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

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2020

☐ 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	**75-3254381**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
999 Skyway Road, Suite 150, San Carlos, California	**94070**
(Address of Principal Executive Offices)	(Zip Code)

(650) 260-7120
(Registrant's Telephone Number, Including Area Code)

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

Title of Each Class	**Trading Symbol(s)**	**Name Of Each Exchange On Which Registered**
Common Stock, $ 0.000041666 Par Value per Share	IOVA	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 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 such files). Yes ☒ No ☐

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

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

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

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock, par value $0.000041666 per value	IOVA	The Nasdaq Stock Market, LLC

The aggregate market value of the registrant's common stock held by non-affiliates on June 30, 2020, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $3.7 billion. 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 17, 2021, there were 146,979,253 shares of the registrant's common stock outstanding.

Documents Incorporated By Reference

Portions of registrant's proxy statement relating to registrant's 2021 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," "might," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "aim," "potential," "continue," "ongoing," "goal," "forecast," "guidance," "outlook," 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, enrollment, and timing of our clinical trials;
- the success, cost and timing of our product development activities;
- the ability of us or our third-party contract manufacturers to continue to manufacture tumor infiltrating lymphocytes, or TIL, in accordance with our selected process;
- our ability to design, construct and staff our own manufacturing facility on a timely basis and within the estimated expenses;
- the success of competing therapies that are or may become available;
- regulatory developments in the United States of America, or U.S., and foreign countries;
- the timing of and our ability to obtain and maintain U.S. Food and Drug Administration, or FDA, or other regulatory authority approval of, or other action with respect to, our product candidates;
- 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;
- fluctuations in the trading price of our common stock; and
- our use of cash and other resources.

Actual results may differ from those set forth in this Annual Report on Form 10-K due to the risks and uncertainties inherent in our business, including, without limitation: the FDA may not agree with our interpretation of the results of its clinical trials; later developments with the FDA that may be inconsistent with already completed FDA meetings; the preliminary clinical results, including efficacy and safety results, from ongoing Phase 2 may not be reflected in the final analyses of these trials including new cohorts within these trials; the results obtained in our ongoing clinical trials, such as the studies and trials referred to in this 10-K, may not be indicative of results obtained in future clinical trials or supportive of product approval; regulatory authorities may potentially delay the timing of FDA or other regulatory authority approval of, or other action with respect to, our product candidates, specifically, our description of FDA interactions are subject to FDA's interpretation, as well as FDA's authority to request new or additional information; we may not be able to obtain or maintain FDA or other regulatory authority approval of its product candidates; our ability to address FDA or other regulatory authority requirements relating to our clinical programs and registrational plans, such requirements including, but not limited to, clinical and safety requirements as well as manufacturing and control requirements; risks related to our accelerated FDA review designations; our ability to obtain and maintain intellectual property rights relating to our product pipeline; and the acceptance by the market of our product candidates and their potential reimbursement by payors, if approved.

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 cell therapies as novel cancer immunotherapy products designed to harness the power of a patient’s own immune system to eradicate cancer cells. Tumor infiltrating lymphocyte, or TIL, therapy is an autologous cell therapy platform technology that was originally developed by the National Cancer Institute, or NCI, which conducted initial clinical trials of this therapy in diseases such as metastatic melanoma and cervical cancer. We have developed a new, shorter manufacturing process for TIL known as Generation 2, or Gen 2, which yields a cryopreserved TIL product. This proprietary and scalable manufacturing method is being investigated in multiple indications. Our lead product candidates include lifileucel for metastatic melanoma and metastatic cervical cancer. In addition to metastatic melanoma and metastatic cervical cancer, we are investigating the effectiveness and safety of TIL for the treatment of head and neck squamous cell carcinoma, or HNSCC, and non-small cell lung cancer, or NSCLC, as well as in other solid tumor oncology indications through collaborations. We are also investigating peripheral blood lymphocyte, or PBL, therapy for patients with relapsed or refractory chronic lymphocytic leukemia, or CLL, and small lymphocytic lymphoma, or SLL.

We are conducting a Phase 2 clinical trial, C-144-01, of our lead product candidate, lifileucel, for the treatment of metastatic melanoma. This multicenter pivotal trial enrolled melanoma patients with disease progression following treatment with at least one systemic therapy, including a PD-1 inhibitor and if BRAF mutated, a BRAF inhibitor, or a combination of BRAF and MEK inhibitors. Cohort 4 of the C-144-01 clinical trial is a single-arm cohort intended to support a biologics license application, or BLA, submission for lifileucel. Cohorts 2 and 4 of the C-144-01 trial use our Gen 2 manufacturing process. We completed and closed enrollment of patients into Cohort 2 of the C-144-01 trial in 2018. Results from Cohort 2 of the C-144-01 clinical trial were initially reported at the American Society of Clinical Oncology, or ASCO, annual meeting on June 1, 2019 and subsequently updated at the ASCO annual meeting on May 29, 2020. In 66 patients with metastatic melanoma, treatment with lifileucel resulted in an objective response rate, or ORR, of 36%, as assessed by investigator, with 2 complete responses and 22 partial responses. The disease control rate, or DCR, was 80.3%. Patients were heavily pretreated and had a mean of 3.3 prior therapies. We have reported durable responses across a wide age range of metastatic melanoma patients, and among those who have received prior anti-CTLA-4 and BRAF targeted treatments, regardless of BRAF mutation status, and equally in patients with PD-L1 high and low status. We have provided several updates on the median duration of response, or DOR, for Cohort 2 and most recently, in January 2021, we announced that median DOR in Cohort 2 had still not been reached after 28.1 months of median study follow up, as assessed by investigator. The adverse event profile was generally consistent with the underlying advanced disease and the profile of the lymphodepletion and IL-2 regimens.

Pivotal Cohort 4 of the C-144-01 trial was enrolled to evaluate ORR as read out by an Independent Review Committee, or IRC, as the primary endpoint based on our interpretation of discussions with the FDA as part of an End of Phase 2, or EOP2, meeting held with the FDA in the third quarter of 2018. In October 2018, based on the data provided to the FDA during the EOP2 meeting, we announced that lifileucel had received a Regenerative Medicine Advanced Therapy, or RMAT, designation from the FDA. Enrollment in Cohort 4 of the C-144-01 trial commenced in March 2019 and patient dosing was completed in January 2020. A total of 87 patients were dosed in Cohort 4. Initial results from Cohort 4 are available for 68 patients with two radiological assessments, as determined by investigator. Lifileucel showed a 32.4% ORR, including one complete response and 21 partial responses, two of which were yet to be confirmed with follow up visits at the time of the data cut, and a DCR of 72.1% as of the data cut off of March 16, 2020, corresponding to 5.3 months of median study follow up. This data is consistent with the Cohort 2 data read out at a similar median duration of study follow up. The ORR of Cohort 2 at a median study follow up of 6 months was 33%. In October 2020, after a Type B meeting with the FDA, we announced that we had delayed our BLA submission for lifileucel in metastatic melanoma as a result of FDA feedback, in order to allow us to simultaneously refine existing and develop new potency assays, and we anticipate submitting

our BLA in 2021. At the same time, we also announced that we had reached agreement with the FDA on the minimum duration of follow up for Cohort 4 to support our BLA submission for lifileucel in the treatment of metastatic melanoma.

We are also conducting a Phase 2 clinical trial, C-145-04, which is a multicenter pivotal trial that will assess the safety and efficacy of lifileucel for the treatment of patients with recurrent, metastatic or persistent cervical cancer. In February 2019, lifileucel received Fast Track designation from the FDA for development in the treatment of cervical cancer with disease progression on or after chemotherapy. In March 2019, the protocol for this trial was amended to modify the primary endpoint of ORR to be determined by IRC. In May 2019, lifileucel received Breakthrough Therapy designation, or BTD, from the FDA for development in the treatment of cervical cancer. Updated results from the C-145-04 clinical trial were reported at the ASCO annual meeting on June 1, 2019. In 27 patients with metastatic cervical cancer, treatment with lifileucel resulted in an ORR of 44%. At the time of the study data cut, there were 3 complete responses and 9 partial responses. The DCR was 85%. Patients were heavily pretreated and had a mean of 2.4 prior therapies. The median DOR had not been reached. The adverse event profile was generally consistent with the underlying advanced disease and the profile of the lymphodepletion and IL-2 regimens. Based on an EOP2 meeting held with the FDA in June 2019, we believe that results from the C-145-04 clinical trial may be sufficient to support registration of lifileucel for the treatment of patients with metastatic cervical cancer. In accordance with the FDA's recommendations, the protocol was amended to further define the patient population. In November 2019, in order to evaluate lifileucel in broader lines of therapy in cervical cancer, we have further amended the C-145-04 trial to collect additional data on early-line patients as well as late-line patients by adding additional cohorts, in anticipation of a changing landscape in this indication, including Cohort 2 for patients that had previously received anti-PD-1 therapy. These additional cohorts also allow access to TIL therapy after completion of the enrollment in the registrational cohorts. A more detailed description of these and other cohorts in the C-145-04 trial is provided in the section entitled "Lifileucel for Cervical Cancer" in this Annual Report on Form 10-K. In January 2021, we announced that Cohort 2 of the C-145-04 trial had completed enrollment and that data from this cohort may be supportive of registration because of the expected changing landscape of care for cervical patients. We intend to initiate a dialog with the FDA in 2021 to discuss BLA submission plans for lifileucel in cervical cancer.

In November 2020, we announced that we had finalized the protocol for our potential registrational clinical trial in NSCLC, IOV-LUN-202, to investigate LN-145 in patients with recurrent or metastatic NSCLC, without driver mutations, who previously received a single line of approved systemic therapy of combined checkpoint inhibitor and chemotherapy. The IOV-LUN-202 clinical trial includes three cohorts. Cohorts 1 and 3 of the IOV-LUN-202 clinical trial will enroll patients with a PD-L1 tumor proportion score, or TPS, of less than one percent, and Cohort 2 will enroll patients with a PD-L1 TPS of greater than or equal to one percent. We intend to enroll patients in the IOV-LUN-202 clinical trial throughout 2021.

C-145-03 is our Phase 2, multicenter trial to assess the safety and efficacy of our product candidate LN-145 for the treatment of patients with recurrent metastatic HNSCC. In October 2018, we reported that, to date, preliminary data for 13 patients in the C-145-03 clinical trial yielded an ORR of 31% with a DOR ranging from 2.8 to 7.6 months. The adverse event profile remained consistent with previous reports. We redesigned our C-145-03 trial to include multiple cohorts, in order to allow for dosing of TIL therapies produced by multiple manufacturing methods, including our Gen 2 manufacturing process, our Generation 3, or Gen 3, manufacturing process, and our PD-1 selected TIL manufacturing process. Our PD-1 selected TIL manufacturing process results in a product that we refer to as LN-145-S1. In January 2021, we announced that we are closing the C-145-03 clinical trial after the trial reached its pre-specified enrollment target.

We are also investigating the potential of our TIL therapies in earlier lines of treatment and in combination with pembrolizumab, and are studying LN-145 as a monotherapy in relapsed refractory non-small cell lung cancer, or NSCLC, patients. IOV-COM-202 is a Phase 2, multicenter trial that is composed of seven cohorts that can enroll up to a total of 135 patients. In May 2019, we reported that the first patient was dosed in the IOV-COM-202 trial. In addition to its ongoing enrollment in the U.S., the IOV-COM-202 trial has also received regulatory approval in Canada and in certain European countries. A more detailed description of these and other cohorts in the C-145-04 trial is provided in the section entitled "Lifileucel and LN-145 in Combination with Pembrolizumab and Other Immunotherapies" in this Annual Report on Form 10-K. In Cohort 2A of the IOV-COM-202 trial, we are enrolling advanced, recurrent, or metastatic HNSCC patients who are naïve to prior immunotherapy including anti-PD-1/anti-PD-L1 therapy. The patients receive LN-145 in combination with pembrolizumab. We reported results from ongoing Cohort 2A of the IOV-COM-202 trial at the Society for Immunotherapy in Cancer, or SITC, meeting in November 2020, as follows. As of October 16, 2020, nine HNSCC patients received LN-145 plus pembrolizumab with a median duration of follow up of 8.6 months. Nine and eight patients were evaluable for safety and efficacy, respectively. Four patients had a confirmed, objective response with an ORR of 44% including one complete response and three partial responses. Median DOR was not reached. The disease control rate at data cutoff was 89% in nine patients. Seven of the eight evaluable patients, or 87.5%, had a reduction in target lesions. The median number of prior therapies was 1.0 with 89% of the patients having received prior chemotherapy. Four patients were human papilloma virus, or HPV,

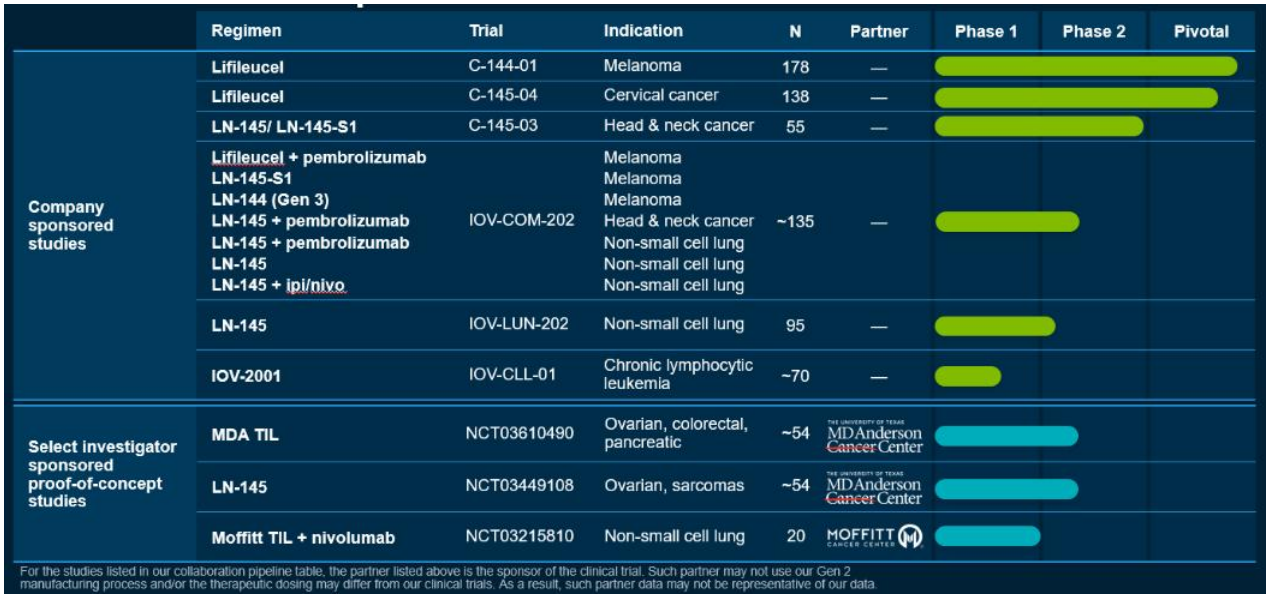
positive, three patients were HPV negative, and two patients had unknown HPV status. The treatment emergent adverse events, or TEAEs, observed were consistent with the underlying advanced disease and the known adverse event profiles of pembrolizumab, lymphodepletion, and IL-2 regimens. The most common TEAEs, occurring in more than 50% of evaluable subjects, were chills, anemia, hypotension, nausea, pyrexia, and thrombocytopenia.

In November 2019, we announced that our investigational new drug application, or IND, for our PBL therapy, IOV-2001, was authorized by the FDA and our sponsored clinical trial using this therapy, IOV-CLL-01, was cleared to proceed. IOV-2001 is a non-genetically modified, polyclonal T cell product that is manufactured using a nine-day process from 50 mL of patient's blood. IOV-CLL-01 is a Phase 1/2 clinical trial evaluating the safety and efficacy of IOV-2001 in patients with relapsed or refractory CLL or SLL. The IOV-CLL-01 trial is expected to enroll up to approximately 70 patients.

As part of our collaboration program with the MD Anderson Cancer Center, or MDACC, two Phase 2 trials were initiated in 2018. Both trials are sponsored by MDACC. The first trial, NCT03449108, is intended to allow for investigation of LN-145 manufactured by us using our manufacturing processes to treat patients with soft tissue sarcoma, osteosarcoma, platinum resistant ovarian cancer, and thyroid cancer. A second trial under the collaboration with MDACC, NCT03610490, is active as well. This trial is treating patients with platinum resistant ovarian cancer, pancreatic cancer, and colorectal cancer. This trial uses TIL manufactured by MDACC using urelumab, a 4-1BB agonistic antibody, as part of the manufacturing process. The data obtained using this manufacturing process may not be representative of our data using our Gen 2 manufacturing process.

We are also collaborating with Centre hospitalier de l'Université de Montreal, or CHUM, Yale University, and Moffitt on investigator-sponsored clinical trials of TIL therapies in other indications. The clinical trials sponsored by CHUM and Moffitt use, or will use, TIL manufactured by different manufacturing processes, which may not be representative of our data using our Gen 2 manufacturing process.

Our current product candidate pipeline and selected investigator-sponsored proof-of-concept studies are summarized in the figure below:



We have developed a third-generation manufacturing process known as Gen 3. Gen 3 is a shorter process than Gen 2. We are using Gen 3 manufacturing in Cohort 1C of the IOV-COM-202 trial in melanoma and in Cohort 3 of the IOV-LUN-202 trial in NSCLC and have previously used it in the C-145-03 trial in HNSCC.

We currently own more than twenty granted or allowed U.S. and international patents for compositions and methods of treatment in a broad range of cancers relating to our Gen 2 manufacturing process, including U.S. Patent Nos. 10,130,659, 10,166,257,

10,272,113, 10,363,273, 10,398,734, 10,420,799, 10,463,697, 10,537,595, 10,646,517, 10,653,723, 10,693,330, 10,695,372, 10,894,063, and 10,905,718. We anticipate that the terms of these patents related to Gen 2 manufacturing processes will extend to January 2038, not including any patent term extensions or adjustments that may be available. Our owned and licensed intellectual property portfolio also includes patent applications relating to TIL, marrow infiltrating lymphocyte, or MIL, and PBL therapies; frozen tumor-based TIL technologies; remnant TIL and digest TIL compositions, methods and processes; methods of treatment of a broad range of cancers using TIL therapies; methods of manufacturing TIL, MIL, and PBL therapies; the use of costimulatory molecules in TIL therapy and manufacturing; stable and transient genetically-modified TIL therapies; methods of using immune checkpoint inhibitors in combination with TIL therapies; TIL selection technologies; and methods of treating patient subpopulations.

In January 2020, we obtained a license from Novartis to develop and commercialize an antibody cytokine engrafted protein, which we refer to as IOV-3001. Under the agreement, we paid an upfront payment to Novartis and may pay milestones involved in initiation of patient dosing in various phases of clinical development for IOV-3001 and approval of a potential product in the U.S., EU and Japan. Novartis is also entitled to low-to-mid single digit percentage royalties from commercial sales of IOV-3001. In addition, in January 2020, we announced a research collaboration and exclusive worldwide licensing agreement with Cellectis S.A., or Cellectis, a clinical-stage biopharmaceutical company focused on developing immunotherapies based on gene-edited allogeneic chimeric antigen receptor modified T cells, whereby we licensed certain transcription activator-like effector nuclease, or TALEN, technology from Cellectis in order to develop TIL that have been genetically edited to create potentially more potent cancer therapeutics. The worldwide exclusive license enables us to use TALEN technology addressing multiple gene targets to modify TIL for therapeutic use in several cancer indications. Financial terms of the license include development, regulatory and sales milestone payments from us to Cellectis, as well as royalty payments based on net sales of TALEN-modified TIL products.

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 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 lifileucel for the treatment of metastatic melanoma.

Based on results of TIL therapy from trials sponsored by the NCI and our own clinical trials in metastatic melanoma, we are focused on expediting the development, regulatory approval and commercialization of our lead product candidate, lifileucel, for the treatment of patients with metastatic melanoma. We filed an investigational new drug application, or IND, with the FDA in December 2014 to initiate a company-sponsored Phase 2 single-arm, multicenter clinical trial of lifileucel in patients with metastatic melanoma. We began enrollment of this trial in the second half of 2015 and expanded it into three cohorts in 2017. In 2019 we expanded into an additional cohort, Cohort 4, which serves as the basis for registration. We held an end of Phase 2 meeting with the FDA in September 2018. Based on the meeting and subsequent dialog with the FDA, we amended the protocol for the C-144-01 trial to include 75 patients in Cohort 4. The primary endpoint is ORR as determined by IRC. We have completed dosing of patients in Cohort 4, have reported preliminary results, and intend to file a BLA for lifileucel in metastatic melanoma in 2021.

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 that we are the only company in the U.S. to have a centralized, demonstrated, and commercially viable TIL manufacturing process. In 2018, we first utilized our Gen 2 TIL manufacturing process, which reduced TIL manufacturing time from 5-6 weeks to 22 days, allowing for a commercially viable product candidate. The Gen 2 process also produces a cryopreserved TIL product for ease of administration and handling. The Gen 2 manufacturing process was utilized in Cohort 2 and Cohort 4 of our C-144-01 trial and has also been selected for use in most of our ongoing TIL clinical development program. We have included Gen 2 as the manufacturing process for registration for our discussions with the FDA and eventually the anticipated BLA filing for lifileucel. Our strategy is to establish our Gen 2 process as a commercial manufacturing process for TIL therapies, including lifileucel. We also continue to develop and evaluate potential future TIL manufacturing processes, including our Gen 3 process and our LN-145-S1 process.

Collaborate with governmental, academic and corporate partners to improve and develop TIL and PBL therapies for new indications or 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. For example, we have ongoing licensing agreements and collaborations with Moffitt, MDACC, Yale University, Cellectis, and Novartis to evaluate several new solid tumor and hematologic indications for TIL and PBL therapy in clinical and preclinical studies as well as, in some cases, new TIL manufacturing approaches. 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 research on unmodified TIL therapy and also addresses human papilloma virus, or HPV-associated cancers (cervical and head and neck), lung, bladder, and breast cancer. A description of certain of these collaborations and related agreements is provided in the following sections of this Annual Report on Form 10-K.

Continue to establish manufacturing capacity for TIL products.

We continue to invest in improving the process and efficiency of manufacturing our product candidates in the U.S. and Europe for TIL manufacturing. Currently we use several contract manufacturing organizations, or CMOs, to supply our TIL-based products for our clinical trials under various manufacturing services agreements, or MSAs. CMOs limit the amount of upfront capital investment as they have existing manufacturing facilities that we can utilize in TIL production.

We began construction of our own manufacturing facility in 2019, in Philadelphia, Pennsylvania, in order to provide for better margins and rapid implementation of innovative changes for TIL therapies that we may develop or commercialize. 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. As of the start of 2021, we have completed most construction and commissioning activities and expect that our manufacturing facility will begin clinical manufacturing in 2021.

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 for two suites. We have since extended our MSA with WuXi until November 2021.

In October 2018, we entered into a three-year MSA and related statement of work with MaSTherCell S.A., or MaSTherCell, a cell therapy CMO that is a subsidiary of Orgenesis Inc., which was acquired by Catalent, Inc. Pursuant to the MSA, MaSTherCell agreed to provide manufacturing and other services for use in our European clinical trials. In December 2019, we provided MaSTherCell with a notice of termination for the statement of work for cell therapy manufacturing. We ceased manufacturing at MaSTherCell in 2020.

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 our European clinical trials. PharmaCell was subsequently acquired by Lonza Group Ltd., or Lonza. Lonza continues to manufacture TIL products for our European clinical trials in its clinical and commercial facility in Geleen, the Netherlands. We have since extended our agreements with Lonza until April 2022.

Also in 2017, we entered into a two-year MSA and related statements of work with Moffitt, to manufacture our autologous cell therapy products for use in clinical trials, which has since been extended until March 2025. Moffitt continues to manufacture TIL products for our clinical trials in the U.S.

Iovance-Sponsored Clinical Trials

We currently have six ongoing Phase 2 clinical studies. The ongoing studies include C-144-01, of our lead product candidate, lifileucel, for the treatment of metastatic melanoma; C-145-04, of our product candidate lifileucel for recurrent, metastatic or persistent cervical cancer; and C-145-03, of our product candidate LN-145, for recurrent and/or metastatic HNSCC, which we are closing because the trial has reached the protocol’s defined enrollment. During 2018, we initiated a Phase 2 clinical trial, IOV-COM-202, a basket trial that will treat checkpoint naïve patients with TIL in combination with pembrolizumab for metastatic melanoma, head and neck cancer and non-small cell lung cancer. The trial also includes a cohort that will treat relapsed and refractory NSCLC patients with TIL alone as well as a cohort for NSCLC for TIL in combination with ipilimumab and nivolumab. Additional melanoma cohorts

are offered in this trial as well. In 2019, we announced that the FDA had cleared our Phase 1/2 clinical trial, IOV-CLL-01, using our PBL therapy, IOV-2001, to proceed. In 2020, we initiated a clinical trial, IOV-LUN-202, in NSCLC, which is now recruiting. Additional information about our clinical trials is presented as follows:

Lifileucel for Metastatic Melanoma

We are developing lifileucel to treat metastatic melanoma. Melanoma is a common type of skin cancer, accounting for approximately 100,350 patients diagnosed and 6,850 deaths each year in the U.S. according to the NCI's Surveillance, Epidemiology and End Results program, or SEER program, as of 2020. Our Phase 2 trial, C-144-01, is a prospective, registrational, four-cohort interventional study evaluating lifileucel in metastatic melanoma patients who have progressed after prior anti-PD-1 therapy and if BRAF mutant, after BRAF or BRAF/MEK inhibitor therapy. Patients enrolled in this trial to date have failed several prior treatment regimens. Lifileucel has received a Regenerative Medicine Advanced Therapy, or RMAT, designation from the FDA in metastatic melanoma.

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, makes 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 or 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. According to estimates from SEER in the U.S. in 2019, approximately there were 7,230 deaths due to melanoma. If approved, we believe lifileucel may be able to treat a portion of the patients that have received all other approved treatment options.

We are using our Gen 2 manufacturing process for most of our ongoing Phase 2 trials, and as a result, Cohort 1 of C-144-01, using our Generation 1, or Gen 1, manufacturing process, was closed to enrollment in 2017 and subsequent patients were enrolled in Cohort 2. The planned enrollment in C-144-01 was reached in late 2018 and Cohort 2 is closed to enrollment. Cohort 3 is a retreatment cohort. Cohort 4, a pivotal cohort, was added in 2019 and has completed dosing.

Updated results from Cohort 2 of the C-144-01 clinical trial were initially reported at the ASCO annual meeting in June 2019 and subsequently updated at the SITC annual meeting in November 2019. In 66 patients with metastatic melanoma, treatment with lifileucel resulted in an ORR of 36%, with 2 complete responses and 22 partial responses. The DCR was 80%. Patients were heavily pretreated and had a mean of 3.3 prior therapies. In January 2021, we announced that median DOR in Cohort 2 had still not been reached after 28.1 months of median study follow up, as assessed by investigator. The adverse event profile was generally consistent with the underlying advanced disease and the profile of the lymphodepletion and IL-2 regimens.

We held an End of Phase 2 meeting with the FDA in September 2018 to discuss the C-144-01 study. In its written minutes to the meeting, the FDA acknowledged that conduct of a randomized Phase 3 study may not be feasible in its intended population of advanced melanoma patients, who have been treated with at least one systemic therapy including an anti-PD-1 antibody and if BRAF mutation positive, a BRAF inhibitor or BRAF inhibitor with MEK inhibitor, and that a randomized study is not required for the registration of lifileucel. The FDA further acknowledged that a single-arm cohort of the C-144-01 trial may be acceptable for registration in this indication. A new cohort, Cohort 4, of 75 patients was enrolled in C-144-01 with a prospective definition of the primary endpoint of ORR to be determined by IRC, to support registration of lifileucel. The FDA recommended that we validate a potency assay prior to starting Cohort 4, which we have done. We initiated Cohort 4 in early 2019 in the U.S. and in Europe and completed dosing in January 2020. A total of 87 patients were dosed in Cohort 4. Initial results from Cohort 4 are available for 68 patients with two radiological assessments, as determined by investigator. In Cohort 4, lifileucel showed a 32.4% ORR, including one complete response and 21 partial responses, two of which are yet to be confirmed with follow up visits, and a DCR of 72.1% as of the data cut off of March 16, 2020, corresponding to 5.3 months of median study follow up. This data is consistent with the Cohort 2 data read out at a similar median duration of study follow up. In October 2020, after a Type B meeting with the FDA, we announced that we had delayed our BLA submission for lifileucel in metastatic melanoma until a date expected to occur in 2021 as a result of FDA feedback, in order to allow us to simultaneously refine existing and develop new potency assays. At the same time, we also announced that we had reached agreement with the FDA on the minimum duration of follow up for Cohort 4 to support our BLA submission for lifileucel in the treatment of metastatic melanoma.

Lifileucel for Cervical Cancer

We are also developing lifileucel, for the treatment of cervical cancer. Lifileucel for metastatic cervical cancer was formerly known as LN-145. According to estimates from the SEER program, approximately 13,800 women were diagnosed with cervical cancer, and approximately 4,290 cervical cancer-related deaths occurred in the U.S. in 2020.

C-145-04 is an ongoing Phase 2, multicenter pivotal trial that will assess the safety and efficacy of lifileucel for the treatment of patients with recurrent, metastatic or persistent cervical cancer. In February 2019, lifileucel received Fast Track designation from the FDA for development in the treatment of cervical cancer with disease progression on or after chemotherapy. In March 2019, the protocol for this trial was amended to modify the primary endpoint of ORR to be determined by IRC. In May 2019, lifileucel received BTD from the FDA for development in the treatment of cervical cancer. Updated results from the C-145-04 clinical trial were reported at the ASCO annual meeting on June 1, 2019. In 27 patients with metastatic cervical cancer, treatment with lifileucel resulted in an ORR of 44%. In the study there were 3 complete responses and 9 partial responses. The DCR was 85%. Patients were heavily pretreated and had a mean of 2.4 prior therapies. The median DOR had not been reached. The median follow-up was 7.4 months. The adverse event profile was generally consistent with the underlying advanced disease and the profile of the lymphodepletion and IL-2 regimens.

Based on an End of Phase 2 meeting held with the FDA in June 2019, the FDA has acknowledged that results from the C-145-04 clinical trial may be sufficient to support registration of lifileucel in the treatment of patients with metastatic cervical cancer. In accordance with the FDA's recommendations, the protocol was amended, to further define the patient population. In November 2019, in order to evaluate lifileucel in broader lines of therapy in cervical cancer, we have amended the C-145-04 trial to collect additional data on early-line patients as well as late-line patients. These additional cohorts also allow access to TIL therapy when the pivotal Cohort 1 is completed and also may support a request from FDA to provide expanded access to lifileucel. Enrollment in these additional cohorts will not impact the timing of the completion of the pivotal cohort nor the size of the registrational program. The C-145-04 trial currently consists of the following cohorts of cervical cancer patients with recurrent, persistent, or metastatic disease:

- Cohort 1 has completed enrollment in patients who have progressed during or after chemotherapy;
- Cohort 2 has closed enrollment to patients for treatment with lifileucel who have progressed during or after treatment with anti-PD-1/anti-PD-L1 checkpoint inhibitor;
- Cohort 3 is enrolling patients who have not received prior systemic therapy for recurrent, metastatic, or persistent disease, and will explore safety and efficacy of the combination of the lifileucel regimen with pembrolizumab;
- Cohort 4 includes patients who have been previously enrolled but are not considered within the registrational population, including patients dosed with product produced by our Gen 1 TIL manufacturing process; and
- Cohort 5 will enroll patients for retreatment with LN-145 for patients who have progressed after initial treatment with lifileucel.

The sample size of the C-145-04 clinical trial is expected to include 138 patients from the appropriate patient populations across these five cohorts. As we continue our work to refine existing and develop new potency assays to support our BLA submission for lifileucel in the treatment of metastatic melanoma, Cohort 2 may be supportive for an expected BLA submission for lifileucel in cervical cancer to further address the emerging treatment landscape for this disease.

