity or other resources needed in the manufacture of Product), proposed remedial measures, and the date such shortage is expected to end. To the extent that a low yield of Product meets the definition of a deviation under the Quality Agreement, the low yield shall further be subject to the deviation procedures in the Quality Agreement.

7.8 Storage, Waste. Company shall, in accordance with all Laws, this Agreement (including the Specifications), the applicable Statement of Work, and Quality Agreement, maintain adequate storage accommodations for all of the materials, Patient Materials and Product. In connection with the Services, Company shall be solely responsible for maintaining safety procedures in connection with the production and manufacture of Product and for the generation, treatment, storage, transportation and/or disposal of waste relating thereto, all of which shall comply with all Laws, including all applicable environmental and occupational safety and health requirements in the jurisdiction of the applicable Facility, this Agreement, the applicable Statement of Work, and the Quality Agreement. Company shall supply certificates of destruction to Iovance upon Iovance's request therefor.

7.9 Changes and Change of Control. Company shall not make any amendments, changes or supplements to the Product Specifications without Iovance's prior written consent. Company shall further not make any amendments, changes or supplements to the Products or Services, including to the raw materials used in the Process (including the specifications therefor or the source thereof), equipment and machinery, the test methods used in connection with the Services and/or Products, the Process and/or Process Specifications, approved, qualified, validated, and/or verified methods (including the method of qualification, validation and/or verification), or the cleaning process or procedures, to the extent that any amendment, change or supplement could reasonably have a direct impact on the quality, safety, purity, potency, or performance of Product or require submissions to or approvals from any regulatory authority or other review authority, such as Institutional Review Boards, without Iovance's prior written approval. All other changes, amendments, and supplements shall be provided to Iovance in the Product Documentation, as defined in the Quality Agreement. All permitted amendments, changes, or supplements shall, in each instance, comply with all Laws and shall be made in accordance with this Agreement, each Statement of Work, and the Quality Agreement. In the event that any amendment, change or supplement is required in order to comply with Law or is required by a regulatory authority or other review authority, including Institutional Review Boards, Company shall immediately notify Iovance in writing. All such amendments, changes, and supplements required in order to comply with Law or that are required by a regulatory or other review authority shall be subject to Iovance's written approval and notification requirements of this Section. Notwithstanding the foregoing, if any amendment, change or supplement requires submissions to or approvals from any regulatory authority or other review authority, including Institutional Review Boards, Company shall not implement such amendment, change or supplement until such submission to or approval has been made and/or obtained by Iovance. All such submissions and approvals shall be subject to Section 10.2. The process for Company and Iovance requested amendments, changes and supplements, as well as implementation of all such amendments, changes and supplements shall be further specified in the Quality Agreement.

8. RECORDS; REPORTS

8.1 Records.

8.1.1 Company will maintain accurate and complete records of documents, accounts, invoices, records and/or other information relating to the Services, including as required by this Agreement, the applicable Statement of Work, the Quality Agreement, all Laws and generally accepted industry practices and standards, and all procedures, records, reports and findings in connection with Company's (or its subcontractor's, as applicable) audit of the suppliers of materials. Company will retain possession of all Batch Records (which Batch Records shall be made accessible through a secured electronic portal) and Company Operating Documents, and will make such records and documents available for review and, solely with respect to Batch Records, copy by Iovance at the Facility upon Iovance's request. Without limitation, Iovance may inspect data and records related to Services, including deviations, discrepancies, out-of-Specifications, failures, investigations, and Batch-specific environmental monitoring data, water and testing data, and Process data as reasonably requested by Iovance. Company Operating Documents will remain Company Confidential Information. Notwithstanding the foregoing, Iovance will have the right to use and reference through a Drug Master File, or other such means as agreed to by the Parties, those portions of Company Operating Documents if required by Law for Iovance to fulfill its responsibilities under such Law, or as required for any filings, submissions, interactions, or communications with any applicable regulatory authority, review authority, including Institutional Review Boards, or clinical trial investigators, sites, and/or subjects. Company shall maintain all records in connection with this Agreement for the longer of (a) ten (10) years after the completion of the Services giving rise to such records; or (b) the period that Company is required by Laws to retain such records for recordkeeping, testing and regulatory purposes. Company shall not dispose of or otherwise destroy any such records without notifying Iovance, obtaining Iovance's written approval for such disposal or destruction, and allowing Iovance to take control of such records (excluding Company Operating Documents) at Iovance's reasonable cost and expense. All such records shall be protected from alteration, destruction, and Security Breaches.

8.1.2 Without limiting the foregoing Section 8.1.1, each Party shall maintain, in accordance with and for the period required under this Agreement, the Quality Agreement, each Statement of Work, and all Laws, complete and adequate records pertaining to the Services, including validation data, stability testing data, as applicable, Batch Records, and the methods and Facilities used for the Services.

8.2 Iovance Regulatory Requirements. Company shall provide Iovance with all requested records, Reports, and documentation related to the Services as required under Law or for any filings, submissions, interactions, or communications with any applicable regulatory authority review authority, including Institutional Review Boards, or clinical trial investigators, sites, and/or subjects; provided, that, to the extent the requested documentation is a Company Operating Document, Company shall provide such documentation to Iovance or, subject to Iovance's prior review, directly to the applicable regulatory authority. The Company will also promptly cooperate with Iovance and respond to all inquiries, audits or information requests etc. from data protection agencies or data subjects, at the Company's own expense, that Iovance or the Company may receive and that pertain to Personal Information or to any Laws mentioned under Section 6.2.4.

8.3 Language. All records and Reports shall be written in or translated into English and in the form as required under the applicable Statement of Work.

8.4 Ownership. Except to the extent required by Law, Iovance shall be the sole owner of the records generated through or in connection with the performance of the Services (excluding Company Operating Documents) and Reports and all rights, title and interest in and to such records and Reports shall vest solely with Iovance. Such records and Reports shall constitute Iovance Confidential Information and are subject to the provisions of Article 12 hereof. Company further agrees to execute any documents or undertake any further actions if requested by Iovance to evidence transfer of title to such records and Reports. Company shall not use such records or Reports for any use, commercial or noncommercial, other than for performing its obligations hereunder, without Iovance's prior written consent. Notwithstanding anything to the contrary in this Agreement, all such records and Reports and the possession/retention thereof will be subject to the terms of this Section 8.

9. **PRODUCT WARRANTIES; INSPECTION AND RELEASE**

9.1 Product Warranties. Unless otherwise requested by Iovance in writing, as further specified in Section 12 and 13 of the Quality Agreement, Company represents, warrants and guarantees that any Product at the time of delivery pursuant to Section 7.3:

9.1.1 conforms to the Specifications;

9.1.2 was subject to Services performed in accordance with the Master Batch Record and Process Specifications;

9.1.3 was subject to Services performed in accordance with this Agreement, the applicable Statement of Work, the Quality Agreement, and all Laws;

9.1.4 was manufactured in Facilities that are in compliance with all Laws at the time of such manufacture;

9.1.5 unless otherwise requested by Iovance in writing, as further specified in Section 12 and 13 of the Quality Agreement, the article comprising each shipment or other delivery hereafter made by Company to, or on the order of Iovance is hereby guaranteed as of the date of such shipment or delivery, to be, on such date, not adulterated by Company within the meaning of the Federal Food, Drug and Cosmetic Act, or similarly designated under other Laws of equivalent intent or effect, and not an article which may not, under the provisions of section 404, 505, or 512 of the Federal Food, Drug, and Cosmetic Act, be introduced into interstate commerce, or similarly designated under other Laws of equivalent intent or effect; and

9.1.6 is being transferred to Iovance free and clear of any pledge, lien, restriction, claim, charge, security interest and/or other encumbrance, except as such existed prior to transfer to Company hereunder.

The foregoing representations and warranties set forth in Sections 9.1.1 through 9.1.6, inclusive, shall be deemed the “Product Warranties”.

9.2 Product Inspection, Shipment and Release.

9.2.1 When the Product ordered by Iovance is ready for shipment, Company will immediately notify Iovance. Product shipment and release procedures, including terms regarding Iovance requests for shipment, shall be specified in the Quality Agreement.

9.2.2 In the event that Product does not meet the Product Warranties, then, at Iovance’s option, which such option shall be articulated in writing, Company shall: (i) destroy such Product, in compliance with Law and all written instructions provided by Iovance, and if such Product’s non-conformance is due to Company’s negligence or willful misconduct, then Company shall produce for Iovance another Batch of Product to replace the non-conforming Product at no additional cost to Iovance, or (ii) re-process such Product in accordance with written instructions provided by Iovance to produce for Iovance another Batch of Product to replace the non-conforming Product at no additional cost to Iovance; provided, that, if Company is unable to replace or re-process Product, as applicable, Company shall refund to Iovance the price of the manufacturing run, raw materials (excluding Patient Materials) and associated testing for that non-conforming Product. Company shall adhere to any instructions provided by Iovance with respect to the disposition of any such non-conforming Product, including delivering such Product to Iovance for further testing. The Parties shall reasonably cooperate to investigate the cause of any such non-conformance. The rights and remedies set forth in this Section 9.2.2 constitute the exclusive rights and remedies of Iovance in respect of the matters identified under this Section 9.2.2 and 9.2.3.

9.2.3 Should either Party discover any Product non-conformance, deficiency, or deviation following the release, issuance of a COA by Company or Iovance, shipment, administration, and/or infusion of Product, immediate notice shall be provided to the other Party. In such circumstances, the Parties shall follow the applicable procedures specified in the Quality Agreement. In the event that an investigation concludes that such Product non-conformance, deficiency, or deviation had an adverse impact on Product quality so as to render the Product to be unusable and such non-conformance, deficiency, or deviation is due to Company's negligence or willful misconduct, then at Iovance's discretion, such non-conforming Product may be treated in accordance with Section 9.2.2. Further terms regarding Product non-conformance and deviations shall be specified in the Quality Agreement. The rights and remedies set forth in this Section 9.2.3 constitute the exclusive rights and remedies of Iovance in respect of the matters identified under this Section 9.2.3, except that where such unusable Product led to a clinical adverse event that gave rise to an indemnifiable Loss, then the rights and remedies under Section 17 also apply.

10. REGULATORY MATTERS; INSPECTIONS; IOVANCE ACCESS

10.1 Permits and Approvals. During the Term, Company will maintain all licenses, permits, registrations, identifications and approvals necessary for the performance of the Services in the Facility(ies). Company will promptly notify Iovance if Company receives notice that any such license, permit, or approval is or may be revoked or suspended, or otherwise limited, or should Company receive notification of any investigation, threat, pending, current, or future proceeding, or notice of the foregoing.

10.2 Inspections by and Interactions with Regulatory Agencies.

10.2.1 Inspections and Regulatory Authority Interactions. Company will allow representatives of any regulatory agency to inspect the relevant parts of the Facility(ies) where the Services are carried out and to inspect any relevant documentation and records, including the Master Batch Record and Batch Records, as such regulatory agency is authorized to inspect by Law, to verify compliance with all Laws and other practices or regulations. Company will immediately notify Iovance of the scheduling of, or without scheduling when a regulatory inspection begins, any such inspection and, if possible, will permit Iovance's attendance at and participation in any such inspection to the extent such inspection is related to the Products and/or Services or would reasonably be expected to affect Company's ability to perform its obligations under this Agreement. Company will promptly send to Iovance a copy of (or in the case of oral interactions, summaries or minutes of) any communications, reports, citations, inspectional findings, establishment inspection reports, FDA Form 483s, warning letters, untitled letters, or other assertions of noncompliance received by Company from a regulatory authority that is related to or would reasonably be expected to otherwise impact the Products and/or Services.

10.2.2 Interactions.

- (a) To the extent permitted by the relevant regulatory authority and by Law, Iovance shall be solely and exclusively responsible for all interactions and communications with and reports to the applicable regulatory authorities related to the Products and/or Services.

