U. S. SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

☑ QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the quarterly period ended **June 30, 2021**

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from __ to __.

Commission File Number 001-36860

IOVANCE BIOTHERAPEUTICS, INC.

(Exact name of issuer as specified in its charter)

Delaware	75-3254381
(State or other jurisdiction of incorporation or organization)	(I.R.S. employer identification number)

999 Skyway Road, Suite 150, San Carlos, CA 94070
(Address of principal executive offices and zip code)

(650) 260-7120
(Registrant’s telephone number, including area code)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes ☑ No ☐

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

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

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

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

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

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

At July 28, 2021, the issuer had 155,032,000 shares of common stock, par value $0.000041666 per share, outstanding.

IOVANCE BIOTHERAPEUTICS, INC.
FORM 10-Q
For the Quarter Ended June 30, 2021

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PART I. FINANCIAL INFORMATION

Item 1. Condensed Consolidated Financial Statements

IOVANCE BIOTHERAPEUTICS, INC.
Condensed Consolidated Balance Sheets
(unaudited; in thousands, except share and per share information)

	June 30, 2021	December 31, 2020
ASSETS		
Current Assets		
Cash and cash equivalents	$ 82,763	$ 67,329
Short-term investments	573,605	562,108
Prepaid expenses and other assets	10,272	6,663
Total Current Assets	666,640	636,100
Property and equipment, net	80,120	59,159
Operating lease right-of-use assets	52,508	54,756
Long-term investments	46,288	—
Restricted cash	6,084	5,525
Long-term assets	1,150	12,918
Total Assets	$ 852,790	$ 768,458
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities		
Accounts payable	$ 21,914	$ 13,513
Accrued expenses	34,192	35,074
Operating lease liabilities - current	4,428	6,284
Total Current Liabilities	60,534	54,871
Non-Current Liabilities		
Operating lease liabilities – noncurrent	46,843	45,375
Long-term note payable	1,000	—
Other liabilities	—	11,714
Total Non-Current Liabilities	47,843	57,089
Total Liabilities	108,377	111,960
Commitments and contingencies		
Stockholders' Equity		
Series A Convertible Preferred stock, $0.001 par value; 17,000 shares designated, 194 shares issued and outstanding as of June 30, 2021 and December 31, 2020	—	—
Series B Convertible Preferred stock, $0.001 par value; 11,500,000 shares designated, 2,842,158 and 3,581,119 shares issued and outstanding as of June 30, 2021 and December 31, 2020, respectively	3	4
Common stock, $0.000041666 par value; 300,000,000 shares authorized, 154,799,721 and 146,874,917 shares issued and outstanding as of June 30, 2021 and December 31, 2020, respectively	7	6
Accumulated other comprehensive income	33	19
Additional paid-in capital	1,731,363	1,486,662
Accumulated deficit	(986,993)	(830,193)
Total Stockholders' Equity	744,413	656,498
Total Liabilities and Stockholders' Equity	$ 852,790	$ 768,458

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

IOVANCE BIOTHERAPEUTICS, INC.
Condensed Consolidated Statements of Operations
(unaudited; in thousands, except per share information)

	Three Months Ended June 30, 2021	Three Months Ended June 30, 2020	Six Months Ended June 30, 2021	Six Months Ended June 30, 2020
Costs and expenses				
Research and development expenses	62,119	49,274	118,068	106,226
General and administrative expenses	19,307	14,353	38,928	28,211
Total costs and expenses	81,426	63,627	156,996	134,437
Loss from operations	(81,426)	(63,627)	(156,996)	(134,437)
Other income				
Interest income, net	75	609	196	1,824
Net Loss	$ (81,351)	$ (63,018)	$ (156,800)	$ (132,613)
Net Loss Per Share of Common Stock, Basic and Diluted	$ (0.53)	$ (0.47)	$ (1.04)	$ (1.02)
Weighted Average Shares of Common Stock Outstanding, Basic and Diluted	153,751	133,162	150,571	129,848

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

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	**2020**	**2021**	**2020**
Net Loss	$ (81,351)	$ (63,018)	$ (156,800)	$ (132,613)
Other comprehensive gain/(loss):				
Unrealized gain on short-term investments	(63)	(595)	14	97
Comprehensive Loss	$ (81,414)	$ (63,613)	$ (156,786)	$ (132,516)

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

IOVANCE BIOTHERAPEUTICS, INC.
Condensed Consolidated Statements of Stockholders' Equity
For the Three Months Ended June 30, 2021 and 2020
(unaudited; 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 - March 31, 2021	194	$ —	2,842,158	$ 3	149,315,299	$ 6	$ 1,552,968	$ 96	$ (905,642)	$ 647,431
Stock-based compensation expense	—	—	—	—	—	—	14,414	—	—	14,414
Common stock issued upon purchase of employee stock purchase plan	—	—	—	—	55,315	—	970	—	—	970
Common stock issued upon exercise of stock options	—	—	—	—	233,251	—	2,742	—	—	2,742
Unrealized loss on short-term investments	—	—	—	—	—	—	—	(63)	—	(63)
Common stock sold in public offering, net of offering costs	—	—	—	—	5,195,856	1	160,269	—	—	160,270
Net loss	—	—	—	—	—	—	—	—	(81,351)	(81,351)
Balance - June 30, 2021	194	$ —	2,842,158	$ 3	154,799,721	$ 7	$ 1,731,363	$ 33	$ (986,993)	$ 744,413
Balance - March 31, 2020	194	$ —	3,581,119	$ 4	126,823,156	$ 5	$ 882,599	$ 912	$ (640,207)	$ 243,313
Stock-based compensation expense	—	—	—	—	—	—	10,537	—	—	10,537
Vesting of restricted shares issued for services	—	—	—	—	6,176	—	—	—	—	—
Tax payments related to shares withheld for vested restricted stock units	—	—	—	—	—	—	(165)	—	—	(165)
Common stock issued upon exercise of stock options	—	—	—	—	129,672	—	1,237	—	—	1,237
Unrealized loss on short-term investments	—	—	—	—	—	—	—	(595)	—	(595)
Common stock sold in public offering, net of offering costs	—	—	—	—	19,475,806.00	1	566,999	—	—	567,000
Net loss	—	—	—	—	—	—	—	—	(63,018)	(63,018)
Balance - June 30, 2020	194	$ —	3,581,119	$ 4	146,434,810	$ 6	$ 1,461,207	$ 317	$ (703,225)	$ 758,309

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

IOVANCE BIOTHERAPEUTICS, INC.
Condensed Consolidated Statements of Stockholders' Equity
For the Six Months Ended June 30, 2021 and 2020
(unaudited; 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 - December 31, 2020	194	$ —	3,581,119	$ 4	146,874,917	$ 6	$ 1,486,662	$ 19	$ (830,193)	$ 656,498
Stock-based compensation expense	—	—	—	—		—	31,355	—	—	31,355
Common stock issued upon purchase of employee stock purchase plan					55,315	—	970	—	—	970
Common stock issued upon exercise of stock options	—	—	—	—	656,429	—	9,221	—	—	9,221
Common stock sold in public offering, net of offering costs	—	—	—	—	6,474,099	1	203,154	—	—	203,155
Common stock issued from preferred stock conversion	—	—	(738,961)	(1)	738,961	—	1	—	—	—
Unrealized gain on short-term investments	—	—	—	—	—	—	—	14	—	14
Net loss	—	—	—	—	—	—	—	—	(156,800)	(156,800)
Balance - June 30, 2021	194	$ —	2,842,158	$ 3	154,799,721	$ 7	$ 1,731,363	$ 33	$ (986,993)	$ 744,413
Balance - December 31, 2019	194	$ —	3,581,119	$ 4	126,411,808	$ 5	$ 869,354	$ 220	$ (570,612)	$ 298,971
Stock-based compensation expense	—	—	—	—	—	—	19,949	—	—	19,949
Vesting of restricted shares issued for services	—	—	—	—	13,449	—	—	—	—	—
Tax payments related to shares withheld for vested restricted stock units	—	—	—	—	—	—	(283)	—	—	(283)
Common stock issued upon exercise of stock options	—	—	—	—	533,747	—	5,188	—	—	5,188
Unrealized gain on short-term investments	—	—	—	—	—	—	—	97	—	97
Common stock sold in public offering, net of offering costs	—	—	—	—	19,475,806	1	566,999	—	—	567,000
Net loss	—	—	—	—	—	—	—	—	(132,613)	(132,613)
Balance - June 30, 2020	194	$ —	3,581,119	$ 4	146,434,810	$ 6	$ 1,461,207	$ 317	$ (703,225)	$ 758,309

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

IOVANCE BIOTHERAPEUTICS, INC.
Condensed Consolidated Statements of Cash Flows
(unaudited; in thousands)

	Six Months Ended June 30, 2021	Six Months Ended June 30, 2020
Cash Flows from Operating Activities		
Net loss	$ (156,800)	$ (132,613)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	31,355	19,949
Non-cash lease expense	2,407	3,328
Accretion (amortization) of discounts and premiums on investments	3,862	(17)
Depreciation and amortization	738	512
Changes in assets and liabilities:		
Prepaid expenses, other assets, and long-term assets	8,159	(1,064)
Right-of-use assets	(159)	—
Operating lease liabilities	(388)	(3,739)
Accounts payable	4,950	(7,096)
Accrued expenses and other liabilities	(10,523)	18,813
Net cash used in operating activities	(116,399)	(101,927)
Cash Flows from Investing Activities		
Maturities of investments	320,151	216,678
Purchase of investments	(381,784)	(534,717)
Purchase of property and equipment	(20,321)	(5,612)
Net cash used by investing activities	(81,954)	(323,651)
Cash Flows from Financing Activities		
Tax payments related to shares withheld for vested restricted stock units	—	(283)
Proceeds from the issuance of common stock upon exercise of options and employee stock purchase plan	10,191	5,188
Proceeds from the issuance of common stock, net	203,155	567,393
Proceeds from the issuance of debt	1,000	—
Net cash provided by financing activities	214,346	572,298
Net increase in cash, cash equivalents, and restricted cash	15,993	146,720
Cash, Cash Equivalents, and Restricted Cash, Beginning of Period	72,854	19,419
Cash, Cash Equivalents, and Restricted Cash, End of Period	$ 88,847	$ 166,139
Supplemental disclosure of non-cash investing and financing activities:		
Net unrealized gain on short-term investments	$ 14	$ 97
Acquisitions of property and equipment included in accounts payable and accrued expense	(1,378)	(5,212)
Accrued offering costs in accrued expenses	—	(393)
Conversion of convertible preferred stock to common stock	(1)	—

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

IOVANCE BIOTHERAPEUTICS, INC.
NOTES TO THE CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
(unaudited)

NOTE 1. 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.

Basis of Presentation of Unaudited Condensed Consolidated Financial Information

The unaudited condensed consolidated financial statements of the Company for the three and six months ended June 30, 2021 and 2020 have been prepared in accordance with accounting principles generally accepted in the United States of America (“GAAP”) for interim financial information and pursuant to the requirements for reporting on Form 10-Q and Regulation S-X. Accordingly, they do not include all the information and footnotes required by GAAP for audited financial statements. However, such information reflects all adjustments (consisting solely of normal recurring adjustments), which are, in the opinion of management, necessary for the fair presentation of the Company's financial position and results of operations. Results shown for interim periods are not necessarily indicative of the results to be obtained for a full fiscal year. The balance sheet information as of December 31, 2020, was derived from the audited financial statements included in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission (the “SEC”) on February 25, 2021. These interim financial statements should be read in conjunction with that report.

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 $156.8 million for the six months ended June 30, 2021 and used $116.4 million of cash in its operating activities during the six months ended June 30, 2021. For the six months ended June 30, 2021, the Company received net proceeds of approximately $203.2 million from the “at the market” offering program the Company has in place with Jefferies LLC, acting as sales agent. As of June 30, 2021, the Company had $708.7 million in cash, cash equivalents, investments, and restricted cash ($82.8 million of cash and cash equivalents, $573.6 million in short-term investments, $46.3 million in long-term investments, and $6.1 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 as well as initiating the construction of the tenant improvements for its new headquarters in San Carlos, California, 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, 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 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, liquidity of investments sufficient to meet cash flow requirements of its business, and maximization of total return while maintaining safety and liquidity.

NOTE 2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Cash, Cash Equivalents, and 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 investments are classified as “available-for-sale” and are presented at fair value as either a current or non-current asset based on the length of maturity from the reporting date. Unrealized gains and losses on available-for-sale securities are included in accumulated other comprehensive 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 three and six months ended June 30, 2021 and 2020. 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 Condensed 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 Condensed 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 commercial papers, and places restrictions on maturities and concentration by type and issuer, except for securities issued by the U.S. government.

Restricted Cash

The Company maintains a required minimum balance, currently $6.1 million in a segregated bank account in connection with three letters of credit, one for $5,450,000 for the benefit of the landlord for its commercial manufacturing facility used as a security deposit for the lease (See Note 10 - Leases), the second one for $74,685 for the benefit of a utilities service provider, and the third one for $559,082 for the benefit of the landlord for its new headquarters lease. The total amount is classified as Restricted Cash on the Condensed Consolidated Balance Sheet. The first 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 second letter of credit of $74,685 expired on March 9, 2021, however, it automatically extends, without written agreement, to the expiration date of December 1, 2022. The third letter of credit of $559,082 expires on February 1, 2032, however, it will be automatically extended, without written agreement, for one year periods to February in each succeeding calendar year. As of June 30, 2021 and December 31, 2020, restricted cash consisted of $6.1 million and $5.5 million, respectively. This amount has been classified as a non-current asset on the Company’s Condensed Consolidated Balance Sheets.

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

	June 30, 2021	June 30, 2020
Cash and cash equivalents	$ 82,763	$ 160,614
Restricted cash (included in non-current assets on the condensed consolidated balance sheets)	6,084	5,525
Total cash, cash equivalents and restricted cash	$ 88,847	$ 166,139

Loss per Share

Basic net loss per share is computed by dividing the net loss by the weighted average number of shares of common stock 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 shares of common stock 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 (iv) conversion of preferred stock, are only included in the calculation of diluted net loss per share when their effect is dilutive.

As of June 30, 2021 and 2020, the following outstanding common stock equivalents have been excluded from the calculation of net loss per share because their impact would be anti-dilutive.

	June 30,	
	2021	2020
Stock options	14,537,031	12,594,736
Series A Convertible Preferred Stock*	97,000	97,000
Series B Convertible Preferred Stock*	2,842,158	3,581,119
2020 ESPP	39,766	—
Restricted stock units	1,253,540	—
	18,769,495	16,272,855

** on an as-converted basis*

The effect of potentially dilutive securities would be reflected in diluted earnings per share of common stock 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.

Fair Value Measurements

Under 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.

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 June 30, 2021 or December 31, 2020.

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

A financial instrument's categorization within the valuation hierarchy is based upon the lowest level of input that is significant to the fair value measurement. The Company's financial instruments consist of Level 1 and Level 2 assets. Where quoted prices are available in an active market, securities are classified as Level 1.

When quoted market prices are not available for a specific security, the Company estimates the fair value by using quoted prices for identical or similar instruments in markets that are not active and model-based valuation techniques for which all significant inputs are observable in the market or can be corroborated by observable market data for substantially the full term of the assets. Where applicable, these models project future cash flows and discount the future amounts to a present value using market-based observable inputs obtained from various third-party data providers, including but not limited to, benchmark yields, interest rate curves, reported trades, broker/dealer quotes and market reference data. Level 2 assets consist of commercial paper and government agency securities. Level 2 inputs for the valuations are limited to quoted prices for similar assets or liabilities in active markets and inputs other than quoted prices that are observable for the asset.

As of June 30, 2021 and December 31, 2020, the fair value of the Company's financial assets, which consist of cash equivalents and investments classified as available-for-sale securities, that were measured 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 June 30, 2021			
	Level 1	Level 2	Level 3	Total
U.S. treasury securities	$ 313,661	$ —	$ —	$ 313,661
U.S. government agency securities	—	11,145	—	11,145
Corporate securities	—	34,207	—	34,207
Commercial paper	—	277,094	—	277,094
Money market funds	46,882	—	—	46,882
Total	$ 360,543	$ 322,446	$ —	$ 682,989

	Assets at Fair Value as of December 31, 2020			
	Level 1	Level 2	Level 3	Total
US treasury securities	$ 470,109	$ —	$ —	$ 470,109
US government agency securities	91,999	—	—	91,999
Money market funds	49,720	—	—	49,720
Total	$ 611,828	$ —	$ —	$ 611,828

The available-for-sale securities in the Company's Condensed Consolidated Balance Sheets are as follows (in thousands):

	June 30, 2021	December 31, 2020
Cash equivalents	$ 63,096	$ 49,720
Short-term investments	573,605	562,108
Long-term investments	46,288	—
Cash Equivalents and Investments total	$ 682,989	$ 611,828

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.

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Iovance Biotherapeutics, Inc. and its wholly-owned subsidiaries, Iovance Biotherapeutics Manufacturing LLC, Iovance Biotherapeutics GmbH, and Iovance Biotherapeutics B.V. All intercompany accounts and transactions have been eliminated. The U.S. dollar is the functional currency for all of the Company's consolidated operations.

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.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC Topic 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances.

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 for the three and six months ended June 30, 2021.

Leases

The Company determines if an arrangement includes a lease at inception. Operating leases are included in its Condensed Consolidated Balance Sheet as Operating lease right-of-use assets and Operating lease liabilities as of June 30, 2021 and 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 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 periodically issues restricted stock units ("RSUs") and restricted stock awards ("RSAs") 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.