LN-145 for NSCLC

We are developing LN-145 to treat NSCLC. According to estimates from the SEER program, approximately 228,820 people were diagnosed with lung and bronchus cancers, and approximately 136,000 deaths occurred related to these cancers in the U.S. in 2020.

In November 2020, we announced that we had finalized the protocol for our potential registrational clinical trial in NSCLC, IOV-LUN-202, to investigate LN-145 in patients with recurrent or metastatic NSCLC, without driver mutations, who previously received a single line of approved systemic therapy of combined checkpoint inhibitor and chemotherapy. The IOV-LUN-202 clinical trial, which is open to recruitment as of January 2021, includes three cohorts. Cohorts 1 and 3 of the IOV-LUN-202 clinical trial will enroll patients with a PD-L1 tumor proportion score, or TPS, of less than one percent, and Cohort 2 will enroll patients with a PD-L1 TPS of greater than or equal to one percent. We intend to enroll patients in the IOV-LUN-202 clinical trial throughout 2021.

LN-145 for Head and Neck Cancer

We are also developing LN-145 to treat head and neck cancer. According to estimates from the SEER program, approximately 65,630 people were diagnosed with head and neck-related cancers, which are referred to by the SEER program as oral cavity, pharynx and larynx cancers, and approximately 14,500 head and neck-related cancer deaths occurred in the U.S. in 2020.

In June 2017, we enrolled our first patient in our ongoing Phase 2 trial, C-145-03, for the treatment of patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck, who have failed one prior therapy. In 2018, preliminary data for 13 patients who were administered a mix of Gen 1 and Gen 2 products, was released showing an ORR of 31%, with 4 partial responses, with the DOR ranging from 2.8 to 7.6 months. Patients in the study had a median of three prior therapies. The safety findings from this study were also consistent with previous reports. The most common treatment emergent adverse events observed at the time of that data cut included chills, hypotension, pyrexia, hyponatremia, and anemia. As additional results are reported for the C-145-03 study, the safety profile of LN-145 may change. We changed the design of our C-145-03 trial so that enrolled patients would also be treated using either LN-145 produced from the Gen 3 manufacturing process or PD-1 selected TIL, or LN-145-S1, from the PD-1 selected TIL manufacturing process in two separate cohorts. In January 2021, we announced that we are closing the C-145-03 clinical trial after the trial reached its pre-specified enrollment target.

Lifileucel and LN-145 in Combination with Pembrolizumab and Other Immunotherapies

In addition to the trials for lifileucel and LN-145 mentioned above, we are developing these products in alone or in combination with pembrolizumab or other immunotherapies for melanoma, head and neck and NSCLC in our clinical trial IOV-COM-202, a Phase 2, multicenter trial that is composed of seven cohorts. In May 2019, we reported that the first patient was dosed in the IOV-COM-202 trial. In addition to the U.S., the IOV-COM-202 trial has also received regulatory approval in Canada and in certain European countries. In January 2021, we announced that we were adding two additional cohorts to the IOV-COM-202 trial, Cohorts 1C and 3C, as described below. The IOV-COM-202 trial now consists of the following cohorts of patients:

- Cohort 1A is enrolling at least 12 patients with advanced unresectable or metastatic melanoma who have not received prior immunotherapy, including checkpoint inhibitors such as anti-PD-1/anti-PD-L1 therapy, for treatment with lifileucel in combination with pembrolizumab;
- Cohort 1B is enrolling up to 27 melanoma patients who have progressed during or after treatment with anti-PD-1/anti-PD-L1 checkpoint inhibitor and if BRAF mutant, after BRAF or BRAF/MEK inhibitor therapy for treatment with LN-145-S1;
- Cohort 1C will enroll up to 27 melanoma patients who have progressed during or after treatment with anti-PD-1/anti-PD-L1 checkpoint inhibitor and if BRAF mutant, after BRAF or BRAF/MEK inhibitor therapy, for treatment with LN-145 manufactured using our Gen 3 process;
- Cohort 2A is enrolling at least 19 patients with advanced, recurrent, or metastatic HNSCC who are naïve to prior immunotherapy including anti-PD-1/anti-PD-L1 therapy, for treatment with LN-145 in combination with pembrolizumab;
- Cohort 3A is enrolling at least 12 patients with NSCLC who are naïve to prior immunotherapy including anti-PD-1/anti-PD-L1 therapy, for treatment with LN-145 in combination with pembrolizumab;
- Cohort 3B is enrolling at least 12 patients with NSCLC who have previously received systemic therapy, which could include checkpoint inhibitors or tyrosine kinase inhibitors, for treatment with LN-145 alone; and
- Cohort 3C will enroll up to 26 patients with NSCLC who have progressed after initial treatment with lifileucel.

The sample size of the IOV-COM-202 clinical trial is expected to include up to 135 patients from the appropriate patient populations across these seven cohorts.

We reported results from ongoing Cohort 2A of the IOV-COM-202 trial at the SITC meeting in November 2020 as follows. As of October 16, 2020, nine HNSCC patients have received LN-145 plus pembrolizumab with a median duration of follow up of 8.6 months. Nine and eight patients were evaluable for safety and efficacy, respectively. Four patients had a confirmed, objective response with an ORR of 44% including one complete response and three partial responses. Median DOR was not reached. The disease control rate at data cutoff was 89% in nine patients, and seven of the eight evaluable patients, 87.5%, had a reduction in target lesions. The median number of prior therapies was 1.0 with 89% of the patients having received prior chemotherapy. Four patients were human papilloma virus, or HPV, positive, three patients were HPV negative, and two patients had unknown HPV status. The treatment emergent adverse event, or TEAE, profile was consistent with the underlying advanced disease and the known adverse event profiles of pembrolizumab, lymphodepletion, and IL-2 regimens. The most common TEAEs, occurring in more than 50% of evaluable subjects, were chills, anemia, hypotension, nausea, pyrexia, and thrombocytopenia.

IOV-2001 PBL for CLL or SLL

In November 2019, we announced that our investigational new drug application, or IND, for IOV-2001 was approved by the FDA and that our sponsored clinical trial using this therapy, IOV-CLL-01, was cleared to proceed. IOV-2001 is a non-genetically modified, polyclonal T cell product that is manufactured using a nine-day process from 50 mL of patient's blood. IOV-CLL-01 is a Phase 1/2 clinical trial evaluating the safety and efficacy of IOV-2001 in patients with relapsed or refractory CLL or SLL. The IOV-CLL-01 trial is expected to enroll up to approximately 70 patients.

Investigator-Sponsored Clinical Trials

TIL in Other Solid Tumor Indications

We are collaborating with MDACC on clinical trials to evaluate TIL therapy in sarcomas, ovarian, colorectal, thyroid, and pancreatic cancers. These trials, NCT03610490 and NCT03449108, began enrolling patients in 2018. Patients in these trials are being treated with LN-145 or LN-145-S1 manufactured by us and TIL manufactured by MDACC.

We are also collaborating with Yale University on a clinical trial to evaluate TIL therapy in TNBC, which opened for enrollment in 2020. Patients in this trial will be treated with LN-145 manufactured by us.

TIL in Combination with Other Immunotherapy Drugs

Checkpoint inhibitors are a class of immunotherapy drugs that 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 provide funding for a clinical trial, NCT03215810, conducted by Moffitt, which seeks to evaluate TIL therapy in combination with the checkpoint inhibitor nivolumab in NSCLC. This study is closed to enrollment. An additional clinical trial, NCT02652455, 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 CTLA-4 checkpoint inhibitor ipilimumab.

In 2019, we entered into a collaboration with Moffitt to fund a Phase 1 trial of lymphodepletion plus TIL therapy with high-dose IL-2 in adolescent and young adult patients with soft tissue sarcoma in clinical trial NCT04052334.

Under our CRADA, we are collaborating with the NCI on a clinical trial, NCT02621021, to evaluate TIL therapy in combination with the checkpoint inhibitor pembrolizumab in a 170-patient clinical trial in patients with advanced melanoma. Enrollment in this trial is currently suspended.

TIL Therapy Background

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.

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

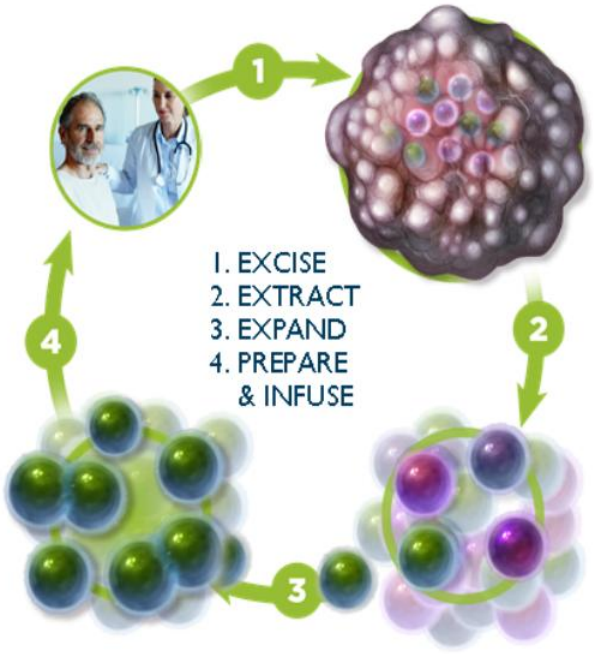
as hundreds or thousands of genes) are mutated, and solid tumors are heterogeneous, (ii) it is not always clear which particular mutations are critical, and (iii) tumors can adapt and find a way to evade treatments that target a single mutation. In addition, the tumor can suppress the patient's natural 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 a significant advancement in the treatment of cancer. These one-time cellular therapies may avoid the long-term side effects associated with current treatments and have the potential to be effective. 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, or NMA, 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

TIL therapy involves the following steps:

1. Excision: A surgical biopsy is conducted to remove about 1.5 cm of the tumor
2. Extraction: The tumor is fragmented and placed in media for TIL to leave the tumor
3. Expansion: TIL are expanded exponentially *ex vivo* to yield $10^9 – 10^{11}$ TIL
4. Preparation and Infusion: The patient receives NMA lymphodepletion to eliminate potentially suppressive tumor microenvironment and maximize engraftment and potential potency of TIL therapy; the 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 at the manufacturing facility until shipping of the final TIL product to the institution for infusion of the TIL back into the patient. We currently treat patients with a single infusion of TIL product, although our protocols allow for evaluation of more than one administration of TIL product. 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

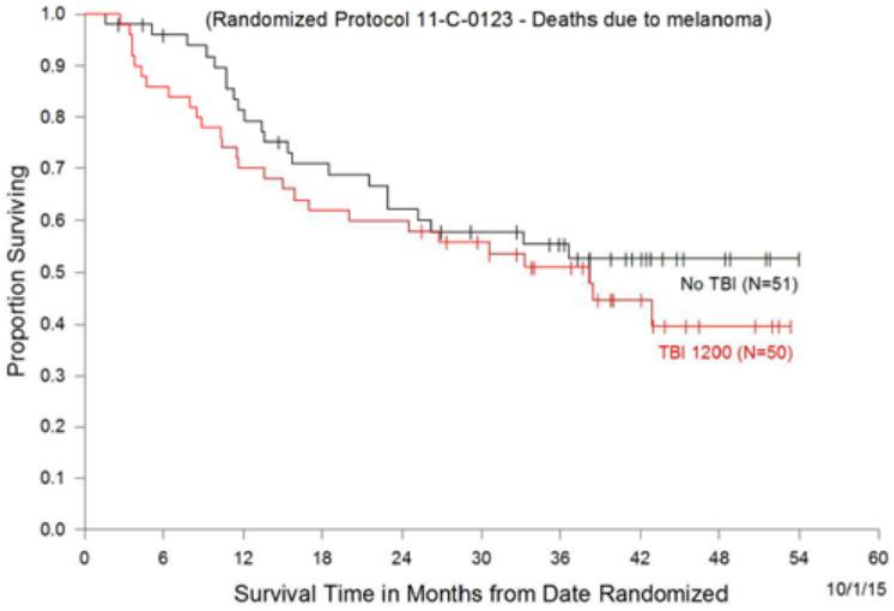
be susceptible due to the hostile tumor microenvironment. In September 2020, we reported data at the European Society for Medical Oncology conference highlighting the reinvigoration of TIL during the Gen 2 manufacturing process.

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 U.S., 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 30% or more, as defined by RECIST criteria) and approximately 22-24% of patients have a complete response (tumor regression of 100%) with no evidence of disease remaining after only one administration. Most patients who have had a complete response remained in response in 3-7 years of follow up. Furthermore, patients can respond to TIL therapy regardless of their prior therapies.

In September 2015, Dr. Steven 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 NMA chemotherapy, with the second group also receiving total body irradiation, or TBI. 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. At the ASCO 2018 meeting, Dr. Goff presented updated findings from the trial. Patients that had prior anti PD-1 treatment had an ORR of 20-25%.

Overall Survival of patients in TIL ± TBI clinical trial



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, 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 an ongoing 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 and was updated at the ASCO meeting in 2018. Out of 18 cervical cancer patients treated with HPV-TIL, two experienced complete remissions reported as ongoing at 53 and 67 months. Another three patients experienced a three-month partial response. 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 clinical programs and we closely monitor our studies to learn about all safety events occurring, as described elsewhere in this Annual Report on Form 10-K. Some of these events may be associated with TIL therapy. Historically, 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.

Next Generation TIL Product Strategies

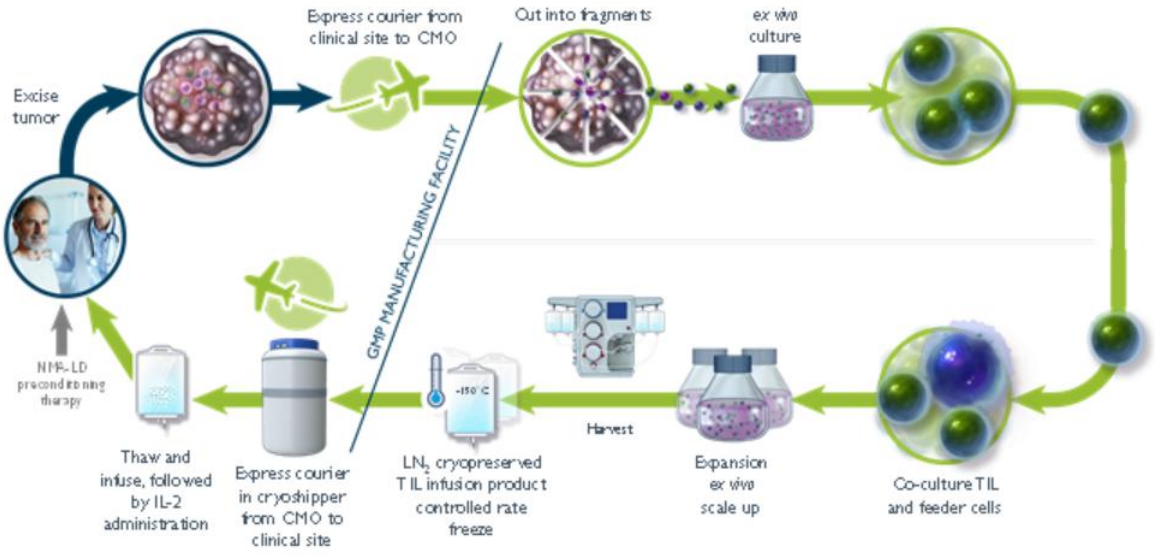
We are developing next generation TIL products using owned and licensed intellectual property rights, in some cases in combination with collaborators such as Cellectis and CHUM, as described elsewhere in this Annual Report on Form 10-K. These products include both genetically-modified TIL and PD-1 selected TIL therapies. We are also developing PBL therapy for CLL and SLL.

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 cGMP environment. This first-generation process expanded the number of TIL over a 5 to 6 week period and produced a non-cryopreserved product for administration to the patient. Our Gen 2 TIL manufacturing process, which was developed by our internal research and process development team, shortens the manufacturing process to 22 days while allowing for a cryopreserved product. The Gen 2 process is currently in use in almost all of our trials in which we manufacture TIL products, including lifileucel and LN-145. We have selected Gen 2 for product registration and ongoing and future TIL clinical development, although we continue to develop new TIL manufacturing processes. We have developed a third-generation manufacturing process, known as Gen 3 which has a shorter manufacturing process than Gen 2. We are testing Gen 3 in multiple clinical trials, as described elsewhere in this Annual Report on Form 10-K. We have also developed a manufacturing process that specifically selects for TIL that are PD-1 positive. This product is known as LN-145-S1.

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 it can be administered to the patient. The following diagram illustrates our Gen 2 TIL manufacturing process.



We have completed most construction and commissioning activities for our own manufacturing facility to manufacture TIL product using the Gen 2 manufacturing process. In addition, we have entered into MSAs with WuXi, Moffitt, and PharmaCell, which was acquired by Lonza, 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 two suites is also available to manufacture TIL for commercial use. Cell processing activities are conducted at all facilities 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 expect to rely on our own manufacturing facility and these CMOs to meet anticipated clinical trial and if approved, commercial demands. In the future, we may rely on them or other third parties, or our own manufacturing capabilities for the manufacturing and processing of TIL-based product candidates for our clinical trials.

To meet projected needs for commercial quantities of TIL products, we have built our own commercial manufacturing facility, which is expected to begin clinical manufacturing of TIL products in 2021. 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 may need to rely on CMOs, including both current and alternate suppliers, to ensure sufficient capacity is available for commercial purposes.

Orphan Drug Designations

During 2015, we received an Orphan Drug Designation, or ODD, for lifileucel in the U.S. to treat malignant melanoma stages IIB-IV. If approved, an ODD provides seven years of market exclusivity in the U.S., subject to certain limited exceptions. However, an ODD does not convey any advantage in, or shorten the duration of, the regulatory review or approval process. The benefits and limitations of ODD are described in more detail elsewhere in this Annual Report on Form 10-K.

During 2018, we received an ODD from the FDA for lifileucel for the treatment of cervical cancer with a tumor size of greater than 2 cm in diameter.

Fast Track Designations

In August 2017, we announced that the FDA had granted Fast Track designation for lifileucel 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 the possibility for rolling review of a BLA by FDA, and also potential eligibility (if criteria are met) for accelerated approval. In 2019, we announced that the FDA had granted Fast Track designation for lifileucel in the treatment of metastatic cervical cancer.

Regenerative Medicine Advanced Therapy Designation

In October 2018, we announced that the FDA had granted RMAT designation for lifileucel for the treatment of patients with metastatic melanoma. The RMAT designation is based on data provided to the FDA from our C-144-01 trial. RMAT designation is granted for regenerative medicine drugs and allows for increased access to FDA during development. Under this designation, surrogate endpoints can be used to receive approval for a product, accelerated approval may be granted, and a rolling review of a BLA may be permitted by FDA.

Breakthrough Therapy Designation

In May 2019, we announced that the FDA had granted Breakthrough Therapy Designation, or BTD, for lifileucel for the treatment of patients with metastatic cervical cancer. The BTD was granted based on data provided to the FDA from our C-145-04 trial. Under a BTD, the FDA may take actions that help expedite the development and review of the application for a product candidate, including seeking to provide timely advice and interactive communications to the sponsor with intensive guidance during development, to help the sponsor design and conduct a more efficient development program. Product candidates with BTD may be suitable for alternative clinical trial designs when scientifically appropriate, which may result in smaller trials or more efficient trials that require less time to complete. BTD also allows the sponsor to file sections of the BLA on an ongoing basis for rolling review where the FDA may consider beginning review portions of a marketing application before the full submission is complete. In addition, BTD status allows for the potential to request priority review of our BLA at the time of BLA submission if supported by clinical data. The clinical evidence needed to support breakthrough designation is preliminary, and the FDA has authority to rescind a BTD if a product candidate no longer meets the qualifying criteria.

Commercialization Plan

We currently have limited sales, marketing or commercial product distribution capabilities and as a company we have no experience in commercializing cell therapy products. We are continuing to build our U.S. commercial and medical affairs infrastructure and intend to build our own global commercialization capabilities over time in certain geographies for our TIL product candidates including lifileucel for metastatic melanoma and cervical cancer. If any of our TIL product candidates are approved, we expect to commercialize those products in the U.S. with an experienced sales, marketing, payer access and distribution organization including a national specialty oncology sales force. We have started and continue to build a dedicated team of medical affairs professionals to help educate health professionals about our TIL therapy and to assist in any training necessary for individual centers to administer our therapy. Outside the U.S., we are in the process of defining our regulatory and commercial strategy. As additional product candidates advance through our pipeline, our commercial plans will evolve as we consider elements such as the market potential.

The five primary areas of our pre-launch efforts include:

- center engagement for commercial launch;
- development of a close collaboration with healthcare professionals, or HCPs, who will be handling or administering our product;
- operational excellence by us in provision of our product;
- communication with payors; and
- building a patient-centric organization

To date, in the U.S., lifileucel has been administered in 20 centers for melanoma and 17 centers for cervical cancer. We anticipate that centers with prior TIL experience will be among the initial targets for launch upon approval, as well as other centers.

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 ODDs, available regulatory exclusivities and patent term extensions where available. To achieve this objective, a strategic focus for us has been to develop our own intellectual property, while also identifying and licensing patents that provide protection and serve as an optimal platform to enhance our intellectual property and technology base. We expect to further develop our patent portfolio as a strategic focus in 2021.

We have developed our own patent portfolio based on internal research and development activities. As a result, we now own a number of pending patent applications and granted patents in the fields of TIL therapy, MIL therapy, and PBL therapy, TIL, MIL, and PBL manufacturing processes, and TIL, MIL, and PBL expansion methods. For example, we own more than twenty granted or allowed U.S. and international patents related to our Gen 2 TIL manufacturing process, including patents directed to compositions and methods of treatment in a broad range of cancers, such as U.S. Patent Nos. 10,130,659, 10,166,257, 10,272,113, 10,363,273, 10,398,734, 10,420,799, 10,463,697, 10,537,595, 10,646,517, 10,653,723, 10,693,330, 10,695,372, 10,894,063, and 10,905,718. We anticipate that the terms of these patents related to Gen 2 manufacturing processes will extend to January 2038, not including any patent term extensions or adjustments that may be available. Our owned and licensed intellectual property portfolio also includes patent applications relating to TIL, MIL, and PBL therapies; frozen tumor-based TIL technologies; remnant TIL and digest TIL compositions, methods and processes; methods of treatment of a broad range of cancers using TIL therapies; methods of manufacturing TIL, MIL, and PBL therapies; the use of costimulatory molecules in TIL therapy and manufacturing; stable and transient genetically-modified TIL therapies; methods of using immune checkpoint inhibitors in combination with TIL therapies; TIL selection technologies; and methods of treating patient subpopulations.

Research, Development and License Agreements

Currently, preclinical research and development is conducted primarily at our own internal research and development laboratory in Tampa, Florida, and additionally with the NCI, Moffitt, and MDACC, as described below. We also have entered into preclinical collaborations with MDACC. We sponsor our own clinical trials and also collaborate on investigator-sponsored clinical trials with the NCI, Moffitt, and MDACC.

In addition, we hold exclusive, co-exclusive, and non-exclusive licenses to certain patent and other intellectual property rights with the National Institutes of Health, or NIH, an agency of the U.S. Public Health Service within the Department of Health and Human Services, Moffitt, MDACC, Novartis, and Cellectis as described 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 Human Papilloma Virus (“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 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 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 a TIL-based product candidate, we will be responsible for all patent-related expenses and fees, past and future, relating to the TIL-based product candidate. In addition, we may be required to supply certain test articles, including TIL, grown and processed under cGMP conditions, suitable for use in clinical trials, where we hold the investigational new drug application for such clinical trial. The extended CRADA has a five-year term expiring in August 2021. We 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.

Patent License Agreement Related to the Development and Manufacture of TIL

Effective October 5, 2011, we entered into an Exclusive Patent License Agreement, or the Patent License Agreement, with the NIH, an agency of the U.S. Public Health Service within the Department of Health and Human Services, which was subsequently amended on February 9, 2015 and October 2, 2015. Pursuant to the Patent License Agreement as amended, the NIH granted us 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 us 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. We anticipate making a milestone payment in conjunction with the submission of a BLA for any of our product candidates 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, or the 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 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. Under the Exclusive Patent License Agreement, we 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 U.S., and the first commercial sale of a licensed product or process in any foreign country.

H. Lee Moffitt Cancer Center

Research Collaboration and Clinical Grant Agreements with Moffitt

In December 2016, we entered into a new three-year Sponsored Research Agreement with H. Lee Moffitt Cancer Center, or Moffitt, which expired in December 2019. In June 2020, we entered into a new Sponsored Research Agreement with Moffitt, with a term that ends either upon completion of the research thereunder or on July 1, 2022, whichever is sooner, and under which immaterial payments will be made to Moffitt in connection with the research services thereunder. Further, we entered into a clinical grant agreement with Moffitt in December 2016 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 June 2017, we 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, under which we obtained a non-exclusive, royalty-free license to any new Moffitt inventions made in the performance of the agreement. Under both clinical grant agreements with Moffit, we have non-exclusive rights to clinical data arising from the respective clinical trials.

Exclusive License Agreements with Moffitt

We entered into a license agreement with Moffitt, or the First 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 using toll-like receptor agonists. 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 First 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 First 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 First Moffitt License related to the treatment of any cancers in the U.S., Europe and Japan and in other countries designated by us in agreement with Moffitt.

We entered into a license agreement with Moffitt in May 2018, or the Second Moffitt License, under which we received a license to Moffitt's rights to patent-pending technologies related to the use of 4-1BB agonists in conjunction with TIL manufacturing processes and therapies. We continue to develop TIL therapies using a 4-1BB agonist in manufacturing in conjunction with M.D. Anderson Cancer Center. Pursuant to the Second Moffitt License, we paid an upfront licensing fee in the amount of $0.1 million in 2018. An annual license maintenance fee will be also payable commencing on the first anniversary of the effective date. In addition, we agreed to pay an annual commercial use payment for each indication for which a first sale has occurred, which in the aggregate amounts to up to $0.4 million a year.

M.D. Anderson Cancer Center

On April 2017, we entered into a Strategic Alliance Agreement, or the SAA, with MDACC under which we and MDACC agreed to conduct clinical and preclinical research studies. We 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, we acquired 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 MDACC reasonably necessary to exploit, including the commercialization thereof. We have also been granted certain rights in clinical data generated by MDACC 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 us of all deliverables due from MDACC thereunder. In May 2017, we made a prepayment of $1.4 million under this agreement. In light of the disease caused by the novel coronavirus, SARS-CoV-2, which was declared a public health emergency on January 31, 2020, under section 319 of the Public Health Service Act (42 U.S.C. 247d) by the Secretary of Health and Human Services, and which we refer to herein as the COVID-19 pandemic, MDACC temporarily suspended their research programs and decommissioned their research labs, and as a result, enrollment in our MDACC-sponsored studies under the SAA was temporarily paused in the first half 2020, but has since been restarted.

WuXi

In November 2016, we entered into a three-year manufacturing and services agreement, or MSA, with WuXi pursuant to which WuXi agreed to provide manufacturing and other services, which has since been amended and assigned to our subsidiary Iovance Biotherapeutics Manufacturing LLC. Under the agreement, we entered into two statements of work for two cGMP manufacturing suites to be established and operated by WuXi for us, and both of the suites are expected to be capable of being used for the commercial manufacturing of our products. The statements of work for the first suites were amended in 2019 and September 2020, and the second suite was amended in 2019. The statements of work for facility include a fixed component to reserve a dedicated suite and a trained work force and a variable component, mainly materials and testing used during the manufacturing processes. Both statements of work provide for adjustments to the targeted production capacity levels and corresponding fixed quarterly fees upon written notice from us of 30 and 90 days for the first and second dedicated suites, respectively. The terms of the related statements of work for the first and second dedicated manufacturing suites currently extend to August 2022 and June 2021, respectively.

Cellectis

In June 2018, we entered into a preclinical research collaboration with Cellectis S.A., or Cellectis, a clinical-stage biopharmaceutical company, to investigate TALEN for genetic editing in conjunction with TIL therapy. In January 2020, we entered into a research collaboration and exclusive worldwide license agreement whereby we licensed gene-editing technology from Cellectis, in order to develop TIL therapies that have been genetically edited. Financial terms of the license include development, regulatory and sales milestone payments from us to Cellectis, as well as royalty payments based on net sales of TALEN-modified TIL products.

Novartis

In January 2020, we obtained a license from Novartis Pharma AG, or Novartis, to develop and commercialize an antibody cytokine engrafted protein, which we refer to as IOV-3001. Under the agreement, we have paid an upfront payment to Novartis and may pay future milestones related to initiation of patient dosing in various phases of clinical development for IOV-3001 and approval of the product in the U.S., EU and Japan. Novartis is also entitled to low-to-mid single digit percentage royalties from commercial sales of the product.

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 University Hospital at Herlev, 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 the promising clinical therapeutic effect of their therapies in clinical exploratory trials, we anticipate substantial direct competition from other organizations developing advanced T cell therapies targeting patients who have received prior anti-PD-1/PD-L1 therapies. In particular, we expect to compete with other new therapies for our lead indications developed by companies such as Bristol-Myers Squibb, Merck, Nektar Therapeutics, Idera Pharmaceuticals, Checkmate Pharmaceuticals, OncoSec Medical, Instil Bio, Achilles Therapeutics, WindMIL Therapeutics, Seagen, and others. We also may compete with therapies based on genetically engineered T cell receptors rendered reactive against tumor-associated antigens prior to their administration to patients, as well as TIL therapies that are designed to be specific to neoantigens, including products developed by Adaptimmune, Ziopharm Therapeutics, Marker Therapeutics, and others. To date, these technologies have been primarily applicable to hematologic malignancies, but their application in solid tumor indications may create competition with us.

Competition for late-stage melanoma patients may come, if approved, from several therapies currently under development. In 2020, Idera Pharmaceuticals reported results from an ongoing Phase 1/2 clinical trial of the TLR9 agonist tilsotolimod in combination with ipilimumab indicating an ORR of 22% in 53 melanoma patients who had previously received anti-PD-1 therapy. Idera Pharmaceuticals is currently conducting a Phase 3 trial of tilsotolimod in combination with ipilimumab in melanoma patients refractory to anti-PD-1 therapy. In 2020, OncoSec Medical announced preliminary results from an ongoing Phase 2 trial of intratumoral electroporation of plasmid IL-12, or tavokinogene telseplasmid, in combination with pembrolizumab, reporting an ORR of 30% in 54 melanoma patients. Checkmate Pharmaceuticals reported preliminary results from an ongoing Phase 1b clinical trial of the TLR9 agonist CMP-001 in combination with pembrolizumab indicating an ORR of 25% in 82 patients who had received prior anti-PD-1 therapy. Competition for late-stage cervical cancer patients also may arise from therapies under development by companies such as Seagen, which reported an ORR of 24% in 2020 from an ongoing trial of cervical cancer patients who progressed on standard therapy. We may also face competition for NSCLC patients from a large number of therapies that target specific, emerging driver mutations in populations that overlap with our patient populations of interest.

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, Pfizer, Regeneron, and Roche. Immunotherapies are also being pursued by several biotechnology companies as well as by large 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 FDCA, 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, 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 Risk Evaluation and Mitigation Strategy, 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 U.S. 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 or 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 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 U.S., 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, and also to certify to FDA our compliance with these requirements when we make FDA submissions. Failure to make required ClinicalTrials.gov submissions, submitting false or misleading information to ClinicalTrials.gov, or making false certifications to FDA could result in enforcement actions, including civil money penalties and adverse publicity.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap. Although these are the typical phases for progression, and characteristics of the phases of a clinical development program, certain

expedited programs allow for variations that could support a marketing application based on surrogate endpoints, intermediate clinical endpoints, or single-arm as opposed to comparative or placebo-controlled studies.