- (b) To the extent that the relevant regulatory authority will not or is not permitted by Law to directly interact with Iovance, copies of (or summaries in the case of oral communications, interactions, and reports) all interactions and communications with, and reports to, the applicable regulatory authority related to the Products and/or Services (whether written or oral) shall be submitted to Iovance by Company, in reasonable and sufficient time prior to submission to the applicable regulatory authority, for Iovance's prior review and approval. For clarity, this may include Iovance providing on-site, but indirect, assistance to Company in connection with a regulatory interaction. Company will incorporate all of Iovance's comments in good faith that are factually accurate and not contrary to Company's responsibility under Law.
- (c) Company shall be responsible for all interactions and communications with and reports to the applicable regulatory authorities that are not related to the Products and/or Services, but that could reasonably be expected to impact the Products and/or Services. Company, however, shall provide copies of all communications, interactions, and reports proposed for submission (or summaries in the case of oral communications, interactions, and reports) that could reasonably be expected to impact the Product and/or Services, to Iovance, in reasonable and sufficient time prior to submission to the applicable regulatory authority, for Iovance's prior comment. Company will consider all of Iovance's comments in good faith.
- (d) In addition to the requirements of the foregoing subsections (b) and (c), Company shall furnish Iovance with final copies (or summaries or minutes in the case of oral communications, interactions, and reports) of all communications and interactions with, and reports to any applicable regulatory authority that relate to or could reasonably be expected to otherwise impact the Products and/or Services.
- (e) After any of the foregoing interactions, communications, or reports, Company shall notify Iovance and provide Iovance with copies (or summaries or minutes in the case of oral communications, reports, and interactions) of any further communications with or received from, or reports to such regulatory agency relating to the subject matter of the response to the extent such response relates to the Products and/or Services or could reasonably be expected to impact the Products and/or Services. Any further interactions and communications with, or reports to the applicable regulatory authority to the extent related to the Products and/or Services or could reasonably be expected to impact the Products and/or Services shall be governed by the terms of this Section 10.2.2 (including with respect to Iovance's right to comment on and/or approve the interaction, communication, or report prior to any submission to a regulatory authority), applied *mutatis mutandis*. Company shall further keep Iovance promptly and fully informed of the steps taken by Company to resolve any outstanding issues with such regulatory agency and the anticipated timetable of resolution of such issues to the extent that they do not involve interactions and communications with, or reports to an applicable regulatory authority, which shall be subject to Iovance's prior written approval to the extent such steps relate to the Products and/or Services, or which shall be subject to Iovance's comment prior to implementation to the extent such steps could reasonably be expected to impact the Products and/or Services. In the former case, Company shall incorporate all of Iovance's comments in good faith. In the latter case, Company will consider all of Iovance's comments in good faith.

10.2.3 All documentation, summaries, minutes and information provided to Iovance by Company under this Section may be redacted for any Third Party confidential or proprietary information.

10.2.4 Company shall take all necessary, requested, or required corrective actions as a result of any communications, reports, citations, inspectional findings, establishment inspection reports, FDA Form 483s, warning letters, untitled letters, or other assertions of noncompliance received by Company from a regulatory authority that are related to or may otherwise impact the Products and/or Services and shall, as agreed to by the Parties, update Iovance on the implementation of such corrective actions. As requested by Iovance, Company shall confer with Iovance on, and seek Iovance's prior written consent before implementing, such corrective actions to the extent they impact the Products and/or Services or affect Company's ability to perform its obligations under this Agreement.

10.2.5 Company shall provide Iovance with all information, records, documentation, and assistance that Iovance may request and that is reasonably necessary or useful for Iovance to address any interaction or communication with, or report to a regulatory authority; provided, that, to the extent the requested documentation is a Company Operating Document, Company shall provide such documentation to Iovance or, subject to Iovance's prior review, directly to the applicable regulatory authority.

10.3 Other Interactions. Interactions and communications with any clinical trial site, investigator, subject, and/or Institutional Review Boards, as well as with any other manufacturing establishments and/or consignees pursuant to 21 C.F.R. § 1271.160 shall be governed by the Quality Agreement.

10.4 Inspections by Iovance.

10.4.1 At agreed-upon dates and times, which agreement Company shall not unreasonably withhold, condition or delay, Iovance and/or its Representatives may visit, inspect, or audit any Facility and/or Services, be present in any Facility during the performance of the Services, and review documents, operations, procedures, and records as they pertain to the performance of the Services, including to: (a) determine Company's compliance with, to the extent applicable, the requirements of this Agreement and the Quality Agreement; (b) inspect for compliance with Law (including, to the extent applicable, cGMPs, and environmental, health and safety Laws); (c) perform risk and loss control assessments to support Iovance's insurance and self-insurance programs; (d) inspect storage facilities and quality systems for Product; (e) review Company's practices, controls, technologies, and procedures with regard to the electronic storage, access, and transmission of records, reports, data, and information relating to the Services to conduct and (f) review, copy (excluding Company Operating Documents), and audit records of Company with respect to Company's performance of its obligations with respect to the Services or Products. As part of Iovance's audit or inspection of a Facility, Iovance's audit or inspection may include the auditing or inspection of any documentation of Company's suppliers (including suppliers of materials) and Third Party service providers who perform Services, to the extent it relates to the Products and Services, including documentation relating to the Company's Third Party service providers who perform Services and/or supplier qualification procedures; the initial and ongoing qualification (including any appropriate validation or verification of Services, including, to the extent applicable, equipment to be used by any such Third Party) of any Third Party service provider who performs Services, including risk assessments, audit reports or questionnaires, and associated corrective actions. Should, in Iovance's reasonable judgment, Iovance need to conduct a for-cause audit, Iovance shall provide Company with two (2) days' prior written notice where practicable and where such notice would not frustrate the purpose of the audit in Iovance's reasonable determination.

10.4.2 In accordance with the terms of the applicable agreement with Company and Third Party manufacturers, suppliers, or other persons or entities providing Services, Iovance may participate in or independently conduct, itself or through a Representative, an audit or inspection of Company's Third Party manufacturers, suppliers, or other persons or entities providing Services in furtherance of this Agreement. Company's quality assurance department shall cooperate with Iovance, as necessary or useful, in any such inspection or audit.

10.4.3 In the event Iovance identifies any deficiency with respect to the performance of the Services or compliance with this Agreement, the Quality Agreement or any applicable Statement of Work during any inspection, audit, or review pursuant to Section 10.4.1 or 10.4.2, or otherwise, Iovance shall notify Company of such deficiency. Company shall investigate and respond to any such deficiency, including the timely implementation of a corrective action plan (if, and as applicable), the process for which shall be further set forth in the Quality Agreement. Company shall fully implement any such corrective action plan prior to producing any further Product; provided, however, that Iovance may (but shall not be obligated to), in its sole discretion, accept Product and/or request the production of Product from Company prior to completion of the corrective action. During the pendency of such deviation(s) and/or corrective action(s), Company shall comply with Iovance's instructions concerning the shipment of Product and/or the continued provision of Services. Iovance shall have the right to review all relevant documentation in connection with such deficiency and corrective action. If the corrective actions taken do not reasonably address a deficiency that would reasonably impact Product quality, then Iovance shall have the right to terminate this Agreement effective immediately pursuant to Section 16.2 and without any further cure period under Section 16.2. The rights and remedies set forth in this Section 10.4.3 constitute the exclusive rights and remedies of Iovance with respect to the subject matter herein, except that where such deficiency causes Iovance to experience a related cost, loss or expense, then the foregoing limitation does not constitute a waiver of any right otherwise available to Iovance under this Agreement or at law.

10.4.4 In the event an audit or inspection of a Third Party service provider who performs Services or raw material supplier reveals a material quality compliance issue related to the Services, Iovance shall have the right to direct Company promptly identify and qualify a new Third Party, or raw material supplier, as applicable, acceptable to and approved by Iovance in writing and to provide the Services or raw materials impacted by such material quality compliance issue, as applicable. Notwithstanding the foregoing, Company shall be fully responsible for sourcing and testing of materials (other than Iovance Materials), and qualification and management of its subcontractors, supplier(s) of materials (other than Iovance Materials), and Third Parties providing Services under an applicable Statement of Work.

10.4.5 Company shall ensure that Third Parties involved in the performance of the Services (or any component thereof including materials suppliers) permit and afford Iovance the same rights as set forth in Section 10.4.1; provided that if Company expects that it will not be able to include all such terms and conditions in its agreement with a particular Third Party or supplier, Company shall notify Iovance of same and the Parties will discuss and mutually agree upon an appropriate course of action; provided further that if the Parties do not agree on an appropriate course of action and any such Third Party or supplier does not afford Iovance such rights, then Iovance shall have the right to terminate this Agreement effective immediately.

10.4.6 For clarity, any such inspection or audit (or failure to inspect or audit) shall not relieve Company of its obligation to comply with all Laws, each Statement of Work, this Agreement and the Quality Agreement and does not constitute a waiver of any right otherwise available to Iovance. In addition, for critical raw material suppliers as well as for Third Party manufacturers of Product, Company shall be required to audit each and Iovance shall have the right to review the audit reports and findings and Company's procedures for auditing such suppliers.

10.4.7 While on-site at a Facility, Iovance will abide by standard policies, operating procedures and the security procedures established by such Facility with respect to conduct at such Facility provided to Iovance in advance in writing and with any reasonable instructions or requests by Company while at such Facility, which could not reasonably be provided to Iovance in advance. During any such on-site visit of the Facility, Iovance will cooperate with Company in taking reasonable precautions to avoid exposure of its Representatives to information regarding activities unrelated to Product manufactured for Iovance. Notwithstanding the above, Company shall not impose any restrictions or other procedures that would impede Iovance's ability to conduct a reasonable and comprehensive audit.

10.5 Iovance Access. Without limiting Iovance's obligations under Section 10.4.7, Representatives of Iovance may act as a person-in-plant and observe the Services. For the avoidance of doubt, Iovance Personnel may not physically participate in the production or manufacture of any Product that may be used in or on humans.

10.6 Procedures. Representatives of Iovance working at, visiting, or otherwise having access to a Facility will abide by applicable Company Operating Documents, standard policies and security procedures with respect to conduct at such Facility provided to Iovance in advance in writing and with any reasonable instructions or requests by Company while at such Facility, which could not reasonably be provided to Iovance in advance. During any such on-site work, visit, or access to a Facility, Iovance will cooperate with Company in taking reasonable precautions to avoid exposure of its Representatives to information regarding activities unrelated to Product or the Services. Representatives of Iovance working at the Facility will be and remain employees of Iovance, and Iovance will be solely responsible for the payment of compensation for such Representatives of Iovance (including applicable federal, state and local withholding, FICA and other payroll taxes, workers' compensation insurance, health insurance, and other similar statutory and fringe benefits).

11. FINANCIAL TERMS

11.1 Payments. Iovance will make payments to Company in the amounts and as set forth in the applicable Statement of Work.

11.2 Invoices. In accordance with payment schedule set forth in the applicable Statement of Work, Company will provide Iovance with invoices each setting forth a detailed account of amounts payable by Iovance. The undisputed amounts set forth in each such invoice will be due and payable within sixty (60) days of receipt of such invoice by Iovance. Iovance will have the right to audit any necessary documents associated with such invoices either by itself or by a certified public accountant ("CPA") reasonably acceptable to Company. In case the audit of the CPA reveals a discrepancy that resulted in (a) an overpayment by Iovance to Company, then Company shall credit the deviated amount with the next invoice to Iovance (or if no more invoices are required Company shall promptly pay such amount to Iovance), or (b) an underpayment by Iovance to Company, then Iovance shall promptly pay such amount to Company. In the event an invoice is disputed, the Parties shall work together in good faith to resolve such dispute as expeditiously as possible and payment on any such disputed amount shall be due thirty (30) days after the dispute is resolved.

11.3 Taxes. Iovance agrees that it is responsible for and will pay any sales, use or other taxes (the "Taxes") resulting from Company's production of Product under this Agreement (except for income or personal property taxes payable by Company). Company will list the Taxes as separate line item(s) in the applicable invoices. Company will not collect any sales and use taxes from Iovance in connection with the production of any Product hereunder if Iovance provides to Company the appropriate valid exemption certificates.

11.4 Method of Payment. All payments to Company hereunder by Iovance will be in United States currency and will be by check, wire transfer, money order, or other method of payment approved by the Parties.

11.5 Iovance shall not have the right to set off any of its payment obligations owed to Company against any damages, credits, claims or charges assessed by Iovance against Company.

11.6 Late Payment. In the event of a default of payment of any amounts by Iovance on the due date, then (a) interest shall accrue on any amount overdue at the annual rate of one per cent (1%) above the prime rate of interest published from time to time in the Wall Street Journal (or similar successor rate), interest to accrue on a day to day basis both before and after judgment; and (b) Company shall, without prejudice to any other of its accrued rights, be entitled to suspend or immediately terminate those Services and/or Statement(s) of Work to which such late payment relates.

12. CONFIDENTIAL INFORMATION

12.1 Definition. “Confidential Information” means all confidential, proprietary and/or trade secret information or materials owned or controlled by a Party, including technical, scientific and other know-how and information, trade secrets, knowledge, technology, means, methods, processes, practices, formulas, instructions, skills, techniques, procedures, controls, specifications, data, results and other material, pre-clinical and clinical trial results, manufacturing procedures, test procedures and purification and isolation techniques, other procedures related to the Services, and any tangible embodiments of any of the foregoing, and any scientific, manufacturing, marketing and business plans, any financial and personnel matters relating to a Party or its present or future products, sales, suppliers, customers, employees, investors or business, that has been disclosed by or on behalf of such Party to the other Party either in connection with the discussions and negotiations pertaining to this Agreement or in the course of performing this Agreement, or that has been developed under this Agreement. Without limiting the foregoing, (a) the terms of this Agreement are deemed the “Confidential Information” of both Parties and will be subject to the terms and conditions set forth in this Article 12, and (b) the Product, the Process, the Master Batch Record, Specifications, and all other Intellectual Property of Iovance and/or its Affiliates (including New Iovance Intellectual Property) are deemed Iovance Confidential Information, as to which Iovance will be deemed the disclosing Party and Company will be deemed the receiving Party in all circumstances, and are subject to the terms and conditions of this Article 12.