Accrued Research and Development Costs

Research and development costs are expensed as incurred. Clinical development costs compose a significant component of research and development costs. The Company has a history of contracting with third parties that perform various clinical trial activities on its behalf. Service agreements with contract research organizations ("CROs") and contract manufacturing organizations ("CMOs") are recognized as the services are incurred. The Company accrues for expenses resulting from obligations under agreements with its third-parties for which the timing of payments does not match the periods over which the materials or services are provided to the Company. Accruals are recorded based on estimates of services received and efforts expended pursuant to agreements established with CROs, CMOs and other outside service providers. These estimates are typically based on contracted amounts applied to the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the services. The Company makes judgements and estimates in determining the accrual balance in each reporting period.

In the event advance payments are made to a CRO, CMO or other outside service provider, the payments are recorded within prepaid expenses and other current assets and subsequently recognized as research and development expense when the associated services have been performed. As actual costs become known, the Company adjusts its liabilities and assets. Inputs, such as the extent of services received and the duration of services to be performed, may vary from the Company's estimates, which will result in adjustments to research and development expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations. The Company's historical estimates have not been materially different from actual amounts recorded.

Preferred Stock

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

Recent Accounting Standards Adopted

In December 2019, the Financial Accounting Standards Board ("FASB") issued ASU No. 2019-12, Income Taxes (Topic 740): *Simplifying the Accounting for Income Taxes*, which simplifies accounting for income taxes by eliminating certain exceptions to the guidance in Topic 740 related to the approach for allocating income tax expense or benefit for the year to continuing operations, discontinued operations, other comprehensive income, and other charges or credits recorded directly to stockholders' equity; the methodology for calculating income tax expense or benefit in an interim period; and the recognition of deferred tax liabilities outside basis difference. This ASU became effective for the Company on January 1, 2021, however, the adoption of this new standard did not have a material impact on its condensed consolidated financial statements and related disclosures.

NOTE 3. CASH EQUIVALENTS AND INVESTMENTS

Cash equivalents consist of the following (in thousands):

	June 30, 2021	December 31, 2020
Cash equivalents	$ 63,096	$ 49,720
Cash equivalents total	$ 63,096	$ 49,720

Cash equivalents in the tables above exclude cash demand deposits of $19.7 million and $17.6 million as of June 30, 2021 and December 31, 2020, respectively (in thousands).

The following table summarizes the Company's investments that are classified as available-for-sale debt securities (in thousands):

	June 30, 2021	December 31, 2020
Short-term investments	$ 573,605	$ 562,108
Long-term investments	46,288	—
Investments total	$ 619,893	$ 562,108

The following table summarizes the classification of the Company's available-for-sale debt securities in its Condensed Consolidated Balance Sheets (in thousands):

Investments	June 30, 2021	December 31, 2020
U.S. treasury securities	$ 313,661	$ 470,109
U.S. government agency securities	11,145	91,999
Corporate securities	27,193	—
Commercial paper	267,894	—
Investments total	$ 619,893	$ 562,108

The cost and fair value of investments as of June 30, 2021 and December 31, 2020 were as follows (in thousands):

As of June 30, 2021	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	$ 313,655	$ 28	$ (22)	$ 313,661
U.S. government agency securities	11,144	1	—	11,145
Corporate securities	27,203	—	(10)	27,193
Commercial papers	267,858	44	(8)	267,894
Total	$ 619,860	$ 73	$ (40)	$ 619,893

As of December 31, 2020	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	$ 470,108	$ 30	$ (29)	$ 470,109
U.S. government agency securities	91,981	20	(2)	91,999
Total	$ 562,089	$ 50	$ (31)	$ 562,108

The following table summarizes the Company's available-for-sale debt securities by contractual maturity (in thousands):

	June 30, 2021	
	Amortized Cost	Fair Value
Within one year	$ 573,549	$ 573,605
One year to two years	46,311	46,288
Investments total	$ 619,860	$ 619,893

All available-for-sale securities held as of June 30, 2021 and December 31, 2020 had contractual maturities of less than two years. No significant available-for-sale securities held as of the periods presented have been in a continuous unrealized loss position for more than 12 months. As of June 30, 2021, unrealized losses on available-for-sale investments are not attributed to credit risk. The Company determined that it has the ability and intent to hold all marketable securities that have been in a continuous loss position until maturity or recovery. To date, the Company has not recorded any impairment charges on its marketable securities.

NOTE 4. PROPERTY AND EQUIPMENT

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

	June 30, 2021	December 31, 2020
Lab equipment	$ 5,534	$ 4,656
Leasehold improvements	3,630	2,573
Computer equipment	608	270
Office furniture and equipment	480	480
Machinery and equipment	82	—
Construction in progress	76,102	56,758
Total Property and equipment, cost	86,436	64,737
Less: Accumulated depreciation and amortization	(6,316)	(5,578)
Property and Equipment, net	$ 80,120	$ 59,159

Depreciation expense for the three months ended June 30, 2021 and 2020, was approximately $0.3 million and $0.2 million, respectively. Depreciation expense for the six months ended June 30, 2021 and 2020 was approximately $0.7 million and $0.5 million, respectively.

NOTE 5. ACCRUED EXPENSES

Accrued expenses consist of the following (in thousands):

	June 30, 2021	December 31, 2020
Clinical related	$ 13,086	$ 15,661
Accrued payroll and employee related expenses	10,210	9,032
Commercial manufacturing facility related	1,703	4,342
R&D Manufacturing related	6,402	3,266
Legal and related services	998	1,061
Accrued other	1,793	1,712
	$ 34,192	$ 35,074

NOTE 6. STOCKHOLDERS' EQUITY

Common Stock

The Company's certificate of incorporation, as amended, authorizes the issuance of up to 300,000,000 shares of the Company's common stock, par value $0.000041666. As of June 30, 2021, 154,799,721 shares of the Company's common stock were issued and outstanding.

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

Preferred Stock

The Company's certificate of incorporation authorizes the issuance of up to 50,000,000 shares of "blank check" preferred stock. As of June 30, 2021, 17,000 shares were designated as Series A Convertible Preferred Stock ("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 six months ended June 30, 2021 or 2020. As of June 30, 2021 and December 31, 2020, 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 shares 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.

During the six months ended June 30, 2021, a total of 738,961 of Series B Convertible Preferred Stock were converted into 738,961 shares of common stock. No shares of Series B Convertible Preferred Stock were converted during the six months ended June 30, 2020. As of June 30, 2021 and December 31, 2020, 2,842,158 and 3,581,119 shares of Series B Preferred Stock (that are convertible into 2,842,158 and 3,581,119 shares of common stock) remained outstanding, respectively.

At the Market Offering Program

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, (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, which became effective immediately upon filing with the Securities and Exchange Commission on May 27, 2020.

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. 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.

For the three and six months ended June 30, 2021, the Company received approximately $160.3 million and $203.2 million, respectively, in net proceeds, net of offering costs, through the sale of 5,195,856 and 6,474,099 shares of its common stock through the Sales Agreement at a weighted average price per share of $31.49 and $32.12, respectively.

NOTE 7. STOCK BASED COMPENSATION

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. As of June 30, 2021, 11,240 shares were available for future grant under the 2011 Plan. Per the terms of the 2011 Plan, no equity awards may be granted under the 2011 Plan after the ten-year anniversary of the plan's adoption by the Board.

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. As of June 30, 2021, 75,023 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. As of June 30, 2021, 3,608,727 shares of common stock were available for grant under the Company's 2018 Plan.

Stock Options

A summary of the status of stock options as of June 30, 2021, and the changes during the six months 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 as of December 31, 2020	12,615,638	$ 18.08		
Granted	4,476,724	41.80		
Exercised	(656,429)	14.05		
Expired/Forfeited	(1,898,902)	32.32		
Outstanding as of June 30, 2021	14,537,031	$ 23.70	6.95	$ 104,461
Options exercisable as of June 30, 2021	7,832,437	$ 14.35	5.03	$ 94,264

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 quarter ended June 30, 2021 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 June 30, 2021. The intrinsic value of the Company's stock options changes based on the closing price of the Company's common stock.

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 its 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 expenses related to the 2020 ESPP for the three and six months ended June 30, 2021 were $0.5 million and $0.8 million, respectively. No compensation expenses related to the 2020 ESPP were recognized for the same periods in 2020. As of June 30, 2021, 55,315 shares were issued under the 2020 ESPP and there was $0.3 million of unrecognized compensation cost associated with the 2020 ESPP, which will be recognized over the remaining 5.4 months.

Restricted Stock Units

On June 1, 2016, the Company entered into an RSU agreement with the Company's former Chief Executive Officer, Maria Fardis, Ph.D., M.B.A., pursuant to which the Company granted Dr. Fardis 550,000 non-transferrable RSUs at a fair market value price of $5.87 per share as an inducement to her employment pursuant to the exception to The Nasdaq Global Market rules that generally require stockholder approval of equity incentive plans. The 550,000 RSUs vested in installments as follows: (i) 137,500 restricted stock units vested upon the first anniversary of the effective date of Dr. Fardis' employment agreement; (ii) 275,000 restricted stock units vested upon the satisfaction of certain clinical trial milestones; and (iii) 137,500 restricted stock units vested in equal monthly installments over the 36-month period following the first anniversary of the effective date of Dr. Fardis' employment. These RSUs were fully vested as of June 1, 2020 and no RSUs associated with this agreement were outstanding as of June 30, 2021 or December 31, 2020.

In June 2021, under the terms of the 2018 Plan, the Company granted 1,253,540 RSUs to its executives and employees. The awards are time-based and each award has one of two vesting conditions. For some RSU awards, 100% of the RSUs will vest on the first anniversary of the grant date, and for others, 50% of the RSUs will vest on the first anniversary of the grant date with the remaining 50% vesting on December 31, 2022, assuming all time-based conditions are achieved.

A summary of the RSU activity during the six months ended June 30, 2021 is presented in the following table:

	Number of RSUs	Weighted Average Grant Date Fair Value
Outstanding, non-vested as of December 31, 2020	—	$ —
Granted	1,253,540	23.87
Vested	—	—
Canceled/Forfeited	—	—
Outstanding, non-vested as of June 30, 2021	1,253,540	$ 23.87

As of June 30, 2021, there was approximately $28.8 million of related unrecognized compensation cost associated with RSUs, which the Company expects to recognize over a remaining weighted-average period of 1.14 years. The aggregate intrinsic value of the nonvested RSUs outstanding as of June 30, 2021 was $32.6 million.

Stock-Based Compensation

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Research and development	$ 8,585	$ 5,465	$ 17,787	$ 9,783
General and administrative	5,829	5,072	13,568	10,166
Total stock-based compensation expenses	$ 14,414	$ 10,537	$ 31,355	$ 19,949

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Stock option expenses	$ 12,783	$ 10,492	$ 29,443	$ 19,837
Restricted stock unit expenses	1,099	45	1,099	112
2020 ESPP expenses	532	—	813	—
Total stock-based compensation expenses	$ 14,414	$ 10,537	$ 31,355	$ 19,949

As of June 30, 2021, there was $118.8 million of total unrecognized compensation expense related to the options to be recognized over a weighted average period of 2.02 years.

The weighted average grant date fair value for employee options granted under the Company's stock option plans during the six months ended June 30, 2021 and 2020 was $24.38 and $16.20. per option, respectively.

NOTE 8. 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 TIL therapies that are designed to destroy metastatic melanoma cells.

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 products licensed by the U.S. Food and Drug Administration ("FDA") and commercially available reagents routinely used for adoptive cell therapy. The parties have continued 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 $0.5 million for the three months ended June 30, 2021 and 2020, and $1.0 million for the six months ended June 30, 2021 and 2020 respectively, as research and development expenses.

Patent License Agreement Related to the Development and Manufacture of TIL

Effective October 5, 2011, the Company entered into 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 TIL adoptive cell therapy products for the treatment of metastatic melanoma, lung, breast, bladder and HPV-positive cancers (the "Indications"). The Patent License Agreement required 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 Indications and other direct costs incurred by the NIH pursuant to the agreement.

Effective May 6, 2021, the Company entered into an Amended and Restated Patent License Agreement with NIH (the “Amended and Restated Patent License Agreement”), which includes the grant of additional exclusive, worldwide patent rights in the Indications to cytokine-tethered TIL technology, and expands the non-exclusive, worldwide field of use to all cancers. The Amended and Restated Patent License Agreement requires the Company to pay royalties based on a percentage of net sales in jurisdictions where patent rights exist, which percentage can fall into a tier that may be less than one percent to mid-single digits depending upon certain events, including the exclusivity of the rights, and a percentage of revenues from sublicensing arrangements, and the Company expects lower overall royalty payments as a result. The Company also agreed to potential milestone payments on the achievement of certain clinical, regulatory and commercial sales milestones for each of the Indications and other direct costs incurred by the NIH pursuant to the Amended and Restated Patent License Agreement. The Company anticipates making a milestone payment in the low single-digit millions of dollars in conjunction with the approval of a Biologics License Application for any of its product candidates covered by the Amended and Restated Patent License Agreement. The term of the Amended and Restated Patent License Agreement continues until the expiry of the last-to-expire patent rights licensed thereunder, and the agreement contains standard termination provisions.

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 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. The Company recorded a de minimis amount and $0.1 million of research and development costs of for the three months ended June 30, 2021 and 2020 respectively, and $0.2 million for the six months ended June 30, 2021 and $0.5 million for the six months ended June 30, 2020, 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 three and six months ended June 30, 2021 and 2020.

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 a de minimis amount for the three months ended June 30, 2021 and 2020, respectively, and a de minimis amount for the six months ended June 30, 2021 and 2020, respectively, as research and development expenses in connection with the Second Moffit License.

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. The Company recorded $0.1 million and zero expenses associated with the MDACC SAA for the three months ended June 30, 2021 and 2020, respectively, and $0.1 million and $0.2 million for the six months ended June 30, 2021 and 2020, respectively, as research and development expenses.

WuXi Apptec, Inc.

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 its 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, September 2020 and February 2021, and the statement of work for the second suite was amended in 2019. The statements of work for the 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 fees upon written notice from the Company of 30 days and 90 days for the first and second suites, respectively. The terms of the related statements of work for the first suite currently extends to February 2022 and the terms of the second manufacturing suite were extended to December 2022.

The Company recorded costs associated with agreements with WuXi of $4.8 million and $5.7 million for the three months ended June 30, 2021 and 2020, respectively, and $8.2 million and $12.3 million for the six months ended June 30, 2021 and 2020, 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 agreements with Cellectis of $0.1 million for the three months ended June 30, 2021 and 2020 and $0.2 million for the six months ended June 30, 2021 and 2020, respectively, as research and development expenses.

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. No expenses were recorded for the three and six months ended June 30, 2021. The Company recorded costs associated with the license agreement from Novartis of $10.0 million as research and development expenses for the six months ended June 30, 2020.

NOTE 9. 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.

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 February 10, 2021, the Company filed its opening brief in support of its appeal of the court’s grant of the Solomon Plaintiff’s motion for reconsideration.

On March 24, 2021, the Solomon Plaintiffs filed their brief in opposition to the Company's appeal of the court's grant of the Solomon Plaintiff's motion for reconsideration. On April 2, 2021, the Company filed its reply brief in support of the Company's appeal of the court's grant of the Solomon Plaintiffs' motion for reconsideration. On May 3, 2021, the Solomon Plaintiffs filed their opening brief in support of their appeal of the court's grant of summary judgment limiting the Solomon Plaintiffs' damages for the Equity Claim to $47,420. On May 11, 2021, the Appellate Division upheld the court's grant of the Solomon Plaintiffs' motion for reconsideration of the dismissal of the First Solomon Suit for want of prosecution.

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. 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. On March 26, 2021, the Court denied the Company's motion to dismiss for lack of personal jurisdiction. The Company filed a response to the complaint in the Second Solomon Suit on April 30, 2021. On May 26, 2021, the Company and Singh filed motions for judgment on the pleadings with respect to the second and third claims asserted against the Company and all claims asserted against Singh, respectively, in the Second Solomon Suit. On June 25, 2021, the Solomon Plaintiffs filed an opposition brief against the motions for judgment on the pleadings. On July 16, 2021, the Company and Singh filed reply briefs in support of the motions for judgement on the pleadings.

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.

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 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.

New Headquarters Lease

On February 8, 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 “Headquarters 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 of the New Headquarters Lease (the “Commencement Date”), which is February 9, 2022, or (ii) the date that the Tenant Improvements (as defined therein) are substantially completed, which is currently expected to be at the end of 2021; 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 United States, 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. 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 approximately $280,000, subject to an annual increase of 3%. Beginning in 2022, the Company will also be responsible for paying operating expenses.

The 120-month term of the New Headquarters Lease is expected to commence in late 2021. Minimum rental payments under the New Headquarters Lease total $36.5 million, which does not include rental payments related to the Company’s one-time option to extend for an additional five years. There was no right-of-use asset or lease liability reflected on the balance sheet as of June 30, 2021 for the New Headquarters Lease, as the Company has not yet obtained control over the use of the Headquarters Premises.

San Carlos Existing Headquarters Leases

On August 4, 2016, the Company entered into an agreement with Hudson Skyway Landing, LLC (the “Suite 150 Lease”) to lease 8,733 square feet of space for its corporate headquarters 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 Lease was 54 months subsequent to the commencement date and expired in April 2021. Monthly lease payments were approximately $38,000.

On October 19, 2018, the Company entered into an agreement (the “Lease”) to lease 12,322 square feet of office space located adjacent to the Company’s headquarters in San Carlos, California. The term of the lease expired on April 30, 2021. Monthly lease payments were 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 the Lease for additional space at its corporate headquarters in San Carlos, California. Under the Amended Lease, the Company leased 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 Skyway Landing II. The term of the Amended Lease expired on April 30, 2021. Monthly lease payments were approximately $39,000 for the first year and $40,000 for the second year.

On February 8, 2021, the Company entered into two amendments (the “Suite 100 and 125 Second Amendment” and the “Suite 150 First Amendment”) to the Amended Lease and the Suite 150 Lease, respectively.