- 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 relationship 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 U.S. are also subject to regulation by the FDA relating to their labeling and distribution. Further, the export of investigational products outside of the U.S. is subject to regulatory requirements of the importing country as well as U.S. export requirements under the FDCA. Additional U.S. 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, under the Prescription Drug User Fee Act, 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. There are numerous FDA personnel assigned to review different aspects of a BLA, and uncertainties can be presented by their ability to exercise judgment and discretion during the review process. The development and provision of additional data and information requested by FDA during review of a BLA may be time consuming and expensive.

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 products under the Accelerated Approval Pathway 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 Therapy designation also allows the sponsor to file sections of the BLA for review on a rolling basis.

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 lifileucel for advanced metastatic melanoma. The Fast Track designation does not change the standards for approval but may expedite the development or approval process. In October 2018, we announced that lifileucel had received an RMAT designation for metastatic melanoma. In 2019, the FDA granted us a Fast Track designation and BTD for lifileucel for metastatic cervical cancer.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant ODD 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 U.S., or a patient population greater than 200,000 individuals in the U.S. and when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the U.S. will be recovered from sales in the U.S. for that drug or biologic. Additionally, sponsors must present a plausible hypothesis for clinical superiority to obtain ODD 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. ODD must be requested before submitting a BLA. After the FDA grants ODD, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has ODD 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 the 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 ODD 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 ODD 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 U.S. 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.

During 2015, we received an ODD for lifileucel in the U.S. to treat malignant melanoma stages IIB-IV. We plan to seek ODD for some or all of our other product candidates in specific orphan indications in which there is a medically plausible basis for the use of such products. During 2018, we received an ODD from the FDA for lifileucel for the treatment of cervical cancer with a tumor size of greater than 2 cm in diameter.

Market and Data Exclusivity and Biosimilars

While under the Biologics Price Competition and Innovation Act of 2009, or BPCIA, 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 ODDs, 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 12-year time period, the FDA may not make an approval of a biosimilar product effective and may not accept a biosimilar application until after four years from the date of first 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 governing patent litigation over patents that are directed to the reference products. The biosimilar product sponsor and reference product sponsor may, but are not required to, exchange certain patent and product information for the purpose of negotiating and determining the scope of patent litigation, including the patents to be asserted and challenged. 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 under certain circumstances.

The 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 U.S. and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity. Under the Best Pharmaceuticals for Children Act, a 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. Pediatric exclusivity is thus an "add-on" exclusivity and is unique in this regard among the various regulatory exclusivities provided by FDA. The FDA can also require pediatric studies of a drug submitted in a new drug application if the FDA determines that the product is likely to be used in a substantial number of pediatric patients, or if the product would provide a meaningful benefit in the pediatric population over existing treatments. This requirement may be waived in certain circumstances, for example, where the indication does not occur or is not highly prevent in the pediatric population.

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 signature requirements, 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 or otherwise consistent with the FDA-approved product labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, rules regarding communication of health care economic information regarding biopharmaceutical products to payors and formularies, 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. Recent court decisions have impacted FDA's enforcement activity regarding off-label promotion in light of First Amendment considerations; however, there are still significant risks in this area, in part due to the potential for False Claims Act exposure.

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 and list their products with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other applicable 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 to the product labeling, are also subject to further FDA review and approval.

Commercial products must meet the requirements of the Drug Supply Chain Security Act, or DSCSA, which imposes obligations on manufacturers of prescription biopharmaceutical products for commercial distribution, regulating the distribution of the products at the federal level, and sets certain standards for federal or state registration and compliance of entities in the supply chain, including manufacturers and repackagers, wholesale distributors, third-party logistics providers, and dispensers. The DSCSA preempts previously enacted state laws and the pedigree requirements of the Prescription Drug Marketing Act, or PDMA. Trading partners within the drug supply chain must now ensure certain product tracing requirements are met that they are doing business with other authorized trading partners; and they are required to exchange transaction information, transaction history, and transaction statements. Product identifier information, an aspect of the product tracing scheme, is required. The DSCSA requirements, development of standards, and the system for product tracing have been and will continue to be phased in over a period of years, with the FDA indicating that it would exercise enforcement discretion on certain aspects due to the COVID-19 pandemic. The distribution of product samples continues to be regulated under the PDMA, and some states also impose regulations on drug sample distribution.

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 U.S. 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 U.S., and in addition to the FDA, these entities may include 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, or AKS, 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 AKS 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 AKS has been interpreted broadly to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. The term "remuneration" includes kickbacks, bribes or rebates and also has been broadly interpreted to include anything of value, including, for example, gifts, discounts, waivers of payment, ownership interest and providing anything at less than its fair market value. Additionally, the intent standard under the federal AKS provides that a person or entity need not have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, a claim including items or services resulting from a violation of the federal AKS constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution or other regulatory sanctions. 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 AKS. 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. The safe harbors are subject to change through legislative and regulatory action, and we may decide to adjust our business practices or be subject to heightened scrutiny as a result.

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 for payment, or approval 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.

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. A claim includes "any request or demand" for money or property presented directly or indirectly 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. In addition, federal AKS violations (which may be alleged based on certain marketing practices, including allegations of off-label promotion) implicate the FCA.

The compliance and enforcement landscape, and related risk, is informed by government litigation and settlement precedent, Advisory Opinions, and Special Fraud Alerts. Our approach to compliance may evolve over time in light of these types of developments.

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 U.S. to comply with accounting provisions requiring us 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 U.S., can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from securing 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.

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 BLA or a New Drug Application, or 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, which imposes criminal and civil penalties prohibits, 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, any healthcare benefit program, regardless of whether the payor is public or private third-party, 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. A

person or entity does not need to have actual knowledge of the statute, or the specific intent to violate it, to have committed a violation.

We may also be subject to data privacy and security laws and 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 specific requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates. While we would not be a "covered entity" under HIPAA, it is possible that we may enter into a service or business arrangement that would cause us to serve as a "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. The Department of Health and Human Services Office of Civil Rights, or the OCR, has increased its focus on compliance and continues to train state attorneys general for enforcement purposes.

Even for entities that are not deemed "covered entities" or "business associates" under HIPAA, according to the U.S. Federal Trade Commission, or the FTC, failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act, or the FTCA, 15 USC § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Medical data is considered sensitive data that merits stronger safeguards. The FTC's guidance for appropriately securing consumers' personal information is similar to what is required by the HIPAA Security Rule.

In addition to the laws discussed above, we may see more stringent state and federal privacy legislation in 2021 and beyond, as the increased cyber-attacks during the pandemic have heightened attention data privacy and security in the U.S. and other jurisdictions. We cannot predict where new legislation might arise, the scope of such legislation, or the potential impact to our business and operations.

Payments made to physicians and other healthcare providers, and other financial interests, have been the subject of a range of federal and state laws. The federal physician payment transparency requirements, sometimes referred to as the Physician Payments Sunshine Act, or the Sunshine Act, was created under the ACA. The Sunshine Act, among other things, imposes 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 and up to an additional 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. As of 2021, applicable manufacturers are subject to tracking payments and transfers of value to physician assistants, nurse practitioners, and other mid-level HCPs as well as physicians, with reporting relative to these mid-level practitioners beginning in 2022. Additionally, 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 HCPs.

Analogous state laws and regulations, such as state anti-kickback and false claims laws, and other state laws addressing the pharmaceutical and healthcare industries, which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and in some cases may apply regardless of payor, i.e., even if reimbursement is not available. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, known as the PhRMA Code, and the relevant compliance program guidance promulgated by the federal government in addition to requiring drug manufacturers to report pricing and marketing information, including, among other things, information related to gifts, payments, or other remuneration to physicians and other healthcare providers or marketing expenditures, state and local laws that require the registration of pharmaceutical sales representatives, and state laws governing the privacy and security of health information and the use of prescriber-identifiable data in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. For example, California enacted the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020 and was recently amended and expanded by the California Privacy Rights Act, or

CPRA, passed on November 3, 2020. While the majority of the CPRA's substantive provisions will not take effect until January 1, 2023, the CPRA's expansion of the "Right to Know" impacts personal information collected on or after January 1, 2022. Companies must still comply with the CCPA during the ramp up period before CPRA goes into effect. The CCPA and CPRA, among other things, create new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also created a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. It remains unclear what, if any, additional modifications will be made to the CPRA by the California legislature or how it will be interpreted. Therefore, the effects of the CCPA and CPRA are significant and will likely require us to modify our data processing practices, and may cause us to incur substantial costs and expenses to comply.

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 HCPs.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under such laws, it is possible that certain business activities could be subject to challenge under one or more of such laws. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring that business arrangements with third parties comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert management's attention from the business.

If our operations are found to be in violation of any of such health regulatory laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including, without limitation, civil, administrative, and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and individual imprisonment, injunctions, private qui tam actions brought by individual whistleblowers in the name of the government, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, 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, with a recent focus on prioritization of "equivalent," less expensive alternatives when available. 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. There are additional pressures on pricing as a result of other, peripheral policies impacting reimbursement across both government and private payors. Non-health specific policies may impart downstream impacts on private insurance reimbursement decision-making. In consideration of these numerous factors, 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 U.S., 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. Further, some stakeholders have recently questioned whether the market price of prescription drugs may be inflated by virtue of the built-in cost imparted by the government rebate model, often negotiated indirectly in exchange for a coverage determination or formulary placement where relevant.

In the U.S., 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 U.S. 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 U.S. 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 U.S. 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 U.S., 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.

In recent years, there have been and continue to be proposals by the federal government, state governments, regulators, and third-party payors to control these costs and, more generally, to reform the U.S. health care system. Certain of these proposals could limit the prices we are able to charge for our products or the amounts of reimbursement available for our products. These laws and future 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 U.S., 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 U.S. 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 and the United Kingdom, 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. By law, a company can only start to market a medicine once it has received a marketing authorization.

Employees and Human Capital Management

As of December 31, 2020, we had 241 employees, 176 of whom were engaged in research and development activities and 65 of whom were engaged in general and administrative support activities. None of our employees are subject to a collective bargaining agreement. Our employees are highly skilled, and many hold advanced degrees. Most of our employees have experience with the development of cell therapies. 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 and our continued ability to attract and retain highly skilled employees. We provide our employees with competitive salaries and bonuses, opportunities for equity

ownership, development programs that enable continued learning and growth and a robust employment package that promotes well-being across all aspects of their lives. In addition to salaries, these programs include potential annual discretionary bonuses, stock awards, a 401(k) plan, healthcare and insurance benefits, health savings and flexible spending accounts, paid time off, family leave, and flexible work schedules, among other benefits. We have taken proactive, aggressive action throughout the COVID-19 pandemic to protect the health and safety of our employees. We expect to continue to implement these measures until we determine that the COVID-19 pandemic is adequately contained for purposes of our business. We may take further actions, in compliance with all appropriate government regulations, that we determine to be in the best interest of our employees.

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, or SEC, as soon as is reasonably practicable after filing. 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 or SEC.

Risk Factors Summary

Our business is subject to a number of risks and uncertainties, including those risks discussed at length below. These risks include, among others, the following principal risk factors that make an investment in our company speculative or risky. You are encouraged to carefully review our full discussion of the material risk factors relevant to an investment in our business, which follows the brief bulleted list of our principal risk factors set forth below:

- *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 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;*
- *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;*
- *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 manufacture of our product candidates is complex, and we may encounter difficulties in production, particularly with respect to process development, quality control, or scaling-up 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;*
- *Cell-based therapies and biologics 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;*
- *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;*
- *We may 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;*

- *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;*
- *We are required to pay substantial royalties and lump sum benchmark payments under our license agreements with the NIH, Moffitt, Novartis, and Cellectis, and we must meet certain milestones to maintain our license rights;*
- *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;*
- *No assurance can be given that the Gen 2 manufacturing process we have selected will be FDA-compliant, more efficient and lower the cost to manufacture TIL products;*
- *We face significant competition from other biotechnology and pharmaceutical companies and from non-profit institutions;*
- *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;*
- *A Fast Track product designation, Breakthrough Therapy 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;*
- *While lifileucel has received ODD for melanoma stages IIB-IV and for cervical cancer patients with tumors greater than 2 cm, there is no guarantee that we will be able to maintain this designation, receive these designations for any of our other product candidates, or receive or maintain any corresponding benefits, including periods of exclusivity;*
- *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;*
- *We may be 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, and as a result, we may be unable to generate product revenues;*
- *If our product candidates do not achieve broad market acceptance, the revenues that we generate from their sales will be limited;*
- *Our business could be adversely affected by the effects of health epidemics, including the recent spread of the COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations. The COVID-19 pandemic could materially affect our operations, including at our headquarters in San Carlos, California and at our manufacturing facility in Philadelphia, Pennsylvania, which are currently subject to state executive orders and shelter-in-place orders, and at our clinical trial sites, as well as the business or operations of our other manufacturers, CROs or other third parties with whom we conduct business;*
- *We will need to grow the size and capabilities of our organization, and we may experience difficulties in managing this growth;*
- *We may rely on third parties to perform many essential services for any products that we commercialize, including services related to 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;*
- *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;*
- *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;*
- *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; and*
- *Governments outside the U.S. tend to impose strict price controls, which may adversely affect our revenues, if any.*

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. We do not have products approved for commercial sale and have not generated revenue from operations. As of December 31, 2020, we had an accumulated deficit of $830.2 million. In addition, during the year ended December 31, 2020, we incurred a net loss of $259.6 million.

Since our inception we have not generated any revenues from operations. We are preparing for the commercial launch of our products, if approved, in 2021. We do not expect to generate any meaningful product sales or royalty revenues until we have a product approved. 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.

Our current line of business, and the biotechnology industry in which we operate, 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 and Board of Directors. While we believe that we have a reasonable 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 pre-commercial 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 pre-commercial 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 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 sale. We have invested a significant portion of our efforts and financial resources in the development of our current product candidates, including lifileucel, LN-145, IOV-2001, and IOV-3001, 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, including the negative impact of the COVID-19 pandemic.

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 U.S. 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 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. Furthermore, although we do not expect to submit our BLA with comparisons to existing or more established therapies and likewise do not expect FDA to base its determination with respect to product approval on such comparisons, FDA may factor these comparisons into its decision whether to approve our TIL therapies, including lifileucel for metastatic melanoma and metastatic cervical cancer. FDA may also consider its approvals of competing products, which may alter the treatment

landscape concurrently with their review of our BLA filings, and which may lead to changes in FDA's review requirements that have been previously communicated to us and our interpretation thereof, including changes to requirements for clinical data or clinical study design. Such changes could delay approval or necessitate withdrawal of our BLA filings.

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:

- price our product candidates competitively such that third-party and government reimbursement leads to broad product adoption;
- prepare a broad network of clinical sites for administration of our product;
- 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 the targeted patient population(s) and claims that are necessary or desirable for successful marketing;
- effectively commercialize our products;
- manufacture product candidates through CMOs or in our own manufacturing facility 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, pharmacies, and group purchasing organizations on commercially reasonable terms;
- maintain patent and trade secret protection and regulatory exclusivity for our product candidates;
- launch commercial sales of our product candidates;
- maintain compliance with applicable laws, regulations, and guidance specific to commercialization including interactions with health care professionals, patient advocacy groups, and communication of health care economic information to payors and formularies;
- achieve market acceptance of our product candidates by patients, the medical community, and third-party payors;
- achieve appropriate reimbursement for our product candidates;
- maintain a distribution and logistics network capable of product storage within our specifications and regulatory guidelines, and further capable of timely product delivery to commercial clinical sites;
- effectively compete with other therapies or competitors; and
- following launch, assure that our product will be used as directed and that additional unexpected safety risks will not arise.

We may face risks due to the need to rely on third parties, including clinical trial sites.

We are heavily reliant on third parties to conduct our clinical trials. We have a limited history of conducting 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. As a result of the COVID-19 pandemic, institutions and research sites that currently conduct clinical trials may not be able to return to normal clinical trial operations for some time, or may no longer choose to participate in studies in the future. As a result, clinical trials may be delayed or otherwise may be more difficult to execute in the future.

We have recruited a team that has experience with clinical trials and in the development of preclinical assets for translation into clinical trials; however, we as a company have limited experience completing pivotal clinical trials for cell therapy products or developing preclinical immunotherapy products. In part because of this lack of experience, we cannot be certain that our ongoing pivotal 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 or initiated in a timely manner, progress according to our plans or expectations, or be completed on time, if they are completed at all.

Large-scale clinical trials require significant financial and management resources, and reliance on third-party clinical investigators, Contract Research Organizations, or CROs, Contract Manufacturing Organizations, or 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 CMOs in the U.S. and Europe to manufacture TIL for use in our trials. We may not be able to demonstrate sufficient comparability between products manufactured at different facilities to allow for inclusion of the clinical results from patients treated with products from these different facilities, or with our own manufacturing facility, in our product registrations. Further, our CMOs may not be able to manufacture TIL or otherwise fulfill their obligations to us because of interruptions to their business, including the loss of their key staff or interruptions to their raw material supply.

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, independent review organizations 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 these oversight 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 Good Laboratory Practices, or GLPs, as appropriate. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with 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 (including pre-approval inspections once a BLA is filed with the FDA) of trial sponsors, clinical investigators, trial sites and certain third parties including CMOs. 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 comply 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 failure to comply or our CMOs' 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 could 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 alternative 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 manufacture and ship our products for the clinical trials that we conduct. Any performance failure on the part of these third parties 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, head and neck and non-small cell lung cancers, and in other indications in collaboration with third parties. We have completed enrollment in the pivotal clinical trial for melanoma, C-144-01. In May 2020, we disclosed interim results for Cohort 4 of the C-144-01 clinical trial. Although the data is consistent with the Cohort 2 data read out at a similar median duration of study follow up, the interim results speak only to data available as of March 16, 2020, and although such data have been reviewed by the investigators, they have not been reviewed by IRC. We plan to initiate trials in new indications, and new cohorts in existing trials. Even as these trials progress, issues may arise that could require us to suspend or terminate such clinical trials or could cause the results of one cohort to differ from a prior cohort. For example, we may experience slower than anticipated enrollment in our pivotal clinical trials, which may consequently delay our BLA filing timelines or permit competitors to obtain approvals that may alter our BLA filing strategy. 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:

- regulators 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 or inability to obtain agreement 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 biologically or mechanistically similar therapeutic or therapeutic candidate;
- delays in recruiting suitable patients to participate in our clinical studies;
- delay in adding new investigators or clinical trial sites, or withdrawal of clinical trial sites from a study;

- delay or change in strategic direction for an indication resulting from differences in results between cohorts in a clinical trial, such as Cohort 2 and Cohort 4 of the C-144-01 clinical trial or the previously disclosed preliminary results for the C-145-04 trial and the final patient population and results, including differences in patient population, such as differences that might arise due to the impact of the existing immunotherapy treatment landscape, or from different interpretations of investigator results by IRC;
- 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 cGCP 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, potentially affecting our timelines for approval of our product candidates;
- 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;
- early results from our clinical studies of our product candidates may be negatively affected by changes in efficacy measures such as overall response rate and duration of response as more patients are enrolled in our clinical trials or as new cohorts of our clinical trials are tested, and overall response rate and duration of response may be negatively affected by the inclusion of unconfirmed responses in preliminary results that we report if such responses are not later confirmed;
- 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;
- delays in patient enrollment due to the ongoing COVID-19 pandemic;
- 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 making a decision on our product candidates;
- transfer of our manufacturing processes to our CMOs or other larger-scale facilities operated by a CMO or by us and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process;
- our use of different manufacturing processes within our clinical trials, including our Gen 1 and Gen 2 manufacturing processes, and any effects that may result from the use of different processes on the clinical data that we have reported and will report in the future; 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 academic, pharmaceutical, 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 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 FDA approval or notification, may not have their desired effect, or 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. For example, while we currently intend to file our first BLA using our Gen 2 manufacturing process, in the future we may seek to commercialize other manufacturing processes, such as our Gen 3 manufacturing process or our PD-1 selected TIL manufacturing process. We may find that commercialization of these manufacturing processes has unintended consequences that necessitate additional development and manufacturing work or additional clinical and preclinical studies, or results in a refusal to file or 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 any product candidates we may seek to develop in the future will never 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, difficulties in identifying and enrolling patients who meet trial eligibility criteria, and the ongoing COVID-19 pandemic, 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 are currently enrolling our company-sponsored, Phase 2 clinical trials to assess its overall safety and efficacy in patients with melanoma, cervical, head and neck and lung cancers. However, we may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. Our ability to enroll or treat patients in our other studies, or the duration or costs of those studies, could be affected by multiple factors, including, preliminary clinical results, which may include efficacy and safety results from our ongoing Phase 2 studies, but may not be reflected in the final analyses of these trials. For example, our studies of our TIL therapy lifileucel in patients with metastatic cervical cancer and metastatic melanoma utilize an "open-label" trial design. An open-label trial is one where both the patient and investigator know whether the patient is receiving the test article or either an existing approved drug or placebo, which has the potential to create selection bias in the investigators. In our Phase 2 open-label studies of TIL therapy lifileucel in patients with metastatic cervical cancer and metastatic melanoma, the investigators have significant discretion over the selection of patient participants. Although preliminary data from these trials was generally positive, that data may not necessarily be representative of interim or final results, as new patients are cycled through the applicable treatment regimes. As the trials continue, the investigators may prioritize patients with more progressed forms of cancer than the initial patient population, based on the success or perceived success of that initial population. Patients with more progressed forms of cancer may be less responsive to treatment, and accordingly, interim efficacy data may show a decline in patient response rate or other assessment metrics. As the trials continue, investigators may shift their approach to the patient population, which may ultimately result in a decline in both interim and final efficacy data from the preliminary data, or conversely, an increase in final efficacy data following a decline in the interim efficacy data, as patients with more progressed forms of cancer are cycled out of the trials and replaced by patients with less advanced forms of cancer. This opportunity for investigator selection bias in our trials as a result of open-label design may not be adequately handled and may cause a decline in or distortion of clinical trial data from our preliminary results. Depending on the outcome of our open-label studies, we may need to

conduct one or more follow-up or supporting studies in order to successfully develop our products for FDA approval. Many companies in the biotechnology, pharmaceutical and medical device industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we cannot be certain that we will not face such setbacks.

Furthermore, 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, including the ability of us or our collaborators to conduct clinical trials under the constraints of the COVID-19 pandemic. 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 and biologic products for clinical trials. If they fail to commence or complete, or experiences delays in, manufacturing our adoptive cell therapy and other biologic 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 include candidates 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. We are also responsible for the manufacturing costs of products for patients that may have a tumor resection but ultimately do not receive an infusion. Depending on the number of patients that we ultimately screen and enroll in our trials, and the number of trials that 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 U.S. 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 test 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, or similar patients in the pivotal program to the Phase 2, 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;
- the ongoing COVID-19 pandemic limiting our access to patients who would otherwise be eligible for enrollment, including treatment-naïve patients who may be more likely to seek standard of care therapies available at local treatment centers rather than enroll in a clinical trial at a larger hospital;
- approval of new indications for existing therapies or approval of new therapies in general;
- 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 any 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 other 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. Amendments to our clinical protocols may affect enrollment in, or results of, our trials, including amendments we have made to further define the patient population to be studied.

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, DSMBs, 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 indications for use 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 or side effects arise in the development of our product candidates, we, an IRB, DSMB 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, thrombocytopenia, chills, anemia, pyrexia, febrile neutropenia, diarrhea, neutropenia, vomiting, hypotension,

and dyspnea. For example, the update in October 2018 from the C-144-01 trial included two grade 5 treatment emergent adverse events. In addition, these side effects and deaths 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, quality control, or scaling-up 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, isolating the T cells from the tumor fragments, 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 fragments, 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 material, interruptions in the manufacturing process, contamination, equipment failure, assay failures, improper installation or operation of equipment, vendor or operator error, inconsistency in cell growth, meeting pre-specified release criteria, 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 starting material, 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, including resection of the proper amount of tumor fragment and the resulting delay may adversely affect that patient's outcome. If microbial, viral, environmental 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-up, process reproducibility, stability issues, lot consistency, and timely availability of raw materials. This includes potential risks associated with FDA not agreeing with all of the details of our validation data or our potency assay or assays for Cohort 4 of our C-144-01 clinical trial. For example, on October 5, 2020, we announced that we and the FDA have not been able to agree on the required potency assays to fully define our TIL therapy, which is required as part of a BLA submission, and that as a result of these developments, our BLA submission is not expected by the end of 2020 and is anticipated instead to occur in 2021. 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, Lonza Netherlands, 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 and quality 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 May 2019 we entered into a lease agreement to build a commercial-scale manufacturing facility in Philadelphia, Pennsylvania for commercial and clinical production of autologous TIL products, including our product candidate lifileucel. We expect that development of our own manufacturing facility will provide us with enhanced control of material supply for both clinical trials and the commercial market, enable the more rapid implementation of process changes, and allow for better long-term margins. However, we have no experience as a company in developing a manufacturing facility and we may not be successful in finalizing the development of 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 cell therapy products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of cell therapy products 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, local 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 the 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 submit to pre-approval inspections by the FDA that will be conducted after we submit our marketing applications, including our BLAs, to the FDA. Manufacturers are also subject to continuing regulatory oversight by FDA and other regulatory authorities, including inspections following marketing approval. Further, we, in cooperation with our CMOs, must supply all necessary chemistry, manufacturing, and control documentation for a pre-approval inspection in support of a BLA on a timely basis. There is no guarantee that we or our CMOs will be able to successfully pass all aspects of a pre-approval inspection by the FDA or other foreign regulatory authorities.

Our, or our CMOs' 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, 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 and biologics 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 requires 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.

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

With the exception of lifileucel for metastatic melanoma and metastatic cervical cancer, 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 could 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.

Even if our lead product lifileucel is approved and commercialized, we may not become profitable.

Our lead product, lifileucel, is initially targeting a small population of refractory patients that suffer from metastatic melanoma and metastatic cervical cancer. Even if the FDA approves these new therapies, and even if we obtain significant market share for each product candidate, because the potential target population for lifileucel in refractory patients may be small, we may never achieve profitability without obtaining regulatory approval for additional indications. 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.

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 2017-2020, we announced our continued collaborations with Moffitt, MDACC, Ohio State University, and CHUM 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. 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 reported or over 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, or may have a negative impact on us if the results of such studies are imputed to our products or proposed indications, even if such imputation is improper. For example, we have entered into collaborations with Moffitt, MDACC and CHUM to perform clinical trials using TIL products that differ from our products, but the results of these clinical trials, if negative, may adversely impact our stock price and our development plans for our products. 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 may 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, 2020, we have an accumulated deficit of $830.2 million. In addition, our research and development and our operating costs have also been substantial and are expected to increase. For example, in October 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 offering expenses payable by us, were $236.7 million. In June 2020, we closed another underwritten offering of our common stock. The net proceeds from the offering, after deducting the underwriting discounts and commissions and other offering expenses payable by us, were $567.0 million. In addition to our continued spending for our product candidates, we expect to spend approximately $40 million over the next year for equipment and construction costs for our commercial-scale production facility in Philadelphia, Pennsylvania. As of December 31, 2020, we had approximately $629.4 million in cash, cash equivalents and short-term investments ($67.3 million of cash and cash equivalents and $562.1 million in short-term investments).

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 twelve months from the date this Annual Report on Form 10-K is issued. However, in order to complete the development of our current product candidates, and in order to affect our business plan, including establishing our own manufacturing facility, we anticipate that we will have to spend more than the funds currently available to us. Furthermore, 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;
- cost of building, staffing and validating our own manufacturing facility in the U.S.;
- 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.

Unless and 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 our Board of Directors, our management will have broad discretion in the use of the net proceeds from our capital raises, including our June 2020, October 2018 and January 2018 public offerings and the proceeds from sales pursuant to our "at-the-market" sales agreement with Jefferies LLC, and may not use them effectively.

Our management will have discretion in the application of the net proceeds from our capital raises, and our stockholders will not have the opportunity as part of their investment decision to assess whether the net proceeds from our 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, their ultimate use may vary substantially from their currently intended use. Our failure to apply the net proceeds of our capital raises 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 our capital raises. Pending their use, we may invest the net proceeds from our capital raises in interest and non-interest bearing cash accounts, 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, 2020, we had U.S. federal net operating loss carryforwards of approximately $662.4 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.

Prior to December 31, 2020, we may have experienced multiple ownership changes. 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. Depending on our future tax position, limitation 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., changes to existing tax laws, or challenges to our tax positions could adversely affect our business and financial condition.

On December 22, 2017, the Tax Cuts and Jobs Act of 2017, or the 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.

In recent years, various tax legislations were signed into law. On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, was enacted in response to the COVID-19 pandemic. Certain provisions of the CARES Act amend or suspend certain provisions of the Tax Act. For example, the tax relief measures under the CARES Act for businesses include a five-year net operating loss carryback, suspension of annual deduction limitation of 80% of taxable income from net operating losses generated in a tax year beginning after December 31, 2017, changes in the deductibility of interest, acceleration of alternative minimum tax credit refunds, payroll tax relief, and a technical correction to allow accelerated deductions for qualified improvement property. There are also potential state tax law provisions that may have an effect on our business. For example, on June 15, 2020, Assembly Bill 85 was passed in California which suspended the use of net operating losses and limited the use of credits for certain corporations. These changes to existing federal and state tax laws and newly enacted tax reform legislation in the U.S. could adversely impact our business, results of operations and financial position as the overall impact of such changes and reform is uncertain.

In addition, U.S. federal, state and local tax laws are extremely complex and subject to various interpretations. Although we believe that our tax estimates and positions are reasonable, including our decision to build our commercial manufacturing facility at the Navy Yard in Philadelphia in order to take advantage of the site's designation as a Keystone Opportunity Zone, Keystone Opportunity Expansion Zone, or Keystone Opportunity Improvement Zone, or collectively KOZ, which allows incentives for business development, as well as certain other financial incentives provided by the Commonwealth of Pennsylvania, the City of Philadelphia and the Philadelphia Industrial Development Corporation, there can be no assurance that our tax positions will not be challenged by relevant tax authorities or that we would be successful in any such challenge. Further, challenges to the site's designation as a KOZ or broader challenges to Pennsylvania's KOZ program could result in the revocation of the site's designation as a KOZ and the attendant tax advantages associated with such designation. If we are unsuccessful in such a challenge, or if the site's status as a KOZ is revoked, the relevant tax authorities may assess additional taxes, which could result in adjustments to, or impact the timing or amount of, taxable income, deductions or other tax allocations, which may adversely affect our results of operations and financial position.

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 U.S. 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 by 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, 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 technology from third parties.

An element of our intellectual property portfolio is to license additional rights and technologies from third parties, including the NIH and others. 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 third parties, including 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.

Our projections regarding the market opportunities for our product candidates may not be accurate, and the actual market for our products may be smaller than we estimate.

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 lifileucel 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, Moffitt, Novartis, and Cellectis, and we must meet certain milestones to maintain our license rights.

Under our license agreements with the NIH, Novartis, and Cellectis for our adoptive cell therapy and immunotherapy 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. These payments could adversely affect the overall profitability for us of any products that we may seek to commercialize under these license agreements. In order to maintain our license rights under the NIH, Moffitt, Novartis, and Cellectis 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 therapies and our other therapies 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 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 governmental or private third party medical insurers.

No assurance can be given that the Gen 2 manufacturing process we have selected will be FDA-compliant, more efficient and lower the cost to manufacture TIL products.

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 methods for large-scale production of autologous TILs that are in accord with current cGMP procedures. We have developed a new and more efficient TIL manufacturing process that we believe can be more efficient and cost effective, and in a more automated manner than previous processes. The production and control of 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 the Gen 2 process or any future process that we select will be 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, we and our third-party manufacturers will have to continually adhere to current cGMP regulations enforced by the FDA through its facilities inspection program. If our facilities or any of the facilities of these manufacturers cannot demonstrate adequate assurance of compliance with FDA standards during a pre-approval inspection, the FDA 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;
- decrease in the price of our stock and overall value of our company;
- exhaustion of our available insurance coverage and our capital resources; or
- the inability to commercialize our product candidates.

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.