12.2 Exclusions. Notwithstanding the foregoing Section 12.1, any information disclosed by a Party to the other Party will not be deemed “Confidential Information” to the extent that such information:

12.2.1 At the time of disclosure is in the public domain, other than as a result of a breach of an obligation of confidentiality or non-use or other misappropriation;

12.2.2 Becomes part of the public domain, by publication or otherwise, other than as a result of a breach of an obligation of confidentiality or non-use or other misappropriation;

12.2.3 At the time of disclosure is already in possession of the Party who received such information, without restriction as to confidentiality or use, as established by contemporaneous written records;

12.2.4 Is lawfully provided to a Party, without restriction as to confidentiality or use, by a Third Party lawfully entitled to possess and make unrestricted disclosures of such information; or

12.2.5 Is independently developed by a Party without use of or reference to the other Party's Confidential Information, as established by contemporaneous written records.

12.3 Disclosure and Use Restriction. Each receiving Party agrees to keep confidential all Confidential Information it receives and not to disclose, transfer or use it for any purpose other than as expressly permitted under this Agreement. The receiving Party will not use the Confidential Information of the other Party for any purpose other than the performance of its obligations and exercise of its rights under this Agreement. Subject to the terms of Article 8, the receiving Party (a) agrees to return or destroy promptly (and certify such destruction) at the owning Party's request all Confidential Information of the owning Party, and (b) if not earlier requested, upon termination of this Agreement, shall promptly return to the disclosing Party such Confidential Information, and shall destroy all copies thereof, together with all notes, drawings, abstracts and other information relating to the disclosing Party's Confidential Information prepared by the receiving Party or any of its representatives, regardless of the medium in which such information is stored; provided, however, that the receiving Party may maintain one (1) archival copy of the disclosing Party's Confidential Information, which such archival copy shall remain subject to the obligations of confidentiality and non-use set forth herein. The return or destruction of the Confidential Information as provided above shall not relieve the receiving Party of its other obligations under this Article 12.

12.4 Security and Use. Each receiving Party agrees to (i) institute and maintain reasonable and customary security procedures to identify, protect and account for all copies of Confidential Information of the disclosing Party, and (ii) limit disclosure of the disclosing Party's Confidential Information to its Representatives having a need to know such Confidential Information for purposes of the receiving Party exercising its rights and performing its obligations under this Agreement; provided that such Representatives are informed of the confidential nature of the information, and are subject to obligations of confidentiality, non-disclosure, non-use and inventions similar to and at least as restrictive as those set forth in this Agreement. The receiving Party shall notify the owning Party as promptly as practicable of any unauthorized use or disclosure of the Confidential Information, but in any event no later than seventy-two (72) hours thereafter; provided, that, for clarity, such notification shall not excuse the receiving Party from any liability in connection with such unauthorized use or disclosure.

12.5 Government-Required Disclosure. If a duly constituted government authority, court or regulatory agency orders that a Party hereto disclose information with respect to which it is subject to an obligation of confidentiality under this Agreement, such Party shall comply with the order, but shall (a) give prompt written notice to the disclosing Party of the proposed disclosure, and allow the disclosing Party at least thirty (30) days to object to all or any portion of the disclosure before it is disclosed; (b) if advance notice is not possible, provide written notice of disclosure immediately thereafter; (c) to the extent possible, minimize the extent of such disclosure; and (d) use reasonable efforts to secure confidential treatment of such information prior to its disclosure (whether through protective orders or otherwise), it being understood that any information so disclosed shall otherwise remain subject to the limitations on use and disclosure hereunder. The Party permitted to disclose any Confidential Information under this Section shall take into consideration all comments and objections raised by the other Party. The Party permitted to disclose any Confidential Information under this Section shall further cooperate with and provide the other Party with the opportunity to seek any protective order reasonably deemed necessary by such Party.

12.6 Permitted Iovance Disclosure. Notwithstanding anything else in this Agreement, Iovance shall further be permitted to disclose information subject to an obligation of confidentiality under this Agreement to the extent reasonably necessary for Iovance to comply with any Laws, make any filings, submissions or reports to an applicable regulatory authority, and to preserve the safety of any subjects in a Iovance clinical trial.

12.7 Publicity. Neither Party will refer to, display or use the other's name, trademarks or trade names confusingly similar thereto, alone or in conjunction with any other words or names, in any manner or connection whatsoever, including any publication, article, or any form of advertising or publicity, except with the prior written consent of the other Party. Neither Party shall disclose to any Third Party nor to the public generally (a) the terms of this Agreement, or (b) the specific relationship between the Parties established hereunder, except where such disclosure is necessary for Regulatory Approval of Product. Notwithstanding the foregoing, the Parties shall have the right to disclose the material commercial terms of this Agreement to any potential acquirer, merger or commercial partner or significant investor; provided, however, that prior to any such disclosure, such Party (1) shall require the intended recipient to sign an undertaking agreeing to accord confidential treatment to such information at least as restrictive as the terms set forth herein and not use such information except to evaluate the proposed acquisition, merger, commercial arrangement or investment, and (2) shall take such other steps reasonably necessary to secure confidential treatment of such information.

13. **INTELLECTUAL PROPERTY**

13.1 Generally. For purposes of this Agreement, "Intellectual Property" means collectively all legal rights in works or ideas, including any patents, copyrights, trade secrets, know-how, inventions (whether or not patentable), discoveries, improvements, and all other intellectual property rights, including all applications and registrations with respect thereto, and all data, information (including Confidential Information), reports and any and all related documentation. Neither Party will, as a result of this Agreement, acquire any right, title or interest in to any Intellectual Property owned or controlled by the other Party or the other Party's Affiliates prior to the Effective Date (including Intellectual Property owned or controlled by the other Party or the other Party's Affiliates prior to the Original Effective Date) or developed independently of this Agreement and the Original Agreement ("Background Intellectual Property"), or, except for the limited licenses expressly granted under this Agreement, any license or right to use any Intellectual Property owned or controlled by the other Party or the other Party's Affiliates. For the avoidance of doubt, Iovance is not granted any rights, licenses, or sublicenses to any cell lines, plasmids, or other products or processes that are licensed by Company that may be used in Services; provided, that, Company shall not use any such cell lines, plasmids, or other products or processes that are licensed by Company in the performance of the Services without first obtaining the prior written consent of Iovance. As between the Parties, Iovance shall own all Iovance Confidential Information and Company shall own all Company Confidential Information.

13.2 New Iovance Intellectual Property and Assignment.

13.2.1 Iovance shall own all right, title, and interest in and to any and all Intellectual Property that Company or its Representatives develops, conceives, invents, first reduces to practice or makes, solely or jointly with Iovance or others, that is a development, improvement, modification, addition, adaptation, enhancement, derivative, variant or progeny resulting from the use of or access to Product, Process, Iovance Materials, Iovance Confidential Information or Background Intellectual Property of Iovance (collectively, "New Iovance Intellectual Property"), including any and all moral rights and Intellectual Property rights inherent therein and appurtenant thereto, including all patent rights, copyrights, trademarks, know-how and trade secrets and the rights to apply for the same. Company further acknowledges and agrees that all original works of authorship that are made by Company (solely or jointly with others) in the performance of a Statement of Work (a "Work") and that are protectable by copyright are "works made for hire," as that term is defined in the United States Copyright Act. However, to the extent that any Work may not, by operation of any Laws, be a work made for hire, Company hereby assigns, transfers and conveys to Iovance all of Company's worldwide right, title and interest in and to such Work, including all Intellectual Property rights relating thereto. For avoidance of doubt, "New Iovance Intellectual Property" shall include any material (including biological material), processes or other items that embody, or that are claimed or covered by, any of the foregoing Intellectual Property. Notwithstanding the foregoing, Iovance agrees that New Iovance Intellectual Property does not include Company Background Intellectual Property or improvements thereto that are developed by Company through the performance of the Services, provided, that such improvements (i) are made without the benefit of Iovance Intellectual Property, Iovance Materials and/or Iovance Confidential Information, and (ii) could have been developed without performance of the Services (i.e., in the event that unique aspects of the Services and/or Iovance Intellectual Property, Iovance Materials or Iovance Confidential Information were not a "but for" cause of such improvement) ("Improvements").

13.2.2 Company hereby assigns and shall assign to Iovance all of its right, title and interest in and to any New Iovance Intellectual Property. Company shall promptly disclose to Iovance in writing all New Iovance Intellectual Property. Company shall execute, and shall require its Representatives, to execute, any documents reasonably required to confirm Iovance's ownership of the New Iovance Intellectual Property, and any documents required to apply for, maintain and enforce any patent or other right in the New Iovance Intellectual Property. In the event that Iovance requires an appointment as an agent or attorney in fact, and cannot reasonably obtain such appointment from Company for any reason other than Company's reasonable dispute regarding the claims associated with such New Iovance Intellectual Property infringe Company Background Intellectual Property or Improvements, Company hereby irrevocably designates and appoints Iovance and its duly authorized officers and agents as Company's agent and attorney in fact, to act for and in Company's behalf and stead to execute and file and prosecute any such applications for United States or foreign patents, trademarks, copyrights or other registration covering New Iovance Intellectual Property or Works assigned to Iovance hereunder, and to do all other lawfully permitted acts to further the prosecution, issuance, enforcement and defense of patents, trademarks, copyrights or other registrations thereon with the same legal force and effect as if executed by Company.

13.2.3 Each Party confirms and shall ensure that its Representatives are subject to and bound by the same assignment obligations of the Parties under this Section 13.2.

13.3 License. Company hereby grants to Iovance a non-exclusive, world-wide, fully paid-up, irrevocable, transferable license, including the right to grant sublicenses under, in and to Company Background Intellectual Property and Improvements to the extent such Background Intellectual Property or Improvements are embedded in any deliverable provided hereunder or used in the manufacturing of Product for which there is no reasonable substitute available to Iovance, to develop, conduct clinical trials for, formulate, manufacture, test, label, package, seek Regulatory Approval for, market, commercialize, make, have made, use, sell and import Product.

13.4 Prosecution, Maintenance and Enforcement of Patents. Iovance will have the sole right and discretion to file, prosecute, maintain and enforce patent applications and patents claiming New Iovance Intellectual Property at Iovance's expense. Company will cooperate with Iovance in Iovance's activities to file, prosecute and maintain patent applications and patents claiming New Iovance Intellectual Property, and will, upon Iovance's request, review and provide comments to Iovance relating to such patent applications and patents.

13.5 Nonassertion. Except to the extent required to protect Company Background Intellectual Property or Improvements rights, and without limiting Section 13.3, Company and its Affiliates hereby covenant and agree not to, alone or in cooperation with any Third Party, sue or bring any cause of action against Iovance, its Representatives, suppliers, distributors, salespersons, customers, licensees or end-users for any patent infringement based on any development, manufacturing or commercialization activities relating to the Product, the Process or Iovance's Background Intellectual Property conducted by Iovance and any Third Party for Iovance. This covenant will run with and attach to any and all patent rights owned or controlled, in whole or in part, by Company and shall be binding upon any assignee or sublicensee of any Intellectual Property from Company.

13.6 Other Covenants. Company agrees that (a) it will not publish or publicly present the results of any data or other information generated from the activities hereunder that includes or consists of Iovance Confidential Information, Iovance Materials or Iovance Intellectual Property without Iovance's prior written consent, and (b) it will at no time file or have filed any patent application or initiate any procedure purporting to obtain any legal rights covering any discovery or inventions that would infringe New Iovance Intellectual Property, or that it first develops, conceives, invents, reduces to practice or makes while using Iovance Confidential Information or Iovance Materials, without Iovance's prior written consent.

14. **REPRESENTATIONS AND WARRANTIES**

14.1 By Iovance. Iovance hereby represents, warrants and covenants to Company that:

14.1.1 it is a corporation duly organized and validly existing under the laws of its jurisdiction of incorporation or organization;

14.1.2 the execution, delivery, and performance of this Agreement by Iovance has been duly authorized by all requisite corporate action and does not require any shareholder action or approval;

14.1.3 it has the power and authority to execute and deliver this Agreement and all Statements of Work and to perform its obligations hereunder and thereunder; and

14.1.4 the execution, delivery, and performance by Iovance of this Agreement, its compliance with the provisions of this Agreement does not and shall not conflict with or result in a breach of any of the terms and provisions of or constitute a default under (a) any other agreement to which it is a party; (b) its certificate of incorporation or bylaws; or (c) any order, writ, injunction, or decree of any governmental authority entered against it or by which any of its property is bound.