Under the Suite 100 and Suite 125 Second Amendment, the Company extended the Amended Lease which 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 approximately $103,000. 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 extended the Suite 150 Lease, which also expired on April 30, 2021, to December 31, 2021. The Company’s monthly base rent under the Suite 150 First Amendment are approximately $44,000. 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.

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 30, 2025 for approximately $34,500 a month.

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 to 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 the Company closed its 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 “Manufacturing Premises”). The construction of the commercial manufacturing facility began in July 2019 and has been substantially completed. The construction of tenant improvements in the commercial manufacturing facility is expected to be completed in the third quarter of 2021, at which time the assets will be placed in service.

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 Manufacturing 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.

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 (in thousands):

	June 30, 2021	December 31, 2020
Operating lease right-of-use assets	$ 52,508	$ 54,756
Operating lease liabilities		
Current portion included in current liabilities	4,428	6,284
long-term portion included in non-current liabilities	46,843	45,375
Total Operating lease liabilities	$ 51,271	$ 51,659

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Operating lease cost	$ 3,380	$ 2,073	$ 6,777	$ 3,709
Variable lease cost	1,578	1,260	2,288	2,631
Short-term lease cost	39	14	75	31
Total lease cost	$ 4,997	$ 3,347	$ 9,140	$ 6,371
Other information				
Cash paid for amounts included in the measurement of lease liabilities included in Operating cashflows	$ 2,512	$ 1,906	$ 4,834	$ 4,102
Right-of-use assets obtained from entering new leases	$ —	$ —	$ —	$ —
Increase (decrease) in right-of-use assets from lease modifications	$ (215)	$ (151)	$ 1,943	$ 328
Weighted-average remaining lease terms (years)			17.97	1.69
Weighted-average discount rates			7.5%	7.5%

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 June 30, 2021, the maturities of the Company's operating lease liabilities were as follows (in thousands):

	Facility leases	CMO embedded leases	Total
2021	$ 3,084	$ 2,334	$ 5,418
2022	4,414	361	4,775
2023	4,423	—	4,423
2024	4,516	—	4,516
2025	4,372	—	4,372
Thereafter	74,899	—	74,899
Total lease payments	$ 95,708	$ 2,695	$ 98,403
Less: Present value adjustment	(47,114)	(18)	(47,132)
Operating lease liabilities	$ 48,594	$ 2,677	$ 51,271

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.

NOTE 11. LONG-TERM NOTE

On January 26, 2021, the Company entered into a 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 February 18, 2021, 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 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.

The Company concludes that it is not reasonably assured that all or a portion of the loan will be forgiven as of June 30, 2021, and therefore accounted for the Job Creation Loan as debt in accordance with ASC Topic 470 – Debt, as opposed to an in-substance government grant, and classified as a long-term debt in its Condensed Consolidated Balance Sheet as of June 30, 2021.

NOTE 12. 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. This stock option was fully vested in September 2020. No expense was recognized for the three and six months ended June 30, 2021 related to this consulting agreement. The Company recognized $0.1 million and $0.2 million in stock-based compensation expense related to this consulting agreement for the three and six months ended June 30, 2020, respectively.

NOTE 13. INCOME TAXES

The Company did not record income tax expenses for the three and six months ended June 30, 2021 and 2020, respectively as the Company expected to be in a taxable loss position in 2021 and 2020, and the net deferred tax assets are fully offset by a valuation allowance as it is not more likely than not that the benefit will be realized. Therefore, the Company's effective tax rate was 0.0%, for the three and six months ended June 30, 2021 and 2020, respectively. As of June 30, 2021, the Company remains in a cumulative book loss position and does not have sufficient positive evidence to realize its net deferred tax assets. As such, the Company continues to maintain a full valuation allowance against its net deferred tax assets.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The management's discussion and analysis of our financial condition as of June 30, 2021 and results of operations for the three and six months ended June 30, 2021, should be read in conjunction with management's discussion and analysis of financial condition and results of operations included in our Annual Report on Form 10-K for the year ended December 31, 2020 which was filed with the Securities and Exchange Commission, or SEC, on February 25, 2021. 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 of our Annual Report on Form 10-K and elsewhere in this report and other reports we file with the SEC. 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. Unless the context requires otherwise, references in this Quarterly Report on Form 10-Q to "Iovance," "we," "us" and "our" refer to Iovance Biotherapeutics, Inc. and our subsidiaries.

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, polyclonal 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 TIL manufacturing process 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 therapy for the treatment of squamous cell carcinoma of the head and neck, non-small cell lung cancer, or NSCLC, and are investigating peripheral blood lymphocyte, or PBL, therapy for patients with relapsed or refractory chronic lymphocytic leukemia, or CLL, and small lymphocytic lymphoma, 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 TIL 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 June 6, 2021. As of the data extract in April 2021, in 66 patients with metastatic melanoma in Cohort 2, treatment with lifileucel resulted in an objective response rate, or ORR, of 36%, as assessed by investigator, with 3 complete responses and 21 partial responses. The disease control rate, or DCR, was 80.3%. Median duration of response, or DOR, in Cohort 2 had not been reached after 33.1 months of median study follow up. Results from Cohort 2 presented at ASCO in June 2021 also suggest that early intervention with lifileucel at the time of initial progression on anti-PD-1 therapy may maximize benefit. Patients in Cohort 2 were heavily pretreated and had a mean of 3.3 prior therapies. We have previously reported durable responses across a wide age range of metastatic melanoma patients, among those who have received prior anti-CTLA-4 and BRAF targeted treatments, regardless of BRAF mutation status, and in patients with PD-L1 high and low status. The adverse event profile was generally consistent with the underlying advanced disease and the profile of the lymphodepletion and IL-2 regimens. In addition, detailed Cohort 2 data was published in the Journal of Clinical Oncology on May 12, 2021.

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 U.S. Food and Drug Administration, or 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 Medicines 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 with Gen 2 product released for Cohort 4. We previously disclosed initial results from Cohort 4 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 ORR data was 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%. Previously, we reported the submission of additional potency assay data to the FDA, and 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. In May 2021, we announced that we had received regulatory feedback from the FDA regarding our potency assays for lifileucel. Following FDA feedback, we have continued our ongoing work developing and validating our potency assays and plan to submit additional assay data and to meet with the FDA in the second half of 2021. Our BLA submission for lifileucel in metastatic melanoma is now expected to occur during the first half of 2022.

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 our lead product candidate 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. In November 2019, we 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 may 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 cancer patients. We intend to initiate a dialog with the FDA to discuss these cohorts and potential BLA submission plans for lifileucel in cervical cancer after resolution of regulatory discussions regarding our potency assays.

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. In June 2021, we reported that the first patient was dosed in the IOV-LUN-202 clinical trial. We intend to continue to enroll patients in the IOV-LUN-202 clinical trial throughout 2021 and 2022.

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 head and neck squamous cell carcinoma, or 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 we 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 1A of the IOV-COM-202 trial, we are enrolling advanced unresectable or metastatic melanoma patients who are naïve to anti-PD-1 therapy. We reported results from ongoing Cohort 1A of the IOV-COM-202 trial at the ASCO meeting in June

2021, as follows. Seven patients received lifileucel in combination with pembrolizumab. Six of the seven patients had a confirmed objective response, with an ORR of 86%, including two complete responses, one unconfirmed complete response who had not yet reached the confirmatory complete response assessment, and three partial responses, with one best response of stable disease. The complete response rate, including the unconfirmed complete response, was 43%. The median follow up was 8.2 months. The Cohort 1A results also demonstrated that lifileucel can be safely combined with pembrolizumab. The treatment-emergent adverse event, or TEAE, profile was consistent with the underlying disease and known adverse event profiles of pembrolizumab, non-myeloablative lymphodepletion, or NMA-LD, and IL-2.

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 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 DCR 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 positive for Human Papilloma Virus, or HPV, 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.

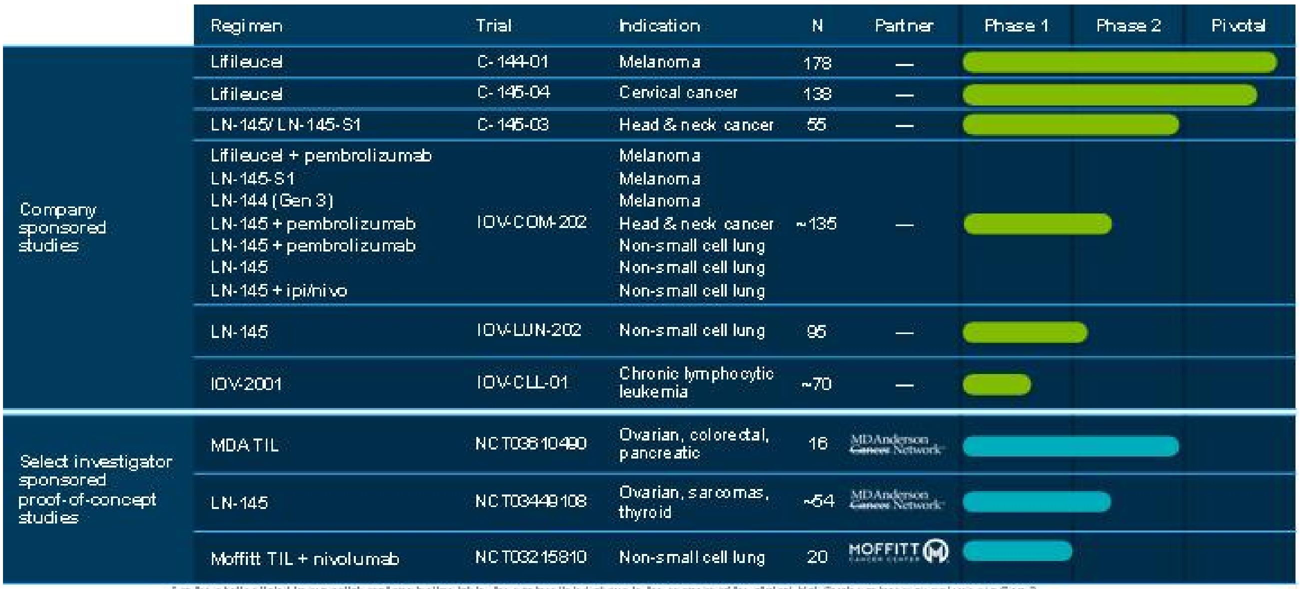
In Cohort 3B of the IOV-COM-202 trial, we enrolled patients with metastatic NSCLC that had progressed on prior immune checkpoint inhibitor therapy, including patients with oncogene-driven tumors who received prior tyrosine kinase inhibitor therapy. Patients were treated with LN-145 monotherapy. We reported results from Cohort 3B of the IOV-COM-202 trial in June 2021, as follows. The ORR was 21.4% for the 28 patients that participated in the trial, including one complete response and five partial responses, and the DCR was 64.3%, including two responders with PD-L1 negative tumors. Median DOR was not reached at a median study follow up of 8.2 months. The treatment-emergent adverse event profile was consistent with the underlying disease and known adverse event profiles of non-myeloablative lymphodepletion and IL-2. All patients treated in Cohort 3B of the IOV-COM-202 trial received prior anti-PD-1/L1 therapy and all six responding patients also received prior chemotherapy. Historically, ORRs of approximately 20% were reported with ICIs as second-line therapy in ICI-naïve patients who progressed on front-line chemotherapy. We anticipate presenting additional Cohort 3B data at a medical meeting in the second half of 2021

In November 2019, we announced that our investigational new drug, or IND, application 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 M.D. 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, was previously active. This trial treated patients with platinum resistant ovarian cancer, pancreatic and colorectal cancer with TIL manufactured by MDACC. 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:



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

We have developed a third-generation TIL 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-five 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, 10,639,330, 10,646,517, 10,653,723, 10,695,372, 10,894,063, 10,905,718, 10,918,666, 10,925,900, 10,933,094, 10,946,044, 10,946,045, 10,953,046, 10,953,047, and 11,013,770. 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 and patents 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, 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.

Components of Operating Results

Revenue

We have not yet generated any revenues since our formation, 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 months 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.

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. We have a history of contracting with third parties that perform various clinical trial activities on our behalf in connection with the ongoing development of our 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. We accrue and expense costs for clinical trial activities performed by third parties based upon estimates of work completed to date of the individual trial in accordance with agreements established with contract research organizations and clinical trial sites. We determine our 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.

We expect our research and development expenses to increase over the next couple of 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.

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, information technology and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to corporate matters and intellectual property, insurance, public company expenses relating to maintaining compliance with Nasdaq listing rules and SEC requirements, investor relations costs, and fees for accounting and consulting services. General and administrative costs are expensed as incurred, and we accrue 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.

We anticipate general and administrative expenses will increase in 2021 as we continue to prepare for commercialization and support an expected growth of the internal general and administrative team.

Interest Income

Interest income results from our interest-bearing cash and investment balances.

Results of Operations

Comparison of the Three and Six Months Ended June 30, 2021 and 2020

<u>Revenues</u>

We did not generate any revenues during the three and six months ended June 30, 2021 or June 30, 2020.

Research and Development expenses (in thousands)

	Three Months Ended June 30, 2021	Three Months Ended June 30, 2020	Increase / (Decrease) $	Increase / (Decrease) %	Six Months Ended June 30, 2021	Six Months Ended June 30, 2020	Increase / (Decrease) $	Increase / (Decrease) %
Research and development	$ 62,119	$ 49,274	12,845	26 %	$ 118,068	$ 106,226	11,842	11 %
Stock-based compensation expense included in research and development expense	8,585	5,465	3,120	57 %	17,787	9,783	8,004	82 %

Research and development expense for the three months ended June 30, 2021 increased by $12.8 million, or 26%, compared to the same period in 2020. The increase was primarily attributable to (i) a $7.1 million increase in payroll and related expenses, (ii) a $3.1 million increase in stock-based compensation expenses, (iii) a $2.3 million increase in our commercial manufacturing facility related cost, and (iv) a $2.8 million increase in manufacturing costs. These increases were partially offset by a $3.6 million decrease in clinical trial costs due to completion of enrollment in pivotal cohorts for melanoma and cervical cancer, and head and neck clinical trials.

Research and development expense for the six months ended June 30, 2021 increased by $11.8 million, or 11%, compared to the same period in 2020. The increase was primarily attributable to (i) a $14.0 million increase in payroll and related expenses, (ii) a $8.0 million increase in stock-based compensation expenses, and (iii) a $4.0 million increase in our commercial manufacturing facility related activities. These increases were partially offset by a $10.0 million decrease in the license cost to further develop IOV-3001 obtained from Novartis for which we recognized in January 2020 in full, and a $5.6 million decrease in clinical trial costs and related manufacturing costs due to completion of enrollment in pivotal cohorts for melanoma and cervical cancer, and head and neck clinical trials.

General and Administrative expenses (in thousands)

	Three Months Ended June 30, 2021	Three Months Ended June 30, 2020	Increase / (Decrease) $	Increase / (Decrease) %	Six Months Ended June 30, 2021	Six Months Ended June 30, 2020	Increase / (Decrease) $	Increase / (Decrease) %
General and administrative	$ 19,307	$ 14,353	4,954	35 %	$ 38,928	$ 28,211	10,717	38 %
Stock-based compensation expense included in general and administrative	5,829	5,072	757	15 %	13,568	10,166	3,402	33 %

General and administrative expenses for the three months ended June 30, 2021 increased by $5.0 million, or 35%, compared to the same period in 2020. The increase was primarily attributable to (i) a $2.6 million increase in payroll and related expenses, including $0.8 million of stock-based compensation expenses, (ii) $1.4 million increase in intellectual property filing related costs, and (iii) $0.8 million increase in insurance, license and professional fees.

General and administrative expenses for the six months ended June 30, 2021 increased by $10.7 million, or 38%, compared to the same period in 2020. The increase was primarily attributable to (i) a $4.7 million increase in payroll and related expenses, (ii) a $3.4 million increase in stock-based compensation expenses, and (iii) $2.3 million increase in intellectual property filing related costs, insurance and license fees.

Interest Income (in thousands)

	Three Months Ended June 30, 2021	Three Months Ended June 30, 2020	Increase / (Decrease) $	Increase / (Decrease) %	Six Months Ended June 30, 2021	Six Months Ended June 30, 2020	Increase / (Decrease) $	Increase / (Decrease) %
Net interest income	$ 75	$ 609	(534)	(88)%	$ 196	$ 1,824	(1,628)	(89)%

Net interest income for the three and six months ended June 30, 2021 and 2020 decreased by $0.5 million, or 88%, and $1.6 million, or 89%, respectively, due primarily to less interest income earned from our investment portfolio during the continued low interest rate environment during the current COVID-19 pandemic.

Net Loss (in thousands)

	Three Months Ended June 30,		Increase / (Decrease)		Six Months Ended June 30,		Increase / (Decrease)	
	2021	2020	$	%	2021	2020	$	%
Net loss	$ (81,351)	$ (63,018)	(18,333)	29 %	$ (156,800)	$ (132,613)	(24,187)	18 %

Net loss for the three and six months ended June 30, 2021 increased by $18.3 million or 29% and $24.2 million or 18%, respectively, compared to the same periods in 2020. The increase in our net loss was due to the continued expansion of our research and development activities and the overall growth of our corporate infrastructure. We anticipate that we will continue to incur net losses in the future as we further invest in our research and development activities and commercial preparation activities.

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 June 30, 2021, we had outstanding 154,799,721 shares of our $0.000041666 par value common stock, 194 shares of our $0.001 par value Series A Convertible Preferred Stock, and 2,842,158 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 2,842,158 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.