Due to the promising clinical therapeutic effect of competitor therapies in clinical exploratory trials, we anticipate substantial direct competition from other organizations developing advanced T cell therapies targeting patients who have received prior anti-PD-1/PD-L1 therapies. In particular, we expect to compete with other new therapies for our lead indications developed by companies such as Bristol-Myers Squibb, Merck, Nektar Therapeutics, Idera Pharmaceuticals, Checkmate Pharmaceuticals, Oncosec Medical, Instil Bio, Achilles Therapeutics, WindMIL Therapeutics, Seagen and others. We also may compete with therapies based on genetically engineered T cell receptors rendered reactive against tumor-associated antigens prior to their administration to patients, as well as TIL therapies that are designed to be specific to neoantigens, including products developed by Adaptimmune, Ziopharm Therapeutics, Marker Therapeutics, and others. To date, these technologies have been primarily applicable to hematologic malignancies, but their application in solid tumor indications may create competition with us. We may also face competition from immunotherapy treatments offered by companies such as Amgen, AstraZeneca, Bristol-Myers Squibb, Merck, Pfizer, Regeneron, and Roche. Many of these companies and 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 U.S. 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 trial 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 lifileucel is a therapy for the treatment of metastatic melanoma and metastatic cervical cancer. Currently, there are numerous companies that are developing various alternate treatments for melanoma and cervical cancer, including patients that have progressed after prior treatment with checkpoint inhibitors and chemotherapy. Accordingly, lifileucel faces significant competition in the melanoma and cervical cancer treatment space from multiple companies. Even if we obtain regulatory approval for lifileucel, the availability and price of our competitors' products could limit the demand and the price we are able to charge for our therapies. 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 portion of our technology from others. 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, Cellectis, Yale University, Novartis, and CHUM. 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, or may be unable to enroll patients, which has occurred in one of our prior collaborations. 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;
- collaborators 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; and
- 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 delayed 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 lifileucel as part of a regimen which uses IL-2. We and our collaborators are also studying TIL therapy along with other products, such as pembrolizumab, ipilimumab and nivolumab. 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 trials could show that any positive 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. Additionally, the FDA review process can be more complicated for combination products, and may result in delays, particularly if complex therapeutics are involved. 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, Breakthrough Therapy 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 lifileucel in metastatic melanoma and metastatic cervical cancer. We were granted Breakthrough Therapy designation, or BTD, for lifileucel for metastatic cervical cancer and Regenerative Medicine Advanced Therapy, or RMAT, designation for lifileucel in advanced melanoma. We may seek Fast Track or Breakthrough 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 lifileucel has received ODD for melanoma stages IIB-IV and for cervical cancer patients with tumors greater than 2 cm, there is no guarantee that we will be able to maintain this designation, receive these designations for any of our other product candidates, or receive or maintain any corresponding benefits, including periods of exclusivity.

We received ODD in the U.S. for lifileucel to treat malignant melanoma stages IIB-IV and cervical cancer patients with tumors greater than 2 cm. We may also seek ODD for our other product candidates, as appropriate. ODD, 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 ODDs to multiple of the same products for the same indication. If another sponsor receives FDA approval for an ODD-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 U.S. 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. For 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, or ALL, that is refractory or in second or later relapse, the FDA required significant post-marketing commitments, including a Phase 4 trial, 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.

We may be 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, and as a result, we may be unable to generate product revenues.

We currently have a small commercial team focused on our commercial strategy, but we 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 a comprehensive healthcare compliance program, 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, sales and commercial support personnel. In the event we are unable to develop a commercial 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 and generate product revenues include:

- if the COVID-19 pandemic continues or reoccurs it may negatively impact our ability to establish commercial operations, educate and interact with healthcare professionals, and successfully launch our product on a timely basis;
- 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 and time associated with the initial and ongoing training of 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 approved product's FDA-required 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 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 branded 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 and authorized 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 trial data from completed or ongoing clinical trials 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 are dependent on information technology, systems, infrastructure and data.

We are dependent upon information technology systems, infrastructure and data. The multitude and complexity of our computer systems make them inherently vulnerable to service interruption or destruction, malicious intrusion and random attack. Likewise, data privacy or security breaches by third parties, employees, contractors or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients, or other business partners may be exposed to unauthorized persons or to the public. Cyberattacks are increasing in their frequency, sophistication and intensity. Cyberattacks could include the deployment of harmful malware, denial-of-service, social engineering and other means to affect service reliability and threaten data confidentiality, integrity and availability. Our business and technology partners face similar risks and any security breach of their systems could adversely affect our security posture. While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, there can be no assurance that our efforts, or the efforts of our partners and vendors, will prevent service interruptions, or identify breaches in our systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or

reputational harm to us. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related breaches.

Our business could be adversely affected by the effects of health epidemics, including the recent spread of the COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations. The COVID-19 pandemic could materially affect our operations, including at our headquarters in San Carlos, California and at our manufacturing facility in Philadelphia, Pennsylvania, which are currently subject to state executive orders and shelter-in-place orders, and at our clinical trial sites, as well as the business or operations of our other manufacturers, CROs or other third parties with whom we conduct business.

Our business could be adversely affected by health epidemics in regions where we have offices, manufacturing facilities, concentrations of clinical trial sites or other business operations, and could cause significant disruption in the operations of clinical trial sites, third party manufacturers and CROs upon whom we rely. For example, starting in December 2019, the COVID-19 Pandemic has spread to multiple countries, including the U.S. and several European countries. Our headquarters is located in the San Francisco Bay Area. The President of the U.S. declared the COVID-19 pandemic a national emergency. Similarly, the State of California declared a state of emergency related to the spread of the COVID-19 pandemic. In March 2020, the health officers of six San Francisco Bay Area counties, including San Mateo County where our headquarters in San Carlos are located, issued shelter-in-place orders. The shelter-in-place orders took effect on March 17, 2020 and will continue through the end of May 2020, unless further extended. In addition, on March 19, 2020, the Governor of California and the State Public Health Officer and Director of the California Department of Public Health ordered all individuals living in the State of California to stay at their place of residence for an indefinite period of time (subject to certain exceptions to facilitate authorized necessary activities) to mitigate the impact of the COVID-19 pandemic. Similar executive orders have been issued by state and local governments in Pennsylvania, Florida, and elsewhere, and states of emergency have been declared at the state and local level in most jurisdictions throughout the U.S.

Quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to the COVID-19 pandemic or other infectious diseases could impact personnel at third-party manufacturing facilities in the U.S. and other countries, or the availability or cost of materials, which would disrupt our supply chain. In addition, our clinical trials may be affected by the COVID-19 pandemic. Clinical site initiation, patient enrollment and patient monitoring may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic. Some sites may no longer be available to see patients for clinical trials. Some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Patients may also miss follow-up visits after receiving our therapies during our clinical trials, which may or may not be rectified by future patient visits and which may result in the exclusion of data from such patients from the clinical trial data. Similarly, our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to the virus that causes the COVID-19 pandemic and adversely impact our clinical trial operations. The COVID-19 pandemic may also affect our ability to recruit treatment-naïve patients into our clinical trials, because those patients may be more likely to seek standard of care therapies available at local treatment centers rather than enroll in a clinical trial at a larger hospital.

We continue to monitor the impact, if any, of the COVID-19 pandemic on our current and future operations, including our regulatory filing timelines and strategy as well as our preparation for commercial launch. As the COVID-19 pandemic continues for an extended period of time, and with travel, face to face interactions, and resources are not allowed or are severely limited, either by us or our contractors, including our CMOs, our regulatory strategy, BLA filing timelines, or commercial launch preparations may be negatively impacted. The COVID-19 pandemic may also impact the FDA and their ability to timely review our regulatory filings and conduct the pre-approval inspections necessary for ultimate approval of BLA.

Our failure to comply with international data protection laws and regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

European Union, or EU, member states and other foreign jurisdictions, including Switzerland and the United Kingdom, have adopted data protection laws and regulations which impose significant compliance obligations on us. Moreover, the collection and use of personal health data in the EU, which was formerly governed by the provisions of the EU Data Protection Directive, was replaced with the EU General Data Protection Regulation, or the GDPR, in May 2018. The GDPR, which is wide-ranging in scope, imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the security and confidentiality of the personal data, data breach notification and the use of third-party processors in connection with the processing of personal data. The GDPR also imposes strict rules on the transfer of personal data out of the EU to the U.S., provides an enforcement authority and imposes large penalties for noncompliance, including the potential for fines of up to

€20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. The GDPR requirements apply not only to third-party transactions, but also to transfers of information between us and our subsidiaries, including employee information. The recent implementation of the GDPR has increased our responsibility and liability in relation to personal data that we process, including in clinical trials, and we may in the future be required to put in place additional mechanisms to ensure compliance with the GDPR, which could divert management's attention and increase our cost of doing business. In addition, new regulation or legislative actions regarding data privacy and security (together with applicable industry standards) may increase our costs of doing business. In this regard, we expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy and data protection in the U.S., the EU and other jurisdictions, and we cannot determine the impact such future laws, regulations and standards may have on our business.

Our failure to comply with state and/or national data protection laws and regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

There are numerous other laws and legislative and regulatory initiatives at the federal and state levels addressing privacy and security concerns, and some state privacy laws apply more broadly than the Health Insurance Portability and Accountability Act, or HIPAA, and associated regulations. For example, California recently enacted legislation, the California Consumer Privacy Act, or CCPA, which went into effect January 1, 2020 and was recently amended and expanded by the California Privacy Rights Act, or CRPA, passed on November 3, 2020. The CCPA and CPRA, among other things, create new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also created a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach.

Although the law includes limited exceptions, including for certain information collected as part of clinical trials as specified in the law, it may regulate or impact our processing of personal information depending on the context. It remains unclear what, if any, additional modifications will be made to the CPRA by the California legislature or how it will be interpreted. Therefore, the effects of the CCPA and CPRA are significant and will likely require us to modify our data processing practices, and may cause us to incur substantial costs and expenses to comply.

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 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.

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 or product, 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 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 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.

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. For example, following our End of Phase 2 meeting with the FDA, we increased enrollment in Cohort 1 of our ongoing C-145-04 clinical trial of TIL therapy lifileucel to at least 75 patients of the appropriate population to address the expected sample size in anticipation of a BLA submission in 2021. Additionally, the patient population is defined per the discussion with FDA as patients who have progressed following initial systemic therapy for recurrent or metastatic disease which include many of the more advanced patients enrolled to date. Our current beliefs regarding the registration pathway for the lifileucel product candidate in metastatic cervical cancer are based on our interpretation of communications with the FDA to date and our efforts to address such communications, which may be incorrect. Our statements that the study may support a BLA submission also assume that our as-adjusted study has addressed the additional requests by the FDA that were raised at our End of Phase 2 meeting. Further, enrollment in this study may need to be further adjusted based on future feedback from the FDA or other regulatory agency input. The revised protocol which further defines the patient population to include more advanced patients in the study, may have an adverse effect on the results reported to date, changes to implement an independent review committee and assay validation and implementation, and the data within this study may not ultimately be supportive of product approval, all of which could result in significant delays to our currently anticipated timeline for development and approval of our product candidate or prevent its approval entirely. Similarly, our current beliefs for our lifileucel product candidate for the treatment of melanoma are based on our interpretation of communications received from the FDA to date regarding this product candidate and our ongoing C-144-01 clinical trial, and may also be incorrect.

A BLA must also include significant information regarding the chemistry, manufacturing and controls for the product. Additionally, 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. We may also not be able to successfully utilize the BTD or RMAT designations we have received for metastatic cervical cancer and advanced melanoma, respectively, to successfully complete the development and commercialization of lifileucel. We may not be able to reach agreement with FDA on an interpretation of outcomes from our meetings, including meetings we have held with FDA in relation to our C-145-04 and C-144-01 clinical trials and future meetings. For example, on October 5, 2020, we announced that we and the FDA have not been able to agree on the required potency assays to fully define our TIL therapy, which is required as part of a BLA submission, and that as a result of these developments, our BLA submission is not expected by the end of 2020 and is anticipated to occur in 2021. 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, including delays arising from the need to increase enrollment, 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 contract 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 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;
- manufacturing sufficient quantities of qualified materials under cGMPs and applying them on a subject-by-subject basis for use in clinical trials; or

- timely implementing or validating changes to our manufacturing or quality control processes and methods needed to address FDA feedback.

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 DSMBs 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 U.S., 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 U.S., 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 U.S., 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 U.S. on a timely basis, if at all.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the U.S. 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 ongoing surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a 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, establishment 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, 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 U.S. 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 biopharmaceutical company, we are subject to many federal and state healthcare laws, including the federal AKS, the federal civil and criminal FCA, 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 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 U.S. 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 U.S., 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. Moreover, the factors noted above have continued to be the focus of policy and regulatory debate that has, thus far, shown the potential for movement towards permanent policy changes; this trend is apt to continue, and may result in more or less favorable impacts on pricing. 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 U.S., 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. Moreover, the recent and ongoing series of congressional hearings relating to drug pricing has presented heightened attention to the biopharmaceutical industry, creating the potential for political and public pressure, while the potential for resulting legislative or policy changes presents uncertainty.

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 U.S. 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 U.S. 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 U.S. 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, with primary focus on the hospital outpatient setting and ancillary services, 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. On December 14, 2018, the U.S. District Court for the Northern District of Texas struck down the ACA, deeming it unconstitutional given that Congress repealed the individual mandate in 2017; on July 9, 2019, the U.S. Court of Appeals for the Fifth Circuit heard arguments on appeal in this matter. On December 18, 2019, the Fifth Circuit ruled that the ACA's individual mandate is unconstitutional given that the Tax Act eliminated the tax penalty associated with the individual mandate. In concluding that the individual mandate is unconstitutional, the question remains whether, or how much of, the rest of the ACA is severable from that constitutional defect. The Fifth Circuit further remanded the case to the U.S. District Court for the Northern District of Texas to further analyze whether the other provisions of the ACA are severable as they currently exist under the law. Following appeal of the Fifth Circuit's decision, the Supreme Court heard oral arguments in *California v. Texas* on November 2, 2020. The Court has yet to issue its opinion, and we cannot say for certain what the decision will be or what impact, if any, it may have on our business.

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 policy, legislative and regulatory proposals aimed at changing the pharmaceutical industry. The U.S. government, state legislatures and foreign governmental entities have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and coverage and requirements for substitution of generic products for branded prescription drugs.

Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could exclude or limit our product candidates from coverage and limit payments for pharmaceuticals. Under the Trump Administration there were a number of actions taken relative to drug pricing. With the change in administration it is possible that President Biden may issue Executive Orders with the potential to change a number of prior executive branch actions on drug pricing. We continue to monitor the potential impact of proposals to lower prescription drug costs at the federal and state level.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We are unable to predict the future course of federal or state healthcare legislation in the U.S. directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. The ACA and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could also have a material and adverse effect on our business, financial condition and results of operations.

Governments outside the U.S. 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 EU and the United Kingdom, 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 U.S. 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 U.S., 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 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 U.S. 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 U.S. 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 U.S., 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 U.S. 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 MDACC if any of 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 U.S., 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 U.S. 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, MDACC, 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 have conducted an extensive freedom-to-operate, or FTO, analyses of the patent landscape with respect to our lead product candidates. Although we continue to undertake FTO analyses of our manufacturing processes, our lead TIL products, and contemplated future processes and products, because patent applications do not publish for 18 months, and because the claims of patent applications can change over time, no FTO analysis can be considered exhaustive. Furthermore, patent and other intellectual property rights in biotechnology remains an evolving area with many risks and uncertainties. As such, we may not be able to ensure that we can market our product candidates without conflict with the rights of others.

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 cell therapy and 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 U.S. 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 U.S. 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 U.S. can be less extensive than those in the U.S. 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 U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. 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 U.S. 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 and our employees and contractors. 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 or pursue these claims. For example, we are currently engaged in litigation involving counterclaims that we have brought relating to theft of certain of our trade secrets, breach of confidentiality, and related counterclaims. Even if we are successful in resolving these claims, litigation could result in substantial cost and be a distraction to our management and employees.

Risks Related to Our Securities

Our officers, directors and principal stockholders own a substantial percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Our officers, directors, and principal stockholders currently beneficially own a substantial portion of our outstanding voting stock. Therefore, these stockholders have the ability and may continue to have the ability to influence our corporate decision making. Given current ownership levels, these stockholders may be able to determine some or all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control or influence elections of directors, amendments to our certificate of incorporation or bylaws, or approval of any merger, sale of assets, or other major corporate transaction. This level of control may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

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:

- volatility and instability in the capital markets due to the COVID-19 pandemic;
- announcements of the results of clinical trials by us, our collaborators, or our competitors, or negative developments with respect to similar products, including those being developed by our collaborators;
- 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 equities research 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 conducing our business;
- regulatory developments within, and outside of, the U.S.;
- 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 may 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 December 31, 2020, we had 146,874,917 shares of common stock outstanding. In addition, we had 16,293,757 shares of common stock equivalents that would increase the number of common stock outstanding if these instruments were exercised or converted to purchase common stock based on vesting requirements of stock options 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. On June 10, 2019, our certificate of incorporation was amended to increase the number of authorized shares of our common stock, par value $0.000041666, from 150,000,000 shares to 300,000,000 shares, which was approved by our stockholders on that date.

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 and October 2018, we issued 15,000,000 shares and 25,300,000 shares of common stock, respectively, in connection with underwritten public offerings. Further, in June 2020, we issued 19,475,806 shares of common stock in connection with an underwritten public offering, and we may offer additional shares under our automatic shelf registration statement in the future. Future issuances may result in substantial dilution to our existing stockholders and could cause our stock price to decline.

If equities 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 equities 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.

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 Promotions*. 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. Some of the limitations placed on us as a result of the SEC administrative order relating to ineligibility

for statutory safe harbors, including under the Private Securities Litigation Reform Act, and limitations on our communications and status as an ineligible issuer under Rule 405 of the Securities Act, have ended as of April 2020. The foregoing order may negatively impact our reputation with current and future investors, and will disqualify us from effecting private placement transactions in reliance upon any of the exemptions from Securities Act registration afforded by Regulation D. As a result, the SEC's order may it more difficult for us to raise capital in future private offerings.

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.

Federal and state securities and related legal actions may result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business or affect our reputation. We may not be successful in defending future claims and cannot provide assurance that insurance proceeds will be sufficient to cover any costs or liability under such claims.

For example, on December 11, 2020, a purported stockholder derivative complaint was filed by plaintiff Leo Shumacher against us, as nominal defendant, and our current directors, as defendants, in the Court of Chancery in the State of Delaware. The complaint alleges breach of fiduciary duty and a claim for unjust enrichment in connection with alleged excessive compensation of certain of our non-executive directors and seeks unspecified damages on behalf of our company. While we intend to vigorously defend against the foregoing complaint, it is not possible to estimate the amount or range of possible loss that might result from these matters.

Our Board of Directors 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, as amended, authorizes the issuance of up to 50,000,000 shares of "blank check" preferred stock (of which only 17,000 shares were issued as Series A Convertible Preferred Stock and 11,500,000 shares were issued 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 of Directors 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, as amended, 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 has the authority to issue up to 38,483,000 additional 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, as amended, designates the Court of Chancery of 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, as amended, provides that, subject to limited exceptions, the Court of Chancery of the State of Delaware shall, to the fullest extent permitted by law, 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, employees or agents to us or our stockholders, creditors or other constituents (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation, as amended, 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. Further, this choice of forum provision does not preclude or contract the scope of exclusive federal or concurrent jurisdiction for any actions brought under the Securities Act or the Exchange Act. Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. As a result, the exclusive forum provision will not apply to suits brought to enforce any duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. In addition, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. As a result, the exclusive forum provision will not apply to suits brought to enforce any duty or liability created by the Securities Act or any other claim for which the federal and state courts have concurrent jurisdiction. Accordingly, our exclusive forum provision will not relieve us of our duties to comply with the federal securities laws and the rules and regulations thereunder, and our stockholders will not be deemed to have waived our compliance with these laws, rules and regulations.

If a court were to find these provisions of our certificate of incorporation, as amended 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, results of operations and financial condition. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management and other employees.

Provisions in our amended and restated bylaws could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the U.S. shall be the exclusive forum for the resolution of any complaint asserting a cause of action under the Securities Act. This provision limits the ability of our shareholders to bring claims under the Securities Act in any court other than the U.S. federal courts, which ultimately may disadvantage our shareholders or be cost prohibitive. Notwithstanding the foregoing, there is uncertainty as to whether a court (other than state courts in the State of Delaware, which have recently upheld the validity of such a provision) would enforce such a provision and whether investors can waive compliance with the federal securities laws and the rules and regulations thereunder. Furthermore, the exclusive forum provision only applies to claims brought under the Securities Act, and does not apply to actions arising under the Exchange Act, which is already subject to federal courts as the exclusive forum.

If a court were to find these provisions of our amended and restated bylaws 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, results of operations and financial condition. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management and other employees.

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 connection with our reincorporation from Nevada to Delaware in 2017, we (as a Delaware corporation) untimely filed a post-effective amendment to adopt a Form S-8 registration statement that we filed (as a Nevada corporation) to register the shares underlying our 2011 Equity Incentive Plan. Before we filed the required post-effective amendment, options to purchase 200,000 shares were exercised under the 2011 Equity Incentive Plan. The effect of the delayed post-effective amendment filing on the 200,000 option shares is uncertain, but the issuance and sale of the shares may not have been in compliance with the Form S-8 registration

statement. The existence of any liability to us, and the amount of any such liability to us, as a result of the issuance of the 200,000 shares is uncertain. Accordingly, no accrual for a potential claim has been made in our financial statements.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

San Carlos Lease

Since August 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. In October 2018, we entered into an agreement to lease 12,322 square feet of office space located adjacent to our headquarters in San Carlos, California. This lease replaced the sublease of 11,449 square feet of office space in the same facility that expired on October 31, 2018. The term of the lease is 30 months subsequent to the commencement date, November 1, 2018, and will expire in April 2021. Monthly lease payments are approximately $59,000, subject to an annual increase of 3%.

In June 2019, we entered into a first amendment to our previously disclosed lease agreement with Hudson Skyway Landing, LLC for additional space at our corporate headquarters in San Carlos, California. Under the amended lease, we leased an additional 8,110 square feet, for a total of approximately 20,432 square feet of space on the first floor of the building located at 999 Skyway Road, San Carlos, California, commonly known as Skyway Landing II. The term of the amended lease remains the same as that of the original lease and expires on April 30, 2021, unless earlier terminated. Our monthly base rent for the additional space is approximately $39,000 for the first year, and $40,000 for the second year.

See Note 14 of the financial statements for subsequent events relating to our San Carlos, California corporate headquarters leases.

New York Lease

We leased office space in New York, 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. On April 20, 2018, we entered into an agreement to extend the lease term to January 31, 2019 for approximately $7,000 a month. On November 2, 2018, we extended the lease term to July 31, 2019 for approximately $4,000 a month. On October 24, 2019, we entered into an agreement to extend the lease term to April 30, 2020 for approximately $4,000 a month. On January 23, 2020, we entered into an agreement to extend the lease term to July 31, 2020 for approximately $4,000 a month. On May 24, 2020, we entered into an agreement to extend the lease term to October 31, 2020 for approximately $4,000 a month. On September 1, 2020, we entered into an agreement to extend the lease term to January 31, 2021, for approximately $4,000 a month. On January 31, 2021, the lease terminated, and we closed our New York office, which did not have an effect on any of our employees, who continue to be employed by us.

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 expired in December 2019 and rent payments were approximately $20,000 per month. In December 2019, we entered into an agreement to extend the lease term to December 18, 2024 for approximately $20,500 a month. In June 2020, we amended the lease agreement to further increase the rentable space to 13,139 square feet and extend the lease term to June 5, 2025 for approximately $34,500 a month.

Philadelphia Office Lease

In May 2019, we entered into an agreement to lease approximately 1,500 square feet of office space in Philadelphia, Pennsylvania until July 1, 2019 for a rate of $2,000 a month, and then approximately 4,500 square feet of office space for the remainder of a three-year term at an initial rate of $11,063 per month, subject to annual increases of 2.5%. In August 2020, we entered into an agreement to lease approximately 2,965 square feet of a training facility space in Philadelphia, Pennsylvania for a twelve month term at a rate of approximately $6,500 per month.

Commercial Manufacturing Facility Agreement

In May 2019, we entered into a lease agreement with 300 Rouse Boulevard, LLC, which we refer to as the Commercial Manufacturing Facility Lease, for a build-to-suit commercial manufacturing facility, laboratories, and offices located in Philadelphia, Pennsylvania. Under the Commercial Manufacturing Facility Lease, we will lease approximately 136,000 rentable square feet of space in a building to be located at 300 Rouse Boulevard, Philadelphia, Pennsylvania, or the Premises. The commercial manufacturing facility is expected to be constructed in two phases: Phase I-A, the construction of the commercial manufacturing facility, with approximately 66,000 rentable square feet of space; and Phase I-B, the construction of offices and laboratories, with approximately 70,000 rentable square feet of space. The Commercial Manufacturing Facility Lease is for a term of 242 months, commencing on the earlier of (i) the date on which we occupy any portion of the Premises for the normal operation of its business or (ii) the date that is the later of (A) one hundred sixty (160) days after the Phase I-A substantial completion date, July 16, 2020, or (B) the Phase I-B Substantial Completion Date, or the Commencement Date. The Commencement Date shall be extended by one day for each day of landlord delay, net of any tenant delay, as defined in the Lease. The Commercial Manufacturing Facility Lease includes an option to extend the term of the lease, exercisable under certain conditions as described in the Commercial Manufacturing Facility Lease, such that the overall term, when added to the initial term, shall be 359 months, by giving the landlord prior written notice thereof at least 18 months in advance of the expiration date.

Beginning on the Commencement Date, our monthly base rent under the Lease will be approximately $320,000, subject to an annual increase of 2% for the first ten years, and an annual increase of the greater of 2% or 75% of the average ten-year consumer price index. We will also be responsible for paying operating expenses, which are expected to be approximately $72,000 per month in 2020.

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

The information in Note 11 to the Consolidated Financial Statements contained in Part III, Item 15 of this Annual Report on Form 10-K is incorporated herein by reference. There are no matters which constitute material pending legal proceedings to which we are a party other than those incorporated into this item by reference from Note 11 to our Consolidated Financial Statements for the year ended December 31, 2020 contained in this Annual Report on Form 10-K

Item 4. Mine Safety Disclosures

Not Applicable.

PART II

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

Market Information

Our common stock is traded on the Nasdaq Global Market under the symbol “IOVA”.

Stockholders

As of December 31, 2020, there were approximately 15 holders of record of our common 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

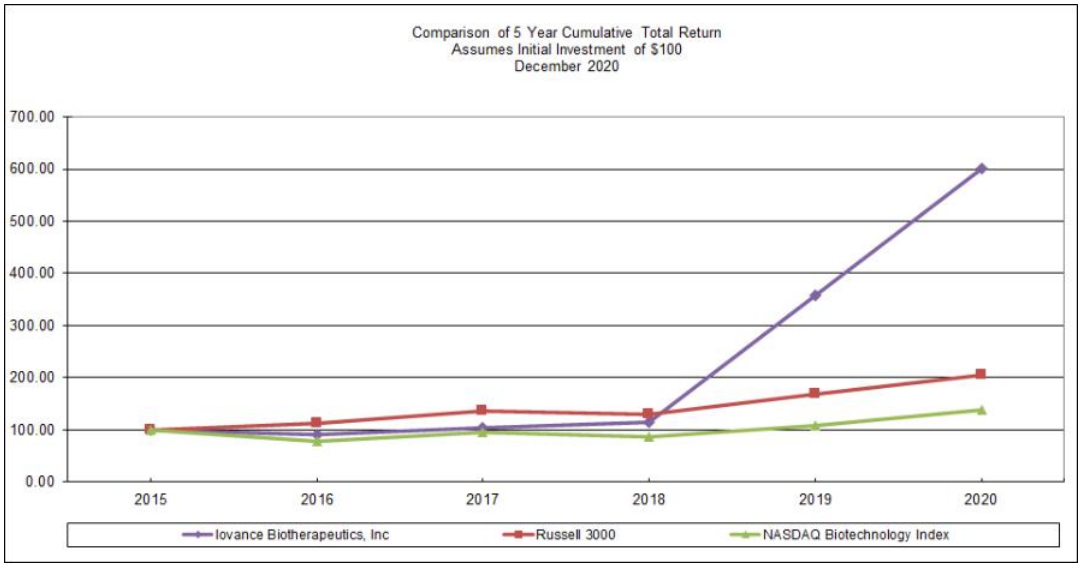
None.

Repurchases of Common Stock

There were no share repurchases during the year ended December 31, 2020.

Stock Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since December 31, 2015 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 2021 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, 2020, 2019, and 2018 and the balance sheet data as of December 31, 2020 and 2019 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, 2017 and 2016 and the balance sheet data as of December 31, 2018, 2017, and 2016 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,				
	2020	2019	2018	2017	2016
			(in thousands)		
Revenue	$ —	$ —	$ —	$ —	$ —
Operating expenses:					
Research and development	201,727	166,023	99,828	71,615	26,941
General and administrative	60,210	40,849	28,430	21,262	26,698
Other income	2,356	9,316	4,678	813	745
Net loss	$ (259,581)	$ (197,556)	$ (123,580)	$ (92,064)	$ (52,894)
Net loss Per Common Share	$ (1.88)	$ (1.59)	$ (1.27)	$ (1.41)	$ (1.85)

	As of December 31,				
	2020	2019	2018	2017	2016
Total assets	$ 768,458	$ 344,655	$ 480,821	$ 155,373	$ 171,886
Total liabilities	$ 111,960	$ 45,684	$ 14,628	$ 9,892	$ 4,968
Total stockholders' equity	$ 656,498	$ 298,971	$ 466,193	$ 145,481	$ 166,918

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 "may," "will," "might," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "aim," "potential," "continue," "ongoing," "goal," "forecast," "guidance," "outlook," or the negative of these terms or other similar expressions to identify forward-looking statements, although not all forward-looking statements contain these words. 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 cell therapies as novel cancer immunotherapy products designed to harness the power of a patient's own immune system to eradicate cancer cells. TIL therapy is an autologous cell therapy platform technology that was originally developed by the NCI, which conducted initial clinical trials of this therapy in diseases such as metastatic melanoma and cervical cancer. We have developed a new, shorter manufacturing process for TIL known as Gen 2, which yields a cryopreserved TIL product. This proprietary and scalable manufacturing method is being investigated in multiple indications. Our lead product candidates include lifileucel for metastatic melanoma and metastatic cervical cancer. In addition to metastatic melanoma and metastatic cervical cancer, we are investigating the effectiveness and safety of TIL for the treatment of squamous cell carcinoma of the head and neck, non-small cell lung cancer, and are investigating PBL therapy for CLL or SLL through our sponsored trials, as well as in other oncology indications through collaborations.

We are conducting a Phase 2 clinical trial, C-144-01, of our lead product candidate, lifileucel, for the treatment of metastatic melanoma. This multicenter pivotal trial enrolled melanoma patients with disease progression following treatment with at least one systemic therapy, including a PD-1 inhibitor and if BRAF mutated, a BRAF inhibitor, or a combination of BRAF and MEK inhibitors. Cohort 4 of the C-144-01 clinical trial is a single-arm cohort intended to support a BLA submission for lifileucel. Cohorts 2 and 4 of the C-144-01 trial use our Gen 2 manufacturing process. We completed and closed enrollment of patients into Cohort 2 of the C-144-01 trial in 2018. Results from Cohort 2 of the C-144-01 clinical trial were initially reported at the ASCO annual meeting on June 1, 2019 and subsequently updated at the ASCO annual meeting on May 29, 2020. In 66 patients with metastatic melanoma, treatment with lifileucel resulted in an ORR of 36%, as assessed by investigator, with 2 complete responses and 22 partial responses. The DCR was 80.3%. Patients were heavily pretreated and had a mean of 3.3 prior therapies. We have reported durable responses across a wide age range of metastatic melanoma patients, and among those who have received prior anti-CTLA-4 and BRAF targeted treatments, regardless of BRAF mutation status, and equally in patients with PD-L1 high and low status. We have provided several updates on the median DOR for Cohort 2 and most recently, in January 2021, we announced that median DOR in Cohort 2 had still not been reached after 28.1 months of median study follow up, as assessed by investigator. The adverse event profile was generally consistent with the underlying advanced disease and the profile of the lymphodepletion and IL-2 regimens.