14.2 By Company. Company hereby represents, warrants and covenants to Iovance that:

14.2.1 it is a corporation or entity duly organized and validly existing under the laws of its jurisdiction of incorporation or organization;

14.2.2 the execution, delivery, and performance of this Agreement by Company have been duly authorized by all requisite corporate action and do not require any shareholder action or approval;

14.2.3 it has the power and authority to execute and deliver this Agreement and to perform its obligations hereunder;

14.2.4 the execution, delivery, and performance by Company of this Agreement and its compliance with the provisions of this Agreement does not and shall not conflict with or result in a breach of any of the terms and provisions of or constitute a default under (a) any other agreement to which it is a party; (b) the provisions of its charter or organizational documents or bylaws; or (c) any order, writ, injunction, or decree of any governmental authority entered against it or by which any of its property is bound;

14.2.5 the Product released to Iovance conforms to the Specifications, has been and shall be the subject of Services performed in accordance with this Agreement, the applicable Statement of Work, the Quality Agreement, unless otherwise waived in writing by Iovance, and all Laws; and is and will be free and clear of all liens and encumbrances;

14.2.6 the operation of the Facility(ies) are and will continue to be in compliance with all Laws (including the receipt and possession of all applicable licenses, permits, registrations and authorizations);

14.2.7 it has maintained and will continue to maintain, in accordance with and for the period required under this Agreement, the applicable Statement of Work, the Quality Agreement, and all Laws, complete and adequate records pertaining to the Services, Products, methods and the Facility(ies) used in the performance of this Agreement;

14.2.8 it, and its Representatives providing Services under this Agreement, are not, have not, and will not be, at the time of performance of any of the Services hereunder, charged, named in an action, found liable, or convicted for conduct relating to the development or approval of, or otherwise relating to the regulation of, any health care product under any Law. In the event that the foregoing should occur or should Company receive notification of any investigation, threat, pending, current, or future proceeding, or notice of the foregoing, Company shall immediately notify Iovance;

14.2.9 save for security interests expressly given in favor of Iovance, it will have good and marketable title, free and clear of any pledge, lien, restriction, claim, charge, security interest and/or other encumbrance, to all Product to be delivered hereunder;

14.2.10 it, and its Representatives, is and are not and will not be, at the time of performance of any Services hereunder, disqualified, excluded or debarred by any regulatory agency or other governmental authority for any purpose pursuant to Law. Debarment, disqualification, and exclusion shall include, but shall not be limited to, FDA debarment, temporary denial, and suspension pursuant to 21 C.F.R. § 335a, FDA investigator disqualification or restriction pursuant to 21 U.S.C. §§ 312.70, 511.1(c), or 812.119, exclusion from participation in federal or state healthcare programs, and debarment, suspension, or ineligibility to participate in federal procurement and non-procurement programs. Prior to employing or otherwise engaging any individual or entity in connection to the Services, Company agrees to review all applicable public lists to ensure that such individuals or entities are not disqualified, excluded, or debarred and agrees not to employ or otherwise engage any individual or entity who is presently or has ever been disqualified, excluded or debarred. In the event that the foregoing should occur or should Company receive notification of any investigation, threat, pending, current, or future proceeding, or notice of the foregoing, Company shall immediately notify Iovance;

14.2.11 it will conduct the Services in compliance with all Laws, including those dealing with occupational safety and health, those dealing with public safety and health, those dealing with patient privacy, those dealing with protecting the environment, and those dealing with disposal of wastes;

14.2.12 any processes or materials used by Company in the Services or otherwise used in the manufacturing of Product (other than the Process) do not infringe any Intellectual Property rights of any Third Party;

14.2.13 it will not enter into any agreement or arrangement with any party which will hinder it or prevent it from performing its obligations under this Agreement;

14.2.14 each of its Representatives is subject to a written agreement that assigns to Company all Intellectual Property made by such individual in the course of his or her employment with Company or the performance of activities hereunder, and Company will not use any of its Representatives in the performance of its obligations hereunder, including the performance of any Services or Statement of Work, that are not each subject to such written obligations; and

14.2.15 it shall comply with all rules and obligations vis-à-vis employees and self-employed consultants (if any), and, as set out by all Laws, collective and individual agreements, including (a) payment of salaries, social security charges, insurances and withholding taxes on the income received by the workers involved in the performance of this Agreement, as well as (b) any other obligations deriving from the employment agreement and/or self-employment agreement, including provisions protection of the personnel, safety and physical integrity, in full compliance with all Laws and the individual and collective agreements. Company expressly undertakes to perform this Agreement using only personnel duly employed or otherwise engaged in accordance with all Laws.

15. **DISCLAIMER; LIMITATION OF LIABILITY**

15.1 Disclaimer. EXCEPT AS EXPRESSLY SET FORTH WITHIN THIS AGREEMENT, A STATEMENT OF WORK OR THE QUALITY AGREEMENT AND TO THE EXTENT PERMITTED BY LAW, NEITHER PARTY MAKES ANY EXPRESS OR IMPLIED WARRANTIES RELATING TO THE SERVICES OR OTHER ACTIVITIES HEREUNDER, INCLUDING WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR NON-INFRINGEMENT.

15.2 Limitation of Liability. UNDER NO CIRCUMSTANCES SHALL EITHER PARTY BE LIABLE TO THE OTHER PARTY FOR INDIRECT, MULTIPLE, SPECIAL, CONSEQUENTIAL, LIQUIDATED, OR PUNITIVE DAMAGES, INCLUDING LOST PROFITS, OR LOST REVENUE AND THE TOTAL LIABILITY OF EITHER PARTY AND ITS REPRESENTATIVES TO THE OTHER PARTY AND ANYONE CLAIMING BY OR THROUGH THE OTHER PARTY, FOR ANY AND ALL CLAIMS, LOSSES, COSTS OR DAMAGES, INCLUDING ATTORNEYS' FEES AND COSTS AND EXPERT-WITNESS FEES AND COSTS OF ANY NATURE WHATSOEVER OR CLAIMS EXPENSES RESULTING FROM OR IN ANY WAY RELATED TO AN APPLICABLE STATEMENT OF WORK FROM ANY CAUSE OR CAUSES SHALL NOT EXCEED, ON A CLAIM-BY-CLAIM BASIS, THE FEES PAID OR OWED FOR THE [***] OF THE SERVICES GIVING RISE TO SUCH LIABILITY UNDER [***] STATEMENT OF WORK (WITH [***] UNDERSTOOD TO MEAN A GIVEN [***] AS OPPOSED TO A [***] OF A [***] (E.G., IN THE CONTEXT OF A [***], A [***] WOULD BE [***], RATHER THAN A [***] IN THE [***] RELATED TO SUCH [***])). THE FOREGOING LIMITATIONS OF LIABILITY SHALL NOT APPLY TO A PARTY'S (A) BREACH OF ITS OBLIGATIONS PURSUANT TO ARTICLE 12 (CONFIDENTIALITY) OR ARTICLE 13 (INTELLECTUAL PROPERTY), (B) GROSS NEGLIGENCE OR WILLFUL MISCONDUCT HEREUNDER, (C) OBLIGATIONS PURSUANT TO SECTION 17.1 OR SECTION 17.2 (INDEMNIFICATION), OR (D) FRAUD.

15.3 Further Limitation. Whereas there are inherent risks of microorganism contamination of Product resulting from the open process steps associated with Patient Tumor acquisition and the Process as of the Original Effective Date, Iovance agrees that notwithstanding anything to the contrary in this Agreement, for so long as the Process has such open process steps, Company shall not be liable for any damages of any kind whatsoever, including Losses where such damages or Losses arise or result from the contamination of Product by microorganisms, including viruses. This limitation shall not apply if the contamination was caused by the negligence, willful misconduct or breach of this Agreement by Company.

16. TERM AND TERMINATION

16.1 Term. The term of this Agreement shall be deemed to have commenced on the Original Effective Date and shall expire on the third (3rd) anniversary of the Original Effective Date, unless earlier terminated in accordance with this Agreement (the "Term"); provided, that the Term may be extended upon the mutual written consent of the Parties.

16.2 Termination for Material Breach. Either Party may terminate this Agreement, by written notice to the other Party, for any material breach of this Agreement by the other Party, if such breach is not cured within thirty (30) days after the breaching Party receives written notice of such breach from the non-breaching Party; provided, however, that if such breach (other than a breach for non-payment) is not capable of being cured within such thirty (30) -day period and the breaching Party has commenced and diligently continued actions to cure such breach within such thirty (30)-day period, the cure period may be extended, with the written consent of the non-breaching Party, to ninety (90) days, so long as the breaching Party is making diligent efforts to cure such breach. Such termination shall be effective upon expiration of such cure period. In the event of termination by Iovance under this Section 16.2, any termination fees in the applicable Statements of Work will not apply.

16.3 Termination of Clinical Trials; Frustration of Purpose. Iovance may immediately terminate a Statement of Work or the manufacturing of a lot under a given Statement of Work upon written notice to Company if (a) any clinical trial for which Product is being produced hereunder has been or will be terminated, or (b) the purpose of such Statement of Work or manufacturing such lot becomes fundamentally frustrated (e.g., TILs cannot be harvested from the applicable patient, the patient can no longer use the Product, or TILs are not being produced in sufficient quantities for use in a patient or the FDA requires that the production of Product must be terminated).

16.4 Termination by Iovance or Company. Iovance may terminate this Agreement or any Statement of Work by providing written notice of termination not less than thirty (30) days in advance of the date of termination. Company may terminate this Agreement by providing written notice of termination not less than one hundred eighty (180) days in advance of the date of termination; provided, that, this Agreement shall remain in full force and effect with respect to any Statements of Work outstanding at the time that such termination becomes effective. For the avoidance of doubt, in the event of termination by Iovance under this Section 16.4, Iovance shall, at minimum, remain liable for all fees owed by Iovance or earned by Company pursuant to any outstanding Statement of Work, including in the case of termination by Iovance under Sections 16.3, or 16.4 or termination by Company under Section 16.5 any termination fees agreed to by the parties in such Statement of Work.

16.5 Termination or Insolvency. Either Party may terminate this Agreement upon notice to the other Party, upon (a) the dissolution, termination of existence, liquidation or business failure of the other Party; (b) the appointment of a custodian or receiver for the other Party who has not been terminated or dismissed within thirty (30) days of such appointment; or (c) the institution by the other Party of any proceeding under national, federal or state bankruptcy, reorganization, receivership or other similar laws affecting the rights of creditors generally or the making by such Party of a composition or any assignment for the benefit of creditors under any national, federal or state bankruptcy, reorganization, receivership or other similar law affecting the rights of creditors generally, which proceeding is not dismissed within thirty (30) days of filing. All rights and licenses granted pursuant to this Agreement are, and shall otherwise be deemed to be, for purposes of Section 365(n) of Title 11 of the United States Code, licenses of rights of "intellectual property" as defined therein.

16.6 Effects of Termination.

16.6.1 Accrued Rights. Termination or expiration of this Agreement or any Statement of Work for any reason will be without prejudice to any rights that will have accrued to the benefit of a Party prior to such termination or expiration. Such termination or expiration will not relieve a Party of obligations that are expressly indicated to or which by their nature should survive the termination or expiration of this Agreement.

16.6.2 Disposition of Remaining Confidential Information. Upon termination or expiration of a Statement of Work or this Agreement, Company will cease use of and store any property (including Intellectual Property) of Iovance in its possession and, at Iovance's option (and subject to the terms of Article 8), return or destroy any Iovance Confidential Information and, except as provided in Section 16.6.3, any other Iovance property in its possession or control. Notwithstanding the foregoing provisions, each Party may retain in its secure archival files a single copy of the other Party's Confidential Information for documentation purposes only and which shall remain subject to the obligations of nonuse and confidentiality set forth in this Agreement.

16.6.3 Purchased Equipment. Upon termination or expiration of a Statement of Work or this Agreement, Company will, if so requested by Iovance, pack and ship at Company's expense any Purchased Equipment related to the Statement of Work, or, in the case of termination or expiration of this Agreement, any Purchased Equipment generally, to a destination or destinations designated by Iovance. Company shall insure that any Purchased Equipment so returned to Iovance is in its original condition but for reasonable wear and tear of the Purchased Equipment contemplated by this Agreement.

16.6.4 Survival. The provisions of this Agreement that by their nature should survive the termination or expiration of this Agreement, including Articles 8, 12, 13, 15, 17 and 18, and Sections 5.4, 6.4 and 16.6 of this Agreement, together with any appendices referenced therein.