On February 8, 2021, we entered into an Open Market Sale Agreement, or the Sales Agreement, with Jefferies LLC, or Jefferies, with respect to an “at the market” offering program, under which we may, from time to time, in our sole discretion, issue and sell through Jefferies, acting as sales agent, up to $350.0 million of shares of our common stock. The issuance and sale, if any, of shares of our common stock under the Sales Agreement will be made pursuant to a prospectus supplement, dated February 8, 2021, to the 2020 Automatic Shelf Registration Statement. For the three and six months ended June 30, 2021, we received approximately $160.3 million and $203.2 million in net proceeds through the sale of 5,195,856 and 6,474,099 shares of our common stock, respectively.

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 Automatic 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 $156.8 million for the six months ended June 30, 2021 and used $116.4 million of cash in our operating activities for the same period ended June 30, 2021. As of June 30, 2021, we had $82.8 million of cash, cash equivalents, $619.9 million of investments ($573.6 million of short-term investments, and $46.3 million of long-term investments), $744.4 million of stockholders’ equity and had working capital of $606.1 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 Quarterly Report on Form 10-Q, 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

The following table summarizes our cash flows for the periods presented from Operating, Investing and Financing Activities (in thousands):

	Six Months Ended June 30,	
	2021	**2020**
Net cash (used in) provided by:		
Operating activities	$ (116,399)	$ (101,927)
Investing activities	(81,954)	(323,651)
Financing activities	214,346	572,298
Net increase in cash, cash equivalents and restricted cash	$ 15,993	$ 146,720

Operating Activities

Net cash used in operating activities for the six months ended June 30, 2021 was $116.4 million compared to $101.9 million for the same period in 2020. The increase of $14.5 million was primarily due to the increased costs in research and development and pre-commercial activities

Investing Activities

Net cash used by investing activities for periods presented primarily relate to the purchase, sale and maturity of investments used to fund the day-to-day needs of our business. Net cash used by investing activities for the six months ended June 30, 2021 was $81.9 million compared to net cash used by investing activities of $323.7 million for the same period in 2020. The decrease in cash provided by investing activities of $241.7 million was primarily due to increase in the purchase of property and equipment related to the commercial manufacturing facility and the timing of maturities and purchases of investments.

Financing Activities

Net cash provided by financing activities for the six months ended June 30, 2021 was $214.3 million compared to $572.3 million for the same period in 2020. The decrease of $358.0 million was primarily due to net proceeds of $567.4 million received from our June 2020 public offering as compared to net proceeds of $203.2 million received from the "at the market" offering program during the six months ended June 30, 2021.

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 three and six months ended June 30, 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

As of June 30, 2021, we had no obligations that would require disclosure as off-balance sheet arrangements.

Significant Accounting Policies and Recent Accounting Standards

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

Inflation

Inflation has not had a material effect on our business, financial condition or results of operations over our two most recent fiscal years.

Item 3. Quantitative and Qualitative Disclosures About Market 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. As of June 30, 2021, we had $619.9 million invested in marketable securities with a maturity date of less than two years. 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 June 30, 2021, the fair value of our investment portfolio would increase or decrease by approximately $2.7 million.

Item 4. Controls and Procedures

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of our disclosure controls and procedures, as such term is defined under Rule 13a-15(e) promulgated under the Exchange Act as of the end of the period covered by this Quarterly Report on Form 10-Q. Based on this evaluation, our principal executive officer and our principal financial officer concluded that our disclosure controls and procedures were effective as of the end of the period covered by this Quarterly Report on Form 10-Q.

Changes in Internal Controls Over Financial Reporting

There have not been any changes in our internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended June 30, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. Legal Proceedings

The information in Note 9 to the Condensed Consolidated Financial Statements contained in Part I, Item 1 of this Quarterly Report on Form 10-Q 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 9 to our Condensed Consolidated Financial Statements for the quarter ended June 30, 2021 contained in this Quarterly Report on Form 10-Q.

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 our Annual Report on Form 10-K for the year ended December 31, 2020 filed on February 25, 2021, 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

We have marked with an asterisk (*) those risk factors below that reflect a substantive change from the risk factors included in our Annual Report on Form 10-K filed with the SEC on February 25, 2021.

Our business is subject to a number of risks and uncertainties, including those risks discussed at length below. These risks include, among others, the brief bulleted list of our principal risk factors set forth below 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 June 30, 2021, we had an accumulated deficit of $987.0 million. In addition, during the six months ended June 30, 2021, we incurred a net loss of $156.8 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 2022. 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. In addition, differences in patient population may affect the clinical results of Cohort 4 as compared to Cohort 4. 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 was not expected by the end of 2020 and was anticipated instead to occur in 2021. Previously, we reported the submission of assay data to the FDA, and on May 18, 2021, we announced that we had received regulatory feedback from the FDA regarding our potency assays for lifileucel. Following FDA feedback, we will continue our ongoing work developing and validating our potency assays and plan to submit additional assay data and to meet with the FDA in the second half of 2021. Our BLA submission for lifileucel is now expected to occur during the first half of 2022. 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 June 30, 2021, we have an accumulated deficit of $987.0 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 February 2021 we entered into an open market sale agreement, or the Sales Agreement, with Jefferies LLC, which provides for the sale of up to $350.0 million of our common stock from time to time. For the six months ended June 30, 2021, we received approximately $203.2 million in net proceeds through the sale of 6,474,099 shares of our common stock. As of June 30, 2021, we had approximately $702.7 million in cash, cash equivalents and investments ($82.8 million of cash and cash equivalents, $573.6 million in short-term investments, and $46.3 million of long-term investments).

Accordingly, we believe that our existing cash, cash equivalents and investments will be sufficient to fund our operations for at least the next twelve months from the date this Quarterly Report on Form 10-Q 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, including our June 2020, October 2018, and January 2018 public offerings, and the proceeds from sales pursuant to the Sales Agreement with Jefferies LLC, which provides for the sale of up to $350.0 million of our common stock from time to time, 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 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, ransomware, social engineering and other means to affect service reliability and threaten data confidentiality, privacy, 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, changes in the competitive environment, 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 was not expected by the end of 2020 and was anticipated to occur in 2021. Previously, we reported the submission of assay data to the FDA, and on May 18, 2021, we announced that we had received regulatory feedback from the FDA regarding our potency assays for lifileucel. Following FDA feedback, we will continue our ongoing work developing and validating our potency assays and plan to submit additional assay data and to meet with the FDA in the second half of 2021. Our BLA submission for lifileucel is now expected to occur during the first half of 2022. 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 Quarterly Report on Form 10-Q or our Annual Report on Form 10-K filed with the SEC on February 25, 2021.

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 June 30, 2021, we had 154,799,721 shares of common stock outstanding. In addition, we had 18,769,495 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 through purchases of employee stock purchase plan, or 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.

Item 2. Unregistered Sales of Securities and Use of Proceeds.

Nothing to report.

Item 3. Defaults Upon Senior Securities.

Nothing to report.

Item 4. Mine Safety Disclosures

Nothing to report.

Item 5. Other Information.

Nothing to report.

Item 6. Exhibits

EXHIBIT INDEX

Exhibit	Description
3.1	Second Amended and Restated Bylaws of Iovance Biotherapeutics, Inc. (incorporated by reference herein to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the Commission on April 26, 2021).
10.1 ++*	Amended and Restated Patent License Agreement, by and between Iovance Biotherapeutics, Inc. and the National Institutes of Health.
10.2++#	Form of Stock Unit Notice and Stock Unit Agreement under the Iovance Biotherapeutics, Inc. 2018 Equity Incentive Plan, as amended (June 2021 Retention Equity Awards).
10.3++#	Form of Nonqualified Stock Option Award Agreement under the Iovance Biotherapeutics, Inc. 2018 Equity Incentive Plan, as amended (June 2021 Retention Equity Awards).
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 Quarterly Report on Form 10-Q of Iovance Biotherapeutics, Inc. for the quarter ended June 30, 2021, formatted in iXBRL (Inline eXtensible Business Reporting Language): (1) Condensed Consolidated Balance Sheets as of June 30, 2021 and December 31, 2020; (2) Condensed Consolidated Statements of Operations for the three and six months ended June 30, 2021 and 2020; (3) Condensed Consolidated Statements of Comprehensive Loss for the three and six months ended June 30, 2021 and 2020; (4) Condensed Consolidated Statements of Stockholders' Equity as of June 30, 2021 and December 31, 2020; (5) Condensed Consolidated Statements of Cash Flows for the three and six months ended June 30, 2021 and 2020; and (6) Notes to Condensed Consolidated 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.

#	Indicates a management contract or compensatory plan or arrangement.
++	Filed herewith (unless otherwise noted as being furnished herewith).
*	Certain portions of the Exhibit have been redacted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

	Iovance Biotherapeutics, Inc.
August 5, 2021	By: /s/ Frederick G. Vogt, Ph.D., Esq. Frederick G. Vogt, Ph.D., Esq. Interim Chief Executive Officer and President, and General Counsel (Principal Executive Officer)
August 5, 2021	By: /s/ Jean-Marc Bellemin Jean-Marc Bellemin Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)

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 "[***]"

PUBLIC HEALTH SERVICE

AMENDED AND RESTATED PATENT LICENSE AGREEMENT – *EXCLUSIVE*

This **Agreement** is based on the model Patent License Exclusive Agreement adopted by the U.S. Public Health Service ("**PHS**") Technology Transfer Policy Board for use by components of the National Institutes of Health ("**NIH**"), the Centers for Disease Control and Prevention ("**CDC**"), and the Food and Drug Administration ("**FDA**"), which are agencies of the **PHS** within the Department of Health and Human Services ("**HHS**").

This Cover Page identifies the Parties to this **Agreement**:

The U.S. Department of Health and Human Services, as represented by
The National Institutes of Health
an Institute or Center (hereinafter referred to as the "**IC**") of the
NIH

and

Iovance Biotherapeutics, Inc. (f/k/a Lion Biotechnologies, Inc.)
hereinafter referred to as the "**Licensee**",
having offices at 999 Skyway Road, Suite 150, San Carlos, CA 94070,
created and operating under the laws of the State of Delaware
Tax ID No: 75-3254381

For the **IC** internal use only:

License Number: L-107-2015-3

License Application Numbers: A-286-2014; A-128-2015; and A-168-2021

Serial Number(s) of Licensed Patent(s) or Patent Application(s): The patents and patent applications listed in Appendix A are incorporated by reference herein.

Licensee: Iovance Biotherapeutics, Inc.

Cooperative Research and Development Agreement (CRADA) Number: None

Public Benefit(s):

The public will benefit from the development of Licensed Products by the Licensee that are granted FDA approval. There is a long-felt need for better treatments for metastatic melanoma. The development of novel TIL-based therapies will provide patients with new cancer treatment options in the realm of personalized medicine to support public health.

This Amended and Restated Patent License Agreement, hereinafter referred to as the "**Agreement**", consists of this Cover Page, an attached **Agreement**, a Signature Page, Appendix A (List of Patent(s) or Patent Application(s)), Appendix B (Fields of Use and Territory), Appendix C (Royalties), Appendix D (Benchmarks and Performance), Appendix E (Commercial Development Plan), Appendix F (Example Royalty Report), and Appendix G (Royalty Payment Options).

The **IC** and the **Licensee** agree as follows:

1. BACKGROUND

1.1 In the course of conducting biomedical and behavioral research, the **IC** or the **FDA** investigators made inventions that may have commercial applicability.

1.2 By assignment of rights from **IC** or **FDA** employees and other inventors, **HHS**, on behalf of the **Government**, owns intellectual property rights claimed in any United States or foreign patent applications or patents corresponding to the assigned inventions. **HHS** also owns any tangible embodiments of these inventions actually reduced to practice by the **IC** or the **FDA**.

1.3 The Secretary of **HHS** has delegated to the **IC** the authority to enter into this **Agreement** for the licensing of rights to these inventions.

1.4 The **IC** desires to transfer these inventions to the private sector through commercialization licenses to facilitate the commercial development of products and processes for public use and benefit.

1.5 The **Licensee** desires to acquire commercialization rights to certain of these inventions in order to develop processes, methods, or marketable products for public use and benefit.

1.6 The parties previously entered into that certain Patent License Agreement, dated as of February 9, 2015 ("**Original Agreement**"), as amended by First Amendment to L-107-2015/0, dated as of October 2, 2015 and corrected as of December 10, 2015, (the "**First Amendment**") and desire to enter into this **Agreement** to further amend and fully restate the **Original Agreement** (including the **First Amendment**).

1.7 The parties acknowledge that after execution of the **Original Agreement** and the **First Amendment**, **Licensee** changed its name from Lion Biotechnologies, Inc. to Iovance Biotherapeutics, Inc.

2. DEFINITIONS

2.1 "**Affiliate(s)**" means a corporation or other business entity, which directly or indirectly is controlled by or controls, or is under common control with the **Licensee**. For this purpose, the term "control" shall mean ownership of more than fifty percent (50%) of the voting stock or other ownership interest of the corporation or other business entity, or the power to elect or appoint more than fifty percent (50%) of the members of the governing body of the corporation or other business entity.

2.2 "**Benchmarks**" mean the performance milestones that are set forth in Appendix D.

2.3 “**Commercial Development Plan**” means the written commercialization plan attached as Appendix E.

2.4 “**Commercially Reasonable Efforts**” means, with respect to the efforts to be expended by **Licensee** with respect to any objective, the reasonable, diligent, good faith efforts to accomplish such objective as **Licensee** would normally use to accomplish a similar objective under similar circumstances. It is understood and agreed that with respect to the research, development and sale of **Licensed Products** or **Licensed Process(es)** by **Licensee**, such efforts shall be substantially equivalent to those efforts and resources commonly used by **Licensee** for products owned by it or to which it has rights, which product is at a similar stage in its development or product life cycle. **Commercially Reasonable Efforts** shall be determined on a market-by-market basis, and it is anticipated that the level of effort will be different for different markets, and will change over time, reflecting changes in the status of the **Licensed Products** or **Licensed Process(es)** and the market(s) involved.

2.5 “**CRADA**” means a Cooperative Research and Development Agreement.

2.6 “**FDA**” means the U.S. Food and Drug Administration.

2.7 “**First Commercial Sale**” means the initial transfer by or on behalf of the **Licensee** or its sublicensees of the **Licensed Products** or the initial practice of a **Licensed Process** by or on behalf of the **Licensee** or its sublicensees in a country after obtaining regulatory approval by the **FDA** or any foreign equivalent necessary for the marketing and sale of such **Licensed Product** or practice of such **Licensed Process** in exchange for cash or some equivalent consideration to which value can be assigned for the purpose of determining **Net Sales**.

2.8 “**Government**” means the Government of the United States of America.

2.9 “**Licensed Fields of Use 1 and 2**” means the **Licensed Field of Use 1** and the **Licensed Field of Use 2**; “**Licensed Field of Use 1**” and “**Licensed Field of Use 2**” shall mean the fields of use identified for such terms, respectively, in Appendix B.

2.10 “**Licensed Patent Rights**” shall mean:

(a) patent applications (including provisional patent applications and PCT patent applications) or patents listed in Appendix A, all divisions and continuations of these applications, all patents issuing from these applications, divisions, and continuations, and any reissues, reexaminations, and extensions of these patents;

(b) to the extent that the following contain one or more claims directed to the invention or inventions disclosed in Paragraph 2.10(a):

(i) continuations-in-part of Paragraph 2.10(a);

(ii) all divisions and continuations of these continuations-in-part;

(iii) all patents issuing from these continuations-in-part, divisions, and continuations;

(iv) priority patent application(s) of Paragraph 2.10(a); and

(v) any reissues, reexaminations, and extensions of these patents;

(c) to the extent that the following contain one or more claims directed to the invention or inventions disclosed in Paragraph 2.10(a): all counterpart foreign and U.S. patent applications and patents to Paragraphs 2.10(a) and 2.10(b), including those listed in Appendix A; and

(d) **Licensed Patent Rights** shall *not* include Paragraphs 2.10(b) or 2.10(c) to the extent that they contain one or more claims directed to new matter which is not the subject matter disclosed in Paragraph 2.10(a).

2.11 “**Licensed Processes**” means processes which, in the course of being practiced, would be within the scope of one or more claims of the **Licensed Patent Rights** that have not been held unpatentable, invalid or unenforceable by an unappealed or unappealable judgment of a court of competent jurisdiction.

2.12 “**Licensed Products**” means tangible materials which, in the course of manufacture, use, sale, or importation, would be within the scope of one or more claims of the **Licensed Patent Rights** that have not been held unpatentable, invalid or unenforceable by an unappealed or unappealable judgment of a court of competent jurisdiction.

2.13 “**Licensed Territory**” means the geographical area identified in Appendix B.

2.14 “**Net Sales**” means the total gross receipts received by **Licensee** for sales of **Licensed Products** or practice of **Licensed Processes** by or on behalf of the **Licensee** or its sublicensees, and from leasing, renting, or otherwise making the **Licensed Products** available to others for consideration without sale or other dispositions, whether invoiced or not, less returns and allowances, packing costs, insurance costs, freight out, taxes or excise duties imposed on the transaction (if separately invoiced), and wholesaler and cash discounts in amounts customary in the trade to the extent actually granted. No deductions shall be made for commissions paid to individuals, whether they are with independent sales agencies or regularly employed by the **Licensee**, or sublicensees, and on its payroll, or for the cost of collections. “**Net Sales**” shall not include (a) the supply of **Licensed Products** or use of **Licensed Processes**, for use in pre-clinical or clinical studies, or for process development, quality control or assurance, storage as safety stock, transfer as a charitable donation or any other transaction for which no gross revenue is received or (b) sales made in a country or region in which no **Licensed Patent Rights** exist.

2.15 "**Practical Application**" means to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and in each case, under these conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or **Government** regulations available to the public on reasonable terms not inconsistent with the terms applicable to similar products or processes and taking into account the efficacy and safety profile of the **Licensed Product** or the utility of the **Licensed Process** and other relevant commercial, scientific, technical and other factors.