Pivotal Cohort 4 of the C-144-01 trial was enrolled to evaluate ORR as read out by an IRC as the primary endpoint based on our interpretation of discussions with the FDA as part of an EOP2 meeting held with the FDA in the third quarter of 2018. In October 2018, based on the data provided to the FDA during the EOP2 meeting, we announced that lifileucel had received a RMAT designation from the FDA. Enrollment in Cohort 4 of the C-144-01 trial commenced in March 2019 and patient dosing was completed in January 2020. A total of 87 patients were dosed in Cohort 4. Initial results from Cohort 4 are available for 68 patients with two radiological assessments, as determined by investigator. Lifileucel showed a 32.4% ORR, including one complete response and 21 partial responses, two of which were yet to be confirmed with follow up visits at the time of the data cut, and a DCR of 72.1% as of the data cut off of March 16, 2020, corresponding to 5.3 months of median study follow up. This data is consistent with the Cohort 2 data read out at a similar median duration of study follow up. The ORR of Cohort 2 at a median study follow up of 6 months was 33%. In October 2020, after a Type B meeting with the FDA, we announced that we had delayed our BLA submission for lifileucel in metastatic melanoma as a result of FDA feedback, in order to allow us to simultaneously refine existing and develop new potency assays, and we anticipate submitting our BLA in 2021. At the same time, we also announced that we had reached agreement with the FDA on the minimum duration of follow up for Cohort 4 to support our BLA submission for lifileucel in the treatment of metastatic melanoma.

We are also conducting a Phase 2 clinical trial, C-145-04, which is a multicenter pivotal trial that will assess the safety and efficacy of lifileucel for the treatment of patients with recurrent, metastatic or persistent cervical cancer. In February 2019, lifileucel received Fast Track designation from the FDA for development in the treatment of cervical cancer with disease progression on or after chemotherapy. In March 2019, the protocol for this trial was amended to modify the primary endpoint of ORR to be determined by IRC. In May 2019, lifileucel received BTD from the FDA for development in the treatment of cervical cancer. Updated results from the C-145-04 clinical trial were reported at the ASCO annual meeting on June 1, 2019. In 27 patients with metastatic cervical cancer, treatment with lifileucel resulted in an ORR of 44%. At the time of the study data cut, there were 3 complete responses and 9 partial responses. The DCR was 85%. Patients were heavily pretreated and had a mean of 2.4 prior therapies. The median DOR had not been reached. The adverse event profile was generally consistent with the underlying advanced disease and the profile of the lymphodepletion and IL-2 regimens. Based on an EOP2 meeting held with the FDA in June 2019, we believe that results from the C-

145-04 clinical trial may be sufficient to support registration of lifileucel for the treatment of patients with metastatic cervical cancer. In accordance with the FDA's recommendations, the protocol was amended to further define the patient population. In November 2019, in order to evaluate lifileucel in broader lines of therapy in cervical cancer, we have further amended the C-145-04 trial to collect additional data on early-line patients as well as late-line patients by adding additional cohorts, in anticipation of a changing landscape in this indication, including Cohort 2 for patients that had previously received anti-PD-1 therapy. These additional cohorts also allow access to TIL therapy after completion of the enrollment in the registrational cohorts. In January 2021, we announced that Cohort 2 of the C-145-04 trial had completed enrollment and that data from this cohort may be supportive of registration because of the expected changing landscape of care for cervical patients. We intend to initiate a dialog with the FDA in 2021 to discuss BLA submission plans for lifileucel in cervical cancer.

In November 2020, we announced that we had finalized the protocol for our potential registrational clinical trial in NSCLC, IOV-LUN-202, to investigate LN-145 in patients with recurrent or metastatic NSCLC, without driver mutations, who previously received a single line of approved systemic therapy of combined checkpoint inhibitor and chemotherapy. The IOV-LUN-202 clinical trial includes three cohorts. Cohorts 1 and 3 of the IOV-LUN-202 clinical trial will enroll patients with a PD-L1 TPS of less than one percent, and Cohort 2 will enroll patients with a PD-L1 TPS of greater than or equal to one percent. We intend to enroll patients in the IOV-LUN-202 clinical trial throughout 2021.

C-145-03 is our Phase 2, multicenter trial to assess the safety and efficacy of our product candidate LN-145 for the treatment of patients with recurrent metastatic HNSCC. In October 2018, we reported that, to date, preliminary data for 13 patients in the C-145-03 clinical trial yielded an ORR of 31% with a DOR ranging from 2.8 to 7.6 months. The adverse event profile remained consistent with previous reports. We redesigned our C-145-03 trial to include multiple cohorts, in order to allow for dosing of TIL therapies produced by multiple manufacturing methods, including our Gen 2 manufacturing process, our Gen 3 manufacturing process, and our PD-1 selected TIL manufacturing process. Our PD-1 selected TIL manufacturing process results in a product that we refer to as LN-145-S1. In January 2021, we announced that we are closing the C-145-03 clinical trial after the trial reached its pre-specified enrollment target.

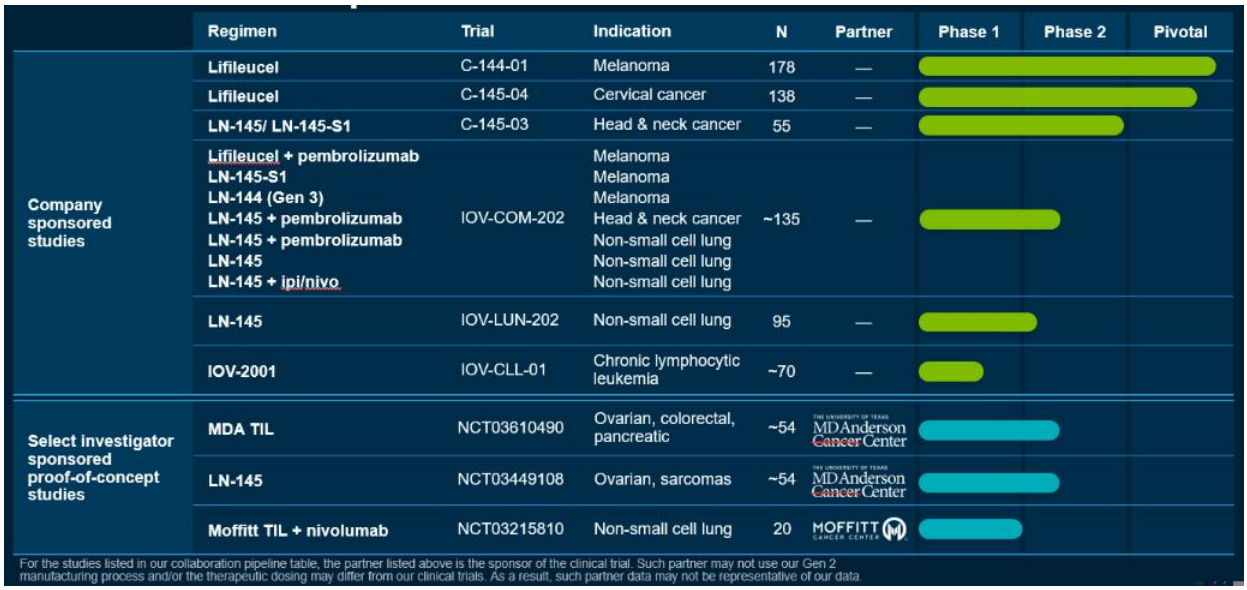
We are also investigating the potential of our TIL therapies in earlier lines of treatment and in combination with pembrolizumab, and are studying LN-145 as a monotherapy in relapsed refractory NSCLC patients. IOV-COM-202 is a Phase 2, multicenter trial that is composed of seven cohorts that can enroll up to a total of 135 patients. In May 2019, we reported that the first patient was dosed in the IOV-COM-202 trial. In addition to its ongoing enrollment in the U.S., the IOV-COM-202 trial has also received regulatory approval in Canada and in certain European countries. In Cohort 2A of the IOV-COM-202 trial, we are enrolling advanced, recurrent, or metastatic HNSCC patients who are naïve to prior immunotherapy including anti-PD-1/anti-PD-L1 therapy. The patients receive LN-145 in combination with pembrolizumab. We reported results from ongoing Cohort 2A of the IOV-COM-202 trial at the SITC meeting in November 2020, as follows. As of October 16, 2020, nine HNSCC patients have received LN-145 plus pembrolizumab with a median duration of follow up of 8.6 months. Nine and eight patients were evaluable for safety and efficacy, respectively. Four patients had a confirmed, objective response with an ORR of 44% including one complete response and three partial responses. Median DOR was not reached. The disease control rate at data cutoff was 89% in nine patients, and seven of the eight evaluable patients, or 87.5%, had a reduction in target lesions. The median number of prior therapies was 1.0 with 89% of the patients having received prior chemotherapy. Four patients were HPV positive, three patients were HPV negative, and two patients had unknown HPV status. The TEAE profile was consistent with the underlying advanced disease and the known adverse event profiles of pembrolizumab, lymphodepletion, and IL-2 regimens. The most common TEAEs, occurring in more than 50% of evaluable subjects, were chills, anemia, hypotension, nausea, pyrexia, and thrombocytopenia.

In November 2019, we announced that our IND for our PBL therapy, IOV-2001, was authorized by the FDA and our sponsored clinical trial using this therapy, IOV-CLL-01, was cleared to proceed. IOV-2001 is a non-genetically modified, polyclonal T cell product that is manufactured using a nine-day process from 50 mL of patient's blood. IOV-CLL-01 is a Phase 1/2 clinical trial evaluating the safety and efficacy of IOV-2001 in patients with relapsed or refractory CLL or SLL. The IOV-CLL-01 trial is expected to enroll up to approximately 70 patients.

As part of our collaboration program with MDACC, two Phase 2 trials were initiated in 2018. Both trials are sponsored by MDACC. The first trial, NCT03449108, is intended to allow for investigation of LN-145 manufactured by us using our manufacturing processes to treat patients with soft tissue sarcoma, osteosarcoma, platinum resistant ovarian cancer, and thyroid cancer. A second trial under the collaboration with MDACC, NCT03610490, is active as well. This trial is treating patients with platinum resistant ovarian cancer, pancreatic and colorectal cancer. This trial uses TIL manufactured by MDACC using urelumab, a 4-1BB agonistic antibody, as part of the manufacturing process. The data obtained using this manufacturing process may not be representative of our data using our Gen 2 manufacturing process.

We are also collaborating with CHUM, Yale University, and Moffitt on investigator-sponsored clinical trials of TIL therapies in other indications. The clinical trials sponsored by CHUM and Moffitt use, or will use, TIL manufactured by different manufacturing processes, which may not be representative of our data using our Gen 2 manufacturing process.

Our current product candidate pipeline and selected investigator-sponsored proof-of-concept studies are summarized in the figure below:



We have developed a third-generation manufacturing process known as Gen 3. Gen 3 is a shorter process than Gen 2. We are using Gen 3 manufacturing in Cohort 1C of the IOV-COM-202 trial in melanoma and in Cohort 3 of the IOV-LUN-202 trial in NSCLC and have previously used it in the C-145-03 trial in HNSCC.

We currently own more than twenty granted or allowed U.S. and international patents for compositions and methods of treatment in a broad range of cancers relating to our Gen 2 manufacturing process, including U.S. Patent Nos. 10,130,659, 10,166,257, 10,272,113, 10,363,273, 10,398,734, 10,420,799, 10,463,697, 10,537,595, 10,646,517, 10,653,723, 10,693,330, 10,695,372, 10,894,063, and 10,905,718. We anticipate that the terms of these patents related to Gen 2 manufacturing processes will extend to January 2038, not including any patent term extensions or adjustments that may be available. Our owned and licensed intellectual property portfolio also includes patent applications relating to TIL, MIL, and PBL therapies; frozen tumor-based TIL technologies; remnant TIL and digest TIL compositions, methods and processes; methods of treatment of a broad range of cancers using TIL therapies; methods of manufacturing TIL, MIL, and PBL therapies; the use of costimulatory molecules in TIL therapy and manufacturing; stable and transient genetically-modified TIL therapies; methods of using immune checkpoint inhibitors in combination with TIL therapies; TIL selection technologies; and methods of treating patient subpopulations.

In January 2020, we obtained a license from Novartis to develop and commercialize an antibody cytokine engrafted protein, which we refer to as IOV-3001. Under the agreement, we paid an upfront payment to Novartis and may pay milestones involved in initiation of patient dosing in various phases of clinical development for IOV-3001 and approval of a potential product in the U.S., EU and Japan. Novartis is also entitled to low-to-mid single digit percentage royalties from commercial sales of IOV-3001. In addition, in January 2020, we announced a research collaboration and exclusive worldwide licensing agreement with Cellectis, a clinical-stage biopharmaceutical company focused on developing immunotherapies based on gene-edited allogeneic chimeric antigen receptor modified T cells, whereby we licensed certain TALEN technology from Cellectis in order to develop TIL that have been genetically edited to create potentially more potent cancer therapeutics. The worldwide exclusive license enables us to use TALEN technology addressing multiple gene targets to modify TIL for therapeutic use in several cancer indications. Financial terms of the license include

development, regulatory and sales milestone payments from us to Cellectis, as well as royalty payments based on net sales of TALEN-modified TIL products.

Results of Operations for the Years Ended December 31, 2020 and 2019

Research and development activities are central to our business model. Product candidates in later stage 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. Since 2017 our primary source of funds has been from the public sale of our common stock.

Revenues

We did not generate any revenues during the years ended December 31, 2020 and 2019, respectively, and we currently do not anticipate that we will generate any significant revenues from the sale or licensing of our product candidates during the 12 month period from the date these financial statements are issued. 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.

Costs and expenses

Research and Development Expense (in thousands)

	Years Ended December 31,		Increase (Decrease)	
	2020	2019	$	%
Research and development	$ 201,727	$ 166,023	$ 35,704	22 %
Stock-based compensation expense included in research and development expense	19,727	11,396	8,331	73 %

Research and development expense for the year ended December 31, 2020 increased by $35.7 million, or 22%, compared to the year ended December 31, 2019. The increase was primarily attributable to (i) a $20.9 million increase in payroll and related expenses driven by a higher number of full-time research and development employees and outside services, (ii) a $10.0 million increase for the license to further develop IOV-3001 obtained from Novartis, (iii) a $8.3 million increase in stock-based compensation expenses, and (iv) a $6.6 million increase in clinical trial costs due to an increase in enrollment across all the trials and initiation of new clinical trials. Further, a $0.8 million increase in research consumables cost contributed to the increase. These increases were partially offset by lower manufacturing costs by $9.1 million due to decreased production runs in 2020 as a result of completion of enrollment in the melanoma pivotal program and a $2.3 million decrease in research alliance expenses due to the COVID-19 pandemic’s impact on patient enrollment in the clinical trials with our research alliance partners.

We expect our research and development expenses to increase over the next several years as we prepare for commercial manufacturing of our products and continue to conduct our clinical trials for other 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)	
	2020	2019	$	%
General and administrative	$ 60,210	$ 40,849	$ 19,361	47 %
Stock-based compensation expense included in general and administrative	21,160	12,881	8,279	64 %

General and administrative expense for the year ended December 31, 2020 increased by $19.4 million, or 47%, compared to the year ended December 31, 2019. The increase was primarily attributable to (i) a $8.3 million increase in stock-based compensation expenses and a $7.1 million increase in payroll and related expenses driven by a higher number of full-time general and administrative employees and higher average stock price, (ii) a $2.1 million increase in director's and officer's insurance premiums, (iii) a $1.1 million increase in intellectual property legal costs, and (iv) a $1.1 million in market research activities as we prepare for commercialization. These increases were partially offset by a $0.7 million decrease in travel expenses.

General and administrative expenses include personnel costs for our employees engaged in general and administrative activities, legal fees, and expenses related to marketing and commercial activities, audit and tax fees, consultants and professional services, and general corporate expenses. We anticipate general and administrative expenses will increase in 2021 as we continue to prepare for commercialization, complete our manufacturing facility and support an expected increase in total headcount.

Interest Income (in thousands)

	Years Ended December 31,		Increase (Decrease)	
	2020	2019	$	%
Net interest income	$ 2,356	$ 9,316	$ (6,960)	(75)%

Interest income results from our interest-bearing cash and investment balances. Net interest income decreased by $7.0 million, or 75%, due primarily to a decrease in interest rates in 2020 as compared to the same period in 2019.

Net Loss (in thousands)

	Years Ended December 31,		(Increase) Decrease	
	2020	2019	$	%
Net loss	$ (259,581)	$ (197,556)	$ (62,025)	31 %

Net loss for the year ended December 31, 2020 increased by $62.0 million or 31%, compared to the year ended December 31, 2019. The increase in our net loss was due to the continued expansion of our research and development activities, increased clinical trials, 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 commercial readiness and clinical development.

Results of Operations for the Years Ended December 31, 2019 and 2018

Revenues

We did not generate any revenues during the years ended December 31, 2019 and 2018, respectively.

Costs and expenses

Research and Development Expense (in thousands)

	Years Ended December 31,		Increase (Decrease)	
	2019	2018	$	%
Research and development expenses	$ 166,023	$ 99,828	$ 66,195	66 %
Stock-based compensation expense included in research and development expense	11,396	9,305	2,091	22 %

Research and development expense for the year ended December 31, 2019 increased by $66.2 million, or 66%, compared to the year ended December 31, 2018. The increase was primarily attributable to (i) a $27.4 million increase in manufacturing costs due to increased production runs and additional manufacturing capacity costs to support the ongoing clinical trials, (ii) a $21.4 million increase in clinical trial costs due to an increase in the number of patients in the clinical trials and purchases of clinical trial drugs, and (iii) a $12.6 million increase in payroll and related expenses and $2.1 million increase in share-based compensation expenses driven by a higher number of full-time research and development employees and dedicated consultants as we expanded our internal research and clinical development programs in 2019.

General and Administrative Expense (in thousands)

	Years Ended December 31,		Increase (Decrease)	
	2019	2018	$	%
General and administrative expenses	$ 40,849	$ 28,430	$ 12,419	44 %
Stock-based compensation expense included in general and administrative expense	12,881	10,722	2,159	20 %

General and administrative expense for the year ended December 31, 2019 increased by $12.4 million, or 44%, compared to the year ended December 31, 2018. The change was primarily attributable to a $3.8 million increase in payroll and related expenses, $2.2 million increase in stock-based compensation expenses driven by a higher number of full-time general and administrative employees, a $3.2 million increase in intellectual property legal costs and a $2.0 million increase in market research activities as we prepare for commercialization.

Interest Income (in thousands)

	Years Ended December 31,		Increase (Decrease)	
	2019	2018	$	%
Interest income, net	$ 9,316	$ 4,678	$ 4,638	99 %

Interest income results from our interest-bearing cash and investment balances. Net interest income increased by $4.7 million due to the higher interest income earned from full-year short-term investments for a full-year as compared to the prior year when we started purchasing short-term investments during the second half of 2018. As our cash, cash equivalents and short term investment balance decrease, we anticipate interest income to decrease.

Net Loss (in thousands)

	Years Ended December 31,		(Increase) Decrease	
	2019	2018	$	%
Net loss	$ (197,556)	$ (123,580)	$ (73,976)	60 %

Net loss for the year ended December 31, 2019 increased by $74.0 million or 60%, compared to the year ended December 31, 2018. The increase in our net loss 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.

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 2021 and may incur significant losses and negative cash flows from operations for the foreseeable future. Historically, we have funded our operations from various public and private offerings of our equity securities (both common stock and preferred stock), from option and warrant exercises, and from interest income. Since 2017, our primary source of funds has been from the public sale of our common stock.

Corporate Capitalization

As of December 31, 2020, we had outstanding 146,874,917 shares of our $0.000041666 par value common stock, 194 shares of our $0.001 par value Series A Convertible Preferred Stock, and 3,581,119 shares of our $0.001 par value Series B Convertible Preferred Stock. The outstanding shares of Series A Convertible Preferred Stock are currently convertible into 97,000 shares of our common stock, and the outstanding shares of Series B Convertible Preferred Stock are currently convertible into 3,581,119 shares of our common stock. The shares of Series A Convertible Preferred Stock and Series B Convertible Preferred Stock do not have voting rights or accrue dividends.

On December 28, 2017, 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 $250 million, which we refer to as the 2017 Shelf Registration Statement. The 2017 Shelf Registration Statement was declared effective on January 19, 2018. On January 29, 2018, we sold 15,000,000 shares of our common stock at a public offering price of $11.50 per share pursuant to the 2017 Shelf Registration Statement. We received gross proceeds of approximately $172.5 million and net proceeds of approximately $162.0 million, after deducting underwriting discounts and offering expenses. The 2017 Shelf Registration Statement was terminated upon effectiveness of the 2018 Shelf Registration Statement (as discussed below).

On September 7, 2018, 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 $250 million, which we refer to as the 2018 Shelf Registration Statement. The 2018 Shelf Registration Statement was declared effective on October 3, 2018 and the aggregate amount of securities we could issue thereunder was subsequently increased by $50 million through a post-effective amendment that we filed on October 11, 2018, pursuant to Rule 462(b) of the Securities Act. On October 17, 2018, we sold 25,300,000 shares of our common stock at a public offering price of $9.97 per share pursuant to the 2018 Shelf Registration Statement. We received gross proceeds of approximately $252.2 million and net proceeds of $236.7 million, after deducting underwriting discounts and offering expenses. The 2018 Shelf Registration Statement is no longer available for future offerings.

On September 17, 2019, we filed a shelf registration statement with the SEC for the issuance up to an aggregate amount of $400 million, which we refer to as the 2019 Shelf Registration Statement. The 2019 Shelf Registration Statement was declared effective on September 24, 2019. The 2019 Shelf Registration Statement was terminated upon effectiveness of the 2020 Automatic Shelf Registration Statement (as discussed below). No shares were sold under the 2019 Shelf Registration Statement prior to its termination.

On May 27, 2020, we filed an automatic shelf registration statement with the SEC for the issuance of an indeterminate amount of Shelf Securities, which we refer to as the 2020 Automatic Shelf Registration Statement. The 2020 Automatic Shelf Registration Statement was immediately effective upon filing with the SEC, and the 2019 Shelf Registration Statement was simultaneously terminated.

On June 2, 2020, we sold 19,475,806 shares of our common stock at a public offering price of $31.00 per share pursuant to the 2020 Automatic Shelf Registration Statement. We received gross proceeds of $603.7 million and net proceeds of $567.0 million, after deducting underwriting discounts and offering expenses. Following the public offering, the 2020 Automatic Shelf Registration Statement remains available for the future issuance of an indeterminate amount of Shelf Securities.

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. If any of the securities covered by the 2020 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 such offering at that time.

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

significant revenues from the sale or licensing of any products during the 12 months from the date these financial statements are issued. We have incurred a net loss of $259.6 million for the year ended December 31, 2020 and used $205.1 million of cash in our operating activities for the year ended December 31, 2020. As of December 31, 2020, we had $629.4 million of cash, cash equivalents, and short-term investments ($67.3 million of cash and cash equivalents and $562.1 million of short-term investments), $656.5 million of stockholders' equity and had working capital of $581.2 million.

We expect to further increase our research and development activities, especially continuing pre-commercial activities and completing the construction of our tenant improvements to our new commercial manufacturing facility, which will increase the amount of cash we will use during 2021 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 including building our own facility. Based on the funds we have available as of the date of the filing of this Annual Report on Form 10-K, we believe that we have sufficient capital to fund our anticipated operating expenses and capital expenditure for at least 12 months from the date of filing this report.

Cash Flows

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

	Years Ended December 31,		
	2020	2019	2018
Net cash (used in) provided by:			
Operating activities	$ (205,134)	$ (158,889)	$ (101,249)
Investing activities	(317,853)	90,025	(386,279)
Financing activities	576,422	6,131	424,307
Net increase in cash, cash equivalents and restricted cash	$ 53,435	$ (62,733)	$ (63,221)

Operating Activities

Net cash used in operating activities represents cash disbursements related to all of our activities other than investing and financing activities. Operating cash flow is derived by adjusting our net loss for non-cash items and changes in operating assets and liabilities. Net cash used in operating activities for the year ended December 31, 2020 increased by $46.2 million to $205.1 million in 2020 from $158.9 million for the same period in 2019. The increase was primarily attributable to (i) a $62.0 million increase in net loss due to increased costs in research and development activities and growth of our corporate infrastructure, which was adjusted by (ii) a $16.6 million increase in stock-based compensation costs. Included in $46.2 million of the increase in cash used in operating activities was the $10.0 million upfront payment we made to Novartis in connection with the license for IOV-3001.

Net cash used in operating activities for the year ended December 31, 2019 increased by $57.6 million to $158.9 million in 2019 from of $101.2 million for the same period in 2018. The increase was primarily attributable to (i) a $73.4 million increase in net loss, which was adjusted by (ii) a $4.2 million increase in stock-based compensation expense, (iii) a $7.0 million increase in noncash lease expense. Further, it was adjusted for a $11.2 million increase in accounts payable primarily due to increases in activities by our company and the timing of payments, which were offset by a $6.1 million increase in right-of-use assets due to the adoption of the new lease accounting standard.

Net cash used in operating activities for the year ended December 31, 2018 increased by $22.5 million to $101.2 million from $78.8 million in 2017. The increase was primarily attributable to a $31.5 million increase in net loss, which was adjusted by a $8.1 million increase in stock-based compensation costs.

Investing Activities

Net cash (used in) / provided by investing activities primarily consists of purchases, maturities of our short-term investments and capital expenditures. Net cash used in investing activities for the year ended December 31, 2020 was $317.9 million compared to net cash provided by $90.0 million for the same period in 2019. The increase in net cash used in investing activities was due primarily to a $368.0 million increase in net purchases of short-term investments from our June 2020 public offering and a $39.9 million increase in the purchase of property and equipment for the commercial manufacturing facility.

Net cash provided by investing activities for the year ended December 31, 2019 was $90.0 million compared to net cash used in investing activities of $386.3 million for the same period in 2018. The increase in net cash provided in 2019 was due primarily to $482.0 million increase in net maturities of short-term investments, which was partially offset by a $5.7 million increase in the purchases of property and equipment.

Net cash used in investing activities for the year ended December 31, 2018 was $386.3 million compared to net cash provided in investing activities of $58.7 million for the same period in 2017. The increase in net cash used in 2018 was due to our reinvestment of the proceeds from January 2018 public offering.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2020 was $576.4 million compared to net cash provided of $6.1 million for the same period in 2019. The increase in net cash provided was primarily due to the cash proceeds of $567.0 million from the June 2020 public offering and a $3.2 million increase in proceeds from the exercise of stock options.

Net cash provided by financing activities for the year ended December 31, 2019 was $6.1 million compared to net cash provided of $424.3 million for the same period in 2018. The decrease in net cash provided was due primarily to higher proceeds in 2018 obtained from the January 2018 public offering and exercise of warrants.

Net cash provided by financing activities of for the year ended December 31, 2018 was $424.3 million compared to $58.7 million for the same period in 2017. The increase was primarily due to a $345.2 million increase in cash proceeds from the public offering in January 2018 as compared to the October 2017 public offering, and a $19.4 million increase in cash proceeds from the exercise of warrants and stock options.

Significant Accounting Policies and Recent Accounting Standards

The preparation of our consolidated financial statements requires us to make estimates and judgments that affect the reported amounts in the financial statements and related disclosures. On an ongoing basis, we evaluate our significant accounting policies and estimates. We base our estimates on historical experience and on various market-specific and other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Estimates are assessed each period and updated to reflect current information. Actual results may differ from these estimates. See Note 2 of the financial statements for a discussion of our significant accounting policies.

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-cancellable contractual obligations as of December 31, 2020 that will require future cash payments are as follows (in thousands):

Contractual Obligations	Payments due by period						
	Total	2021	2022	2023	2024	2025	Thereafter
Operating lease obligations	$ 103,411	$ 10,200	$ 6,063	$ 4,286	$ 4,375	$ 4,281	$ 74,206
CMO contractual obligations	9,877	9,583	294	—	—	—	—
Total	$ 113,288	$ 19,783	$ 6,357	$ 4,286	$ 4,375	$ 4,281	$ 74,206

Operating lease obligations consist of obligations under non-cancelable operating leases for our facilities in San Carlos, CA, Philadelphia, PA, Tampa, FL, and New York, NY.

Contract Manufacturing Organization, or CMO, contractual obligations consist of embedded lease obligations for the manufacturing facilities and minimum fixed commitment fees included in our manufacturing contracts, such as personnel, general support fee, and minimum production or material fees. See Note 10 of the financial statements.

The contractual obligations table above excludes approximately $40 million over the next year for equipment and construction costs for our commercial-scale production facility in Philadelphia, PA.

Impact of COVID-19 on our Business

Operations and Liquidity

The full impact of the COVID-19 pandemic is unknown and rapidly evolving. While the potential economic impact brought by and over the duration of the COVID-19 pandemic may be difficult to assess or predict, the COVID-19 pandemic has resulted in significant disruption of global financial markets, which could in the future negatively affect our liquidity. In addition, a recession or market volatility resulting from the COVID-19 pandemic could affect our business. We have taken proactive, aggressive action throughout the COVID-19 pandemic to protect the health and safety of our employees, and expect to continue to implement these measures until we determine that the COVID-19 pandemic is adequately contained for purposes of our business. We may take further actions as government authorities require or recommend or as we determine to be in the best interests of our employees. We do not believe that the COVID-19 pandemic had a material impact on our liquidity or results of operations for the year ended December 31, 2020. Further, to date, the COVID-19 pandemic has not had significant effects on our clinical trial enrollment. Given the nature and type of our short-term investments in U.S. government securities, we do not believe that the COVID-19 pandemic will have a material impact on our current investment liquidity.

Outlook

Although there is uncertainty related to the anticipated impact of the recent COVID-19 pandemic on our future results, we believe our current cash reserves leave us well-positioned to manage our business through this crisis as it continues to unfold. However, the impacts of the COVID-19 pandemic are broad-reaching and continuing and the financial impacts associated with the COVID-19 pandemic are still uncertain.

The COVID-19 pandemic is ongoing, and its dynamic nature, including uncertainties relating to the ultimate geographic spread of the virus, the severity of the disease, the duration of the pandemic, and actions that would be taken by governmental authorities to contain the pandemic or to treat its impact, makes it difficult to forecast any effects on our results for the fiscal year ending December 31, 2021.

Despite the economic uncertainty resulting from the COVID-19 pandemic, we intend to continue to focus on the development of our product candidates. We continue to monitor the rapidly evolving situation and guidance from international and domestic authorities, including federal, state and local public health authorities and may take additional actions based on their recommendations. In these circumstances, there may be developments outside our control requiring us to adjust our operating plan. As such, given the dynamic nature of this situation, we cannot reasonably estimate the impacts of COVID-19 on our financial condition, results of operations or cash flows in the future.

Off-Balance Sheet Arrangements

At December 31, 2020, 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 market risk is limited primarily to interest income sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because a significant portion of our investments are in interest bearing cash accounts consisting of short-term debt securities issued by the U.S. government. The primary objective of our investment activities is to preserve principal. We adhere to an investment policy that requires us to limit amounts invested in securities based on credit rating, maturity, industry group and investment type and issuer, except for securities issued by the U.S. government. We do not have any derivative financial instruments or foreign currency instruments. At December 31, 2020, we had $562.1 million invested in short-term marketable securities with a maturity date of less than one year. As such we believe that we are not exposed to any material market risk. If interest rates had varied by 1% in the year ended December 31, 2020, the fair value of our investment portfolio would increase or decrease by approximately $2.6 million.