17. **INDEMNIFICATION**

17.1 Indemnification of Iovance. Company will indemnify Iovance and its Affiliates and subcontractors, and their respective directors, officers, employees and agents (the "Iovance Parties"), and defend and hold each of them harmless, from and against all claims, lawsuits or other action or threat by a Third Party, including any and all losses, damages, liabilities, costs and expenses (including reasonable attorneys' fees and expenses) incurred in the defense or settlement thereof or in damages awarded therein (collectively, "Losses") to the extent such Losses arise out of or result from: (a) any material breach by Company (or any Company Parties) of this Agreement or the Original Agreement, or (b) the negligence or willful misconduct of any Company Parties in the performance of this Agreement or the Original Agreement. Company's obligation to indemnify Iovance shall be reduced to the extent that any Losses are caused by the negligence, willful misconduct, breach of this Agreement or the Original Agreement, or fraud of Iovance.

17.2 Indemnification of Company. Iovance will indemnify Company and its Affiliates and subcontractors, and their respective directors, officers, employees and agents (the “Company Parties”), and defend and hold each of them harmless, from and against any and all Losses to the extent such Losses arise out of or result from: (a) any material breach by Iovance of this Agreement or the Original Agreement, (b) the research, development, distribution, use, sales or other disposition by or on behalf of Iovance of the Product, or (c) the negligence or willful misconduct of any Iovance Parties in the performance of this Agreement or the Original Agreement. Iovance’s obligation to indemnify Company shall be reduced to the extent that any Losses are caused by the negligence, willful misconduct, breach of this Agreement or the Original Agreement, or fraud of Company.

17.3 Limitation. The obligation of Company under Section 17.1 and Iovance under Section 17.2 is limited to [***] dollars (\$[***]) per indemnifiable claim, except that this limitation will not apply with respect to any such claim arising out of or relating to fraud, gross negligence or willful misconduct by the Indemnitor. For the avoidance of doubt, this limitation will not apply with respect to any Loss relating to personal injury or death arising out of or relating to fraud, gross negligence, willful misconduct or breach of this Agreement or the Original Agreement.

17.4 Indemnification Procedure.

17.4.1 An “Indemnitor” means the indemnifying Party. An “Indemnitee” means the indemnified Party, its Affiliates and subcontractors, and their respective directors, officers, employees and agents, who shall be represented through the Party to this Agreement with whom they are associated.

17.4.2 An Indemnitee which intends to claim indemnification under Section 17.1 or Section 17.2 hereof shall promptly notify the Indemnitor in writing of any claim, lawsuit or other action in respect of which the Indemnitee, its Affiliates, or any of their respective directors, officers, employees and agents intend to claim such indemnification. The Indemnitee shall permit, and shall cause its Affiliates and subcontractors and their respective directors, officers, employees and agents to permit, the Indemnitor, at its discretion, to settle any such claim, lawsuit or other action and agrees to the complete control of such defense or settlement by the Indemnitor; provided, however, that in order for the Indemnitor to exercise such rights, such settlement shall not adversely affect the Indemnitee’s rights under this Agreement or impose any obligations on the Indemnitee in addition to those set forth in this Agreement. No such claim, lawsuit or other action shall be settled without the prior written consent of the Indemnitor and the Indemnitor shall not be responsible for any legal fees or other costs incurred other than as provided herein. The Indemnitee, its Affiliates and subcontractors and their respective directors, officers, employees and agents shall cooperate fully with the Indemnitor and its legal representatives in the investigation and defense of any claim, lawsuit or other action covered by this indemnification, all at the reasonable expense of the Indemnitor. The Indemnitee shall have the right, but not the obligation, to be represented by counsel of its own selection and expense. It is understood that only Company or Iovance may claim indemnity under this Article 17 (on its own behalf or on behalf of its indemnitees), and other Indemnitees may not directly claim indemnity hereunder.

17.4.3 Exclusivity. The rights and remedies set forth in this Section 17 constitute the exclusive rights and remedies of the Parties in respect of the matters indemnified under Section 17.1 and 17.2.

17.5 Insurance. Iovance will maintain, at all times during the Term and for five (5) years thereafter, a products liability insurance policy (the "Insurance Policy"), with a per occurrence limit of at least two million dollars (\$2,000,000) and an aggregate limit of at least five million dollars (\$5,000,000). Likewise, Company will maintain, at all times during the Term and for at least five (5) years thereafter, commercial general liability insurance including contractual liability coverage and product liability coverage, with a per occurrence limit of at least two million dollars (\$2,000,000) and an aggregate limit of at least five million dollars (\$5,000,000). In addition, Company will, and has a contractual responsibility to, maintain, at all times during the Term insurance of a type and in an amount necessary to fully cover the loss of all Purchased Equipment on Company premises or under Company's control and will arrange for Iovance to be named as loss payee on all such insurance. Upon Iovance's request, Company shall furnish to Iovance certificates that all insurance required under this Agreement. Any failure by Company to provide such certifications shall be deemed a material breach of this Agreement. Company shall provide thirty (30) days' prior written notice of all cancellation, non-renewal or material changes in such policy(ies); provided, that, for clarity, at all times Company must comply with the insurance minimums set forth above.

18. MISCELLANEOUS

18.1 Independent Contractors. Each of the Parties is an independent contractor and nothing herein contained shall be deemed to constitute the relationship of partners, joint venturers, nor of principal and agent between the Parties. Neither Party shall at any time enter into, incur, or hold itself out to Third Parties as having authority to enter into or incur, on behalf of the other Party, any commitment, expense, or liability whatsoever.

18.2 Force Majeure. Neither Party shall be in breach of this Agreement if and to the extent there is any failure of performance under this Agreement occasioned by an act of God, fire, flood, act of government or state, war, civil commotion, insurrection, acts of terrorism, embargo, sabotage, prevention from or hindrance in obtaining energy or other utilities, or any other similar reason beyond the control and without the fault or negligence of the Party affected thereby (a "Force Majeure Event"). Such excuse shall continue as long as the Force Majeure Event continues to affect performance. Upon cessation of such Force Majeure Event, the affected Party shall promptly resume performance under this Agreement as soon as it is commercially reasonable for the Party to do so. Each Party agrees to give the other Party prompt written notice of the occurrence of any Force Majeure Event, the nature thereof, and the extent to which the affected Party will be unable to fully perform its obligations under this Agreement. Each Party further agrees to use commercially reasonable efforts to correct the Force Majeure Event as quickly as practicable (provided that in no event shall a Party be required to settle any labor dispute) and to give the other Party prompt written notice when it is again fully able to perform such obligations. This Section shall be without prejudice to Iovance's termination rights under Article 16.

18.3 Condemnation. If the Facility(ies) are, or any individual Facility is, condemned or taken as a result of the exercise of the power of eminent domain or will be conveyed to a governmental agency having power of eminent domain under the threat of the exercise of such power (any of the foregoing, a “Condemnation”), then this Agreement will terminate as of the date on which title to the Facility(ies) vests in the authority so exercising or threatening to exercise such power and Iovance will not have any right to the Condemnation proceeds. This Section shall be without prejudice to Iovance’s termination rights under Article 16.

18.4 Notices. Any notice required or permitted to be given under this Agreement by any Party shall be in writing and shall be (a) delivered personally, (b) sent by registered mail, return receipt requested, postage prepaid, (c) sent by a nationally-recognized courier service guaranteeing next-day or second day delivery, charges prepaid, or (d) delivered by facsimile (with documented evidence of transmission), to the addresses or facsimile numbers of the other Party set forth below, with an electronic copy of the notice sent to the email address provided, or at such other addresses as may from time to time be furnished by similar notice by any Party. The effective date of any notice under this Agreement shall be the date of receipt by the receiving Party.

If to Company:

WuXi AppTec, Inc.
Attention: Alan Moore
4751 League Island Blvd.
Philadelphia, PA 19112

With a copy to “Vice President, Manufacturing” at the above address.

If to Iovance:

Iovance Biotherapeutics, Inc.
Attention: Richard Gaeto
999 Skyway Road, Suite 150
San Carlos, CA 94070

With a copy to:

Iovance Biotherapeutics, Inc.
Attention: Legal Department
999 Skyway Road, Suite 150
San Carlos, CA 94070

With an electronic copy to:
legal@iovance.com

Either Party may change its address for notice by giving notice thereof in the manner set forth in this Section 18.4.

18.5 Entire Agreement, Amendments, Initial Agreement.

18.5.1 This Agreement, including the Quality Agreement and the Statements of Work and Change Orders entered into by the Parties from time to time and the Appendices attached hereto or thereto and referenced herein or therein, constitutes the full understanding of the Parties, a complete and fully integrated agreement and a complete and exclusive statement of the terms of their agreement with respect to the specific subject matter hereof and supersedes all prior agreements and understandings, oral and written, among the Parties with respect to the subject matter hereof (including the Original Agreement). No terms, conditions, understandings or agreements purporting to amend, modify or vary the terms of this Agreement (including any Appendix hereto) shall be binding unless hereafter made in a written instrument referencing this Agreement and signed by each of the Parties.

18.5.2 The Parties were previously parties to that certain Cell Therapy Development, Manufacturing and/or Tissue Processing Terms and Conditions with an effective date of September 25, 2015 (the "Initial Agreement"), which predates this Agreement and the Original Agreement, and under such Initial Agreement the Parties have executed several work orders, including WO A-4, executed September 6, 2016 ("WO A-4"). The Parties desire that the Original Agreement, as amended and restated by this Agreement, govern WO A-4. The Parties acknowledge and agree that this Section 18.5.2 constitutes an amendment to WO A-4 under Section 14 of the Initial Agreement. In furtherance thereof, from and after the Original Effective Date, the Original Agreement, as amended and restated by this Agreement, shall solely govern the performance of WO A-4. Accordingly, references to Statements of Work herein shall also be deemed to refer to WO A-4.

18.6 Governing Law. This Agreement and any disputes hereunder will be governed by and construed in accordance with the laws of the State of New York, without giving effect to its conflicts of laws provisions. The United Nations Convention on Contracts for the International Sale of Goods will not apply to this Agreement. This provision shall operate without prejudice to either Party's ability to seek injunctive or other interlocutory relief in any court accepting jurisdiction in order to protect and enforce its Intellectual Property rights.

18.7 Equitable Relief. The Parties agree that the obligations contained in Articles 12 and 13 are necessary and reasonable in order to protect the Parties' respective businesses. The Parties further agree that monetary damages may be inadequate to compensate a Party for any breach by the other Party of its covenants and agreements with respect to Articles 12 and 13, and that each Party shall be entitled to seek injunctive or other equitable relief against the threatened or continued breach of those provisions, and agree that no bond or other security shall be required in obtaining such equitable relief. Furthermore, except as expressly set forth in this Agreement, none of the remedies set forth in this Agreement are intended to be exclusive, and each Party shall have available to it all remedies available under law or in equity.

18.8 Counterparts. This Agreement and any amendment hereto may be executed in any number of counterparts, each of which shall for all purposes be deemed an original and all of which shall constitute the same instrument. This Agreement shall be effective upon full execution by facsimile, PDF or original, and a facsimile or scanned signature shall be deemed to be and shall be as effective as an original signature. Signature pages may be exchanged via email.

18.9 Severability. As a fully integrated agreement, each right or obligation of each Party to this Agreement is fully dependent on the Party retaining all of its other rights and performing all of its other obligations under this Agreement. Nevertheless, if any part of this Agreement shall be found to be invalid or unenforceable under Law in any jurisdiction, such part shall be ineffective only to the extent of such invalidity or unenforceability in such jurisdiction, without in any way affecting the remaining parts of this Agreement in that jurisdiction or the validity or enforceability of this Agreement as a whole in any other jurisdiction. In addition, the part that is ineffective shall be reformed in a mutually agreeable manner so as to as nearly approximate the intent of the Parties as possible.

18.10 Titles and Subtitles. All headings, titles and subtitles used in this Agreement (including any Appendix hereto) are for convenience only and are not to be considered when construing or interpreting any term or provision of this Agreement (or any Appendix hereto).

18.11 Recitals, Definitions and Appendices. All “RECITALS”, “DEFINITIONS” and Appendices referred to herein form an integral part of this Agreement and are incorporated into this Agreement by such reference.

18.12 Interpretation and Construction.

18.12.1 Where the context requires, (i) all pronouns used herein will be deemed to refer to the masculine, feminine or neuter gender as the context requires and (ii) the singular context will include the plural and vice versa.

18.12.2 The words “include”, “includes” and “including” (and words of similar meaning) shall be deemed to be followed by the phrase “without limitation”.

18.12.3 For purposes of interpretation of this Agreement, the following shall apply:

- (a) “Personal Information” shall be understood to include personal data.
- (b) With respect to the Use of Personal Information, “Use” shall be understood to include the processing of Personal Information.
- (c) “patients” shall be understood to be synonymous with study subjects.
- (d) “regulatory agency” shall be understood to be synonymous with regulatory authority.