2.16 "**Research License**" means a nontransferable, nonexclusive license to make and to use the **Licensed Products** or the **Licensed Processes** as defined by the **Licensed Patent Rights** for purposes of research only and not for purposes of commercial sale, manufacture or distribution or in lieu of purchase.

3. GRANT OF RIGHTS

3.1 The **IC** hereby grants and the **Licensee** accepts, subject to the terms and conditions of this **Agreement**, an exclusive license to Group A of the **Licensed Patent Right**s in the **Licensed Territory** to make and have made, to use and have used, to sell and have sold, to offer to sell, and to import any **Licensed Products** in the **Licensed Field of Use 1** and to practice and have practiced any **Licensed Process(es)** in such **Licensed Field of Use 1**.

3.2 The **IC** hereby grants and the **Licensee** accepts, subject to the terms and conditions of this **Agreement**, a non-exclusive license to Group B of the **Licensed Patent Right**s in the **Licensed Territory** to make and have made, to use and have used, to sell and have sold, to offer to sell, and to import any **Licensed Products** in **Licensed Fields of Use 1** and **2** and to practice and have practiced any **Licensed Process(es)** in **Licensed Fields of Use 1** and **2**.

3.3 This **Agreement** confers no license or rights by implication, estoppel, or otherwise under any patent applications or patents of the **IC** other than the **Licensed Patent Rights** regardless of whether these patents are dominant or subordinate to the **Licensed Patent Rights**.

4. SUBLICENSING

4.1 Upon written approval, which shall include prior review of any sublicense agreement by the **IC** and which shall not be unreasonably withheld or delayed, the **Licensee** may enter into sublicensing agreements under the **Licensed Patent Rights**.

4.2 The **Licensee** agrees that any sublicenses shall provide that the obligations to the **IC** of Paragraphs 5.1-5.4, 8.1, 10.1, 10.2, 12.5, and 13.8-13.10 of this **Agreement** shall be binding upon the sublicensee as if it were a party to this **Agreement**. The **Licensee** further agrees to attach copies of these Paragraphs to all sublicense agreements.

4.3 Any sublicenses granted by the **Licensee** shall provide for the termination of the sublicense, or the conversion to a license directly between the sublicensees and the **IC**, at the option of the sublicensee, upon termination of this **Agreement** under Article 13. This conversion is subject to the **IC** approval, which will not be unreasonably denied or delayed, and contingent upon acceptance by the sublicensee of the remaining provisions of this **Agreement**.

4.4 The **Licensee** agrees to forward to the **IC** a complete copy of each fully executed sublicense agreement postmarked within thirty (30) days of the execution of the agreement. To the extent permitted by law, the **IC** agrees to maintain each sublicense agreement in confidence.

5. STATUTORY AND IC REQUIREMENTS AND RESERVED GOVERNMENT RIGHTS

5.1

(a) the **IC** reserves on behalf of the **Government** an irrevocable, nonexclusive, nontransferable, royalty-free license for the practice of all inventions licensed under the **Licensed Patent Rights** throughout the world by or on behalf of the **Government** and on behalf of any foreign government or international organization pursuant to any existing or future treaty or agreement to which the **Government** is a signatory. Prior to the **First Commercial Sale**, the **Licensee** agrees to provide the **IC** with reasonable quantities of the **Licensed Products** or materials made through the **Licensed Processes** for **IC** research use. Given the nature of the envisioned **Licensed Products** as personalized autologous cell therapy products, if any **Licensed Products** and/or materials made through the **Licensed Processes** are not available in reasonable quantities for **IC** research use, they shall not be subject to the foregoing obligation; and

(b) in the event that the **Licensed Patent Rights** are Subject Inventions made under **CRADA**, the **Licensee** grants to the **Government**, pursuant to 15 U.S.C. §3710a(b)(1)(A), a nonexclusive, nontransferable, irrevocable, paid-up license to practice the **Licensed Patent Rights** or have the **Licensed Patent Rights** practiced throughout the world by or on behalf of the **Government**. In the exercise of this license, the **Government** shall not publicly disclose trade secrets or commercial or financial information that is privileged or confidential within the meaning of 5 U.S.C. §552(b)(4) or which would be considered as such if it had been obtained from a non-Federal party. Prior to the **First Commercial Sale**, the **Licensee** agrees to provide the **IC** with reasonable quantities of the **Licensed Products** or materials made through the **Licensed Processes** for **IC** research use. Given the nature of the envisioned **Licensed Products** as personalized autologous cell therapy products, if any **Licensed Products** and/or materials made through the **Licensed Processes** are not available in reasonable quantities for **IC** research use, they shall not be subject to the foregoing obligation.

5.2 The **Licensee** agrees that products used or sold in the United States embodying the **Licensed Products** or produced through use of the **Licensed Processes** shall be manufactured substantially in the United States, unless a written waiver is obtained in advance from the **IC**.

5.3 The **Licensee** acknowledges that the **IC** may enter into future **CRADAs** under the <u>Federal Technology Transfer Act of 1986</u> that relate to the subject matter of this **Agreement**. The **Licensee** agrees not to unreasonably deny requests for a **Research License** from future collaborators with the **IC** when acquiring these rights is necessary in order to make a **CRADA** project feasible. The **Licensee** may request an opportunity to join as a party to the proposed **CRADA**.

5.4

(a) in addition to the reserved license of Paragraph 5.1, the **IC** reserves the right to grant **Research Licenses** directly or to require the **Licensee** to grant **Research Licenses** on reasonable terms. The purpose of these **Research Licenses** is to encourage basic research, whether conducted at an academic or corporate facility. In order to safeguard the **Licensed Patent Rights**, however, the **IC** shall consult with the **Licensee** before granting to commercial entities a **Research License** or providing to them research samples of materials made through the **Licensed Processes**; and

(b) in exceptional circumstances, and in the event that the **Licensed Patent Rights** are Subject Inventions made under a **CRADA**, the **Government**, pursuant to <u>15 U.S.C. §3710a(b)(1)(B)</u>, retains the right to require the **Licensee** to grant to a responsible applicant a nonexclusive, partially exclusive, or exclusive sublicense to use the **Licensed Patent Rights** in the **Licensed Fields of Use 1 and 2** on terms that are reasonable under the circumstances, or if the **Licensee** fails to grant this license, the **Government** retains the right to grant the license itself. The exercise of these rights by the **Government** shall only be in exceptional circumstances and only if the **Government** determines:

(i) the action is necessary to meet health or safety needs that are not reasonably satisfied by the **Licensee**;

(ii) the action is necessary to meet requirements for public use specified by Federal regulations, and these requirements are not reasonably satisfied by the **Licensee**; or

(iii) the **Licensee** has failed to comply with an agreement containing provisions described in <u>15 U.S.C. §3710a(c)(4)(B)</u>; and

(c) the determination made by the **Government** under this Paragraph 5.4 is subject to administrative appeal and judicial review under 35 U.S.C. §203(b).

6. ROYALTIES AND REIMBURSEMENT

6.1 The **Licensee** agrees to pay the **IC** a non-creditable, nonrefundable license issue royalty as set forth in Appendix C.

6.2 The **Licensee** agrees to pay the **IC** a nonrefundable minimum annual royalty as set forth in Appendix C.

6.3 The **Licensee** agrees to pay the **IC** earned royalties as set forth in Appendix C.

6.4 The **Licensee** agrees to pay the **IC** benchmark royalties as set forth in Appendix C.

6.5 The **Licensee** agrees to pay the **IC** sublicensing royalties as set forth in Appendix C.

6.6 A patent or patent application licensed under this **Agreement** shall cease to fall within the **Licensed Patent Rights** for the purpose of computing earned royalty payments in any given country on the earliest of the dates that:

(a) the application has been abandoned and not continued;

(b) the patent expires or irrevocably lapses, or

(c) the patent has been held to be invalid or unenforceable by an unappealed or unappealable decision of a court of competent jurisdiction or administrative agency.

6.7 No multiple royalties shall be payable because any **Licensed Products** or **Licensed Processes** are covered by more than one of the **Licensed Patent Rights**.

6.8 On sales of the **Licensed Products** by the **Licensee** to sublicensees or on sales made in other than an arms-length transaction, the value of the **Net Sales** attributed under this Article 6 to this transaction shall be that which would have been received in an arms-length transaction, based on sales of like quantity and quality products on or about the time of this transaction.

6.9 With regard to unreimbursed expenses associated with the preparation, filing, prosecution, and maintenance of all patent applications and patents in the E-068-2018 patent family within the **Licensed Patent Rights** and paid by the **IC** prior to the effective date of this **Agreement**, the **Licensee** shall pay the **IC**, as an additional royalty, within sixty (60) days of the **IC's** submission of a statement and request for payment to the **Licensee**, an amount equivalent to these unreimbursed expenses previously paid by the **IC**. As of April 5, 2021 these unreimbursed expenses are approximately [***].

6.10 With regard to unreimbursed expenses associated with the preparation, filing, prosecution, and maintenance of all patent applications and patents to the extent included within the **Licensed Patent Rights** and paid by the **IC** on or after the effective date of this **Agreement**, the **IC**, at its sole option, may require the **Licensee**:

(a) to pay the **IC** on an annual basis, within sixty (60) days of the **IC's** submission of a statement and request for payment, a royalty amount equivalent to these unreimbursed expenses paid during the previous calendar year(s) provided, however, that if the **IC** grants a commercialization license under the **Licensed Patent Rights** to one or more third parties, then the **Licensee** shall pay the **IC** a pro-rated portion of such unreimbursed expenses calculated by dividing the total patent costs paid during the previous calendar year(s) by the number of commercialization licensees of record whose licenses have a licensed field of use which includes the development of therapeutic or diagnostic products and falls within the scope of the **Licensed Patent Rights** as of the date of this statement. For avoidance of doubt, if the **Licensee** is the only commercialization licensee of record whose license has a licensed field of use which includes the development of therapeutic or diagnostic products and falls within the scope of the **Licensed Patent Rights** as of the date of this statement, the **Licensee** shall pay **IC** a royalty amount equivalent to one hundred percent (100%) of these unreimbursed expenses paid during the previous calendar year(s);

(b) to pay these unreimbursed expenses directly to the law firm employed by the **IC** to handle these functions. However, in this event, the **IC** and not the **Licensee** shall be the client of the law firm; or

(c) in limited circumstances, the **Licensee** may be given the right to assume responsibility for the preparation, filing, prosecution, or maintenance of any patent application or patent included with the **Licensed Patent Rights**. In such event, the **Licensee** shall directly pay the attorneys or agents engaged to prepare, file, prosecute, or maintain these patent applications or patents and shall provide the **IC** with copies of each invoice associated with these services as well as documentation that these invoices have been paid.

6.11 The **IC** agrees, upon written request, to provide the **Licensee** with summaries of patent prosecution invoices for which the **IC** has requested payment from the **Licensee** under Paragraphs 6.9 and 6.10. The **Licensee** agrees that all information provided by the **IC** related to patent prosecution costs shall be treated as confidential commercial information and shall not be released to a third party (other than its **Affiliates** or sublicensee) except as required by law or a court of competent jurisdiction.

6.12 The **Licensee** may elect to surrender its rights in any country of the **Licensed Territory** under any of the **Licensed Patent Rights** upon ninety (90) days written notice to the **IC** and owe no payment obligation under Paragraph 6.10 for patent-related expenses incurred in that country after ninety (90) days of the effective date of the written notice.

7. PATENT FILING, PROSECUTION, AND MAINTENANCE

7.1 Except as otherwise provided in this Article 7, the **IC** agrees to take responsibility for, but to consult with, the **Licensee** in the preparation, filing, prosecution, and maintenance of any and all patent applications or patents included in the **Licensed Patent Rights** and shall furnish copies of relevant patent-related documents to the **Licensee**.

7.2 Upon the **IC's** written request, the **Licensee** shall assume the responsibility for the preparation, filing, prosecution, and maintenance of any and all patent applications or patents included in the **Licensed Patent Rights** and shall, on an ongoing basis, promptly furnish copies of all patent-related documents to the **IC**. In this event, the **Licensee** shall, subject to the prior approval of the **IC**, select registered patent attorneys or patent agents to provide these services on behalf of the **Licensee** and the **IC**. The **IC** shall provide appropriate powers of attorney and other documents necessary to undertake this action to the patent attorneys or patent agents providing these services. The **Licensee** and its attorneys or agents shall consult with the **IC** in all aspects of the preparation, filing, prosecution and maintenance of patent applications and patents included within the **Licensed Patent Rights** and shall provide the **IC** sufficient opportunity to comment on any document that the **Licensee** intends to file or to cause to be filed with the relevant intellectual property or patent office.

7.3 At any time, after **Licensee** has assumed responsibility for the preparation, filing, prosecution, and maintenance of **Licensed Patent Rights** as provided in Paragraph 7.2, the **IC** may provide the **Licensee** with written notice that the **IC** wishes to re-assume control of the preparation, filing, prosecution, and maintenance of any and all patent applications or patents included in the **Licensed Patent Rights**. If the **IC** elects to reassume these responsibilities, the **Licensee** agrees to cooperate fully with the **IC**, its attorneys, and agents in the preparation, filing, prosecution, and maintenance of any and all patent applications or patents included in the **Licensed Patent Rights** and to provide the **IC** with complete copies of any and all documents or other materials in **Licensee's** possession or control that the **IC** deems necessary to undertake such responsibilities. The **Licensee** shall be responsible for all costs associated with transferring patent prosecution responsibilities to an attorney or agent of the **IC's** choice.

7.4 Each party shall promptly inform the other as to all material matters that come to its attention that may affect the preparation, filing, prosecution, or maintenance of the **Licensed Patent Rights** and permit each other to provide comments and suggestions with respect to the preparation, filing, prosecution, and maintenance of the **Licensed Patent Rights**, which comments and suggestions shall be considered by the other party.

8. RECORD KEEPING

8.1 The **Licensee** agrees to keep accurate and correct records of the **Licensed Products** made, used, sold, or imported and the **Licensed Processes** practiced under this **Agreement** appropriate to determine the amount of royalties due the **IC**. These records shall be retained for at least five (5) years following a given reporting period and shall be available during normal business hours for inspection, at the expense of the **IC**, by an accountant or other designated auditor selected by the **IC** for the sole purpose of verifying reports and royalty payments hereunder. **Licensee** may require such auditor or accountant to enter into a confidentiality agreement with **Licensee** containing reasonable terms and conditions for the protection of **Licensee**'s non-public and proprietary information. The accountant or auditor shall only disclose to the **IC** information relating to the accuracy of reports and royalty payments made under this **Agreement**. If an inspection shows an underreporting or underpayment in excess of [***]for any twelve (12) month period, then the **Licensee** shall reimburse the **IC** for the cost of the inspection at the time the **Licensee** pays the unreported royalties, including any additional royalties as required by Paragraph 9.8. All royalty payments required under this Paragraph 8.1 shall be due within sixty (60) days of the date the **IC** provides to the **Licensee** notice of the payment due.

9. REPORTS ON PROGRESS, BENCHMARKS, SALES, AND PAYMENTS

9.1 Prior to signing this **Agreement**, the **Licensee** has provided the **IC** with the **Commercial Development Plan** in Appendix E, under which the **Licensee** intends to use **Commercially Reasonable Efforts** to bring **Licensed Product(s)** or **Licensed Process(es)** within the subject matter of the **Licensed Patent Rights** to the point of **Practical Application**. This **Commercial Development Plan** is hereby incorporated by reference into this **Agreement**. Based on this plan, performance **Benchmarks** are determined as specified in Appendix D.

9.2 The **Licensee** shall provide written annual reports on its product development progress or efforts to commercialize any **Licensed Product** under the **Commercial Development Plan** within sixty (60) days after December 31 of each calendar year. These progress reports shall include, but not be limited to: progress on research and development, status of applications for regulatory approvals, manufacturing, sublicensing, marketing, importing, and sales during the preceding calendar year, as well as, plans for the present calendar year. The **IC** also encourages these reports to include information on any of the **Licensee's** public service activities that relate to the **Licensed Patent Rights**. If reported progress differs from that projected in the **Commercial Development Plan** and **Benchmarks**, the **Licensee** shall explain the reasons for these differences. In the annual report, the **Licensee** may propose amendments to the **Commercial Development Plan**, acceptance of which by the **IC** may not be denied unreasonably. The **Licensee** agrees to provide any additional information reasonably required by the **IC** to evaluate the **Licensee's** performance under this **Agreement**. The **Licensee** may amend the **Benchmarks** at any time upon written approval by the **IC**. The **IC** shall not unreasonably withhold approval of any request of the **Licensee** to extend the time periods of this schedule if the request is supported by a reasonable showing by the **Licensee** of diligence in its performance under the **Commercial Development Plan** and toward bringing the **Licensed Products** to the point of **Practical Application** as defined in 37 C.F.R. §404.3(d). The **Licensee** shall amend the **Commercial Development Plan** and **Benchmarks** at the request of the **IC** to address any **Licensed Field of Use 1** not specifically addressed in the plan originally submitted.

9.3 The **Licensee** shall report to the **IC** the dates for achieving **Benchmarks** specified in Appendix D and the **First Commercial Sale** in each country in the **Licensed Territory** within thirty (30) days of such occurrences.

9.4 Following the **First Commercial Sale**, the **Licensee** shall submit to the **IC**, within sixty (60) days after each calendar half-year ending June 30 and December 31, a royalty report, as described in the example in Appendix F, setting forth for the preceding half-year period the amount of the **Licensed Products** sold or **Licensed Processes** practiced by or on behalf of the **Licensee** in each country within the **Licensed Territory**, the **Net Sales**, and the amount of royalty accordingly due. With each royalty report, the **Licensee** shall submit payment of earned royalties due. If no earned royalties are due to the **IC** for any reporting period, the written report shall so state. The royalty report shall be certified as correct by an authorized officer of the **Licensee** and shall include a detailed listing of all deductions made under Paragraph 2.14 to determine **Net Sales** made under Article 6 to determine royalties due. The royalty report shall also identify the site of manufacture for the **Licensed Product(s)** sold in the United States.