Inflation Risk

Inflation has not had a material effect on our business, financial condition or results of operations during the years ended December 31, 2020, 2019, or 2018.

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, 2020 based on the framework in *Internal Control—Integrated Framework*

2013 issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO. Based on that evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2020.

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 consolidated 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.

EXHIBIT INDEX

Exhibit	Description
2.1	Plan of Conversion (incorporated herein by reference to Exhibit 2.1 to the 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 the 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 to the Registrant's Current Report on Form 8-K filed with the Commission on June 2, 2017).
3.3	Certificate of Incorporation (incorporated herein by reference to Exhibit 3.3 to the 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 to the Registrant's Post-Effective Amendment No. 1 to the Registration Statement on Form S-3 (file no. 333-214073) 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 to the Registrant's Post-Effective Amendment No. 1 to the Registration Statement on Form S-3 (file no. 333-214073 incorporated by reference into file no. 333-212373) filed with the Commission on July 31, 2017).
3.6	Certificate of Amendment of Certificate of Incorporation (incorporated herein by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the Commission on June 27, 2017).
3.7	Certificate of Amendment of Certificate of Incorporation (incorporated herein by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8 K filed with the Commission on June 11, 2019).
3.8	Amended and Restated Bylaws (incorporated herein by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the Commission on May 27, 2020).
4.2	Specimen of Stock Certificate (incorporated herein by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K filed with the Commission on March 12, 2018).
4.3	Description of Securities (incorporated herein by reference to Exhibit 4.3 to the Registrant's Annual Report on Form 10-K filed with the Commission on March 6, 2019).
10.1	Genesis Biopharma, Inc. 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8 K filed with the Commission on October 20, 2011).#
10.2	Form of Incentive Stock Option Agreement under the Genesis Biopharma Inc. 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.4 to the Registrant's Annual Report on Form 10-K filed with the Commission on February 25, 2020).#
10.3	Form of Non-Qualified Stock Option Agreement under the Genesis Biopharma Inc. 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.5 to the Registrant's Annual Report on Form 10-K filed with the Commission on February 25, 2020).#
10.4	Lion Biotechnologies, Inc. 2014 Equity Incentive Plan, as amended (incorporated herein by reference to Appendix A to the Registrant's Definitive Proxy Statement on Schedule 14A filed with the Commission on July 7, 2016).#
10.5	Form of Incentive Stock Option Agreement under the Lion Biotechnologies, Inc. 2014 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 to the Registrant's Annual Report on Form 10-K filed with the Commission on February 25, 2020).#
10.6	Form of Non-Qualified Stock Option Agreement under the Lion Biotechnologies, Inc. 2014 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.8 to the Registrant's Annual Report on Form 10-K filed with the Commission on February 25, 2020).#
10.7	Iovance Biotherapeutics, Inc. 2018 Equity Incentive Plan, as amended (incorporated herein by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed with the Commission on June 9, 2020).#
10.8	Form of Incentive Stock Option Agreement under the Iovance Biotherapeutics, Inc. 2018 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.10 of Registrant's Annual Report on Form 10-K filed with the Commission on February 25, 2020).#
10.9	Form of Non-Qualified Stock Option Agreement under the Iovance Biotherapeutics, Inc. 2018 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.11 of Registrant's Annual report on Form 10-K filed with the Commission on February 25, 2020).#
10.10	Iovance Biotherapeutics, Inc, 2020 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed with the Commission on June 9, 2020).#

10.11	Patent License Agreement by and between Genesis Biopharma, Inc. and the National Institutes of Health effective October 5, 2011 (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K/A filed with the Commission on December 13, 2011).*
10.12	Cooperative Research and Development Agreement for Intramural-PHS Clinical Research, dated August 5, 2011, by and between the U.S. Department of Health and Human Services, as represented by the National Cancer Institute, and Genesis Biopharma, Inc. (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K/A (Amendment No. 2) filed with the Commission on November 29, 2011).
10.13	Form of Director Stock Award Agreement (incorporated herein by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed with the Commission on July 25, 2013).#
10.14	Form of Registration Rights Agreement by and among Lion Biotechnologies, Inc. and the Investors thereunder (incorporated herein by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed with the Commission on October 31, 2013).
10.15	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 Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed with the Commission on January 27, 2015).*
10.16	Patent License Agreement, dated February 9, 2015, by and between Lion Biotechnologies, Inc. and the National Institutes of Health (incorporated herein by reference to Exhibit 10.47 to the Registrant's Annual Report on Form 10 K filed with the Commission on March 16, 2015).*
10.17	Patent License Agreement, dated February 10, 2015, by and between Lion Biotechnologies, Inc. and the National Institutes of Health (incorporated herein by reference to Exhibit 10.46 to the Registrant's Annual Report on Form 10-K filed with the Commission on March 16, 2015).*
10.18	First Amendment to Patent License Agreement, effective October 2, 2015, by and between Lion Biotechnologies, Inc. and the National Institutes of Health (incorporated herein by reference to Exhibit 10.47 to the Registrant's Quarterly Report on Form 10-Q filed with the Commission on November 6, 2015).*
10.19	Form of Securities Purchase Agreement, dated June 2, 2016, by and among Lion Biotechnologies, Inc. and the Investors thereunder (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed with the Commission on June 3, 2016).
10.20	Form of Registration Rights Agreement, dated June 2, 2016, by and among Lion Biotechnologies, Inc. and the Investors thereunder (incorporated herein by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed with the Commission on June 3, 2016).
10.21	Amendment #2 to the Cooperative Research and Development Agreement #02734, dated August 18, 2016, by and between the National Cancer Institute and Lion Biotechnologies, Inc. (incorporated herein by reference to Exhibit 10.3 to Amendment No. 2 to Registrant's Registration Statement on Form S 1 filed with the Commission on August 31, 2016).
10.22	Manufacturing Services Agreement, dated November 23, 2015, by and between WuXi AppTec, Inc. and Lion Biotechnologies, Inc. (incorporated herein by reference to Exhibit 10.36 to the Registrant's Annual Report on Form 10-K filed with the Commission on March 9, 2017).*
10.23	Strategic Alliance Agreement, effective as of April 17, 2017, between Lion Biotechnologies, Inc. and The University of Texas M.D. Anderson Cancer Center (incorporated herein by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10 Q filed with the Commission on August 3, 2017).*
10.24	First Amendment to the Strategic Alliance Agreement by and between Iovance Biotherapeutics, Inc. and The University of Texas M.D. Anderson Cancer Center, effective as of August 2, 2017 (incorporated herein by reference to Exhibit 10.34 to the Registrant's Annual Report on Form 10-K filed with the Commission on March 12, 2018).
10.25	Second Amendment to the Strategic Alliance Agreement by and between Iovance Biotherapeutics, Inc. and The University of Texas M.D. Anderson Cancer Center, effective February 16, 2018 (incorporated herein by reference to Exhibit 10.35 to the Registrant's Annual Report on Form 10-K filed with the Commission on March 12, 2018).
10.26	Executive Employment Agreement, effective as of June 1, 2016, by and between Maria Fardis and Lion Biotechnologies, Inc. (incorporated herein by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10 Q filed with the Commission on August 9, 2016).*#
10.27	Severance Agreement and General Release, effective as of July 8, 2020, between Iovance Biotherapeutics, Inc. and Timothy Morris (incorporated herein by reference to Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q filed with the Commission on August 6, 2020).*#

10.28	Executive Employment Agreement, effective as of September 30, 2016, by and between Frederick G. Vogt and Lion Biotechnologies, Inc. (incorporated herein by reference to Exhibit 10.32 to the Registrant's Annual Report on Form 10 K filed with the Commission on March 12, 2018).#
10.29	Executive Employment Agreement effective as of July 18, 2019, by and between Friedrich-Reinhard Graf Finck von Finckenstein, M.D. and Iovance Biotherapeutics, Inc. (incorporated herein by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed with the Commission on August 1, 2019).
10.30	Executive Employment Agreement, effective as of December 14, 2020, by and between Jean-Marc Bellemin and Iovance Biotherapeutics, Inc.#**+
10.31	Office Lease, effective as of August 4, 2016, by and between Lion Biotechnologies, Inc. and Hudson Skyway Landing, LLC (incorporated herein by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8 K filed with the Commission on August 8, 2016).
10.32	Office Lease, effective as of October 19, 2018, by and between Iovance Biotechnologies, Inc. and Hudson Skyway Landing, LLC (incorporated herein by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8 K filed with the Commission on October 25, 2018).
10.33	First Amendment to the Office Lease, effective as of June 19, 2019, between Iovance Biotherapeutics, Inc. and Hudson Skyway Landing, LLC (incorporated herein by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed with the Commission on November 4, 2019).
10.34	Second Amendment to the Office Lease, effective as of February 8, 2021, by and between Iovance Biotherapeutics, Inc. and Hudson Skyway Landing, LLC (incorporated herein by reference to Exhibit 10.2 of the Registrant's Current Report on Form 8-K filed with the Commission on February 9, 2021).
10.35	First Amendment to the Office Lease, effective as of February 8, 2021, by and between Iovance Biotherapeutics, Inc. and Hudson Skyway Landing, LLC (incorporated herein by reference to Exhibit 10.3 of the Registrant's Current Report on Form 8-K filed with the Commission on February 9, 2021).
10.36	Lease Agreement, effective as of May 28, 2019, by and between Iovance Biotherapeutics, Inc. and 300 Rouse Boulevard, LLC (incorporated herein by reference to Exhibit 10.3 of the Registrant's Current Report on Form 8-K filed with the Commission on June 3, 2019).
10.37	First Amendment to the Lease Agreement, effective as of August 20, 2019, between Iovance Biotherapeutics, Inc. and 300 Rouse Boulevard, LLC (incorporated herein by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q filed with the Commission on November 4, 2019).
10.38	Second Amendment to the Lease Agreement, effective as of June 30, 2020, between Iovance Biotherapeutics, Inc. and 300 Rouse Boulevard, LLC (incorporated herein by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q filed with the Commission on August 6, 2020).
10.39	Lease Agreement, effective as of February 8, 2021, by and between Iovance Biotherapeutics, Inc. and ARE-San Francisco No. 63, LLC (incorporated herein by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed with the Commission on February 9, 2021).
21.1	Subsidiaries of the Company.**
23.1	Consent of Independent Registered Public Accounting Firm.**
24.1	Power of Attorney (included on the signature page of this Annual Report).
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, 2020, formatted in XBRL (eXtensible Business Reporting Language): (1) Balance Sheets as of December 31, 2020 and 2019 (2) Statements of Income for the years ended December 31, 2020 and 2019; (3) Statements of Shareholders' Equity for the years ended December 31, 2020 and 2019; (4) Statements of Cash Flows for the years ended December 31, 2020 and 2019; and (5) Notes to Financial Statements.
104	Cover Page Interactive Data File – the cover page interactive date file does not appear in the Interactive Date File because its XBRL tags are embedded within the Inline XBRL document.

* 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.

** Filed herewith.

# Indicates a management contract or compensatory plan or arrangement.

\+ Certain portions of the Exhibit have been redacted pursuant to Item 601(b)(10)(iv) of Regulation S-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.

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: February 25, 2021

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

POWER OF ATTORNEY

Know all persons by these presents, that each person whose signature appears below constitutes and appoints Maria Fardis and Jean-Marc Bellemin, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place, and stead, in any and all capacities, to sign any and all amendments to this Annual Report, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents, or any of them or their or his or her substitute or substituted, may lawfully do or cause to be done by virtue thereof.

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.

Signature	Title	Date
/s/ Maria Fardis Maria Fardis	Chief Executive Officer (Principal Executive Officer) and Director	February 25, 2021
/s/ Jean-Marc Bellemin Jean-Marc Bellemin	Chief Financial Officer and Treasurer (Principal Financial Officer)	February 25, 2021
/s/ Michael C. Swartzburg Michael C. Swartzburg	Vice President, Finance (Principal Accounting Officer)	February 25, 2021
/s/ Merrill A. McPeak Merrill A. McPeak	Director	February 25, 2021
/s/ Michael Weiser Michael Weiser	Director	February 25, 2021
/s/ Ryan D. Maynard Ryan D. Maynard	Director	February 25, 2021
/s/ Iain Dukes Iain Dukes	Director	February 25, 2021
/s/ Wayne Rothbaum Wayne Rothbaum	Director	February 25, 2021
/s/ Athena Countouriotis Athena Countouriotis	Director	February 25, 2021

IOVANCE BIOTHERAPEUTICS, INC.
Index to Financial Statements

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and Board of Directors 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, 2020 and 2019, the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, 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, 2020, 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 February 25, 2021, expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Change in Accounting Principle

As discussed in Note 10 to the consolidated financial statements, the Company changed its method of accounting for leases in 2019.

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.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Incremental Borrowing Rate (Leases)

Description of the Matter

As discussed in Note 10 to the consolidated financial statements, the Company's reported right-of-use assets, current lease liabilities and long-term lease liabilities, utilize discount rates to calculate the estimated present value of future lease payments. Since

the Company's leases do not provide an implicit rate, management utilized a third-party valuation specialist to assist in estimating the incremental borrowing rates used in its present value calculation, which required subjectivity. The incremental borrowing rate is the rate of interest that a lessee would have to pay to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. As of December 31, 2020, the weighted average incremental borrowing rate used to determine the operating lease liability is 8.3%.

Auditing management's assessment of its incremental borrowing rate is highly subjective and judgmental as the Company has no outstanding debt nor committed credit facilities, secured or otherwise, that would have comparable collateral or similar terms as their underlying leases. Further, changes in the incremental borrowing rate may have a material impact on the measurement of the Company's right-of-use assets, current lease liabilities and long-term lease liabilities. Based on the level of management judgment, we have determined the incremental borrowing rate to be a critical audit matter. This required a high degree of auditor judgment and an increased extent of effort, including the need to involve our valuation specialists, when performing audit procedures to evaluate the reasonableness of management's estimation of the incremental borrowing rate.

How We Addressed the Matter in Our Audit

Our audit procedures included, amongst others:

- We obtained an understanding, evaluated the design, and tested the operating effectiveness of management's controls with regards to the methodology, inputs, and assumptions used to determine the incremental borrowing rate, including those over management's review of its third-party specialist valuation report.
- We obtained an understanding of the factors considered and assumptions made by management and the valuation specialists in developing the estimate of the incremental borrowing rate, the sources of data relevant to these factors and assumptions and the procedures used to obtain the data, and the methods used to calculate the estimate.
- We reviewed the contractual terms of the lease agreements to ensure the commencement dates, any lease term extensions and/or early termination clauses were properly considered in determining the appropriate lease term for calculating the incremental borrowing rates.
- With the assistance of our valuation specialists, we performed an independent estimate of the incremental borrowing rate and compared the results to the Company's estimate.
- We evaluated the reasonableness of the valuation methods and assumptions used by management and the Company's valuation specialist to estimate the incremental borrowing rates for borrowing amounts and terms comparable to their outstanding leases by:
    - Developing an independent estimate of the incremental borrowing rates with the assistance of our valuation specialists by utilizing third party data related to comparable company borrowings with comparable payment terms.
    - Performing a sensitivity analysis on incremental borrowing rates used to determine the impact rate changes could have on the present value calculation of the Company's operating lease right-of-use assets and operating lease liabilities.

/s/ Marcum LLP

Marcum LLP

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

New York, NY
February 25, 2021

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

To the Shareholders and Board of Directors 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, 2020, based on criteria established in *Internal Control-Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission. In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on criteria established in *Internal Control-Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated balance sheets as of December 31, 2020 and 2019, and related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows and the related notes for each of the three years in the period ended December 31, 2020 of the Company and our report dated February 25, 2021 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 the 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 degree of compliance with the policies or procedures may deteriorate.

/s/ Marcum LLP

Marcum LLP
New York, NY
February 25, 2021

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

	December 31, 2020	December 31, 2019
ASSETS		
Current Assets		
Cash and cash equivalents	$ 67,329	$ 13,969
Short-term investments	562,108	293,112
Prepaid expenses and other assets	6,663	9,412
Total Current Assets	636,100	316,493
Property and equipment, net	59,159	8,536
Operating lease right-of-use assets	54,756	10,695
Restricted cash	5,525	5,450
Long-term assets	12,918	3,481
Total Assets	$ 768,458	$ 344,655
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities		
Accounts payable	$ 13,513	$ 15,567
Accrued expenses	35,074	16,265
Operating lease liabilities - current	6,284	7,252
Total Current Liabilities	54,871	39,084
Non-Current Liabilities		
Operating lease liabilities – noncurrent	45,375	4,248
Other liabilities	11,714	2,352
Total Non-Current Liabilities	57,089	6,600
Total Liabilities	111,960	45,684
Commitments and contingencies (Note 10 and 11)		
Stockholders' Equity		
Series A Convertible Preferred stock, $0.001 par value; 17,000 shares designated, 194 shares issued and outstanding as of December 31, 2020 and December 31, 2019 (aggregate liquidation value of $194)	—	—
Series B Convertible Preferred stock, $0.001 par value; 11,500,000 shares designated, 3,581,119 shares issued and outstanding as of December 31, 2020 and December 31, 2019 (aggregate liquidation value of $17,010)	4	4
Common stock, $0.000041666 par value; 300,000,000 shares authorized, 146,874,917 and 126,411,808 shares issued and outstanding as of December 31, 2020 and December 31, 2019, respectively	6	5
Accumulated other comprehensive income	19	220
Additional paid-in capital	1,486,662	869,354
Accumulated deficit	(830,193)	(570,612)
Total Stockholders' Equity	656,498	298,971
Total Liabilities and Stockholders' Equity	$ 768,458	$ 344,655

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,		
	2020	2019	2018
Revenues	$ —	$ —	$ —
Costs and expenses			
Research and development expenses	201,727	166,023	99,828
General and administrative expenses	60,210	40,849	28,430
Total costs and expenses	261,937	206,872	128,258
Loss from operations	(261,937)	(206,872)	(128,258)
Other income			
Interest income, net	2,356	9,316	4,678
Net Loss	(259,581)	(197,556)	(123,580)
Net Loss Per Share of Common Stock, Basic and Diluted	$ (1.88)	$ (1.59)	$ (1.27)
Weighted Average Shares of Common Stock Outstanding, Basic and Diluted	138,301	124,336	97,277

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,		
	2020	2019	2018
Net Loss	$ (259,581)	$ (197,556)	$ (123,580)
Other comprehensive loss:			
Unrealized (loss) / gain on short-term investments	(201)	262	(42)
Comprehensive Loss	$ (259,782)	$ (197,294)	$ (123,622)

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 Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholder Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance - January 1, 2018	1,694	—	7,378,241	7	73,164,914	3	394,651	—	(249,180)	145,481
Stock-based compensation expense							20,027			20,027
Vesting of restricted shares issued for services					39,536	—	—			—
Tax payments related to shares withheld for vested restricted stock units						—	(223)			(223)
Common stock issued upon exercise of warrants					6,301,216	1	15,753			15,754
Common stock issued upon exercise of stock options					1,336,514	—	9,959			9,959
Conversion of convertible preferred stock into common stock	(1,500)		(1,523,396)	(1)	2,273,396		1			—
Common stock sold in public offering, net of offering costs					40,300,000	1	398,816			398,817
Unrealized loss on short- term investments								(42)		(42)
Net loss									(123,580)	(123,580)
Balance - December 31, 2018	194	—	5,854,845	6	123,415,576	5	838,984	(42)	(372,760)	466,193
Adoption of ASU 2018-07							296		(296)	—
Stock-based compensation expense							24,277			24,277
Vesting of restricted shares issued for services					27,514	1	(1)			—
Tax payments related to shares withheld for vested restricted stock units							(312)			(312)
Common stock issued upon exercise of stock options					727,492	—	6,443			6,443
Conversion of convertible preferred stock into common stock		—	(2,273,726)	(2)	2,273,726	—	2			—
Unrealized loss on short- term investments								262		262
Cancellation of common shares from settlement of dispute					(32,500)	(1)	(335)			(336)
Net loss									(197,556)	(197,556)
Balance - December 31, 2019	194	$ —	3,581,119	$ 4	126,411,808	$ 5	$ 869,354	$ 220	$ (570,612)	$ 298,971
Stock-based compensation expense							40,775			40,775
Vesting of restricted stock shares issued for service					13,449		112			112
Tax payments related to shares withheld for vested restricted stock units							(284)			(284)
Common stock issued upon exercise of stock options					973,854		9,663			9,663
Common stock sold in public offering, net of offering costs					19,475,806	1	567,042			567,043
Unrealized gain on short- term investments								(201)		(201)
Net loss									(259,581)	(259,581)
Balance - December 31, 2020	194	$ —	3,581,119	$ 4	146,874,917	$ 6	$ 1,486,662	$ 19	$ (830,193)	$ 656,498

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,		
	2020	2019	2018
Cash Flows from Operating Activities			
Net loss	$ (259,581)	(197,556)	(123,580)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	40,887	24,277	20,027
Noncash lease expense	7,572	6,954	—
Depreciation and amortization	1,140	1,169	956
Gain on settlement of dispute	—	(336)	—
Accretion (amortization) of discounts and premiums on investments	1,865	(3,421)	(1,332)
Loss on disposal of assets	—	16	9
Changes in assets and liabilities:			
Prepaid expenses, other assets, and long-term assets	(6,688)	(3,278)	(2,065)
Operating lease liabilities (Right-of-use assets)	(11,474)	(6,148)	—
Accounts payable	(2,964)	12,706	1,507
Accrued expenses and other liabilities	24,109	6,728	3,229
Net cash used in operating activities	(205,134)	(158,889)	(101,249)
Cash Flows from Investing Activities			
Maturities of short-term investments	676,601	514,601	41,000
Purchase of short-term investments	(947,663)	(417,659)	(426,081)
Purchase of property and equipment	(46,791)	(6,917)	(1,198)
Net cash (used in) provided by investing activities	(317,853)	90,025	(386,279)
Cash Flows from Financing Activities			
Tax payments related to shares withheld for vested restricted stock units	(284)	(312)	(223)
Proceeds from the issuance of common stock upon exercise of warrants	—	—	15,754
Proceeds from the issuance of common stock upon exercise of options	9,663	6,443	9,959
Proceeds from the issuance of common stock, net	567,043	—	398,817
Net cash provided by financing activities	576,422	6,131	424,307
Net increase (decrease) in cash, cash equivalents, and restricted cash	53,435	(62,733)	(63,221)
Cash, Cash Equivalents, and Restricted Cash Beginning of Year	19,419	82,152	145,373
Cash, Cash Equivalents, and Restricted Cash End of Year	$ 72,854	$ 19,419	$ 82,152
Supplemental disclosure of non-cash investing and financing activities:			
Net unrealized (loss) gain on short-term investments	$ (201)	$ 262	(42)
Acquisitions of property and equipment included in accounts payable and accrued expense	(5,094)	122	—
Conversion of convertible preferred stock to common stock	—	2	1
Vesting of restricted stock units	—	1	—

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", "we", "us" or "our") is a clinical-stage biopharmaceutical company focused on the development and commercialization of cell therapies as novel cancer immunotherapy products designed to harness the power of a patient's own immune system to eradicate cancer cells. Tumor infiltrating lymphocyte ("TIL") therapy is an autologous cell therapy platform technology that was originally developed by the National Cancer Institute ("NCI"), which conducted initial clinical trials in diseases such as metastatic melanoma and cervical cancer. The Company has developed a new, shorter manufacturing process for TIL therapy known as Generation 2 ("Gen 2"), which yields a cryopreserved TIL product. This proprietary and scalable manufacturing method is being further investigated in multiple indications. The Company's lead product candidates include lifileucel for metastatic melanoma and metastatic cervical cancer. Lifileucel for metastatic cervical cancer was formerly known as LN-145. In addition to metastatic melanoma and metastatic cervical cancer, the Company is investigating the effectiveness and safety of TIL therapy and peripheral blood lymphocyte therapy for the treatment of squamous cell carcinoma of the head and neck, non-small cell lung cancer, and chronic lymphocytic leukemia through its sponsored trials, as well as in other oncology indications through collaborations. On June 1, 2017, the Company reincorporated from a Nevada corporation to a Delaware corporation.

Liquidity

The Company is currently engaged in the development of therapeutics to fight cancer, specifically solid tumors. The Company currently 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 significant revenues from the sale or licensing of any of its product candidates during the 12 months from the date these financial statements are issued. The Company has incurred a net loss of $259.6 million for the year ended December 31, 2020 and used $205.1 million of cash in its operating activities during the year ended December 31, 2020. As of December 31, 2020, the Company had $635.0 million in cash, cash equivalents, short-term investments, and restricted cash ($67.3 million of cash and cash equivalents, $562.1 million in short-term investments and $5.5 million in restricted cash).

The Company expects to continue its research and development activities, increase pre-commercial activities and continue the construction of the tenant improvements for its new manufacturing facility, which will increase the amount of cash used during 2021 and beyond. Specifically, the Company expects continued spending on its current and planned clinical trials, continued expansion of manufacturing activities, including construction of a manufacturing facility, higher payroll expenses as the Company increases its professional and scientific staff and continuation of pre-commercial activities. Based on the funds the Company has available as of the date these financial statements are issued, the Company believes that it has sufficient capital to fund its anticipated operating expenses and capital expenditures as planned for at least the next twelve months from the date these financial statements are issued.

Impact of COVID-19

In December 2019, a novel coronavirus known as SARS-CoV-2 was first detected in Wuhan, Hubei Province, People's Republic of China, causing outbreaks of the coronavirus disease, known as COVID-19, that has now spread globally. On January 30, 2020, the World Health Organization ("WHO") declared COVID-19 a pandemic (the "COVID-19 Pandemic"). The Secretary of Health and Human Services declared a public health emergency on January 31, 2020, under section 319 of the Public Health Service Act (42 U.S.C. 247d), in response to the COVID-19 Pandemic. The full impact of the COVID-19 Pandemic is unknown and rapidly evolving. While the potential economic impact brought by and over the duration of the COVID-19 Pandemic may be difficult to assess or predict, the COVID-19 Pandemic has resulted in significant disruption of global financial markets, which could in the future negatively affect the Company's liquidity. In addition, a recession or market volatility resulting from the COVID-19 Pandemic could affect the Company's business. Given the nature and type of the Company's short-term investments in U.S. government securities, the Company does not believe the COVID-19 Pandemic has had or will have a material impact on the Company's current investment liquidity.

Concentrations of Risk

The Company is subject to credit risk from its portfolio of cash equivalents and short-term investments. Under its investment policy, the Company limits amounts invested in such securities by credit rating, maturity, industry group, investment type and issuer,

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

except for securities issued by the U.S. government. The Company does not believe it is exposed to any significant concentrations of credit risk from these financial instruments. The goals of its investment policy, in order of priority, are as follows: safety and preservation of principal and diversification of risk and liquidity of investments sufficient to meet cash flow requirements.

NOTE 2. SUMMARY OF SIGNIFICANT ACCOUNTING PRACTICES

Cash, Cash Equivalents, and Short-term Investments

The Company's cash and cash equivalents include short-term investments with original maturities of three months or less when purchased. 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 loss or income. Any impairment losses related to credit losses (if any) are included in an allowance for credit losses with an offsetting entry to net loss. No impairment losses related to credit losses were recognized for the years ended December 31, 2020 and 2019. The cost of debt securities is adjusted for the amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in net interest income in the Consolidated Statements of Operations. Gains and losses on securities sold are recorded based on the specific identification method and are included in net interest income in the Consolidated Statements of Operations. The Company has not incurred any realized gains or losses from sales of securities to date. 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, except for securities issued by the U.S. government. Currently the Company invests excess cash only in obligations issued by the U.S. government and U.S. government agencies.

Restricted Cash

The Company maintains a certain minimum balance, approximately $5.5 million in a segregated bank account in connection with a letter of credit, one for $5.45 million for the benefit of the landlord for its commercial manufacturing facility used as a security deposit for the lease (See Note 10 - Leases), and a second one for $74,685 for the benefit of a utilities service provider. The total amount is classified as Restricted Cash on the Consolidated Balance Sheet. The letter of credit originally expired on May 28, 2020, however, it automatically extends for additional one-year periods, without written agreement, to May 28 in each succeeding calendar year, through at least 60 days after the lease expiration date. Further, on the expiration of the seventh year of the lease, and each anniversary date thereafter, the letter of credit may be decreased by $1,000,000, with a minimum security deposit of $1,450,000 maintained through the end of the lease term. The $74,685 letter of credit will expire on March 9, 2021, however, it will be automatically extended, without written agreement, to the expiration date of December 1, 2022. As of December 31, 2020 and 2019, restricted cash consisted of $5.5 million and this amount has been classified as a non-current asset on the Company's Consolidated Balance Sheets.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash, reported within the Consolidated Balance Sheets that sum to the total of the same such amounts shown in the Consolidated Statements of Cash Flows:

	December 31, 2020	December 31, 2019	December 31, 2018
Cash and cash equivalents	$ 67,329	$ 13,969	$ 82,152
Restricted cash (included in non-current assets on the Consolidated Balance Sheets)	5,525	5,450	—
Total cash, cash equivalents and restricted cash	$ 72,854	$ 19,419	$ 82,152

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

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. The depreciation or amortization of capitalized construction in progress costs, a component of property and equipment, net, begins once the underlying asset is placed into service and is recognized over the estimated useful lives:

Computer equipment	2 years
Office furniture and equipment	5 years
Lab equipment	5 years
Leasehold improvements	Lesser of the remaining economic 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 Consolidated 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 undiscounted 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, 2020, 2019, and 2018, the Company did not recognize any impairments for its property and equipment.

Loss per Share

Basic net loss per share is computed by dividing the net loss by the weighted average number of common shares outstanding during the period.

Diluted net loss per share is computed by dividing the net loss by the sum of the weighted average number of shares of common stock outstanding and the dilutive common stock equivalent shares outstanding during the period. The Company’s potentially dilutive common stock equivalent shares, which include incremental common shares issuable upon (i) the exercise of outstanding stock options and warrants, (ii) purchases though the 2020 Employee Stock Purchase Plan (the “2020 ESPP”), (iii) vesting of restricted stock units and restricted stock awards, and (vi) conversion of preferred stock, are only included in the calculation of diluted net loss per share when their effect is dilutive.

At December 31, 2020, 2019, and 2018, 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,		
	2020	2019	2018
Stock options	12,615,638	9,494,712	6,889,287
Series A Convertible Preferred Stock*	97,000	97,000	97,000
Series B Convertible Preferred Stock*	3,581,119	3,581,119	5,854,845
2020 ESPP	37,259	—	—
Restricted stock units	—	22,916	68,742
	16,331,016	13,195,747	12,909,874

**on an as-converted basis*

The dilutive effect of potentially dilutive securities would be reflected in diluted earnings per common share by application of the treasury stock method. Under the treasury stock method, an increase in the fair market value of the Company's common stock could result in a greater dilutive effect from potentially dilutive securities.

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—These are investments where values are based on unadjusted quoted prices for identical assets in an active market that the Company has the ability to access.

Level 2—These are investments where values are based on quoted market prices in markets that are not active or model derived valuations in which all significant inputs are observable in active markets

The Company does not have fair valued assets classified under Level 2 as of December 31, 2020 and 2019.

Level 3—These are financial instruments where values are derived from techniques in which one or more significant inputs are unobservable.

The Company does not have fair valued assets classified under Level 3 as of December 31, 2020 and 2019.

The Company's financial instruments consist of cash and cash equivalents and short-term investments, all of which are reported at their respective fair value on its Consolidated Balance Sheets.

As of December 31, 2020 and 2019, 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, 2020			
	Level 1	Level 2	Level 3	Total
U.S. treasury securities	$ 470,109	$ —	$ —	$ 470,109
U.S. government agency securities	91,999	—	—	91,999
Total	$ 562,108	$ —	$ —	$ 562,108

	Assets at Fair Value as of December 31, 2019			
	Level 1	Level 2	Level 3	Total
US treasury securities	$ 242,249	$ —	$ —	$ 242,249
US government agency securities	50,863	—	—	50,863
Total	$ 293,112	$ —	$ —	$ 293,112

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 the assumptions made in valuing stock instruments issued for services and used in measuring operating right-of-use assets and operating lease liabilities, accounting for potential liabilities, capitalization of internal-use software development costs, and the valuation allowance associated with the Company's deferred tax assets.