18.13 Assignment, Third Party Beneficiaries. This Agreement shall be binding upon the successors and assigns of the Parties and the name of a Party appearing herein shall be deemed to include the names of its successors and assigns. Company may not assign its interest under this Agreement (including the Quality Agreement) without the prior written consent of Iovance, such consent not to be unreasonably withheld. Notwithstanding the above, Iovance may, without Company's prior consent, assign this Agreement, in whole or in part, to Iovance's Affiliates or to any entity that may acquire substantially all of the assets of Iovance to which this Agreement relates. This Agreement shall be binding upon, and inure to the benefits of, the Parties hereto and their respective successors and assigns. Any permitted assignment of this Agreement by either Party will be conditioned upon that Party's permitted assignee agreeing in writing to comply with all the terms and conditions contained in this Agreement, the Statements of Work, the Quality Agreement and all Laws. No assignment shall relieve any Party of responsibility for the performance of any obligation that accrued prior to the effective date of such assignment. None of the provisions of this Agreement shall be for the benefit of or enforceable by any Third Party, including any creditor of either Party hereto. No such Third Party shall obtain any right under any provision of this Agreement or shall by reasons of any such provision make any claim in respect of any debt, liability or obligation (or otherwise) against either Party hereto.

18.14 Waiver. The failure of any Party at any time or times to require performance of any provision of this Agreement (including any Appendix hereto) will in no manner affect its rights at a later time to enforce the same. No waiver by any Party of any term, provision or condition contained in this Agreement (including any Appendix hereto), whether by conduct or otherwise, in any one or more instances, shall be deemed to be or construed as a further or continuing waiver of any such term, provision or condition or of any other term, provision or condition of this Agreement (including any Appendix hereto).

18.15 Dispute Resolution, Arbitration.

18.15.1 If the JSC is unable to resolve a dispute pursuant to Section 3.3.3, despite each Party's good faith efforts, either Party may refer the dispute to the President of each Party's respective business unit (or other designee), who will attempt to resolve such dispute by negotiation and consultation for a thirty (30) day period following receipt of such written notice.

18.15.2 In the event that no agreement is reached by the Presidents (or other designees) with respect to such dispute within thirty (30) days after its referral to them, either Party may refer the matter to binding arbitration pursuant to Section 18.15.3.

18.15.3 In the event Presidents (or other designees) have not resolved a dispute referred to them pursuant to Section 18.15.2 within thirty (30) days of receipt of the written notice referring such dispute to the Presidents (or other designees), either Party may at any time after such thirty (30) day period submit such dispute to be finally settled by arbitration administered in accordance with the procedural rules of the American Arbitration Association (the "AAA") in effect at the time of submission, as modified by this Section 18.15.3. The arbitration will be governed by the Laws of the State of New York. The arbitration will be heard and determined by three arbitrators who are retired judges or attorneys with at least twenty (20) years of relevant experience in the pharmaceutical and biotechnology industry, each of whom will be impartial and independent and will not have worked for or on behalf of either Party for at least five (5) years. Each Party will appoint one (1) arbitrator and the third arbitrator will be selected by the two (2) Party-appointed arbitrators, or, failing agreement within thirty (30) days following appointment of the second arbitrator, by the AAA. Such arbitration will take place in New York, New York. The arbitration award so given will, absent manifest error, be a final and binding determination of the applicable dispute, will be fully enforceable in any court of competent jurisdiction, and will not include any damages expressly prohibited by Section 15.2. Each Party will pay the fees, costs and expenses for the arbitrator it chooses, and the Parties will share payment for the third arbitrator. Except in a proceeding to enforce the results of the arbitration or as otherwise required by Law or securities exchange, neither Party nor any arbitrator may disclose the existence, content or results of any arbitration hereunder without the prior written consent of both Parties.

18.15.4 Nothing in this Agreement will prevent either Party from exercising any right under this Agreement, including the right of termination, or require either Party to forego or delay any proceeding to seek equitable or injunctive relief to stop or prevent any breach of this Agreement if that Party reasonably believes that it would be irreparably harmed by any delay in seeking such relief.

18.16 No Presumption against Drafter. For purposes of this Agreement, each Party hereby waives any rule of construction that requires that ambiguities in this Agreement (including any Appendix hereto) be construed against the drafter.

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IN WITNESS WHEREOF, the Parties have executed this Agreement as of the Effective Date.

IOVANCE BIOTHERAPEUTICS, INC.

WUXI APPTEC, INC.

Name:

Name:

Title:

Title:

APPENDIX A

Statements of Work

APPENDIX B

Iovance Materials

EXECUTIVE EMPLOYMENT AGREEMENT

THIS EXECUTIVE EMPLOYMENT AGREEMENT (the “**Agreement**”) dated August 7, 2016 by and between Lion Biotechnologies, Inc., a Nevada corporation (the “**Company**”), and Frederick Vogt (“**Executive**”) (either party individually, a “**Party**”; collectively, the “**Parties**”).

WHEREAS the Company desires to retain the services of Executive to serve as the Company's Vice President, Intellectual Property.

WHEREAS, the Parties desire to enter into this Agreement to set forth the terms and conditions of Executive's employment by the Company and to address certain matters related to Executive's employment with the Company;

WHEREAS, both the Company and the Executive have read and understood the terms and provisions set forth in this Agreement, and Executive acknowledges Executive has been afforded a reasonable opportunity to review this Agreement with Executive's legal counsel to the extent desired;

NOW, THEREFORE, in consideration of the foregoing and the mutual provisions contained herein, and for other good and valuable consideration, the Parties hereto agree as follows:

1. **Employment.** Effective September 30, 2016 (the “Effective Date”), the Company hereby employs Executive, and Executive hereby accepts such employment, upon the terms and conditions set forth herein.

2. **Duties.**

2.1 **Position.** Executive shall be employed by the Company in the position of Vice President, Intellectual Property shall have the duties and responsibilities consistent with the position of Vice President, Intellectual Property and such other duties and responsibilities assigned by the Company's Chief Executive Officer. Executive shall perform faithfully and diligently such duties as are reasonable and customary for Executive's position, as well as such other duties as the Chief Executive Officer shall reasonably assign from time to time. Executive shall provide his services hereunder from his home office, with travel to the Company's offices in New York City and other offices as required by Company business.

2.2 **Best Efforts/Full-Time.**

2.2(a) Executive understands and agrees that Executive will faithfully devote Executive's best efforts and substantially all of his time during normal business hours to advance the interests of the Company. Executive will abide by all policies duly adopted by the Company, as well as all applicable federal, state and local laws, regulations or ordinances. Executive will act in a manner that Executive reasonably believes to be in the best interest of the Company at all times. Executive further understands and agrees that Executive has a fiduciary duty of loyalty to the Company to the extent provided by applicable law and that Executive will take no action which materially harms the business, business interests, or reputation of the Company.

2.2(b) Executive agrees that Executive will not directly engage in competition with the Company at any time during the existence of the employment relationship between the Company and Executive.

2.2(c) Executive agrees that, during the term of this Agreement, Executive shall work exclusively for the Company. Consequently, Executive agrees to not engage in any other employment, consulting or other business activity without the written consent of the Company.

3. **At-Will Employment.** Executive's employment with the Company will be “at-will” and will not be for any specific period of time. As a result, Executive is free to resign at any time, for any or no reason, as Executive deems appropriate. The Company will have a similar right and may terminate Executive's employment at any time, with or without cause. Executive's and the Company's respective rights and obligations at the time of termination are outlined below in Section 6 of this Agreement.

4. Compensation.

4.1 Base Salary and Sign-On Bonus. As compensation for the performance of all duties to be performed by Executive hereunder, the Company shall pay to Executive a base salary of \$300,000 per year, less required deductions for state and federal withholding tax, social security and all other employment taxes and authorized payroll deductions, payable on a prorated basis as it is earned, in accordance with the normal payroll practices of the Company (the "**Base Salary**"). As a sign-on bonus, Executive will be paid \$50,000 (subject to payroll taxes) with the first paycheck.

4.2 Stock Options. As of the Effective Date, Executive shall receive stock options to purchase an aggregate of 200,000 shares of the Company's common stock. To the extent legally permitted, the stock options shall be incentive stock options. The stock options will have an exercise price equal to the fair market value of the common stock at the close of trading on NASDAQ on the Effective Date. Provided that Executive is still employed with the Company on the following dates, the foregoing stock options will vest in three installments as follows: (i) Options for the purchase of 66,672 shares shall vest on one year anniversary of the Effective Date; and (ii) the remaining stock options shall vest as to 16,672 shares at the end of each quarter over the next two years, commencing with the first quarter following the first anniversary of the Effective Date. Upon the termination of Executive's employment with the Company, except as provided herein, the unvested options will be forfeited and returned to the Company. In addition to the foregoing grant of options, Executive shall also be entitled to receive stock option grants under the Company's stock option plan commencing one year after the Effective Date in such amounts and upon such terms as shall be determined by the Board of Directors, in its sole discretion.

4.3 Incentive Compensation. Executive will be eligible to participate in the Company's annual incentive compensation program ("**Incentive Plan**") applicable to executive employees, as approved by the Board (the year in which the program is implemented, the "**Plan Year**"). The target potential amount payable to Executive under the Incentive Plan, if earned, shall be 30% of Executive's Base Salary earned during the applicable calendar year. Compensation under the Incentive Plan ("**Incentive Compensation**") will be conditioned on the satisfaction of individual and Company objectives, as established in writing by the Company, and the condition that Executive is employed by Company on the Incentive Compensation payment date, which shall be on or before March 15th of the year following the Plan Year. The payment of any Incentive Compensation pursuant to this Section 4.3 shall be made in accordance with the normal payroll practices of the Company, less required deductions for state and federal withholding tax, social security and all other employment taxes and authorized payroll deductions.

4.4 Performance Review. The Company will periodically review Executive's performance on no less than an annual basis and may increase (but not decrease) Executive's salary or other compensation, as it deems appropriate in its sole and absolute discretion.

4.5 Customary Fringe Benefits. Executive understands and agrees that certain employee benefits may be provided to the Executive by the Company incident to the Executive's employment. Executive will be eligible for all customary and usual fringe benefits generally available to executive employees and all other employees of the Company subject to the terms and conditions of the Company's benefit plan documents. Executive understands and agrees that any employee benefits provided to the Executive by the Company incident to the Executive's employment (other than Base Salary, Incentive Compensation and any applicable Severance Payment) are provided solely at the discretion of the Company and may be modified, suspended or revoked at any time, without notice or the consent of the Executive, unless otherwise provided by law. Moreover, to the extent that these benefits are provided pursuant to policies or plan documents adopted by the Company, Executive acknowledges and agrees that these benefits shall be governed by the applicable employment policies or plan documents. The benefits to be provided to Executive shall include group health insurances and participation in a 401 (k) plan. Executive will be eligible to receive paid time off benefits in the form of vacation, sick and holidays.

4.6 Business Expenses. Executive will be reimbursed for all reasonable, out-of-pocket business expenses incurred in the performance of Executive's duties on behalf of the Company, including travel-related expenses. To obtain reimbursement, expenses must be submitted promptly with appropriate supporting documentation in accordance with the Company's policies.

5. Confidentiality and Proprietary Agreement. Executive agrees to abide by the Company's Employee Proprietary Information and Inventions Agreement (the "**Non-Disclosure Agreement**"), which Executive has signed and is incorporated herein by reference.

6. Termination of Executive's Employment.

6.1 Termination for Cause by the Company. The Company may terminate Executive's employment immediately at any time and without notice for "Cause." For purposes of this Agreement, "Cause" shall mean (i) a material breach by Executive of this Agreement or the Non-Disclosure Agreement; (ii) the death of Executive or his disability resulting in his inability to perform his reasonable duties assigned hereunder for a period of 180 days; (iii) Executive's theft, dishonesty, or falsification of any Company documents or records; (iv) Executive's improper use or disclosure of the Company's confidential or proprietary information; or (v) Executive's conviction (including any plea of guilty or nolo contendere) of any criminal act which impairs Executive's ability to perform his duties hereunder or which in the Board's judgment may materially damage the business or reputation of the Company; provided, however, that prior to termination for cause arising under clause (i), Executive shall have a period of ten days after written notice from the Company to cure the event or grounds constituting such cause. Any notice of termination provided by Company to Executive under this Section 6.1 shall identify the events or conduct constituting the grounds for termination with sufficient specificity so as to enable Executive to take steps to cure, if curable, the same if such default is a material breach by Executive of this Agreement of the Non-Disclosure Agreement. In the event Executive's employment is terminated in accordance with this subsection 6.1, Executive shall be entitled to receive only the Base Salary and any earned Incentive Compensation (as defined in Section 4.3 above) then in effect, prorated to the date of termination. All other obligations of the Company to Executive pursuant to this Agreement will be automatically terminated and completely extinguished.