9.5 The **Licensee** agrees to forward semi-annually to the **IC** a copy of these reports received by the **Licensee** from its sublicensees during the preceding half-year period as shall be pertinent to a royalty accounting to the **IC** by the **Licensee** for activities under the sublicense.

9.6 Royalties due under Article 6 shall be paid in U.S. dollars and payment options are listed in Appendix G. For conversion of foreign currency to U.S. dollars, the conversion rate shall be the New York foreign exchange rate quoted in *The Wall Street Journal* on the day preceding the day that the payment is due. Any loss of exchange, value, taxes, or other expenses incurred in the transfer or conversion to U.S. dollars shall be paid entirely by the **Licensee**. The royalty report required by Paragraph 9.4 shall be mailed to the **IC** at its address for **Agreement** Notices indicated on the Signature Page.

9.7 The **Licensee** shall be solely responsible for determining if any tax on royalty income is owed outside the United States and shall pay the tax and be responsible for all filings with appropriate agencies of foreign governments. As reasonably requested by **Licensee**, **IC** shall cooperate with **Licensee** in applying for any valid exemption or obtaining any valid refund of such taxes paid by **Licensee**.

9.8 Additional royalties may be assessed by the **IC** on any payment that is more than ninety (90) days overdue at the rate of [***] percent ([***]%) per [***]. This [***]percent ([***]%) per [***]rate may be applied retroactively from the original due date until the date of receipt by the **IC** of the overdue payment and additional royalties. The payment of any additional royalties shall not prevent the **IC** from exercising any other rights it may have as a consequence of the lateness of any payment.

9.9 All plans and reports required by this Article 9 and marked "confidential" by the **Licensee** shall, to the extent permitted by law, be treated by the **IC** as commercial and financial information obtained from a person and as privileged and confidential, and any proposed disclosure of these records by the **IC** under the Freedom of Information Act (FOIA), 5 U.S.C. §552 shall be subject to the predisclosure notification requirements of 45 C.F.R. §5.65(d).

10. PERFORMANCE

10.1 The **Licensee** shall use its **Commercially Reasonable Efforts** to bring the **Licensed Products** and the **Licensed Processes** to **Practical Application**. **Commercially Reasonable Efforts** for the purposes of this provision shall include reasonable adherence to the **Commercial Development Plan** in Appendix E and performance of the **Benchmarks** in Appendix D in each case as either may be amended from time to time. The efforts of a sublicensee or an **Affiliate** of **Licensee** shall be considered the efforts of the **Licensee**.

10.2 Upon the **First Commercial Sale** in the United States, until the expiration or termination of this **Agreement**, the **Licensee** shall use its **Commercially Reasonable Efforts** to make the **Licensed Products** and the **Licensed Processes** reasonably accessible to the United States public.

10.3 The **Licensee** agrees, after its **First Commercial Sale**, to make reasonable quantities of the **Licensed Products** or materials produced through the use of the **Licensed Processes** within the **Licensed Fields of Use 1 and 2** available to patient assistance programs.

10.4 The **Licensee** agrees, after its **First Commercial Sale** and as part of its marketing and product promotion, to develop educational materials (e.g., brochures, website, etc.) directed to patients and physicians detailing the **Licensed Products** or medical aspects of the prophylactic and therapeutic uses of the **Licensed Products**.

10.5 The **Licensee** agrees to supply, to the Mailing Address for **Agreement** notices indicated on the Signature Page, the Office of Technology Transfer, **NIH** with inert samples of the **Licensed Products** or the **Licensed Processes** or their packaging for educational and display purposes only.

11. INFRINGEMENT AND PATENT ENFORCEMENT

11.1 The **IC** and the **Licensee** agree to notify each other promptly of each infringement or possible infringement of the **Licensed Patent Rights**, as well as, any facts which may affect the validity, scope, or enforceability of the **Licensed Patent Rights** of which either party becomes aware.

11.2 Pursuant to this **Agreement** and the provisions of 35 U.S.C. Chapter 29, the **Licensee** may:

(a) bring suit in its own name, at its own expense, and on its own behalf for infringement of presumably valid claims in the **Licensed Patent Rights**;

(b) in any suit, enjoin infringement and collect for its use, damages, profits, and awards of whatever nature recoverable for the infringement; or

(c) settle any claim or suit for infringement of the **Licensed Patent Rights** provided, however, that the **IC** and appropriate **Government** authorities shall have the first right to take such actions; and

(d) if the **Licensee** desires to initiate a suit for patent infringement, the **Licensee** shall notify the **IC** in writing. If the **IC** does not notify the **Licensee** of its intent to pursue legal action within ninety (90) days, the **Licensee** shall be free to initiate suit. The **IC** shall have a continuing right to intervene in the suit. The **Licensee** shall take no action to compel the **Government** either to initiate or to join in any suit for patent infringement. The **Licensee** may request the **Government** to initiate or join in any suit if necessary to avoid dismissal of the suit. Should the **Government** be made a party to any suit, the **Licensee** shall reimburse the **Government** for any costs, expenses, or fees which the **Government** incurs as a result of the motion or other action, including all costs incurred by the **Government** in opposing the motion or other action. In all cases, the **Licensee** agrees to keep the **IC** reasonably apprised of the status and progress of any litigation. Before the **Licensee** commences an infringement action, the **Licensee** shall notify the **IC** and give careful consideration to the views of the **IC** and to any potential effects of the litigation on the public health in deciding whether to bring suit.

11.3 In the event that a declaratory judgment action alleging invalidity or non-infringement of any of the **Licensed Patent Rights** shall be brought against the **Licensee** or raised by way of counterclaim or affirmative defense in an infringement suit brought by the **Licensee** under Paragraph 11.2, pursuant to this

Agreement and the provisions of 35 U.S.C. Chapter 29 or other statutes, the **Licensee** may:

(a) defend the suit in its own name, at its own expense, and on its own behalf for presumably valid claims in the **Licensed Patent Rights**;

(b) in any suit, ultimately to enjoin infringement and to collect for its use, damages, profits, and awards of whatever nature recoverable for the infringement; and

(c) settle any claim or suit for declaratory judgment involving the **Licensed Patent Rights**; provided, however, that the **IC** and appropriate **Government** authorities shall have the first right to take these actions and shall have a continuing right to intervene in the suit; and

(d) if the **IC** does not notify the **Licensee** of its intent to respond to the legal action within a reasonable time, the **Licensee** shall be free to do so. The **Licensee** shall take no action to compel the **Government** either to initiate or to join in any declaratory judgment action. The **Licensee** may request the **Government** to initiate or to join any suit if necessary to avoid dismissal of the suit. Should the **Government** be made a party to any suit by motion or any other action of the **Licensee**, the **Licensee** shall reimburse the **Government** for any costs, expenses, or fees, which the **Government** incurs as a result of the motion or other action. If the **Licensee** elects not to defend against the declaratory judgment action, the **IC**, at its option, may do so at its own expense. In all cases, the **Licensee** agrees to keep the **IC** reasonably apprised of the status and progress of any litigation. Before the **Licensee** commences an infringement action, the **Licensee** shall notify the **IC** and give careful consideration to the views of the **IC** and to any potential effects of the litigation on the public health in deciding whether to bring suit.

11.4 In any action under Paragraphs 11.2 or 11.3 the expenses including costs, fees, attorney fees, and disbursements, shall be paid by the **Licensee**. The value of any recovery made by the **Licensee** through court judgment or settlement actually collected shall first be applied by **Licensee** to reimburse it for all of its costs and expenses (including attorneys' fees, expert witness fees, and any reimbursement payments made to **IC** or the **Government**) and the balance shall be treated as **Net Sales** and subject to earned royalties as provided in **Appendix C** when and as collected.

11.5 The **IC** shall cooperate fully with the **Licensee** in connection with any action under Paragraphs 11.2 or 11.3. The **IC** agrees promptly to provide access to all necessary documents and to render reasonable assistance in response to a request by the **Licensee**.

12. NEGATION OF WARRANTIES AND INDEMNIFICATION

12.1 The **IC** offers no warranties other than those specified in Article 1.

12.2 The **IC** does not warrant the validity of the **Licensed Patent Rights** and makes no representations whatsoever with regard to the scope of the **Licensed Patent Rights**, or that the **Licensed Patent Rights** may be exploited without infringing other patents or other intellectual property rights of third parties.

12.3 THE **IC** MAKES NO WARRANTIES, EXPRESS OR IMPLIED, OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OF ANY SUBJECT MATTER DEFINED BY THE CLAIMS OF THE **LICENSED PATENT RIGHTS** OR TANGIBLE MATERIALS RELATED THERETO.

12.4 The **IC** does not represent that it shall commence legal actions against third parties infringing the **Licensed Patent Rights**.

12.5 The **Licensee** shall indemnify and hold the **IC**, its employees, students, fellows, agents, and consultants harmless from and against all liability, demands, damages, expenses, and losses, including but not limited to death, personal injury, illness, or property damage in connection with or arising out of:

(a) the use by or on behalf of the **Licensee**, its sublicensees, directors, employees, or third parties of any **Licensed Patent Rights**; or

(b) the design, manufacture, distribution, or use of any **Licensed Products**, **Licensed Processes** or materials by the **Licensee**, or other products or processes developed in connection with or arising out of the **Licensed Patent Rights**.

12.6 The **Licensee** agrees to maintain a liability insurance program consistent with sound business practice.

13. <u>TERM, TERMINATION, AND MODIFICATION OF RIGHTS</u>

13.1 This **Agreement** is effective when signed by all parties, unless the provisions of Paragraph 14.16 are not fulfilled, and shall extend to the expiration of the last to expire of the **Licensed Patent Rights** unless sooner terminated as provided in this Article 13.

13.2 In the event that the **Licensee** is in default in the performance of any material obligations under this **Agreement**, including but not limited to the obligations listed in Paragraph 13.5, and if the default has not been remedied within ninety (90) days after the date of notice in writing of the default, or if not reasonably capable of remedy within such period, **Licensee** has not taken substantial steps to remedy the alleged default within such ninety (90) day period, the **IC** may terminate this **Agreement** by written notice and pursue outstanding royalties owed through procedures provided by the <u>Federal Debt Collection Act</u>.

13.3 In the event that the **Licensee** (a) becomes insolvent or (b) files a petition in bankruptcy, or has such a petition filed against it and, in either case, such petition is not dismissed within sixty (60) days, the **Licensee** shall immediately notify the **IC** in writing.

13.4 The **Licensee** shall have a unilateral right to terminate this **Agreement** or any licenses in any country or territory by giving the **IC** sixty (60) days written notice to that effect. For clarity, in accordance with the foregoing, **Licensee** shall have a unilateral right to terminate any license in any country or territory on a patent (or patent application)-by-patent (or patent application) and country (or territory)-by-country (or territory) basis.

13.5 The **IC** shall specifically have the right to terminate or modify, at its option, this **Agreement**, if the **IC** determines that the **Licensee**:

(a) is not executing the **Commercial Development Plan** in accordance with Appendix E and the **Licensee** cannot otherwise demonstrate to the **IC's** satisfaction that the **Licensee** has taken, or can be expected to take within a reasonable time, effective steps to achieve the **Practical Application** of the **Licensed Products** or the **Licensed Processes**;

(b) has not achieved and is not reasonably likely to achieve the **Benchmarks** as may be modified under Paragraph 9.2;

(c) has willfully made a material false statement of, or willfully omitted a material fact in, the license application or in any report required by this **Agreement**;

(d) has committed a material breach of a covenant or agreement contained in this **Agreement**;

(e) is not keeping the **Licensed Products** or the **Licensed Processes** within the scope of the **Licensed Fields of Use 1 and 2** reasonably accessible to the public after commercial use commences;

(f) cannot reasonably satisfy unmet health and safety needs within the scope of the **Licensed Fields of Use 1 and 2**;

(g) cannot reasonably justify a failure to comply with the domestic production requirement of Paragraph 5.2 unless waived; or

(h) has been found by a court of competent jurisdiction to have violated the Federal antitrust laws in connection with its performance under this **Agreement** without the possibility of appeal.

13.6 In making the determination referenced in Paragraph 13.5, the **IC** shall take into account the normal course of such commercial development programs conducted with sound and reasonable business practices and judgment and the annual reports submitted by the **Licensee** under Paragraph 9.2. Prior to invoking termination or modification of this **Agreement** under Paragraph 13.5, the **IC** shall give written notice to the **Licensee** providing the **Licensee** specific notice of, and a ninety (90) day opportunity to respond to, the **IC's** concerns as to the items referenced in Paragraphs 13.5(a)-13.5(h). If the **Licensee** fails to alleviate the **IC's** reasonable concerns as to the items referenced in Paragraphs 13.5(a)-13.5(h) or fails to initiate corrective action to the **IC's** reasonable satisfaction, the **IC** may terminate this **Agreement**.

13.7 When the public health and safety so require, and after written notice to the **Licensee** providing the **Licensee** a sixty (60) day opportunity to respond, the **IC** shall have the right to require the **Licensee** to grant sublicenses to responsible applicants, on commercially reasonable terms, in any **Licensed Fields of Use 1 and 2** under the **Licensed Patent Rights**, unless the **Licensee** can reasonably demonstrate that the granting of the sublicense would not materially increase the availability to the public of the subject matter of the **Licensed Patent Rights**. The **IC** shall not require the granting of a sublicense unless the responsible applicant has first negotiated in good faith with the **Licensee** for a sublicense on commercially reasonable terms and conditions.

13.8 The **IC** reserves the right according to 35 U.S.C. §209(d)(3) to terminate or modify this **Agreement** if it is determined that this action is necessary to meet the requirements for public use specified by federal regulations issued after the date of the license and these requirements are not reasonably satisfied by the **Licensee**.

13.9 Within thirty (30) days of receipt of written notice of the **IC's** unilateral decision to modify or terminate this **Agreement**, the **Licensee** may, consistent with the provisions of 37 C.F.R. §404.11, appeal the decision by written submission to the designated **IC** official. The decision of the designated **IC** official shall be the final agency decision. The **Licensee** may thereafter exercise any and all administrative or judicial remedies that may be available.

13.10 Within ninety (90) days of expiration or termination of this **Agreement** under this Article 13, a final report shall be submitted by the **Licensee**. Any royalty payments, including those incurred but not yet paid (such as the full minimum annual royalty), and those related to patent expenses, due to the **IC** shall become immediately due and payable upon termination or expiration. If terminated under this Article 13, sublicensees may elect to convert their sublicenses to direct licenses with the **IC** pursuant to Paragraph 4.3. Unless otherwise specifically provided for under this **Agreement**, upon termination or expiration of this **Agreement**, the **Licensee** shall return all **Licensed Products** or other materials included within the **Licensed Patent Rights** to the **IC** or provide the **IC** with certification of the destruction thereof. The **Licensee** may not be granted additional **IC** licenses if the final reporting requirement is not fulfilled.

14. GENERAL PROVISIONS

14.1 Neither party may waive or release any of its rights or interests in this **Agreement** except in writing. The failure of either party to assert a right hereunder or to insist upon compliance with any term or condition of this **Agreement** shall not constitute a waiver of that right by that party or excuse a similar subsequent failure to perform any of these terms or conditions by the that party.

14.2 This **Agreement** constitutes the entire agreement between the parties relating to the subject matter of the **Licensed Patent Rights**, the **Licensed Products** and the **Licensed Processes**, and all prior negotiations, representations, agreements, and understandings are merged into, extinguished by, and completely expressed by this **Agreement**.

14.3 The provisions of this **Agreement** are severable, and in the event that any provision of this **Agreement** shall be determined to be invalid or unenforceable under any controlling body of law, this determination shall not in any way affect the validity or enforceability of the remaining provisions of this **Agreement**.

14.4 If either party desires a modification to this **Agreement**, the parties shall, upon reasonable notice of the proposed modification by the party desiring the change, confer in good faith to determine the desirability of the modification. No modification shall be effective until a written amendment is signed by the signatories to this **Agreement** or their designees.

14.5 The construction, validity, performance, and effect of this **Agreement** shall be governed by Federal law as applied by the Federal courts in the District of Columbia.

14.6 All **Agreement** notices required or permitted by this **Agreement** shall be given by prepaid, first class, registered or certified mail or by an express/overnight delivery service provided by a commercial carrier, properly addressed to the other party at the address designated on the following Signature Page, or to another address as may be designated in writing by the other party. **Agreement** notices shall be considered timely if the notices are received on or before the established deadline date or sent on or before the deadline date as verifiable by U.S. Postal Service postmark or dated receipt from a commercial carrier. Parties should request a legibly dated U.S. Postal Service postmark or obtain a dated receipt from a commercial carrier or the U.S. Postal Service. Private metered postmarks shall not be acceptable as proof of timely mailing.

14.7 This **Agreement** shall not be assigned or otherwise transferred (including any transfer by legal process or by operation of law, and any transfer in bankruptcy or insolvency, or in any other compulsory procedure or order of court) except to the **Licensee's Affiliate(s)** without the prior written consent of the **IC**. The parties agree that the identity of the parties is material to the formation of this **Agreement** and that the obligations under this **Agreement** are nondelegable. In the event that the **IC** approves a proposed assignment, the **Licensee** shall pay the **IC**, as an additional royalty, [***] percent ([***]%) of the fair market value of any consideration received for any assignment of this **Agreement** within sixty (60) days of the assignment.