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 subsidiaries, Iovance Biotherapeutics Manufacturing LLC and Iovance Biotherapeutics GmbH. All intercompany accounts and transactions have been eliminated. The U.S. dollar is the functional currency for all the Company's consolidated operations.

Leases

The Company determines if an arrangement includes a lease at inception. Operating leases are included in its Consolidated Balance Sheet as Operating lease right-of-use assets and Operating lease liabilities as of December 31, 2020. Operating lease right-of-use assets represent the Company's right to use an underlying asset for the lease term and operating lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease right-of-use assets and liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. In determining the net present value of lease payments, the Company uses an estimated incremental borrowing rate that is applicable to the Company based on the information available at the later of the lease commencement date or the date of adoption of Accounting Standard Update (ASU) No. 2016-02 and ASU No. 2018-10, Leases (together "Topic 842"). The operating lease right-of-use assets also include any lease payments made less lease incentives. The Company's leases may include options to extend or terminate the lease, which is considered in the lease term when it is reasonably certain that the Company will exercise any such options. Lease expense is recognized on a straight-line basis over the expected lease term. The Company has elected not to apply the recognition requirements of Topic 842 for short-term leases.

For lease agreements entered into after the adoption of Topic 842 that include lease and non-lease components, such components are generally accounted for separately.

Stock-Based Compensation

The Company periodically grants stock options to employees in non-capital raising transactions as compensation for services rendered. The Company also offers employee stock purchase plans to employees. The Company accounts for all stock-based payment awards made to employee, including the employee stock purchase plans, 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. Upon the adoption of ASU No. 2018-07, Compensation-Stock Compensation ("Topic 718"), the Company accounts for stock option grants to non-employees in a similar manner as stock option grants to employees except for the term used in the grant date fair value, therefore no longer requiring a re-measurement at the then-current fair values at each reporting date until the shares underlying the options have vested. The non-employee awards that contain a performance condition that affects the quantity or other terms of the award are measured based on the outcome that is probable.

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. The stock-based compensation expense is recorded based upon the value derived from the Black-Scholes option pricing model. The assumptions used in the Black-Scholes option pricing model could materially affect compensation expense recorded in future periods.

The Company has in the past issued restricted stock units ("RSU") and restricted stock awards ("RSA") as part of its share-based compensation programs. The Company measures the compensation cost with respect to RSUs and RSAs 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 awards.

The fair value of RSUs and RSAs is based on the closing price of the Company's common stock on the grant date.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Cloud Computing Arrangements

The Company defers implementation costs incurred in cloud computing arrangements in accordance with ASC 2018-15 and amortizes it over the noncancelable term of the cloud computing arrangements plus any optional renewal periods (1) that are reasonably certain to be exercised by the Company or (2) for which exercises of the renewal option is controlled by the cloud service provider. Costs incurred during the application development stage that are directly attributable to developing or obtaining software for internal use are defined as implementation costs and capitalized. Costs incurred during operation and post-implementation stages are charged to expense.

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 trial 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, marketing, commercial 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, 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.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act") was enacted and signed into law, and GAAP requires recognition of the tax effects of new legislation during the reporting period that includes the enactment date. The CARES Act, among other things, includes changes to the tax provisions that benefits business entities and makes certain technical corrections to the 2017 Tax Cuts and Jobs Act. The tax relief measures for business entities include a five-year net operating loss ("NOL") carrybacks, suspension of annual deduction limitation of 80% taxable income from net operating losses generated in a tax year beginning after December 31, 2017, changes in the deductibility of interest, acceleration of alternative minimum tax credit refunds, payroll tax relief, and technical correction to allow accelerated deductions for qualified improvement property. The CARES Act also provides other non-tax benefits to assist those impacted by the pandemic. The Company evaluated the impact of the CARES Act and determined the impact is immaterial.

Concentrations

The Company is subject to credit risk from its portfolio of cash equivalents and short-term investments. Under its investment policy, the Company limits amounts invested in such securities by credit rating, maturity, industry group, investment type and issuer, except for securities issued by the U.S. government. The Company does not believe it is exposed to any significant concentrations of credit risk from these financial instruments. The goals of its investment policy, in order of priority, are as follows: safety and preservation of principal and diversification of risk; liquidity of investments sufficient to meet cash flow requirements. The Company maintains cash, cash equivalents and short-term investment balances at three financial institutions. Management believes that the financial institutions which hold its cash are financially sound and, accordingly, minimal credit risk exists. As of December 31, 2020, and 2019, respectively, the Company's cash balances were in excess of insured limits maintained at the financial institutions.

Recent Accounting Standards

Financial Instruments

In June 2016, the FASB issued ASU 2016-13, Financial Instruments - Credit Losses, and also issued subsequent amendments to the initial guidance, ASU 2018-19, ASU 2019-04, ASU 2019-05, ASU 2019-11, and ASU 2020-03 (collectively, Topic 326), to introduce a new impairment model for recognizing credit losses on financial instruments based on an estimate of current expected credit losses ("CECL"). Under Topic 326, an entity is required to estimate CECL on available-for-sale ("AFS") debt securities only when the fair value is below the amortized cost of the asset and is no longer based on an impairment being "other-than-temporary". Topic 326 also requires the impairment calculation on an individual security level and requires an entity use present value of cash flows when estimating the CECL. The credit-related losses are required to be recognized through earnings and non-credit related losses are reported in other comprehensive income. In April 2019, the FASB further clarified the scope of Topic 326 and addressed issues related to accrued interest receivable balances, recoveries, variable interest rates and prepayment. Topic 326 will be effective for public entities in fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. The new guidance requires modified retrospective application to all outstanding instruments, with a cumulative effect adjustment recorded to opening retained earnings as of the beginning of the first period in which the guidance becomes effective. The Company adopted this guidance on January 1, 2020, however, the adoption of this new guidance did not have any material impact on its consolidated financial statements.

Cloud Computing Arrangements

In August 2018, the FASB issued ASU 2018-15, Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40) Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract (ASU 2018-15). The guidance requires a customer in a cloud computing arrangement that is a service contract to follow the internal use software guidance to determine which implementation costs to defer and recognize as an asset. It therefore requires a customer to defer potentially significant implementation costs incurred in a cloud computing arrangement that were often expensed as incurred under the legacy GAAP and recognize them as expense over the term of the hosting arrangement. ASU 2018-15 is effective for fiscal years beginning subsequent to December 15, 2019. The Company adopted this guidance on January 1, 2020. The Company recorded $1.4 million as prepaid expenses and long-term assets on the Consolidated Balance Sheet as of December 31, 2020. The Company recorded $0.2 million of amortization expense for the year ended December 31, 2020.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Segment reporting

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

Subsequent Events

Management of the Company evaluates events that have occurred after the balance sheet date through the date the financial statements are issued. See Note 14 - Subsequent Events.

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

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

	December 31, 2020	December 31, 2019
Cash equivalents - Money market funds	$ 49,720	$ 10,049
Cash equivalents total	$ 49,720	$ 10,049

Cash equivalents in the tables above exclude cash demand deposits of $17.6 million and $3.9 million as of December 31, 2020 and 2019, respectively (in thousands).

Short-term investments	December 31, 2020	December 31, 2019
U.S. treasury securities	$ 470,109	$ 242,249
U.S. government agency securities	91,999	50,863
Short-term investments total	$ 562,108	$ 293,112

The cost and fair value of cash equivalents and short-term investments at December 31, 2020 and 2019 were as follows (in thousands):

As of December 31, 2020	Cost	Accretion (Amortization)	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	$ 471,702	$ (1,594)	$ 30	$ (29)	$ 470,109
U.S. government agency securities	92,248	(267)	20	(2)	91,999
Total	$ 563,950	$ (1,861)	$ 50	$ (31)	$ 562,108

As of December 31, 2019	Cost	Accretion	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	$ 241,709	$ 364	$ 179	$ (3)	$ 242,249
U.S. government agency securities	50,712	107	44	—	50,863
Total	$ 292,421	$ 471	$ 223	$ (3)	$ 293,112

Unrealized gains and losses are included in accumulated other comprehensive loss. All short-term investments held by the Company as of December 31, 2020 and 2019 have a maturity of less than one year.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 4. PROPERTY AND EQUIPMENT

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

	December 31, 2020	December 31, 2019
Lab equipment	$ 4,656	$ 4,530
Leasehold improvements	2,573	2,372
Computer equipment	270	258
Office furniture and equipment	480	457
Construction in progress	56,758	5,417
Total Property and equipment, cost	64,737	13,034
Less: Accumulated depreciation and amortization	(5,578)	(4,498)
property and equipment, net	$ 59,159	$ 8,536

Depreciation expense for the years ended December 31, 2020, 2019, and 2018 was approximately $1.1 million, $1.2 million and $1.0 million, respectively.

NOTE 5. ACCRUED EXPENSES

Accrued expenses consist of the following (in thousands):

	December 31, 2020	December 31, 2019
Clinical related	$ 15,661	$ 4,692
Accrued payroll and employee related expenses	9,032	6,866
Commercial manufacturing facility related	4,342	—
Manufacturing related	3,266	2,184
Legal and related services	1,061	866
Accrued other	1,712	1,657
	$ 35,074	$ 16,265

NOTE 6. STOCKHOLDERS' EQUITY

Authorized Shares of Common Stock

On June 10, 2019, the certificate of incorporation of the Company was amended to increase the number of authorized shares of the Company's common stock, par value $0.000041666, from 150,000,000 shares to 300,000,000 shares (the "Certificate of Amendment"). The Certificate of Amendment was approved by the Company's stockholders at the Company's 2019 Annual Meeting of Stockholders held on June 10, 2019.

Public Offerings

In June 2020, the Company closed an underwritten public offering of 16,935,484 shares of the Company's common stock at a public offering price of $31.00 per share, before underwriting discounts, which included 2,540,322 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 "June 2020 Public Offering"). The gross proceeds from the offering, before deducting the underwriting discounts and commissions and other offering expenses payable by the Company, were $603.7 million, with net proceeds to the Company of $567.0 million.

In October 2018, the Company completed an underwritten public offering of 25,300,000 shares of the Company's common stock at a public offering price of $9.97 per share, before underwriting discounts, which included 3,300,000 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.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The gross proceeds from the offering, before deducting the underwriting discounts and commissions and other estimated offering expenses payable by the Company, were $252.2 million, with net proceeds to the Company of $236.7 million.

In January 2018, the Company closed an 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 offering expenses payable by the Company, were $172.5 million, with net proceeds to the Company of $162.0 million.

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, 2020, 17,000 shares were designated as Series A Convertible Preferred Stock and 11,500,000 shares were designated as Series B Convertible Preferred Stock ("Series B Convertible Preferred Stock").

Series A Convertible Preferred Stock

A total of 17,000 shares of Series A Convertible 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 Convertible 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. Each share of Series A Preferred Stock is initially convertible into 500 shares of common stock.

The Series A Convertible Preferred Stock may, at the option of each investor, be converted into fully paid and non-assessable shares of common stock. The holders of shares of Series A Convertible 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 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 Convertible Preferred Stock shall first receive an equal dividend on each outstanding share of Series A Convertible Preferred Stock.

No Shares of Series A Convertible Preferred Stock were converted during the year ended December 31, 2020 and 2019. At December 31, 2020 and 2019, 194 shares of Series A Convertible Preferred Stock (that are convertible into 97,000 shares of common stock) remained outstanding.

Series B Convertible Preferred Stock

A total of 11,500,000 shares of Series B Convertible Preferred Stock are authorized for issuance under the Company's Series B Certificate of Designation of Rights, Preferences and Privileges of Series B Convertible Preferred Stock. The shares of Series B Convertible 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. Each share of Series B Preferred Stock is initially convertible into 1 share of common stock.

The Series B Convertible Preferred Stock may, at the option of each investor, be converted into fully paid and non-assessable shares of common stock. The holders of Series B Convertible 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 common stock and preferred stock, pro rata based on the number of shares held by each holder. Holders of Series B Convertible 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 Convertible Preferred Stock or the Company's common stock. So long as any Series B Convertible Preferred Stock remains outstanding, the Company may not redeem, purchase or otherwise acquire any material amount of the Series A Convertible Preferred Stock or any securities junior to the Series B Convertible Preferred Stock.

No Shares of Series B Convertible Preferred Stock were converted during the year ended December 31, 2020. A total of 2,273,726 shares of Series B Convertible Preferred Stock were converted into 2,273,726 shares of common stock during the year ended December 31, 2019. At December 31, 2020 and 2019, 3,581,119 shares of Series B Preferred Stock (that are convertible into 3,581,119 shares of common stock) remained outstanding, respectively.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Cancellation of Common Shares

On September 30, 2013, the Company and a third party entered into an agreement under which the Company issued 50,000 shares of unregistered stock in the Company to the third party. On January 16, 2019, the two parties entered into a confidential settlement agreement in connection with a dispute related to their prior relationship and activities. As part of the settlement, the third party returned 32,500 shares of common stock to the Company for cancellation and retained the remaining 17,500 shares. The Company included a gain of $335,000 on cancellation of 32,500 shares in Other income in its Consolidated Statement of Operations.

Warrants

There were no remaining outstanding warrants as of December 31, 2020 and 2019.

Restricted Stock Units

On June 1, 2016, the Company entered into an RSU agreement with the Company's Chief Executive Officer, Maria Fardis, Ph.D., pursuant to which the Company granted Dr. Fardis 550,000 non-transferrable RSU 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 RSU vest in installments as follows: (i) 137,500 RSU vested upon the first anniversary of the effective date of Dr. Fardis' employment agreement; (ii) 275,000 RSU vest upon the satisfaction of certain clinical trial milestones; and (iii) 137,500 RSU vest in equal monthly installments over the 36-month period following the first anniversary of the effective date of Dr. Fardis' employment, such that the RSUs were fully vested as of June 1, 2020. At December 31, 2020, the Company had no RSUs outstanding.

Stock-based compensation expense for restricted stock units are measured based on the closing fair market value of the Company's common stock on the date of grant. The stock-based compensation expenses relating to restricted stock units were $0.1 million, $0.3 million, and $0.3 million for the years ended December 31, 2020, 2019, and 2018, respectively, recorded as part of general and administrative expenses.

Equity Incentive Plans

On October 14, 2011, the Company's Board of Directors (the "Board") 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 Board 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 Board 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. At December 31, 2020, 11,240 shares were available for future grant under the 2011 Plan.

On September 19, 2014, 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, 2020, 61,575 shares were available for grant under the Company's 2014 Plan.

On April 22, 2018, the Board adopted the Iovance Biotherapeutics, Inc. 2018 Equity Incentive Plan (the "2018 Plan"). The 2018 Plan was approved by the Company's stockholders at the annual meeting of stockholders held in June 2018. The 2018 Plan as

approved by the stockholders authorized the issuance up to an aggregate of 6,000,000 shares of common stock reserved for issuance in the form of incentive (qualified) stock options, non-qualified options, common stock, stock appreciation rights, restricted stock awards, restricted stock units, other stock-based awards, other cash-based awards or any combination of the foregoing. On June 8, 2020, the Company's stockholders approved an amendment to the 2018 Plan to increase the number of shares available for issuance upon the exercise of stock options under the 2018 Plan from 6,000,000 to 14,000,000 shares, which became effective immediately. At December 31, 2020, 7,455,537 shares of common stock were available for grant under the Company's 2018 Plan.

Stock Options

A summary of the status of stock options at December 31, 2020, 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 Contract Life	Aggregate Intrinsic Value (in thousands)
Outstanding at January 1, 2018	6,072,368	$ 7.42		
Issued	2,960,620	14.73		
Exercised	(1,336,514)	7.45		
Expired/Cancelled	(807,187)	10.04		
Outstanding at December 31, 2018	6,889,287	$ 10.25		
Issued	4,166,600	14.73		
Exercised	(727,492)	8.85		
Expired/Cancelled	(833,683)	13.87		
Outstanding at December 31, 2019	9,494,712	$ 12.00		
Issued	4,981,001	28.17		
Exercised	(973,854)	9.92		
Expired/Cancelled	(886,221)	18.67		
Outstanding at December 31, 2020	12,615,638	$ 18.08	7.81	$ 358,726
Options exercisable at December 31, 2020	6,401,443	$ 11.70	6.67	$ 222,631

A summary of outstanding and exercisable stock options as of December 31, 2020 is as follows:

	Options Outstanding			Options Exercisable		
Range of Exercise Prices	Number of Shares	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price Per Share	Number of Shares	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price Per Share
$ 5.05-$ 7.3	1,307,133	5.26	$ 5.98	1,307,133	5.26	$ 5.98
$ 7.4-$ 8.17	1,309,536	5.70	7.67	1,300,911	5.68	7.67
$ 8.3-$ 11.05	1,072,016	6.92	9.60	808,228	6.55	9.54
$ 11.15-$ 11.26	1,377,597	7.93	11.26	812,887	7.76	11.26
$ 11.44-$ 16.8	1,481,860	7.33	15.57	1,282,900	7.30	15.71
$ 16.94-$ 22.9	1,291,100	8.54	19.73	674,672	8.33	19.59
$ 23-$ 23.87	256,300	9.08	23.59	12,375	8.90	23.17
$ 23.88-$ 23.88	1,369,946	9.05	23.88	—	—	—
$ 23.93-$ 25.78	1,406,500	8.97	25.32	76,787	8.56	25.65
$ 27.5-$ 117	1,743,650	9.54	35.25	125,550	8.77	36.54
	12,615,638	7.81	$ 18.08	6,401,443	6.67	$ 11.70

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Employee Stock Purchase Plan

In June 2020, the Company adopted the 2020 ESPP upon its approval by the Company's shareholders at its Annual Stockholders Meeting on June 8, 2020. The Company reserved 500,000 shares of its common stock for issuance under the 2020 ESPP.

Under the 2020 ESPP, employees of the Company can purchase shares of our common stock based on a percentage of their compensation subject to certain limits. The purchase price per share is equal to the lower of 85% of the fair market value of its common stock on the offering date or the purchase date with a six month look-back feature. The 2020 ESPP purchases are settled with common stock from the 2020 ESPP's previously authorized and available pool of shares.

The compensation expense related to the 2020 ESPP for the year ended December 31, 2020 was $0.06 million. As of December 31, 2020, no shares were issued under the 2020 ESPP and there was $0.5 million of unrecognized compensation cost associated with the 2020 ESPP, which will be recognized over 6 months.

Stock-Based Compensation

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

	Years Ended December 31,		
	2020	2019	2018
Research and development	$ 19,727	$ 11,396	$ 9,305
General and administrative	21,160	12,881	10,722
Total stock-based compensation expenses	$ 40,887	$ 24,277	$ 20,027

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

	Years Ended December 31,		
	2020	2019	2018
Stock option expenses	$ 40,714	$ 23,964	$ 19,758
Restricted stock unit expenses	112	313	269
2020 ESPP expenses	61	—	—
Total stock-based compensation expenses	$ 40,887	$ 24,277	$ 20,027

As of December 31, 2020, there was $75.9 million of total unrecognized compensation expenses related to non-vested employee options to be recognized over a weighted average period of 1.90 years.

The weighted average grant date fair value for employee options granted under the Company's stock option plans during the years ended December 31, 2020, 2019, and 2018 was $17.32, $9.48, and $14.44 per option respectively.

The aggregate intrinsic value in the table above reflects the total pre-tax intrinsic value (the difference between the Company's closing stock price on the last trading day of the year ended December 31, 2020 and the exercise price of the options, multiplied by the number of in-the-money stock options) that would have been received by the option holders had all option holders exercised their options on December 31, 2020. The intrinsic value of the Company's stock options changes based on the closing price of the Company's common stock.

The total pre-tax intrinsic value of stock options exercised during the year ended December 31, 2020, 2019, and 2018 were $21.4 million, $5.3 million, and $2.3 million, respectively.

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The following table summarizes the assumptions relating to options granted pursuant to the Company's equity incentive plans for the years ended December 31, 2020, 2019, and 2018:

	Stock Option			ESPP
	Years Ended December 31,			
Assumptions:	2020	2019	2018	2020
Expected term (years)	5.18 - 6.19	6.14 - 6.06	6.50 - 5.13	0.50
Expected volatility	69.99% - 70.99%	71.62% - 70.63%	200.28% - 167.54%	54.90%
Risk-free interest rate	0.28% - 1.83%	2.59% - 1.62%	2.97% - 2.27%	0.09%
Expected dividend yield	0%	0%	0%	0%

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 based on historical exercises, cancellations, and forfeitures of stock options and outstanding option shares

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.

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 $1.2 million, $0.9 million, and $0.5 million for the years ended December 31, 2020, 2019, and 2018, respectively.

NOTE 8. INCOME TAXES

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

	As of December 31,	
	2020	2019
Deferred income tax asset:		
Net operating loss carry forward	$ 144,087	$ 95,473
Stock-based compensation	11,364	8,851
Tax credit carry forwards	32,508	22,711
Lease liabilities	11,051	2,529
Depreciation and amortization	250	98
Reserves and accruals	1,866	1,410
Deferred tax assets before valuation allowance	201,126	131,072
Less: valuation allowance	(189,412)	(128,720)
Net deferred income tax assets	11,714	2,352
Deferred tax liabilities:		
Depreciation and amortization	(11,714)	(2,352)
Net deferred tax assets (liabilities)	$ —	$ —

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

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

	Years ended December 31,		
	2020	2019	2018
Federal statutory tax rate	(21)%	(21)%	(21)%
Orphan Drug & Research credits	(3)	(4)	(3)
Permanent and other differences	1	1	1
Tax rate change	—	—	—
State tax, net of federal benefit	—	(2)	(1)
	(23)%	(26)%	(24)%
Valuation allowance	23 %	26 %	24 %
Effective tax rate	— %	— %	— %

The components of income tax expense (benefit) are as follows (in thousands):

	Years Ended December 31,		
	2020	2019	2018
Federal:			
Current	$ —	$ —	$ —
Deferred	(59,931)	(47,010)	(28,277)
State and Local			
Current	—	—	—
Deferred	(760)	(3,564)	(2,020)
Change in Valuation Allowance	60,691	50,574	30,297
Total income tax expense (benefit)	$ —	$ —	$ —

The Company had net operating loss carryovers (“NOLs”) for federal and state income tax purposes of approximately $662.4 million and $128.9 million, respectively, as of December 31, 2020. $142.4 million of federal NOLs will expire beginning in 2027, while $520.0 million generated after Tax Reform will have an indefinite life. The state NOLs will expire if unused in years 2030 through 2038.

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 Code (“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. The Company’s utilization of NOLs may also be adversely affected by future changes in federal and state tax laws and regulations.

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, 2020, 2019, and 2018, the change in the valuation allowance was approximately $60.7 million, $50.6 million, and $30.3 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 income tax expenses in the Consolidated Statement of Operations. Penalties would be recognized as a component of "General and Administrative Expenses" in the Consolidated Statement of Operations.

A reconciliation of the beginning and ending balances of the unrecognized tax benefits during the years ended December 31, 2020, 2019, and 2018 is as follows (in thousands):

	Years Ended December 31,		
	2020	2019	2018
Unrecognized benefit - beginning of period	$ 10,038	$ 6,344	$ 4,111
Gross decreases - prior period tax positions	—	—	118
Gross increase current period tax positions	4,394	3,694	2,115
Unrecognized benefit - end of period	$ 14,432	$ 10,038	$ 6,344

No interest or penalties on unpaid tax were recorded during the years ended December 31, 2020, 2019, and 2018, 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 U.S. federal and U.S. state taxing authorities may choose to audit tax returns for tax years beyond the statute of limitation period due to significant tax attribute carryforwards from prior years, making adjustments only to carryforward attributes. The Company is not currently under examination by income tax authorities in federal, state or other foreign jurisdictions.

NOTE 9. 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 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, the Company 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 Human Papilloma Virus ("HPV")-associated cancers.

In August 2016, the NCI and the Company entered 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 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, as amended, the Company is 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. The Company recorded costs associated with the CRADA of $2.0 million, $2.2 million, and $2.0 million for the years ended December 31, 2020, 2019 and 2018, respectively, as research and development expenses.

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Patent License Agreement Related to the Development and Manufacture of TIL

Effective October 5, 2011, the Company entered into an Exclusive Patent License Agreement (the "Patent License Agreement") with the NIH, an agency of the U.S. 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. The Company anticipates making a milestone payment in conjunction with the submission of a Biologics License Application for any of its product candidates covered by the Patent License Agreement.

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. Under the Exclusive Patent License Agreement, the Company 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 U.S., and the first commercial sale of a licensed product or process in any foreign country.

H. Lee Moffitt Cancer Center

Research Collaboration and Clinical Grant Agreements with Moffitt

In December 2016, the Company entered into a new three-year Sponsored Research Agreement with H. Lee Moffitt Cancer Center ("Moffitt") which expired in December 2019. In June 2020, the Company entered into a new Sponsored Research Agreement with Moffitt, with a term that ends either upon completion of the research thereunder or on July 1, 2022, whichever is sooner, and under which immaterial payments will be made to Moffitt in connection with the research services thereunder. 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, under which the Company obtained a non-exclusive, royalty-free license to any new Moffitt inventions made in the performance of the agreement. Under both clinical grant agreements with Moffit, the Company has non-exclusive rights to clinical data arising from the respective clinical trials. In the years ended December 31, 2020, 2019 and 2018, the Company recorded research and development costs of $0.6 million, $0.7 million, and $1.2 million, respectively, in connection with the research collaboration and clinical grant agreements with Moffitt.

Exclusive License Agreements with Moffitt

The Company entered into a license agreement with Moffitt (the "First 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 using toll-like receptor agonists. 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 First 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 First 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 First Moffitt License related to the treatment of any cancers in the U.S., Europe and Japan and in other countries designated by the Company in agreement with Moffitt. No expenses were recorded for the First Moffitt License for the year ended December 31, 2020, 2019, and 2018.

The Company entered into a license agreement with Moffitt effective as of May 7, 2018 (the “Second Moffitt License”), under which the Company received a license to Moffitt’s rights to patent-pending technologies related to the use of 4-1BB agonists in conjunction with TIL manufacturing processes and therapies. Pursuant to the Second Moffitt License, the Company paid an upfront licensing fee in the amount of $0.1 million in 2018. An annual license maintenance fee is also payable commencing on the first anniversary of the effective date. In addition, the Company agreed to pay an annual commercial use payment for each indication for which a first sale has occurred, which in the aggregate amounts to up to $0.4 million a year. The Company recorded $0.1 million for the years ended December 31, 2020, 2019 and 2018 as research and development expenses in connection with this agreement.

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 (“MDACC”) under which the Company and MDACC 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 acquired 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 MDACC reasonably necessary to exploit, including the commercialization thereof. The Company has also been granted certain rights in clinical data generated by MDACC 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 MDACC thereunder. In May 2017, the Company made a prepayment of $1.4 million followed by subsequent payment of $2.5 million under this agreement. The Company recorded $1.1 million, $3.4 million and $0.8 million associated with the SAA for the year ended December 31, 2020, 2019, and 2018 as research and development expenses, respectively.

WuXi

In November 2016, the Company entered into a three-year manufacturing and services agreement (“MSA”) with WuXi AppTec, Inc. (“WuXi”) pursuant to which WuXi agreed to provide manufacturing and other services, which has since been amended and assigned to our subsidiary Iovance Biotherapeutics Manufacturing LLC. Under the agreement, the Company entered into two statements of work for two cGMP manufacturing suites to be established and operated by WuXi for the Company, both of the suites are expected to be capable of being used for the commercial manufacture of its products. The statements of work for the first suite were amended in 2019 and September 2020, and the second suite was amended in 2019. The statements of work for facility include a fixed component to reserve a dedicated suite and a trained work force, and a variable component, mainly materials and testing used during the manufacturing processes. Both statements of work provide for adjustments to the targeted production capacity levels and the corresponding fixed quarterly fees upon written notice from the Company of 30 days and 90 days for the first and second dedicated suites, respectively. The terms of the related statements of work for the first and second dedicated manufacturing suites currently extend to August 2022 and June 2021, respectively. The Company recorded costs associated with agreements with WuXi of $20.6 million, $28.4 million, and $15.1 million for the years ended December 31, 2020, 2019, and 2018 respectively, as research and development expenses.

Cellectis

On January 12, 2020, the Company entered into a research collaboration and exclusive worldwide license agreement whereby the Company will license gene-editing technology from Cellectis S.A. ("Cellectis"), a clinical-stage biopharmaceutical company, in order to develop TIL therapies that have been genetically edited. Financial terms of the license include development, regulatory and sales milestone payments from the Company to Cellectis, as well as royalty payments based on net sales of TALEN-modified TIL

products. The Company recorded costs associated with the license agreement from Cellectis of $0.4 million the year ended December 31, 2020, respectively.

Novartis

On January 12, 2020, the Company obtained a license from Novartis Pharma AG ("Novartis") to develop and commercialize an antibody cytokine engrafted protein, which the Company refers to as IOV-3001. Under the agreement, the Company has paid an upfront payment to Novartis and may pay future milestones related to initiation of patient dosing in various phases of clinical development for IOV-3001 and approval of the product in the U.S., EU and Japan. Novartis is also entitled to low-to-mid single digit percentage royalties from commercial sales of the product. The Company recorded costs associated with the license agreement from Novartis of $10.0 million as research and development expenses for the year ended December 31, 2020.

NOTE 10. LEASES

Facilities Leases

The Company has evaluated the following existing facility leases and determined that, effective upon the adoption of Topic 842, they were all operating leases. Operating lease right-of-use assets and liabilities were recognized as of January 1, 2019 based on the present value of the remaining lease payments over the lease term. As the Company's leases do not provide an implicit rate, the Company utilized a third party in determining an incremental borrowing rate based on the information available as of the adoption date of Topic 842 to obtain the present value of lease payments. The Company's lease terms may include options to extend or terminate the lease which are included in the lease term when it is reasonably certain that it will exercise any such options. Lease expense is recognized on a straight-line basis over the expected lease term. The Company elected not to apply the recognition requirements of Topic 842 for short-term leases that have a lease term of 12 months or less.

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 had 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. In December 2019, the Company entered into an agreement to extend the lease term to December 18, 2024 for approximately $20,500 a month.

In June 2020, the Company amended the lease agreement to further increase the rentable space to 13,139 square feet and extend the lease term to June 5, 2025 for approximately $34,500 a month.

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. The sublease for this space expired on October 31, 2018. Monthly lease payments were approximately $26,000.

On October 19, 2018, the Company entered into an agreement to lease 12,322 square feet of office space located adjacent to the Company's headquarters in San Carlos, California. This lease replaces the sublease of 11,449 square feet of office space in the same

facility that expired on October 31, 2018. The term of the lease is 30 months subsequent to the commencement date, November 1, 2018, and will expire in April 2021. Monthly lease payments are approximately $59,000, subject to an annual increase of 3%.

On June 19, 2019, the Company entered into a first amendment (the "Amended Lease") to its previously disclosed lease agreement with Hudson Skyway Landing, LLC (the "Lease") for additional space at its corporate headquarters in San Carlos, California. Under the Amended Lease, the Company will lease an additional 8,110 square feet (the "Expansion Space"), for a total of approximately 20,432 square feet of space on the first floor of the building located at 999 Skyway Road, San Carlos, California, commonly known as Skyway Landing II. The term of the Amended Lease remains the same as that of the Lease and expires on April 30, 2021, unless earlier terminated in accordance with the Amended Lease. The Company's monthly base rent for the Expansion Space under the Amended Lease will be approximately $39,000 for the first year, and $40,000 for the second year.