6.2 Termination Without Cause By The Company/Separation Package. The Company may terminate Executive's employment under this Agreement without Cause (as defined in Section 6.1 above) at any time on thirty (30) days' advance written notice to Executive. In the event of such termination, Executive will receive Executive's Base Salary through the date of termination and a prorated portion of any Incentive Compensation that was earned under Section 4.3 through the date of termination. Upon such termination without Cause, any then unvested stock options granted to Executive by the Company will become fully vested and Executive shall have six months from the date of termination within which to exercise his vested options. In addition, upon a termination of Executive's employment by the Company without Cause, Executive will be eligible to receive a "**Severance Payment**" equivalent to six months of Executive's then Base Salary, payable in full within thirty (30) days after termination, provided that Executive first satisfies the Severance Conditions. For purposes of this Agreement, the "**Severance Conditions**" are defined as (1) Executive's execution and non- revocation of a full general release, in the form attached hereto as Exhibit A, and such release has become effective in accordance with its terms prior to the 30th day following the termination date; and (2) Executive's reaffirmation of Executive's commitment to comply, and actual compliance, with all surviving provisions of this Agreement. Following payment of the Severance Payment, Base Salary, any Incentive Compensation and any benefits required to be paid in accordance with applicable benefit plans through the date of termination, all other obligations of the Company to Executive pursuant to this Agreement will be automatically terminated and completely extinguished.

6.3 Termination Upon a Change of Control. For purposes of this Agreement, "**Change of Control**" shall mean: (1) a merger or consolidation or the sale or exchange by the stockholders of the Company of capital stock of the Company, where the stockholders of the Company immediately before such transaction do not obtain or retain, directly or indirectly, at least a majority of the beneficial interest in the voting stock or other voting equity of the surviving or acquiring corporation or other surviving or acquiring entity, in substantially the same proportion as before such transaction; (2) any transaction or series of related transactions to which the Company is a party in which in excess of fifty percent (50%) of the Company's voting power is transferred; or (3) the sale or exchange of all or substantially all of the Company's assets (other than a sale or transfer to a subsidiary of the Company as defined in section 424(f) of the Internal Revenue Code of 1986, as amended (the "**Code**")), where the stockholders of the Company immediately before such sale or exchange do not obtain or retain, directly or indirectly, at least a majority of the beneficial interest in the voting stock or other voting equity of the corporation or other entity acquiring the Company's assets, in substantially the same proportion as before such transaction; provided, however, that a Change of Control shall not be deemed to have occurred pursuant to any transaction or series of transactions relating to a public or private financing or re-financing, the principal purpose of which is to raise money for the Company's working capital or capital expenditures and which does not result in a change in a majority of the members of the Board. If, within six (6) months immediately preceding a Change of Control or within twelve (12) months immediately following a Change of Control, the Executive's employment is terminated by the Company for any reason other than Cause, then the Executive shall be entitled to receive the Severance Payment and stock option vesting and exercisability set forth in Section 6.2, provided that Executive first satisfies the Severance Conditions. Following payment of the Severance Payment, Base Salary, any Incentive Compensation and any benefits required to be paid in accordance with applicable benefit plans through the date of termination, all other obligations of the Company to Executive pursuant to this Agreement will be automatically terminated and completely extinguished.

6.4 Resignation. Executive shall have the right to terminate this Agreement at any time, for any reason, by providing the Company with thirty (30) days written notice, provided, however, that subsequent to Executive's resignation, Executive shall be required to comply with all surviving provisions of this Agreement. Executive shall not be entitled to any Severance Pay. Executive will only be entitled to receive Executive's Base Salary earned up to the date of termination. Notwithstanding the foregoing, Executive has the right upon thirty (30) days written notice to the Company to terminate Executive's employment for "Good Reason" due to occurrence of any of the following: (i) a material adverse change in Executive's title, duties or responsibilities; (ii) any failure by the Company to pay, or any reduction by Company of, the base salary or any failure by Company to pay any Incentive Compensation to which Executive is entitled pursuant to Section 4; (iii) the Company creates a work environment designed to constructively terminate Executive or to unlawfully harass or retaliate against Executive; (iv) a Change of Control occurs in which the Company is not the surviving entity and the surviving entity fails to offer Executive an executive position at a compensation level at least equal to Executive's then compensation level under this Agreement; or (v) the Company's requirement that Executive report for work at a location more than forty-five (45) miles from his home without the written consent of Executive to such relocation. In the event that Executive terminates his employment for Good Reason, then Executive shall be entitled to receive the Base Salary, any earned Incentive Compensation, Severance Payment and stock option vesting and exercisability as if Executive were terminated by the Company without Cause under Section 6.2, subject to Executive's compliance with all of the Severance Conditions.

6.5 Application of Section 409A.

6.5(a) Notwithstanding anything set forth in this Agreement to the contrary, no amount payable pursuant to this Agreement which constitutes a "deferral of compensation" within the meaning of the Treasury Regulations issued pursuant to Section 409A of the Code (the "**Section 409A Regulations**") shall be paid unless and until Executive has incurred a "separation from service" within the meaning of the Section 409A Regulations.

6.5(b) Company intends that income provided to Executive pursuant to this Agreement will not be subject to taxation under Section 409A of the Code. The provisions of this Agreement shall be interpreted and construed in favor of satisfying any applicable requirements of Section 409A of the Code. **However, Company does not guarantee any particular tax effect for income provided to Executive pursuant to this Agreement.** In any event, except for Company's responsibility to withhold applicable income and employment taxes from compensation paid or provided to Executive, Company shall not be responsible for the payment of any applicable taxes on compensation paid or provided to Executive pursuant to this Agreement.

6.5(c) Furthermore, to the extent that Executive is a "specified employee" within the meaning of the Section 409A Regulations as of the date of Executive's separation from service, no amount that constitutes a deferral of compensation which is payable on account of Executive's separation from service shall be paid to Executive before the date (the "**Delayed Payment Date**") which is first day of the seventh month after the date of Executive's separation from service or, if earlier, the date of Executive's death following such separation from service. All such amounts that would, but for this Section, become payable prior to the Delayed Payment Date will be accumulated and paid on the Delayed Payment Date.

6.5(d) Notwithstanding anything herein to the contrary, the reimbursement of expenses or in-kind benefits provided pursuant to this Agreement shall be subject to the following conditions: (i) the expenses eligible for reimbursement or in-kind benefits in one taxable year shall not affect the expenses eligible for reimbursement or in-kind benefits in any other taxable year; (ii) the reimbursement of eligible expenses or in-kind benefits shall be made promptly, subject to Company's applicable policies, but in no event later than the end of the year after the year in which such expense was incurred; and (iii) the right to reimbursement or in-kind benefits shall not be subject to liquidation or exchange for another benefit.

6.5(e) For purposes of Section 409A of the Code, the right to a series of installment payments under this Agreement shall be treated as a right to a series of separate payments.

7. General Provisions.

7.1 Successors and Assigns. The rights and obligations of the Company under this Agreement shall inure to the benefit of and shall be binding upon the successors and assigns of the Company. Executive shall not be entitled to assign any of Executive's rights or obligations under this Agreement.

7.2 Waiver. Either party's failure to enforce any provision of this Agreement shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Agreement.

7.3 Attorney's Fees. In the event of any dispute or claim relating to or arising out of Executive's employment relationship with Company, this Agreement, or the termination of Executive's employment with Company for any reason, the prevailing party in any such dispute or claim shall be entitled to recover its reasonable attorney's fees and costs.

7.4 Severability. In the event any provision of this Agreement is found to be unenforceable by an arbitrator or court of competent jurisdiction, such provision shall be deemed modified to the extent necessary to allow enforceability of the provision as so limited, it being intended that the parties shall receive the benefit contemplated herein to the fullest extent permitted by law. If a deemed modification is not satisfactory in the judgment of such arbitrator or court, the unenforceable provision shall be deemed deleted, and the validity and enforceability of the remaining provisions shall not be affected thereby.

7.5 Interpretation; Construction. The headings set forth in this Agreement are for convenience only and shall not be used in interpreting this Agreement. Executive has participated in the negotiation of the terms of this Agreement. Furthermore, Executive acknowledges that Executive has had an opportunity to review and revise the Agreement and have it reviewed by legal counsel, if desired, and, therefore, the normal rule of construction to the effect that any ambiguities are to be resolved against the drafting party shall not be employed in the interpretation of this Agreement.

7.6 Governing Law. This Agreement will be governed by and construed in accordance with the laws of the United States and the internal laws of the State of California.

7.7 Notices. Any notice required or permitted by this Agreement shall be in writing and shall be delivered as follows with notice deemed given as indicated: (a) by personal delivery when delivered personally; (b) by overnight courier upon written verification of receipt; (c) by telecopy, facsimile transmission, or electronic transmission such as e-mail, upon acknowledgment of receipt of electronic transmission; or (d) by certified or registered mail, return receipt requested, upon verification of receipt. Notice shall be sent to the addresses set forth below each party's signature, or such other address as either party may specify in writing.

7.8 Entire Agreement. This Agreement constitutes the entire agreement between the Parties relating to this subject matter and supersedes all prior or simultaneous representations, discussions, negotiations, and agreements, whether written or oral. This Agreement may be amended or modified only with the written consent of Executive and the Company. No oral waiver, amendment or modification will be effective under any circumstances whatsoever.

[Execution Page Follows]

THE PARTIES TO THIS AGREEMENT HAVE READ THE FOREGOING AGREEMENT AND FULLY UNDERSTAND EACH AND EVERY PROVISION CONTAINED HEREIN. WHEREFORE, THE PARTIES HAVE EXECUTED THIS AGREEMENT ON THE DATES SHOWN BELOW.

EXECUTIVE:

/s/ Frederick G. Vogt

Frederick Vogt
West Norriton, PA

COMPANY:

Lion Biotechnologies, Inc.

By:

/s/ Maria Fardis

Maria Fardis
President & Chief Executive Officer
112 W. 34th Street 17th Floor
New York, NY 10120

Exhibit A
Form of Release and Waiver of Claims

In consideration for the severance payments and other benefits provided for in the Executive Employment Agreement, effective as of September 30, 2016 (the "Employment Agreement"), I, Frederick Vogt hereby furnish Lion Biotechnologies, Inc., a Nevada corporation (the "Company") with the following release and waiver (the "Release and Waiver").

In exchange for the consideration provided to me by the Employment Agreement, I hereby generally and completely release the Company and its officers, directors, employees, agents, attorneys, predecessors, successors, parent and subsidiary entities, insurers, affiliates, and assigns from any and all claims, liabilities and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring prior to my signing this Release and Waiver. This general release includes, but is not limited to: (1) all claims arising out of or in any way related to my employment with the Company or the termination of that employment; (2) all claims related to my compensation or benefits from the Company, including, but not limited to, salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, or any other ownership interests in the Company; (3) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (4) all tort claims, including, but not limited to, claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (5) all federal, state, and local statutory claims, including, but not limited to, claims for discrimination, harassment, retaliation, attorneys' fees, or other claims arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990, and the federal Age Discrimination in Employment Act of 1967 (as amended) ("ADEA").

I acknowledge that, among other rights, I am waiving and releasing any rights I may have under ADEA and that this Release and Waiver is knowing and voluntary. I further acknowledge that I have been advised, as required by the Older Workers Benefit Protection Act, that: (a) the release and waiver granted herein does not relate to claims under the ADEA which may arise after this Release and Waiver is executed; (b) I should consult with an attorney prior to executing this Release and Waiver; (c) I have 21 days in which to consider this Release and Waiver (although I may choose voluntarily to execute this Release and Waiver earlier); (d) I have seven days following the execution of this Release and Waiver to revoke my consent to this Release and Waiver; and (e) this Release and Waiver shall not be effective until the eighth day after I execute this Release and Waiver and the revocation period has expired. Notwithstanding the foregoing, nothing contained in this Release and Waiver shall waive, release or otherwise diminish any claims that I might have at law or in equity for payment of severance or other benefits to which I am entitled under the terms of the Employment Agreement.

I acknowledge my continuing obligations under my Employee Proprietary Information and Inventions Agreement between myself and the Company (the "Confidentiality Agreement"). I understand and agree that my right to the severance pay I am receiving is in exchange for my agreement to the terms of this Release and Waiver and is contingent upon my continued compliance with my Confidentiality Agreement.

This Release and Waiver, including the Confidentiality Agreement, and the Employment Agreement constitute the complete, final and exclusive embodiment of the entire agreement between the Company and me with regard to the subject matter hereof. I am not relying on any promise or representation by the Company that is not expressly stated herein. This Release and Waiver may only be modified by a writing signed by both me and a duly authorized officer of the Company.

Frederick Vogt

Dated: _____

FIRST AMENDMENT TO THE STRATEGIC ALLIANCE AGREEMENT**Effective Date: August 2, 2017**

THIS FIRST AMENDMENT TO THE STRATEGIC ALLIANCE AGREEMENT (this "Amendment"), is entered into by and between Iovance Biotherapeutics, Inc., a Delaware corporation, successor in interest to Lion Biotechnologies, Inc., with a place of business located at 999 Skyway Road, Suite 150, San Carlos, CA 94070 ("Iovance"), and The University of Texas M. D. Anderson Cancer Center, with a place of business located at 1515 Holcombe Blvd., Houston, TX 77030 ("MD Anderson"), a member institution of The University of Texas System, as of the date set forth above (the "Effective Date"). Iovance and MD Anderson may each be referred to as a "Party" or together, the "Parties".