14.8 The **Licensee** agrees in its use of any **IC**-supplied biological materials that are supplied under this **Agreement** to comply with all applicable statutes, regulations, and guidelines, including **IC** and **HHS** regulations and guidelines. The **Licensee** agrees not to use such biological materials for research involving human subjects or clinical trials in the United States without complying with 21 C.F.R. Part 50 and 45 C.F.R. Part 46. The **Licensee** agrees not to use such biological materials for research involving human subjects or clinical trials outside of the United States without notifying the **IC**, in writing, of the research or trials and complying with the applicable regulations of the appropriate national control authorities. Written notification to the **IC** of research involving such biological materials in human subjects or clinical trials outside of the United States shall be given no later than sixty (60) days prior to commencement of the research or trials.

14.9 The **Licensee** acknowledges that it is subject to and agrees to abide by the United States laws and regulations (including the Export Administration Act of 1979 and Arms Export Control Act) controlling the export of technical data, computer software, laboratory prototypes, biological material, and other commodities. The transfer of these items may require a license from the appropriate agency of the **Government** or written assurances by the **Licensee** that it shall not export these items to certain foreign countries without prior approval of this agency. The **IC** neither represents that a license is or is not required or that, if required, it shall be issued.

14.10 The **Licensee** agrees to mark the **Licensed Products** or their packaging sold in the United States with all applicable U.S. patent numbers and similarly to indicate "Patent Pending" status. All the **Licensed Products** manufactured in, shipped to, or sold in other countries shall be marked in a manner to preserve the **IC's** patent rights in those countries.

14.11 By entering into this **Agreement**, the **IC** does not directly or indirectly endorse any product or service provided, or to be provided, by the **Licensee** whether directly or indirectly related to this **Agreement**. The **Licensee** shall not state or imply that this **Agreement** is an endorsement by the **Government**, the **IC**, any other **Government** organizational unit, or any **Government** employee. Additionally, the **Licensee** shall not use the names of the **IC**, the **FDA** or the **HHS** or the **Government** or their employees in any advertising, promotional, or sales literature without the prior written approval of the **IC**.

14.12 The parties agree to attempt to settle amicably any controversy or claim arising under this **Agreement** or a breach of this **Agreement**, except for appeals of modifications or termination decisions provided for in Article 13. The **Licensee** agrees first to appeal any unsettled claims or controversies to the designated **IC** official, or designee, whose decision shall be considered the final agency decision.

Thereafter, the **Licensee** may exercise any administrative or judicial remedies that may be available.

14.13 Nothing relating to the grant of a license, nor the grant itself, shall be construed to confer upon any person any immunity from or defenses under the antitrust laws or from a charge of patent misuse, and the acquisition and use of rights pursuant to 37 C.F.R. Part 404 shall not be immunized from the operation of state or Federal law by reason of the source of the grant.

14.14 Any formal recordation of this **Agreement** required by the laws of any **Licensed Territory** as a prerequisite to enforceability of the **Agreement** in the courts of any foreign jurisdiction or for other reasons shall be carried out by the **Licensee** at its expense, and appropriately verified proof of recordation shall be promptly furnished to the **IC**.

14.15 Paragraphs 4.3, 8.1, 9.5-9.8, 9.9, 12.1-12.5, 13.9, 13.10, 14.12 and 14.15 of this **Agreement** shall survive termination of this **Agreement**.

14.16 The terms and conditions of this **Agreement** shall, at the **IC's** sole option, be considered by the **IC** to be withdrawn from the **Licensee's** consideration and the terms and conditions of this **Agreement**, and the **Agreement** itself to be null and void, unless this **Agreement** is executed by the **Licensee** and a fully executed original is received by the **IC** within sixty (60) days from the date of the **IC's** signature found at the Signature Page.

SIGNATURES BEGIN ON NEXT PAGE

NIH PATENT LICENSE AGREEMENT – *EXCLUSIVE*

SIGNATURE PAGE

For the **IC**:

_______________________________________ ____________________

Richard U. Rodriguez Date
Associate Director, Technology Transfer Center
National Cancer Institute
National Institutes of Health

Mailing Address or E-mail Address for **Agreement** notices and reports:

License Compliance and Administration
Monitoring & Enforcement
Office of Technology Transfer
National Institutes of Health
6011 Executive Boulevard, Suite 325

Rockville, Maryland 20852-3804 U.S.A.

E-mail: LicenseNotices_Reports@mail.nih.gov

For the **Licensee** (Upon, information and belief, the undersigned expressly certifies or affirms that the contents of any statements of the **Licensee** made or referred to in this document are truthful and accurate.):

by:

______________________________ ______________
Signature of Authorized Official Date

____
Printed Name

____
Title

I. Official and Mailing Address for **Agreement** notices:

Frederick G. Vogt, Ph.D., Esq.
General Counsel
999 Skyway Road, Suite 150
San Carlos, CA 94070
Email: fred.vogt@iovance.com

With an electronic copy to: legal@iovance.com

II. Official and Mailing Address for Financial notices (the **Licensee's** contact person for royalty payments):

Frederick G. Vogt, Ph.D., Esq.
General Counsel
999 Skyway Road, Suite 150
San Carlos, CA 94070
Email: fred.vogt@iovance.com

With an electronic copy to: legal@iovance.com

Any false or misleading statements made, presented, or submitted to the **Government**, including any relevant omissions, under this **Agreement** and during the course of negotiation of this

Agreement are subject to all applicable civil and criminal statutes including Federal statutes 31 U.S.C. §§3801-3812 (civil liability) and 18 U.S.C. §1001 (criminal liability including fine(s) or imprisonment).

APPENDIX A – LIST OF PATENT(S) OR PATENT APPLICATION(S)

Patent(s) or Patent Application(s)

Group A

1. United States Provisional Patent Application No. 61/846,161 filed July 15, 2013 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-US-01];
2. International Patent Application No. PCT/US2014/046478 filed July 14, 2014 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-PCT-02];
3. Australian Patent Application No. 2014290286 filed July 14, 2014 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-AU-03];
4. Canadian Patent Application No. 2918080 filed July 14, 2014 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-CA-04];
5. Chinese Patent No. 105452448 issued July 28, 2020 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-CN-05];
6. European Patent No. 3022294 issued November 20, 2019 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-EP-06];
    a. Validated in DE, ES, FR, GB, IT and NL
7. Japanese Patent No. 6616295 issued December 4, 2019 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-JP-07];
8. Russian Patent No. 2713333 issued February 4, 2020 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-RU-08];
9. United States Patent Application No. 14/905,138 filed January 14, 2016 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-US-09];
10. European Patent Application No. 19209253 filed November 14, 2019 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-EP-10];
11. United States Patent Application No. 16/218,658 filed December 13, 2018 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-US-11];
12. Russian Patent Application No. 2019105050 filed February 22, 2019 entitled "Methods of Preparing Anti-human Papillomavirus Antigen T Cells" [**HHS** Reference No. E-494-2013-0-RU-12];

13. Japanese Patent Application No. 2019-202239 filed November 7, 2019 entitled “Methods of Preparing Anti-human Papillomavirus Antigen T Cells” [**HHS** Reference No. E-494-2013-0-JP-13];
14. Chinese Patent Application No. 202010606868.1 filed June 29, 2020 entitled “Methods of Preparing Anti-human Papillomavirus Antigen T Cells” [**HHS** Reference No. E-494-2013-0-CN-20];
15. Hong Kong Patent Application No. 42020015851.7 filed September 10, 2020 entitled “Methods of Preparing Anti-human Papillomavirus Antigen T Cells” [**HHS** Reference No. E-494-2013-0-HK-21];
16. Australian Patent Application No. 2020233702 filed September 16, 2020 entitled “Methods of Preparing Anti-human Papillomavirus Antigen T Cells” [**HHS** Reference No. E-494-2013-0-AU-22];
17. Macau Patent Application No. J/004455(388) filed October 27, 2020 entitled “Methods of Preparing Anti-human Papillomavirus Antigen T Cells” [**HHS** Reference No. E-494-2013-0-MO-23];
18. United States Patent Application No. 17/113,570 filed December 7, 2020 entitled “Methods of Preparing Anti-human Papillomavirus Antigen T Cells” [**HHS** Reference No. E-494-2013-0-US-24];
19. United States Provisional Patent Application No. 62/628,454 filed February 9, 2018 entitled “Tethered Interleukin-15 and Interleukin-21” [**HHS** Reference No. E-068-2018-0-US-01];
20. International Patent Application No. PCT/US2019/016975 filed February 7, 2019 entitled “Tethered Interleukin-15 and Interleukin-21” [**HHS** Reference No. E-068-2018-0-PCT-02];
21. Australian Patent Application No. 2019218785 filed August 7, 2020 entitled “Tethered Interleukin-15 and Interleukin-21” [**HHS** Reference No. E-068-2018-0-AU-03];
22. Chinese Patent Application No. 201980012443.3 filed August 7, 2020 entitled “Tethered Interleukin-15 and Interleukin-21” [**HHS** Reference No. E-068-2018-0-CN-04];
23. European Patent Application No. 19709154.9 filed August 8, 2020 entitled “Tethered Interleukin-15 and Interleukin-21” [**HHS** Reference No. E-068-2018-0-EP-05];
24. United States Patent Application No. 16/964,796 filed July 24, 2020 entitled “Tethered Interleukin-15 and Interleukin-21” [**HHS** Reference No. E-068-2018-0-US-06]; and
25. Canadian Patent Application No. 3,090,512 filed August 5, 2020 entitled “Tethered Interleukin-15 and Interleukin-21” [**HHS** Reference No. E-068-2018-0-CA-07].

Group B

1. United States Provisional Patent Application No. 60/408,681 filed September 6, 2002 entitled “Immunotherapy with In Vitro-Selected Antigen-Specific Lymphocytes after

Nonmyeloablative Lymphodepleting Chemotherapy" [**HHS** Reference No. E-275-2002-0-US-01];

2. International Patent Application No. PCT/US2003/027873 filed September 5, 2003 entitled "Immunotherapy with In Vitro-Selected Antigen-Specific Lymphocytes after Nonmyeloablative Lymphodepleting Chemotherapy" [**HHS** Reference No. E-275-2002-1-PCT-01];
3. United States Patent No. 8,034,334 issued October 11, 2011 entitled "Immunotherapy with In Vitro-Selected Antigen-Specific Lymphocytes after Nonmyeloablative Lymphodepleting Chemotherapy" [**HHS** Reference No. E-275-2002-1-US-02];
4. European Patent No. 1545204 issued August 10, 2016 entitled "Immunotherapy with In Vitro-Selected Antigen-Specific Lymphocytes after Nonmyeloablative Lymphodepleting Chemotherapy" [**HHS** Reference No. E-275-2002-1-EP-03];
    a. Validated in CH, DE, DK, ES, FR, GB, IT, NL and SE.
5. Canadian Patent No. 2497552 issued May 27, 2014 entitled "Immunotherapy with In Vitro-Selected Antigen-Specific Lymphocytes after Nonmyeloablative Lymphodepleting Chemotherapy" [**HHS** Reference No. E-275-2002-1-CA-04];
6. Australian Patent No. 2003265948 issued May 21, 2009 entitled "Immunotherapy with In Vitro-Selected Antigen-Specific Lymphocytes after Nonmyeloablative Lymphodepleting Chemotherapy" [**HHS** Reference No. E-275-2002-1-AU-05];
7. United States Patent No. 8,287,857 issued October 16, 2012 entitled "Immunotherapy with In Vitro-Selected Antigen-Specific Lymphocytes after Nonmyeloablative Lymphodepleting Chemotherapy" [**HHS** Reference No. E-275-2002-1-US-06];
8. United States Provisional Patent Application No. 61/237,889 filed August 28, 2009 entitled "Adoptive Cell Therapy with Young T Cells" [**HHS** Reference No. E-273-2009-0-US-01];
9. United States Patent No. 8,383,099 issued February 26, 2013 entitled "Adoptive Cell Therapy with Young T Cells" [**HHS** Reference No. E-273-2009-0-US-02];
10. United States Patent No. 9,074,185 issued July 7, 2015 entitled "Adoptive Cell Therapy with Young T Cells" [**HHS** Reference No. E-273-2009-0-US-03];
11. United States Provisional Patent Application No. 61/466,200 filed March 22, 2011 entitled "Methods of Growing Tumor Infiltrating Lymphocytes (TIL) in Gas-Permeable Containers" [**HHS** Reference No. E-114-2011-0-US-01];
12. International Patent Application No. PCT/US2012/029744 filed March 20, 2012 entitled "Methods of Growing Tumor Infiltrating Lymphocytes (TIL) in Gas-Permeable Containers" [**HHS** Reference No. E-114-2011-0-PCT-02];
13. United States Patent Application No. 13/424,646 filed March 20, 2012 entitled "Methods of Growing Tumor Infiltrating Lymphocytes (TIL) in Gas-Permeable Containers" [**HHS** Reference No. E-114-2011-0-US-03];
14. United States Patent Application No. 15/375,289 filed December 12, 2016 entitled "Methods of Growing Tumor Infiltrating Lymphocytes (TIL) in Gas-Permeable Containers" [**HHS** Reference No. E-114-2011-0-US-04]; and

15. United States Patent Application No. 16/211,859 filed December 6, 2018 entitled “Methods of Growing Tumor Infiltrating Lymphocytes (TIL) in Gas-Permeable Containers” [**HHS** Reference No. E-114-2011-0-US-05].

APPENDIX B – FIELDS OF USE AND TERRITORY

I. **Licensed Fields of Use 1 and 2:**

The **Licensed Field of Use 1** means the use of the **Licensed Patent Rights** to develop, manufacture, distribute, sell, and use autologous tumor infiltrating lymphocyte ("**TIL**") adoptive cell therapy products for the treatment of metastatic melanoma, lung, breast, bladder, and HPV-positive cancers.

The **Licensed Field of Use 2** means the use of the **Licensed Patent Rights** to develop, manufacture, distribute, sell, and use autologous TIL adoptive cell therapy products for the treatment of all cancers other than those specified in the **Licensed Field of Use 1**.

Statement applying to both **Licensed Field of Use 1** and **Licensed Field of Use 2**: TIL are a subset of T lymphocytes (T cells) that migrate and are located within a tumor site. TIL isolated from these tumor sites exhibit natural anti-tumor activity without genetic modifications. For the avoidance of doubt, cell therapy products involving TIL genetically modified for reactivity against cancer-specific mutations or TIL selected for reactivity against cancer-specific mutations are excluded from the **Licensed Fields of Use 1 and 2**, unless such cell therapy products are a combination of unselected, unmodified TIL therapy with the **Licensee's** proprietary technologies or the **Licensee**'s in-licensed technologies. Subject to the foregoing, specifically excluded from this **Agreement** are the use of T cell receptors isolated from TIL.

II. **Licensed Territory:** Worldwide.

<u>**APPENDIX C – ROYALTIES**</u>

Royalties:

I. Within sixty (60) days of execution of this **Agreement**, the **Licensee** shall pay the **IC** an amendment issue royalty in the amount of [***].

II. The Parties acknowledge and agree that prior to the execution of this **Agreement**, the **Licensee** paid the **IC** (a) an execution royalty in the sum of [***] pursuant to the terms of the **Original Agreement**, and (b) an amendment issue royalty in the sum of [***] in two installment payments, each in the amount of [***] pursuant to the terms of the **First Amendment**.

III. The **Licensee** agrees to pay to the **IC** a nonrefundable minimum annual royalty in the amount of [***] as follows:

(a) The Parties acknowledge and agree that following the execution of the **Original Agreement**, and prior to the execution of this **Agreement**, **Licensee** paid the **IC** the required minimum annual royalties.

(b) Subsequent minimum annual royalty payments are due and payable on January 1 of each calendar year and may be credited against any earned royalties due for sales made in that year.

(c) In the case of each of (a) and (b) above, such payments shall be due so long as **Licensee** has not terminated this **Agreement** pursuant to Paragraph 13.4.

IV. For **Net Sales** received by or on behalf of **Licensee** or its sublicensees for sales of **Licensed Products** or practice of **Licensed Processes** that are in the **Licensed Field of Use 1** and covered by a claim of a granted patent or a claim of a patent application pending less than ten (10) years from its earliest claimed priority date in the **Licensed Patent Rights** Group A of Appendix A, **Licensee** shall pay the **IC** an earned royalty of [***]. **Licensee** shall be entitled to a credit of [***] against such earned royalty rate for each percentage point in excess of [***] that **Licensee** must pay to an unaffiliated licensor(s) for the manufacture and sale of **Licensed Product(s)** and **Licensed Process(es)**. Said credit however, shall not reduce the earned royalty rate due to **IC** for **Licensed Product(s)** and **Licensed Process(es)** below [***].

For **Net Sales** received by or on behalf of **Licensee** or its sublicensees for sales of **Licensed Products** or practice of **Licensed Processes** covered by a claim of a granted patent in the **Licensed Patent Rights** Group B of Appendix A**, Licensee** shall pay the **IC** an earned royalty of [***].

Licensee agrees to pay the **IC** earned royalties of [***] on **Net Sales** of **Licensed Products** and/or **Licensed Processes** by or on behalf of **Licensee** or its sublicensees in any jurisdiction where **Licensed Patent Rights** exist and in which **Licensed Products** and/or **Licensed Processes** (a) are covered *only* by a claim or claims of a patent application in the **Licensed Patent Rights** pending at least ten (10) years from its earliest claimed priority date, or (b) are not covered by a claim of a granted patent in the **Licensed Patent Rights** in the case where patent prosecution is closed in the jurisdiction. With respect to part (a) of the foregoing sentence, if such claim(s) later issue in a granted patent of the **Licensed Patent Rights** that covers a **Licensed Product** and/or **Licensed Process**, **Licensee** shall pay the **IC** the balance of earned royalties which otherwise would have been due had the claim(s) issued on or before the ten (10) year anniversary of the earliest claimed priority date.