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. On April 20, 2018, the Company entered into an agreement to extend the lease term to January 31, 2019 for approximately $7,000 a month. On November 2, 2018, the Company entered into an agreement to extend the lease term to July 31, 2019 for approximately $4,000 a month. On May 1, 2019, the Company entered into an agreement to extend the lease term to January 31, 2020 for approximately $4,000 a month. On October 24, 2019, the Company entered into an agreement to extend the lease term to April 30, 2020 for approximately $4,000 a month. On January 23, 2020, the Company entered into an agreement to extend the lease term to July 31, 2020 for approximately $4,000 a month. On May 24, 2020, the Company entered into an agreement to extend the lease term to October 31, 2020 for approximately $4,000 a month. On September 1, 2020, the Company entered into an agreement to extend the lease term to January 31, 2021, for approximately $4,000 a month. On January 31, 2021, the lease terminated, and we closed our New York office.

Philadelphia Office Lease

On May 2, 2019, the Company entered into an agreement to lease approximately 1,500 square feet of office space in Philadelphia, Pennsylvania until July 1, 2019 for a rate of $2,000 a month, and then approximately 4,500 square feet of office space for the remainder of a three-year term at an initial rate of $11,063 per month, subject to annual increases of 2.5%.

On August 1, 2020, the Company entered into an agreement to lease approximately 2,965 square feet of a training facility space in Philadelphia, Pennsylvania for a twelve-month term at a rate of approximately $6,500 per month.

Commercial Manufacturing Facility Agreement

On May 28, 2019, the Company entered into a lease agreement with 300 Rouse Boulevard, LLC (the "Commercial Manufacturing Facility Lease") for a build-to-suit commercial manufacturing facility, laboratories, and offices located in Philadelphia, Pennsylvania. Under the Commercial Manufacturing Facility Lease, the Company leases approximately 136,000 rentable square feet of space in a building located at 300 Rouse Boulevard, Philadelphia, Pennsylvania (the "Premises"). The construction of the commercial manufacturing facility began in July 2019 and has been substantially completed.

The Company determined the commencement date of the Commercial Manufacturing Lease to be October 7, 2020 in accordance with Topic 842 when its landlord made the Premise available for the Company's use and the Company obtained control over the use of the Premises. The Commercial Manufacturing Facility Lease includes an option to extend the term of the lease, exercisable under certain conditions as described in the Commercial Manufacturing Facility Lease, such that the overall term, when added to the initial term, shall be 359 months, by giving the landlord prior written notice thereof at least 18 months in advance of the expiration date. In determining the lease term, the Company did not include the periods covered by the option to extend the lease as it determined that it is not reasonably certain that the Company will exercise such option. Upon the commencement date, the Company recognized operating lease liabilities and right-of-use assets of $41.3 million and $45.7 million, respectively.

The Company's monthly base rent under the Lease will be approximately $320,000, subject to an annual increase of 2% for the first ten years, and an annual increase of the greater of 2% or 75% of the average ten-year consumer price index. The Company is also responsible for paying operating expenses, which are expected to be approximately $72,000 per month in 2021.

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Manufacturing Contracts

The Company uses contract manufacturing organizations (collectively the "CMOs" and each a "CMO") to manufacture and supply TILs for clinical and commercial purposes. The CMO contractual obligations consist of the use of manufacturing facilities and minimum fixed commitment fees, such as personnel, general support fees, and minimum production or material fees. In addition to the minimum fixed commitment fees, the CMO contractual obligations include variable costs such as production and material costs in excess of the minimum quantity specified in each CMO agreement. During the term of each CMO agreement, the Company has access to and control of the use of a dedicated suite in each of the CMOs' facilities for manufacturing activities. In conjunction with the adoption of Topic 842 on January 1, 2019, the Company reevaluated all of its material contracts it has, to determine whether they contain a lease under Topic 840. An arrangement is considered a lease or contains a lease if an underlying asset is explicitly or implicitly identified and use of the asset is controlled by the customer. Based on this evaluation, the Company concluded that all of its contracts with CMOs contained embedded operating leases because the suites used for its production are implicitly identified, is only used by the Company exclusively during the contractual term of the arrangements, and the CMOs have no substantive contractual rights to substitute the facilities used by the Company. Further, the Company controls the use of the facilities by obtaining all of the economic benefits from the use of the facilities and direct the use of the facilities throughout the period of use. The terms of the CMO contracts include options to terminate the lease with an advance notice of five to six months. The termination clauses and extension clauses are included in the calculation of the lease term for each of the CMOs when it is reasonably certain that it will not exercise such options.

The guidance requires the Company to first identify a lease deliverable and non-lease deliverable included in the arrangements, and then allocate the fixed contractual consideration to the lease deliverable(s) and the non-lease deliverable(s) on a relative standalone selling price basis to determine the amount of operating lease right-of-use assets and liabilities. The Company identified the use of a dedicated suite as a single lease deliverable, and related labor services as a single non-lease deliverable in each of the CMO arrangements. Judgment is required to determine the relative standalone selling price of each deliverable as the observable standalone selling prices are not readily available. Therefore, management used estimates and assumptions in determining relative standalone selling price of lease of a suite and labor service using information that includes market and other observable inputs to the extent possible.

The Company leases certain furniture and equipment that has a lease term of 12 months or less. Since the commencement date does not include an option to purchase the underlying asset, the Company elected not to apply the recognition requirements of Topic 842 for short-term leases, however, the lease costs that pertain to the short-term leases are disclosed in the components of lease costs table below.

The balance sheet classification of the Company's right-of-use asset and lease liabilities was as follows:

	December 31, 2020	December 31, 2019
Operating lease right-of-use assets	$ 54,756	$ 10,695
Operating lease liabilities		
Current portion included in current liabilities	6,284	7,252
long-term portion included in non-current liabilities	45,375	4,248
Total Operating lease liabilities	$ 51,659	$ 11,500

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The following table summarizes components of lease expenses, which were included in Total expenses in the Company's Consolidated Statement of Operations, and other information related to our operating leases as follows (in thousands except weighted-average remaining lease terms and discount rates):

	For the Year Ended December 31, 2020	For the Year Ended December 31, 2019
Operating lease cost	8,728	$ 9,213
Variable lease cost	5,585	5,801
Short-term lease cost	91	72
Total lease cost	14,404	$ 15,086
Other information		
Cash paid for amounts included in the measurement of lease liabilities included in Operating cashflows	$ 8,372	$ 8,622
Increase in right-of-use assets from the adoption of Topic 842	$ —	$ 10,380
Right-of-use assets obtained from entering new leases	$ 50,327	$ 4,092
Increase in right-of-use assets from lease modifications	$ 1,306	$ 3,660
Weighted-average remaining lease terms (years)	16.76	1.74
Weighted-average discount rates	8.3 %	7.7 %

Variable lease cost is determined based on performance or usage in accordance with the contractual agreements, and not based on an index or rate.

As of December 31, 2020, the maturities of the Company's operating lease liabilities were as follows (in thousands):

	Facility leases	CMO embedded leases	Total
2021	$ 3,912	$ 6,288	$ 10,200
2022	4,281	1,782	6,063
2023	4,286	—	4,286
2024	4,375	—	4,375
2025	4,281	—	4,281
Thereafter	74,206	—	74,206
Total lease payments	$ 95,341	$ 8,070	$ 103,411
Less: Present value adjustment	(51,474)	(278)	(51,752)
Operating lease liabilities	$ 43,867	$ 7,792	$ 51,659

Operating lease liabilities are based on the net present value of the remaining lease payments over the remaining lease term. In determining the present value of lease payments, the Company used its incremental borrowing rate based on the information available at the date of adoption of Topic 842 or the date of lease modifications. As of December 31, 2020, the weighted average remaining lease term is 16.76 years and the weighted average discount rate used to determine the operating lease liabilities was 8.3%.

NOTE 11. LEGAL PROCEEDINGS

Derivative Lawsuit. On December 11, 2020, a purported stockholder derivative complaint was filed by plaintiff Leo Shumacher against the Company, as nominal defendant, and its current directors, as defendants, in the Court of Chancery in the State of Delaware. The complaint alleges breach of fiduciary duty and a claim for unjust enrichment in connection with alleged excessive compensation of certain non-executive directors of the Company and seeks unspecified damages on behalf of the Company. The defendants intend to vigorously defend against the foregoing complaints. Based on the early stage of the litigation, it is not possible to estimate the amount or range of possible loss that might result from these matters.

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Solomon Capital, LLC. On April 8, 2016, a lawsuit ("the First Solomon Suit") 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 ("Solomon Plaintiffs") against the Company in the Supreme Court of the State of New York, County of New York (index no. 651881/2016). The Solomon Plaintiffs allege that, between June and November 2012, they provided to the Company $0.1 million and that they advanced and paid on behalf of the Company 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 1,110 shares to the Solomon Plaintiffs (after the 1-for-100 reverse split of the Company's common stock effected in March 2013) (the "Equity Claim"), and (iii) allow the Solomon Plaintiffs to convert the foregoing funds into its securities in the next financing of the Company on the same terms offered to other investors, which Solomon Plaintiffs allege, should have given them the right to convert their advances and payments into shares of the Company's common stock in the restructuring that took effect in May 2013. Based on the foregoing, the Solomon 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. On June 3, 2016, the Company filed an answer and counterclaims in the lawsuits. The Company has asserted counterclaims for fraudulent inducement, fraudulent misrepresentation, fraudulent concealment, breach of fiduciary duty, and breach of contract, alleging principally that the counterclaim defendants misrepresented their qualifications and failed to disclose that Solomon Sharbat was the subject of an investigation by the Financial Industry Regulatory Authority ("FINRA") that resulted in the loss of his FINRA license. In its counterclaims, 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 shares of Company stock. On May 12, 2020, the court granted the Company's motion for summary judgment limiting the Solomon Plaintiffs' damages for the Equity Claim to $47,420. The Solomon Plaintiffs filed a notice of appeal of this summary judgment on June 9, 2020. On July 2, 2020, the court granted the Company's motion to dismiss the First Solomon Suit for want of prosecution. On July 31, 2020, the Solomon Plaintiffs, through new counsel, filed a motion for reconsideration of the dismissal of the First Solomon Suit for want of prosecution. On August 11, 2020, the Company filed an opposition brief against the Solomon Plaintiffs' motion for reconsideration. On August 17, 2020, the Solomon Plaintiffs filed a reply brief in support of their motion for reconsideration. On September 2, 2020, the Solomon Plaintiffs filed a notice of appeal of the dismissal for want of prosecution. On January 4, 2021, the court granted the Solomon Plaintiffs motion for reconsideration, and reinstituted the case. On January 15, 2021, the Company filed a notice of appeal of the court's grant of the Solomon Plaintiffs motion for reconsideration.

On September 27, 2019, the Solomon Plaintiffs filed a new lawsuit (through new legal counsel) ("the Second Solomon Suit") titled *Solomon Capital, LLC, Solomon Capital 401(K) Trust, Solomon Sharbat and Shelhav Raff v. Iovance Biotherapeutics, Inc., f/k/a/ Lion Biotechnologies Inc. f/k/a/ Genesis Biopharma Inc., and Manish Singh* in the Supreme Court of the State of New York, County of New York (index no. 655668/2019). In the Second Solomon Suit, the Solomon Plaintiffs allege that they are third party beneficiaries of a "finder's fee agreement" that prior management entered into with a third party unlicensed entity in 2012 in connection with seeking financing, that an agreement or understanding existed between the Company and the plaintiffs that the plaintiffs would be paid fees and commissions (in cash and stock) if they obtained financing for the Company, and that they directly and indirectly introduced investors to the Company who invested in the Company, or were willing to invest in the Company. Finally, the Solomon Plaintiffs allege that they were promised a license to use the Company's technology in Israel. The plaintiffs claim that the Company breached the foregoing understandings, promises and agreements and, as a result, they are entitled to certain damages. The Solomon Plaintiffs also allege that Manish Singh, the Company's former Chief Executive Officer, committed fraud and took shares belonging to them. On February 18, 2020, the Company filed a removal petition and removed the Second Solomon Suit to the U.S. District Court for the Southern District of New York, where the case has been assigned case no. 1:20-cv-1391. The Company has not yet responded to the complaint in the Second Solomon Suit. On May 22, 2020, the Company moved to dismiss the Second Solomon Suit for lack of personal jurisdiction. On July 17, 2020, the Solomon Plaintiffs filed an opposition brief against the Company's motion to dismiss for lack of personal jurisdiction. On August 7, 2020, the Company filed a reply brief in support of the Company's motion to dismiss for lack of personal jurisdiction.

The Company intends to vigorously defend these complaints and pursue its counterclaims, as applicable. At the current stage of the litigation, in both the First Solomon Suit and the Second Solomon Suit, 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.

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 $300,000), 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 U.S. District Court for the Southern District of New York, where the case has been assigned case no. 1:17-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 the Company's materials, prohibiting him from disclosing or using the Company's materials, and granting expedited discovery. On June 25, 2018, pursuant to a stipulation between the parties, the court entered a permanent injunction prohibiting Dr. Fischkoff from disclosing, possessing, or using any of the Company's proprietary materials or trade secrets. On July 5, 2018, the court entered an order dismissing two of Dr. Fischkoff's claims against the Company and Dr. Fardis. On October 18, 2018, Dr. Fischkoff amended his complaint to assert a new claim for defamation arising from SEC filings in which the Company provided the information about this litigation. On September 23, 2020, the parties reached a confidential settlement in this matter, and on October 13, 2020, the court approved a stipulation of dismissal with prejudice filed by the parties.

Other Matters. In connection with the Company's reincorporation from Nevada to Delaware in 2017, the Company (as a Delaware corporation) untimely filed a post-effective amendment to adopt a Form S-8 registration statement that the Company filed (as a Nevada corporation) to register the shares underlying the Company's 2011 Equity Incentive Plan. Before the Company filed the required post-effective amendment, options to purchase 200,000 shares were exercised under the 2011 Equity Incentive Plan. The effect of the delayed post-effective amendment filing on the 200,000 option shares is uncertain, but the issuance and sale of the shares may not have been in compliance with the Form S-8 registration statement. The existence of any liability to the Company, and the amount of any such liability to the Company, as a result of the issuance of the 200,000 shares is uncertain. Accordingly, no accrual for a potential claim has been made by the Company in its consolidated financial statements.

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 it 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 its financial position, results of operations or cash flows.

NOTE 12. QUARTERLY UNAUDITED RESULTS

The results of operations by quarter for the years ended December 31, 2020 and 2019 are as follows:

	2020				2019			
	(in thousands, except per share information)							
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Revenue	$ —	$ —	$ —	$ —	$ —	$ —	$ —	$ —
Net loss	$ (69,595)	$ (63,018)	$ (58,571)	$ (68,397)	$ (36,950)	$ (47,551)	$ (49,487)	$ (63,568)
Net loss per share, basic and diluted	$ (0.55)	$ (0.47)	$ (0.40)	$ (0.47)	$ (0.30)	$ (0.38)	$ (0.40)	$ (0.50)
Weighted average share used in computing net loss per share, basic and diluted	126,568	133,162	146,492	146,738	123,415	123,567	124,035	126,273

NOTE 13. RELATED PARTY TRANSACTIONS

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

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Company recognized $0.2 million, $0.4 million and $0.7 million in stock-based compensation expense related to this consulting agreement during the years ended December 31, 2020, 2019 and 2018, respectively.

NOTE 14. SUBSEQUENT EVENTS

New Headquarters Lease

On February 3, 2021, the Company entered into a lease agreement with ARE-San Francisco No. 63, LLC (the "New Headquarters Lease") for laboratories and offices to be constructed in Suite 400 of an existing building located at 825 Industrial Road, San Carlos, California (the "Building"), commonly known as The District. Under the New Headquarters Lease, the Company will lease approximately 49,918 rentable square feet of space in the Building (the "Premises"). The New Headquarters Lease is for a term of 120 months, commencing upon the first day of the first full month (the "Rent Commencement Date") after the earlier to occur of (i) the date that is 12 months and one day after the execution date (the "Commencement Date"), which is January 30, 2022, or (ii) the date that the Tenant Improvements are substantially completed; provided, however, that the Rent Commencement Date shall be delayed 1 day for each day after the Commencement Date that (a) to the extent that, after the Commencement Date, any governmental authority having jurisdiction, as a result of the COVID-19 outbreak in the U.S., declares or implements any order or mandate that restricts construction activities in San Mateo County, California (any such order or mandate, a "Government Mandate"), to the extent that such Government Mandate precludes the construction of tenant improvements, or (b) a landlord delay occurs. Construction of the Company's offices is expected to extend through 2021. The New Headquarters Lease includes an option to extend the term of the lease for 60 months, exercisable under certain conditions and at a market rate as described in the New Headquarters Lease.

Commencing 210 days after the Rent Commencement Date as the result of a rent abatement, the Company's monthly base rent under the New Headquarters Lease will be $279,540.80, subject to an annual increase of 3%. Beginning in 2022, the Company will also be responsible for paying operating expenses.

Extension of Existing Headquarters Leases

On February 3, 2021, the Company entered into two amendments (the "Suite 150 Second Amendment" and the "Suite 100 and Suite 125 First Amendment") to its previously disclosed lease agreements with Hudson Skyway Landing, LLC, for space located on the first floor of the building located at 999 Skyway Road, San Carlos, California, commonly known as Skyway Landing II.

Under the Suite 100 and Suite 125 Second Amendment, the Company will extend its previously disclosed amended lease of approximately 20,432 rentable square feet of space, which would have expired on April 30, 2021, to December 31, 2021. The Company's monthly base rent under the Suite 100 and Suite 125 Second Amendment will be $103,181.60. The Company is also responsible for paying its portion of operating expenses and real estate taxes. The Company has an option to extend the expiration of the Suite 100 and Suite 125 Second Amendment for one month or six months, at its discretion, by providing notice as specified in the Suite 100 and Suite 125 Second Amendment.

Under the Suite 150 First Amendment, the Company will extend its previously disclosed lease of approximately 8,733 rentable square feet of space, which also would have expired on April 30, 2021, to December 31, 2021. The Company's monthly base rent under the Suite 150 First Amendment will be $44,101.65. The Company is also responsible for paying its portion of operating expenses and real estate taxes. The Company has an option to extend the expiration of the Suite 150 First Amendment for one month or six months, at its discretion, by providing notice as specified in the Suite 150 First Amendment.

Economic Stimulus Program Loan

On January 26, 2021, the Company entered into a Loan Note dated January 26, 2021 (the "Loan Note") and accompanying Economic Stimulus Program Loan Agreement with PIDC – Local Development Corporation, a Pennsylvania nonprofit corporation (the "Lender"), pursuant to which the Lender agreed to make a loan (the "Job Creation Loan") to the Company in a principal amount of $1.0 million. The Job Creation Loan will be for a term of five years starting on the date of the issuance of a final certificate of occupancy for the Company's leased premises in Philadelphia, Pennsylvania. The Job Creation Loan is unsecured, bears no interest, and will be forgiven by the Lender in the amount of $2,000 per full-time or "full time equivalent" (defined as two or more part time employees whose working hours total at least 35 hours a week) employee with an average salary of at least $80,000 ("FT Employees"), up to a maximum amount equal to the amount of the Job Creation Loan, as calculated based on the average number of

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FT Employees employed at the Company's premises during the period of the 5-year term beginning on the date that is six months prior to the maturity date and ending on the maturity date. If the Job Creation Loan is not forgiven in full by the maturity date, the remaining balance of the loan not forgiven will become payable on the maturity date. The Loan Note includes customary events of default. Upon the occurrence of an event of default, the Lender will have the right to exercise remedies against the Company, including the right to require immediate payment of all amounts due under the Loan Note.

Entry Into a Material Definitive Agreement

On February 8, 2021, the Company entered into an Open Market Sale Agreement (the "Sales Agreement") with Jefferies LLC ("Jefferies") with respect to an "at the market" offering program, under which the Company may, from time to time, in its sole discretion, issue and sell through Jefferies, acting as sales agent, up to $350.0 million of shares of the Company's common stock, par value $0.000041666 per share (the "Common Shares"). The issuance and sale, if any, of the Common Shares by the Company under the Sales Agreement will be made pursuant to a prospectus supplement, dated February 8, 2021, to the Company's registration statement on Form S-3ASR, originally filed with the Securities and Exchange Commission on May 27, 2020, which became effective immediately upon filing.

Pursuant to the Sales Agreement, Jefferies may sell the Common Shares by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act of 1933, as amended (the "Securities Act"). Jefferies will use commercially reasonable efforts consistent with its normal trading and sales practices to sell the Common Shares from time to time, based upon instructions from the Company (including any price or size limits or other customary parameters or conditions the Company may impose).

The Company will pay Jefferies a commission of up to 3.0% of the gross sales proceeds of any Common Shares sold through Jefferies under the Sales Agreement.

The Company is not obligated to make any sales of Common Shares under the Sales Agreement. The offering of Common Shares pursuant to the Sales Agreement will terminate upon the earlier to occur of (i) the issuance and sale, through Jefferies, of all Common Shares subject to the Sales Agreement and (ii) termination of the Sales Agreement in accordance with its terms.

Exhibit 10.30

Portions of this Exhibit have been redacted because they are both (i) not material and (ii) would be competitively harmful if publicly disclosed. Information that was omitted has been noted in this document with a placeholder identified by the mark "[***]"

EXECUTIVE EMPLOYMENT AGREEMENT

THIS EXECUTIVE EMPLOYMENT AGREEMENT (the "**Agreement**") is entered into as of November 23, 2020 by and between Iovance Biotherapeutics, Inc., a Delaware corporation (the "**Company**"), and Jean-Marc Bellemin ("**Executive**") (either party individually, a "**Party**"; collectively, the "**Parties**").

WHEREAS, the Company desires to employ Executive to serve as the Company's Chief Financial Officer;

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, the promises and obligations set forth below and for other good and valuable consideration, the receipt of which is hereby acknowledged by the Parties, the Company and Executive agree and intend to be legally bound, as follows:

1. Effective Date. Effective December 14, 2020 (the "**Effective Date**"), the Company hereby employs Executive, and Executive hereby accepts such employment, upon the terms and conditions set forth herein.

2. Position and Duties.

2.1 Position. The Company agrees to employ Executive in the position of Chief Financial Officer reporting to the Chief Executive Officer. The Executive shall have the duties and responsibilities consistent with the office of a Chief Financial Officer of a publicly traded corporation, and such other duties and responsibilities as determined from time to time by the Company, including but not limited to the 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 Company and/or Chief Executive Officer shall reasonably assign from time to time. Executive shall perform his duties in the Company's offices in San Carlos, California subject to customary travel as reasonably required.

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 business hours to the faithful and loyal performance of his job duties to the Company (except for permitted vacation periods and reasonable periods of illness or other incapacity). 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 he shall not, directly or indirectly, (i) engage or participate

in any outside activity that would, or may be perceived to, conflict with the best interests of the Company or Executive's duties to the Company, or (ii) provide services to or invest in any corporation or entity that competes or intends to compete with the business of the Company.

2.2(c) Executive agrees that, during the term of this Agreement, Executive shall work exclusively for the Company. Consequently, Executive agrees to not accept employment, of any kind, from any person or entity other than the Company, and to not perform duties or render services to any person or entity other than the Company. Notwithstanding the foregoing, nothing herein shall prohibit Executive from (i) serving as a member of the board of directors of an entity engaged solely in charitable activities or community affairs, provided that, such activity shall be limited by Executive so as not to interfere with the performance of Executive's duties and responsibilities hereunder; (ii) owning, as a passive investment, less than 1% of capital stock of any corporation listed on the national securities exchange or a publicly traded over-the-counter market; or (iii) engaging in any other manner of employment, consulting or other business activity with the written consent of the Company, the Chief Executive Officer, or as approved by the Company's Board of Directors or a committee thereof (collectively, the "**Board**").

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. As compensation for the performance of all duties to be performed by Executive hereunder, the Company shall pay to Executive a base salary of $450,000 per year, less applicable 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**").

4.2 Signing Bonus. As a signing bonus, Executive shall receive two payments of $65,000 (subject to payroll taxes) (the "**Signing Bonus Payments**"). The first payment of the Signing Bonus Payments will be paid on the Company's first regular payroll date in January 2021, and the second payment will be paid in 2021 on the date on which annual bonus payments for 2020 are made to all other Company employees. The Signing Bonus Payments shall be considered earned eighteen (18) months following the Effective Date or, if applicable, the date on which Executive's employment is terminated by the Company without Cause (as defined herein), due to death or Disability (as defined herein), or by Executive for Good Reason (as defined herein) prior to eighteen (18) months from the Effective Date. If Executive's employment is terminated by the Company for Cause or by Executive without Good Reason (including by Executive's resignation) prior to or on the date that is eighteen (18) months from the Effective Date (the "**Separation Date**"), he shall, within ten (10) days after the Separation Date, repay to the Company a portion of the total value of the Signing Bonus Payments (before the deduction of any applicable taxes) in accordance with the table below based on his Separation Date.

Months from the Effective Date through the Separation Date	**Portion of total value of Signing Bonus Payments repayable by Executive to Company**
< 12 months	100%
12 - 18 months	75%
> 18 months	0%

For avoidance of doubt, the Signing Bonus Payments are an advance only and shall not be deemed earned unless the foregoing requirements for the Signing Bonus Payments are satisfied.

4.3 Stock Options. As of the Effective Date, Executive shall receive stock options to purchase an aggregate of 150,000 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 closing trading price of the common stock on the Effective Date. Provided that Executive is still employed with the Company on the following dates, the foregoing stock options will vest in installments as follows: (i) Options for the purchase of one-third of the 150,000 shares shall vest on one year anniversary of the Effective Date; and (ii) the remaining stock options shall vest as to one-twelfth of the 150,000 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.

4.4 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**"), such participation to begin on January 1, 2021. The Incentive Compensation shall be paid in accordance with the terms and conditions outlined in the Incentive Plan and based upon the achievement of certain goals, objectives, and other metrics as decided by the Board. The maximum potential amount payable to Executive under the Incentive Plan, if earned, shall be 40% 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. No Incentive Compensation will be payable to Executive to the extent Executive is not employed on the Incentive Compensation payment date. The payment of any Incentive Compensation pursuant to this Section 4.3 is in the sole discretion of the Board, in accordance with the Incentive Plan, and 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.

4.5 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 and with any necessary Board approval requirements.

4.6 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. The amount, eligibility and extent of these benefits shall be governed by the Company's applicable policy in effect and as amended from time to time and in compliance with applicable law.

4.7 Business Expenses. Executive will be reimbursed for all reasonable and necessary 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, Executive shall provide the

Company with reasonable documentation and receipts establishing the amount and nature of such expenses. Executive shall comply with such reasonable budget limitations and pre-approval, approval, and reporting requirements with respect to expenses as the Company may establish from time to time.

5. Confidentiality and Proprietary Agreement. Executive agrees to abide by the Company's Employee Proprietary Information and Inventions Agreement (the "**EPIIA**"), 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 EPIIA; (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; (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; (vi) failure or refusal to comply with reasonable and lawful Company policies and procedures; or (vii) Executive's failure and/or inability to comply with or meet the requirements of any performance improvement plan reasonably provided to Executive by the Chief Executive Officer and/or the Board; 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 or the EPIIA. 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, 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. Upon such termination of employment 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, 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, as well as any other agreements concerning his employment with and separation from employment, including without limitation, and confidentiality and proprietary information agreements. Following payment of the Severance Payment, Base Salary, 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 following compensation, provided that Executive first satisfies the Severance Conditions: (i) the Severance Payment set forth in Section 6.2 and (ii) any then time-based unvested stock options granted to Executive by the Company to the extent then outstanding at the time of such termination will become fully vested on the last day of Executive's employment with the Company, and Executive shall have three months from the date of termination within which to exercise his vested options. Following payment of the Severance Payment, Base Salary, 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 non-discretionary 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; or (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. In the event that Executive terminates his employment for Good Reason, then Executive shall be entitled to receive the Base Salary, and Severance Payment 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. Employment and Post-Employment Covenants.

7.1 Non-Solicitation. Executive agrees that during a period of 12 months following the termination of the Executive's employment (the "**Restrictive Period**"), Executive shall not (a) solicit or in any manner encourage, either directly or indirectly, any existing employee of the Company to leave the Company for any reason; nor will he interfere in any other manner with the employment or business relationships at the time existing between the Company and its current or prospective employees or consultants; or (b) induce or attempt to induce any customer, supplier, distributor, licensee or other business affiliate of the Company to cease doing business with the Company or in any way interfere with the existing business relationship between any customer, supplier, distributor, licensee or other business affiliate and the Company.

7.2 Non-Disparagement. Executive agrees, at all times following the Effective Date, not to, directly or indirectly, on his behalf or on behalf of any other person or entity, (a) take any action which is intended, or could reasonably be expected, to harm, disparage, defame, slander, or lead to unwanted or unfavorable publicity for the Company, its subsidiaries or any of their respective affiliates, or its or their respective equity holders, directors, officers, members, managers, partners, employees, representatives or agents, or otherwise take any action which could reasonably be expected to detrimentally affect the reputation, image, relationships or public view of any such person or entity or (b) attempt to do any of the foregoing, or assist, entice, induce or encourage any other person or entity to do or attempt to do any activity which, were it done by Executive, would violate any provision of this Section 7.2; provided, however, that Executive shall not be prohibited by this Section 7.2 from making truthful statements (i) when required by order of a court or other body of competent jurisdiction or as required by law or (ii) solely

within the context of seeking judicial enforcement of legal or contractual rights against a person or entity.

7.3 Remedies. Executive acknowledges that the duration of the Restrictive Period is fair is reasonably required for the protection of the Company's business interests, including its goodwill. The Executive (a) acknowledges that his failure to comply with any requirement of this Section 7 this Agreement will cause the Company irreparable harm and that a remedy at law for such a failure would be an inadequate remedy; and (b) consents to the Company's obtaining from a court having jurisdiction specific performance, an injunction, a restraining order or any other equitable relief in order to enforce any such provision. The right to obtain such equitable relief shall be in addition to, and not in lieu of, any other remedy to which the Company is entitled under applicable law (including, but not limited to, monetary damages).

8. General Provisions.

8.1 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.

8.2 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.

8.3 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.

8.4 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.

8.5 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.

8.6 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.

8.7 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.

8.8 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 AS SHOWN BELOW.

EXECUTIVE:

/s/ Jean-Marc Bellemin
Jean-Marc Bellemin

Address:
[***]

COMPANY:

Iovance Biotherapeutics, Inc.

By: /s/ Maria Fardis

Maria Fardis
President & Chief Executive Officer
999 Skyway Road, Suite 150
San Carlos, CA 94070

Exhibit 21.1

Subsidiaries Of The Company

Iovance Biotherapeutics GmbH, a company formed under the laws of Switzerland.

Iovance Biotherapeutics B.V., a company formed under the laws of The Netherlands.

Iovance Biotherapeutics Manufacturing LLC, a limited liability company formed under the laws of the Commonwealth of Pennsylvania.

Exhibit 23.1

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. 333-238724), Form S-3 (File No. 333-214073), Form S-3 (File No. 333-212373), Form S-8 (File No. 333-239317), Form S-8 (File No. 333-239316), Form S-8 (File No. 333-227242), Form S-8 (File No. 333-205097), Form S-8 (File No. 333-217638) and Form S-8 (File No. 333-214567) of our report dated February 25, 2021, with respect to our audits of the consolidated financial statements of Iovance Biotherapeutics, Inc. as of December 31, 2020 and 2019 and for each of the three years in the period ended December 31, 2020 and our report dated February 25, 2021 with respect to our audit of internal control over financial reporting of Iovance Biotherapeutics, Inc. as of December 31, 2020, which reports are included in this Annual Report on Form 10-K of Iovance Biotherapeutics, Inc. for the year ended December 31, 2020.

/s/ Marcum LLP

Marcum LLP
New York, NY
February 25, 2021

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: February 25, 2021

/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, Jean-Marc Bellemin, 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: February 25, 2021

/s/ Jean-Marc Bellemin
Jean-Marc Bellemin
Chief Financial Officer
(Principal Financial 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, 2020 (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: February 25, 2021

/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, Jean-Marc Bellemin, 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, 2020 (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: February 25, 2021

/s/ Jean-Marc Bellemin
Jean-Marc Bellemin
Chief Financial Officer
(Principal Financial Officer)