WHEREAS, the Parties have entered into a Strategic Alliance Agreement effective April 17, 2017 (the "Original Agreement"); and

WHEREAS, the Parties now desire to amend the Original Agreement.

NOW, THEREFORE, in consideration of the mutual covenants contained herein, the Parties hereby agree to be legally bound as follows:

1. The following sentence in Section 2.1(a) of the Original Agreement:

The first three Study Orders are attached to this Agreement as Exhibit I, Exhibit II, and Exhibit III, and the Studies that are the subject of such Study Orders are also referred to herein as the "Initial Studies".

is hereby deleted and replaced in its entirety by the following sentence:

The first three Study Orders, when completed, will be incorporated into this Agreement as Exhibit I, Exhibit II, and Exhibit III, and the Studies that are the subject of such Study Orders are also referred to herein as the "Initial Studies".

2. In the event of any inconsistency or conflict between the terms of this Amendment and the terms of the Original Agreement, the terms of this Amendment shall control.

3. This Amendment, together with the Original Agreement, constitutes the final and complete expression of the parties with respect to the subject matter hereof. This Amendment may not be amended except by a written instrument duly executed and delivered by each of the parties.

4. Except as expressly amended by this Amendment, all of the terms and conditions of the Original Agreement shall remain unchanged and in full force and effect as set forth therein.

5. This Amendment may be executed in any number of counterparts, including by electronic portable document format (PDF) exchange, each of which shall be deemed an original as against any Party whose signature appears thereon, but all of which, taken together, shall constitute one and the same instrument, with the same effect as though such signatures were on the same instrument.

IN WITNESS WHEREOF, the undersigned, intending to be legally bound, have duly executed this Agreement as of the Effective Date.

IOVANCE BIOTHERAPEUTICS, INC.

THE UNIVERSITY OF TEXAS

M.D. ANDERSON CANCER CENTER

By: /s/ Maria Fardis

By: /s/ Chris McKee

Authorized Signature

Authorized Signature

Maria Fardis, Ph.D., M.B.A.

Chris McKee

Printed Name

Printed Name

President and Chief Executive Officer

SVP, Strategy & Business Development

Title

Title

SECOND AMENDMENT TO THE STRATEGIC ALLIANCE AGREEMENT**Effective Date: February 16, 2018**

THIS SECOND AMENDMENT TO THE STRATEGIC ALLIANCE AGREEMENT (this "Amendment"), is entered into by and between Iovance Biotherapeutics, Inc., a Delaware corporation and successor in interest to Lion Biotechnologies, Inc., with a place of business located at 999 Skyway Road, Suite 150, San Carlos, CA 94070 ("Iovance"), and The University of Texas M. D. Anderson Cancer Center, with a place of business located at 1515 Holcombe Blvd., Houston, TX 77030 ("MD Anderson"), a member institution of The University of Texas System, as of the date set forth above (the "Effective Date"). Iovance and MD Anderson may each be referred to as a "Party" or together, the "Parties". Unless otherwise defined in this Amendment, all capitalized terms shall have the meaning ascribed to them in the Original Agreement (as defined hereinafter).

WHEREAS, the Parties have entered into a Strategic Alliance Agreement effective April 17, 2017, as amended by the First Amendment to the Strategic Alliance Agreement effective August 2, 2017 (collectively, the "Original Agreement"); and

WHEREAS, the Parties now desire to amend the Original Agreement.

NOW, THEREFORE, in consideration of the mutual covenants contained herein, the Parties hereby agree to be legally bound as follows:

1. Section 1.3 shall be deleted in its entirety and replaced with the following:

1.1 JSC Responsibilities. The main task of the JSC will be to oversee the Collaboration. In order to achieve the objectives of the Collaboration, the JSC will oversee each Study under the Collaboration. The JSC will provide technical, scientific, clinical, and regulatory guidance regarding the Studies and will be responsible for monitoring the progress of the Studies. Each JSC meeting will include an agenda item related to the safety of the Studies and dedicate sufficient time to discuss safety concerns, safety updates or specific safety issues that have occurred during the performance of the Studies ("Safety Review"). In addition, the JSC agrees to meet quarterly (or more frequently should a specific Study safety event or finding require additional review, provided that each Party mutually agrees to such meeting, with such prompt agreement not to be unreasonably withheld) to review Study safety concerns, findings or events that are reasonably deemed by either or both parties as serious or urgent. In accordance with the aforementioned sentence, the JSC shall promptly schedule such meetings upon reasonable request at a time that is mutually agreeable to both Parties, which shall be conducted in person at a mutually agreeable location or via teleconference. The JSC will also be responsible for coordinating resolution of problems arising during the performance of the Studies or in the Collaboration as a whole. Additional members may be invited by the JSC on a case by case basis should discussion of certain topics require so; provided, that such members will be subject to written obligations of confidentiality and non-use at least as strict as those set forth in Section 5 of the Agreement.

2. Section 2.3(e) shall be deleted in its entirety and replaced with the following:

(e) MD Anderson and Principal Investigator shall be responsible for reporting and tracking of all adverse events with respect to a Study (each an "AE" and collectively, the "AEs") in compliance with all MD Anderson policies and procedures, all Laws, and each applicable Protocol. Principal Investigator shall be responsible for updating all AEs, including any expedited safety reports. Any serious adverse events with respect to a Study (each an "SAE" and collectively the "SAEs") that are serious, related and unexpected will be thoroughly documented in a report and submitted to the MD Anderson Investigational New Drug Office ("IND Office") within twenty-four (24) hours of the Principal Investigator's or MD Anderson's awareness of the SAE. Any SAEs that are not defined as serious, related and unexpected shall be thoroughly documented in a report and submitted to the IND Office within five (5) days of the Principal Investigator's or MD Anderson's awareness of the SAE. All reports will be redacted to delete any patient identifying information and shall be electronically delivered to Iovance at iovacessafety@iovance.com promptly after submission to the IND Office. Within twenty-four (24) hours of receipt of a report related to SAEs that are serious, related and unexpected, and where deemed necessary by Iovance in its sole discretion, Iovance will provide any comments to Principal Investigator. For all other reports, where deemed necessary by Iovance in its sole discretion, Iovance will provide its comments promptly to the Principal Investigator. The Principal Investigator will review Iovance's comments and shall provide such comments to the IND Office. Any updated information shall be submitted by the Principal Investigator as a follow-up SAE report. Iovance will have a reasonable opportunity to discuss any AE or SAE with Principal Investigator promptly if reasonably requested.

Principal Investigator shall provide a list of all safety events that occurred in the performance of the Study to Iovance once per month, which may include, SAEs, special situation reports, and AEs. At Iovance's reasonable request, Principal Investigator shall provide additional relevant information related to any such safety event, SAE, or special situation report. Additionally, the Principal Investigator will promptly provide Iovance with all relevant information in his/her possession or control as may be reasonably needed to assist Iovance in the identification and resolution of problems or unexpected occurrences involving the Study Drug (as defined in an applicable Study Order) or its use in the applicable Study.

MD Anderson and Iovance will share information with each other relating to any Study findings that may impact the safety of the Study Drug, including how the Study Drug may adversely affect the health and safety of any Study patient, influence the conduct of a Study, alter an IRB's approval to continue a Study, or affect the willingness of a patient to continue participation in the Study.

If a Data Safety Monitoring Board ("DSMB") is engaged by MD Anderson in connection with a Study, any DSMB recommendations related to any Study shall be provided to Iovance promptly upon request. MD Anderson represents and certifies that (a) its DSMB operates and functions in an independent manner in accordance with applicable Laws and FDA guidance, and (b) if a DSMB is engaged by MD Anderson to oversee any Study, the DSMB shall consider the unique nature of such Study in connection with its review of the Study data.

3. All references to "LBIO" in the Original Agreement are hereby deleted and replaced by "Iovance".

4. Section 9.5 is amended to replace "Lion Biotechnologies, Inc." with "Iovance Biotherapeutics, Inc." and to replace "legal@lionbio.com" with "legal@iovance.com".

5. Section 4.3(d) is amended to add the following sentence at the end of the paragraph: "MD Anderson shall submit all invoices by electronic mail to ap@iovance.com".

6. In the event of any inconsistency or conflict between the terms of this Amendment and the terms of the Original Agreement, the terms of this Amendment shall control.

7. This Amendment, together with the Original Agreement, constitutes the final and complete expression of the parties with respect to the subject matter hereof. This Amendment may not be amended except by a written instrument duly executed and delivered by each of the parties.

8. Except as expressly amended by this Amendment, all of the terms and conditions of the Original Agreement shall remain unchanged and in full force and effect as set forth therein.

9. This Amendment may be executed in any number of counterparts, including by electronic portable document format (PDF) exchange, each of which shall be deemed an original as against any Party whose signature appears thereon, but all of which, taken together, shall constitute one and the same instrument, with the same effect as though such signatures were on the same instrument.

[Signature page follows]

IN WITNESS WHEREOF, the undersigned, intending to be legally bound, have duly executed this Amendment.

IOVANCE BIOTHERAPEUTICS, INC.

**THE UNIVERSITY OF TEXAS
M. D. ANDERSON CANCER CENTER**

By: /s/ Maria Fardis

Authorized Signature

By: /s/ Ben Melson

Authorized Signature

Maria Fardis, Ph.D., M.B.A.

Printed Name

Ben Melson

Printed Name

President and Chief Executive Officer

Title

Sr. Vice President and Chief Financial Officer

Title

ACKNOWLEDGED FOR STUDY ORDER 1:

ACKNOWLEDGED FOR STUDY ORDER 2:

PRINCIPAL INVESTIGATOR

PRINCIPAL INVESTIGATOR

By: /s/ Amir A. Jazaeri

Signature

By: /s/ Amir A. Jazaeri

Signature

Amir A. Jazaeri, M.D.

Printed Name

Amir A. Jazaeri, M.D.

Printed Name

Ad Interim Chair, Dept of Gynecologic Oncology

Title

Ad Interim Chair, Dept of Gynecologic Oncology

Title

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM'S CONSENT

We consent to the incorporation by reference in the Registration Statements of Iovance Biotherapeutics, Inc. on Form S-3 (File No. 333-222340), Form S-3 (File No. 333-214073), Form S-3 (File No. 333-212373), Form S-8 (File No. 333-217638), Form S-8 (File No. 333-205097), and Form S-8 (File No. 333-214567) of our report dated March 12, 2018, with respect to our audits of the consolidated financial statements of Iovance Biotherapeutics, Inc. as of December 31, 2017 and 2016 and for each of the two years in the period ended December 31, 2017 and our report dated March 12, 2018 with respect to our audit of the effectiveness of internal control over financial reporting of Iovance Biotherapeutics, Inc. as of December 31, 2017, which reports are included in this Annual Report on Form 10-K of Iovance Biotherapeutics, Inc. for the year ended December 31, 2017.

/s/ Marcum LLP

Marcum LLP
New York, NY
March 12, 2018

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements (Forms S-3 No. 333-222340, 333-214073, and 333-212373, Forms S-8 No. 333-217638, 333-205097 and 333-214567) of Iovance Biotherapeutics, Inc. (formerly Lion Biotechnologies, Inc.) of our report dated March 11, 2016, relating to the financial statements of Iovance Biotherapeutics, Inc. (formerly Lion Biotechnologies, Inc.) for the year ended December 31, 2015, included in this Annual Report on Form 10-K for the year ended December 31, 2017.

/s/ Weinberg & Company, P.A.
Weinberg & Company, P.A.

Los Angeles, California
March 12, 2018

**CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002**

I, Maria Fardis, certify that:

1. I have reviewed this Annual Report on Form 10-K of Iovance Biotherapeutics, 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 Rules 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.
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2018

/s/ Maria Fardis

Maria Fardis
Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002**

I, Timothy E. Morris, certify that:

1. I have reviewed this Annual Report on Form 10-K of Iovance Biotherapeutics, 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 Rules 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.
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2018

/s/ Timothy E. Morris

Timothy E. Morris

Chief Financial Officer

(Principal Financial and Accounting Officer)

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002**

I, Maria Fardis, Chief Executive Officer of Iovance Biotherapeutics, Inc. (Company), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

- the Annual Report on Form 10-K of the Company for the year ended December 31, 2017 (Report) fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the periods presented therein.

Date: March 12, 2018

/s/ Maria Fardis

Maria Fardis
Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002**

I, Timothy E. Morris, Chief Financial Officer of Iovance Biotherapeutics, Inc. (Company), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

- the Annual Report on Form 10-K of the Company for the year ended December 31, 2017 (Report) fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the periods presented therein.

Date: March 12, 2018

/s/ Timothy E. Morris

Timothy E. Morris

Chief Financial Officer

(Principal Financial and Accounting Officer)