For **Net Sales** received by or on behalf of **Licensee** or its sublicensees for sales of **Licensed Products** or practice of **Licensed Processes** covered by **Licensed Patent Rights** in both Group A and Group B of Appendix A, **Licensee** shall pay the **IC** an earned royalty of no more than [***].

V. The **Licensee** agrees to pay the **IC Benchmark** royalties within sixty (60) days of achieving each **Benchmark** listed below by **Licensee** or its sublicensees for each **Licensed Product** or **Licensed Process**:

(a) For successful completion of the first **Licensee**-sponsored Phase 2 Clinical Study in each indication of **Licensed Field of Use 1**.

i. Melanoma: [***]

ii. Breast cancer: [***]

iii. Lung cancer: [***]

iv. HPV-positive cancer: [***]

v. Bladder cancer: [***]

(b) For successful completion of the first **Licensee**-sponsored Phase 3 Clinical Study for each indication in **Licensed Field of Use 1**.

i. Melanoma: [***]

ii. Breast Cancer: [***]

iii. Lung cancer: [***]

iv. HPV-positive cancer: [***]

v. Bladder Cancer: [***]

(c) Upon the first **FDA** approval or foreign equivalent for a **Licensed Product** or **Licensed Process** for each indication in the **Licensed Field of Use 1**.

i. Melanoma: [***]

ii. Breast cancer: [***]

iii. Lung cancer: [***]

iv. HPV-positive cancer: [***]

v. Bladder cancer: [***]

(d) For the **First Commercial Sale** of a **Licensed Product** or **Licensed Process** in the United States for each indication in the **Licensed Field of Use 1**.

i. Melanoma: [***]

ii. Breast cancer: [***]

iii. Lung cancer: [***]

iv. HPV-positive cancer: [***]

v. Bladder cancer: [***]

(e) For the **First Commercial Sale** of a **Licensed Product** or **Licensed Process** in any foreign country for each indication in the **Licensed Field of Use 1**.

i. Melanoma: [***]

ii. Breast cancer: [***]

iii. Lung cancer: [***]

iv. HPV-positive cancer: [***]

v. Bladder cancer: [***]

(f) Upon the first time the aggregate **Net Sales** of all **Licensed Products** or **Licensed Processes** achieve the following thresholds, the **Licensee** pays the following one-time **Benchmark** royalties:

(1) [***] when the aggregate **Net Sales** of all **Licensed Products** or **Licensed Processes** reaches [***].

(2) [***] when the aggregate **Net Sales** of all **Licensed Products** or **Licensed Processes** reaches [***].

For purposes of this **Agreement**, "successful completion of a **Licensee-**sponsored Phase 2 Clinical Study" shall mean, with respect to a specified construct, formulation and dose of a specified **Licensed Product** in a specified cancer indication, the statistical demonstration in a pivotal Phase 2 Clinical Study of safety and efficacy, sufficient to support a Phase 3 clinical trial submission by the **Licensee** for such specified construct, formulation and dose of such specified **Licensed Product** for the treatment of such specified cancer indication.

For purposes of this **Agreement**, "successful completion of a **Licensee**-sponsored Phase 3 Clinical Study" shall mean, with respect to a specified construct, formulation and dose of a specified **Licensed Product** in a specified cancer indication, the statistical demonstration in a pivotal Phase 3 Clinical Study of safety and efficacy, sufficient to support a BLA submission by the **Licensee** for such specified construct, formulation and dose of such specified **Licensed Product** for the treatment of such specified cancer indication.

For clarity, under Appendix C- Paragraph V(a-e) only one (1) **Benchmark** royalty payment shall be payable upon achievement of the specified event for each indication. For example, only one (1) **Benchmark** royalty payment shall be due upon achievement of each specified milestone for a first **Licensed Product** or **Licensed Process** treating an HPV-positive cancer indication. Therefore, further **Licensed Products** or **Licensed Processes** treating additional HPV-positive cancer indications will not each require separate benchmark royalty payments.

VI. The **Licensee** agrees to pay the **IC**:

(a) additional sublicensing royalties of [***] on the fair market value of any consideration received for granting each sublicense under **Licensed Patent Rights** for a **Licensed Product** or **Licensed Process** (excluding any consideration received for granting a license or sublicense under any intellectual property which is not the **Licensed Patent Rights**) within sixty (60) days of the execution of each sublicense if any such sublicense is executed prior to the achievement of the **Benchmark** in Appendix D for **FDA** approval or foreign equivalent for a **Licensed Product** or **Licensed Process** within each indication in **Licensed Field of Use 1** from Appendix B; and

(b) additional sublicensing royalties of [***] on the fair market value of any consideration received for granting each sublicense under **Licensed Patent Rights** for a **Licensed Product** or **Licensed Process** (excluding any consideration received for granting a license or sublicense under any intellectual property which is not the **Licensed Patent Rights**) within sixty (60) days of the execution of each sublicense if any such sublicense is executed following the achievement of the **Benchmark** in Appendix D for **FDA** approval or foreign equivalent for a **Licensed Product** or **Licensed Process** within each indication in **Licensed Field of Use 1** from Appendix B.

(c) Notwithstanding anything in this **Agreement** to the contrary, any such consideration will not include the following:

(1) Bona fide support for research and development activities corresponding directly to the development of **Licensed Product(s)** and/or **Licensed Process(es),** which do not exceed **Licensee's** fully-burdened cost for undertaking such research and development, and limited to support which is received after the effective date of this **Agreement** specifically excluding any support which is used by **Licensee** to offset research and

development expenses which are incurred prior to the effective date of this **Agreement**;

(2) Proceeds derived from debt financing received after the effective date of this **Agreement**, to the extent that such financing is at market rates; or

(3) As earned royalties on **Net Sales** or sales by sublicensee(s).

APPENDIX D - BENCHMARKS AND PERFORMANCE

The **Licensee** agrees to the following **Benchmarks** for its performance under this **Agreement** and, within thirty (30) days of achieving a **Benchmark**, shall notify the **IC** that the **Benchmark** has been achieved.

	Benchmark	Deadline
I.	[***]	[***]
II.	[***]	[***]
III.	[***]	[***]
IV.	[***]	[***]
V.	[***]	[***]
VI.	[***]	[***]
VII.	[***]	[***]
VIII.	[***]	[***]
IX.	[***]	[***]
X.	[***]	[***]
XI.	[***]	[***]
XII.	[***]	[***]
XIII.	[***]	[***]

APPENDIX E – COMMERCIAL DEVELOPMENT PLAN

[***]

APPENDIX F – EXAMPLE ROYALTY REPORT

Required royalty report information includes:

- OTT license reference number (L-XXX-200X/0)
- Reporting period
- Catalog number and units sold of each Licensed Product (domestic and foreign)
- Gross Sales per catalog number per country
- Total Gross Sales
- Itemized deductions from Gross Sales
- Total Net Sales
- Earned Royalty Rate and associated calculations
- Gross Earned Royalty
- Adjustments for Minimum Annual Royalty (MAR) and other creditable payments made
- Net Earned Royalty due

Example

Catalog Number	**Product Name**	**Country**	**Units Sold**	**Gross Sales (US$)**
1	A	US	[***]	[***]
1	A	UK	[***]	[***]
1	A	France	[***]	[***]
2	B	US	[***]	[***]
3	C	US	[***]	[***]
4	D	US	[***]	[***]

Total Gross Sales [***]
Less Deductions:
Freight
[***]
Returns
[***]
Total Net Sales [***]

Royalty
Rate [***]
Royalty
Due [***]
Less Creditable Payments [***]
Net
Royalty Due [***]

APPENDIX G – ROYALTY PAYMENT OPTIONS

The License Number MUST appear on payments, reports and correspondence.

Credit and Debit Card Payments: Credit and debit card payments can be submitted for amounts up to $24,999. Submit your payment through the U.S. Treasury web site located at: **https://www.pay.gov/public/form/start/28680443.**

Automated Clearing House (ACH) for payments through U.S. banks only

The **IC** encourages its licensees to submit electronic funds transfer payments through the Automated Clearing House (ACH). Submit your ACH payment through the U.S. Treasury web site located at: https://www.pay.gov/public/form/start/28680443. Please note that the IC "only" accepts ACH payments through this U.S. Treasury web site.

Electronic Funds Wire Transfers: The following account information is provided for wire payments. In order to process payment via Electronic Funds Wire Transfer sender MUST supply the following information within the transmission:

Drawn on a **U.S. bank account** via FEDWIRE:

Please provide the following instructions to your Financial Institution for the remittance of Fedwire payments to the **NIH ROYALTY FUND**.

Fedwire Field Tag	Fedwire Field Name	Required Information
{1510}	Type/Subtype	**1000**
{2000}	Amount	*(enter payment amount)*
{3400}	Receiver ABA routing number*	[***]
{3400}	Receiver ABA short name	**TREAS NYC**
{3600}	Business Function Code	**CTR** (*or CTP*)
{4200}	Beneficiary Identifier (account number)	*(enter 12 digit gateway account #)* [***]
{4200}	Beneficiary Name	*(enter agency name associated with the Beneficiary Identifier)* **DHHS / NIH (75080031)**
{5000}	Originator	*(enter the name of the originator of the payment)* **COMPANY NAME**
{6000}	Originator to Beneficiary Information – Line 1	*(enter information to identify the purpose of the payment)* **ROYALTY**
{6000}	Originator to Beneficiary Information – Line 2	*(enter information to identify the purpose of the payment)*

Fedwire Field Tag	Fedwire Field Name	Required Information
		LICENSE NUMBER
{6000}	Originator to Beneficiary Information – Line 3	*(enter information to identify the purpose of the payment)* ***INVOICE NUMBER***
{6000}	Originator to Beneficiary Information – Line 4	*(enter information to identify the purpose of the payment)*
Notes: *The financial institution address for Treasury's routing number is 33 Liberty Street, New York, NY 10045.		

Agency Contacts: Office of Technology Transfer (OTT) (301) 496-7057 OTT-Royalties@mail.nih.gov

Drawn on a **foreign bank account** via FEDWIRE:

The following instructions pertain to the Fedwire Network. Deposits made in US Dollars (USD).

Should your remitter utilize a correspondent US domestic bank in transferring electronic funds, the following Fedwire instructions are applicable.

Fedwire Field Tag	Fedwire Field Name	Required Information
{1510}	Type/Subtype	**1000**
{2000}	Amount	*(enter payment amount)*
{3100}	Sender Bank ABA routing number	*(enter the US correspondent bank's ABA routing number)*
{3400}	Receiver ABA routing number*	[***]
{3400}	Receiver ABA short name	**TREAS NYC**
{3600}	Business Function Code	**CTR** (*or CTP*)
{4200}	Beneficiary Identifier (account number)**	*(enter 12 digit gateway account #)* [***]
{4200}	Beneficiary Name	*(enter agency name associated with the Beneficiary Identifier)* **DHHS / NIH (75080031)**
{5000}	Originator	*(enter the name of the originator of the payment)* **COMPANY'S NAME**
{6000}	Originator to Beneficiary Information – Line 1	*(enter information to identify the purpose of the payment)* **ROYALTY**
{6000}	Originator to Beneficiary Information – Line 2	*(enter information to identify the purpose of the payment)* **LICENSE NUMBER**

Fedwire Field Tag	Fedwire Field Name	Required Information
{6000}	Originator to Beneficiary Information – Line 3	*(enter information to identify the purpose of the payment)* ***INVOICE NUMBER***
{6000}	Originator to Beneficiary Information – Line 4	*(enter information to identify the purpose of the payment)*

Notes:
*The financial institution address for Treasury's routing number is 33 Liberty Street, New York, NY 10045.
**Anything other than the 12 digit gateway account # will cause the Fedwire to be returned –
SWIFT CODE: [***]

Agency Contacts:

Office of Technology Transfer (OTT) (301) 496-7057 OTT-Royalties@mail.nih.gov

Checks

All checks should be made payable to "NIH Patent Licensing"

Checks drawn on a **U.S. bank account** and sent by US Postal Service should be sent directly to the following address:

> National Institutes of Health
> P.O. Box 979071
> St. Louis, MO 63197-9000

Checks drawn on a U.S. bank account and sent by **overnight or courier** should be sent to the following address:

> US Bank
> Government Lockbox SL-MO-C2GL
> 1005 Convention Plaza
> St. Louis, MO 63101
> Phone: 314-418-4087

Checks drawn on a **foreign bank account** should be sent directly to the following address:

> National Institutes of Health
> Office of Technology Transfer
> License Compliance and Administration
> Royalty Administration
> 6011 Executive Boulevard
> Suite 325, MSC 7660
> Rockville, Maryland 20852

IOVANCE BIOTHERAPEUTICS, INC.

STOCK UNIT NOTICE
UNDER THE
IOVANCE BIOTHERAPEUTICS, INC.
2018 EQUITY INCENTIVE PLAN, AS AMENDED

Name of Grantee:

This Notice evidences the award of Restricted Stock Units (each, an "***RSU***," and collectively, the "***RSUs***") of Iovance Biotherapeutics, Inc., a Delaware corporation (the "***Company***"), that have been granted to you pursuant to the Iovance Biotherapeutics, Inc. 2018 Equity Incentive Plan, as amended (the "***Plan***"), and conditioned upon your agreement to the terms of the attached Stock Unit Agreement (the "***Agreement***"). This Notice constitutes part of and is subject to the terms and provisions of the Agreement and the Plan, which are incorporated by reference herein. Each RSU is equivalent in value to one share of the Company Stock and represents the Company's commitment to issue one share of Company Stock at a future date, subject to the terms of the Agreement and the Plan. The RSUs are credited to a separate account maintained for you on the books and records of the Company (the "***Account***"). All amounts credited to the Account will continue for all purposes to be part of the general assets of the Company.

Grant Date:

Number of RSUs:

Vesting Schedule: All of the RSUs are nonvested and forfeitable as of the Grant Date. So long as your employment or service is continuous from the Grant Date through the applicable date upon which vesting is scheduled to occur:

Notwithstanding the foregoing, effective upon a Change in Control, the RSUs that are unvested as of the date of termination will immediately become 100% exercisable.

______________________________ ______________
Iovance Biotherapeutics, Inc. Date

I acknowledge that I have carefully read the Agreement and the prospectus for the Plan. I agree to be bound by all of the provisions set forth in those documents. I also consent to electronic delivery of all notices or other information with respect to the RSUs or the Company.

______________________________ ______________
Signature of Grantee Date

Iovance Biotherapeutics, Inc.

Stock Unit Agreement
under the
Iovance Biotherapeutics, Inc.
2018 Equity Incentive Plan, as amended

1. Terminology. Unless otherwise provided in this Agreement, capitalized terms used herein are defined in the Glossary at the end of this Agreement.

2. Vesting. All of the RSUs are nonvested and forfeitable as of the Grant Date. So long as your service or employment is continuous from the Grant Date through the applicable date upon which vesting is scheduled to occur, the RSUs will become vested and nonforfeitable in accordance with the vesting schedule set forth in the Notice. Except for the circumstances, if any, described in the Notice, none of the RSUs will become vested and nonforfeitable after your service or employment ceases.

3. Termination of Employment or Service. Unless otherwise provided in the Notice, if your service or employment with the Company ceases for any reason, all RSUs that are not then vested and nonforfeitable will be forfeited to the Company immediately and automatically upon such cessation without payment of any consideration therefor and you will have no further right, title or interest in or to such RSUs or the underlying shares of Company Stock. Notwithstanding the foregoing, if your service or employment with the Company is terminated due to death or Disability, any unvested portion of the RSUs shall become fully vested as of the date of such termination.

4. Restrictions on Transfer. Neither this Agreement nor any of the RSUs may be assigned, transferred, pledged, hypothecated or disposed of in any way, whether by operation of law or otherwise, and the RSUs shall not be subject to execution, attachment or similar process. All rights with respect to this Agreement and the RSUs shall be exercisable during your lifetime only by you or your guardian or legal representative. Notwithstanding the foregoing, the RSUs may be transferred upon your death by last will and testament or under the laws of descent and distribution.

5. Settlement of RSUs.

(a) Manner of Settlement. You are not required to make any monetary payment (other than applicable tax withholding, if required) as a condition to settlement of the RSUs. The Company will issue to you, in settlement of your RSUs and subject to the provisions of Section 6 below, the number of whole shares of Company Stock that equals the number of whole RSUs that become vested, and such vested RSUs will terminate and cease to be outstanding upon such issuance of the shares. Upon issuance of such shares, the Company will determine the form of delivery (e.g., a stock certificate or electronic entry evidencing such shares) and may deliver such shares on your behalf electronically to the Company's designated stock plan administrator or such other broker-dealer as the Company may choose at its sole discretion, within reason.

(b) Timing of Settlement. Your RSUs will be settled by the Company, via the issuance of Company Stock as described herein, on the date that the RSUs become vested and nonforfeitable. However, if a scheduled issuance date falls on a Saturday, Sunday or federal holiday, such issuance date shall instead fall on the next following day that the principal executive offices of the Company are open for business. In all cases, the issuance and delivery of shares under this Agreement is intended to comply with Treasury Regulation 1.409A-1(b)(4) and shall be construed and administered in such a manner.

6. Tax Withholding. On or before the time you receive a distribution of the shares subject to your RSUs, or at any time thereafter as requested by the Company, you hereby authorize any required withholding from the Company Stock issuable to you and/or otherwise agree to make adequate provision in cash for any sums required to satisfy the federal, state, local and foreign tax withholding obligations of the Company or any Affiliate which arise in connection with your RSUs (the "***Withholding Taxes***"). Additionally, the Company may, in its sole discretion, satisfy all or any portion of the Withholding Taxes obligation relating to your RSUs by any of the following means or by a combination of such means: (i) withholding from any compensation otherwise payable to you by the Company; (ii) causing you to tender

a cash payment; (iii) permitting you to enter into a "same day sale" commitment with a broker-dealer that is a member of the Financial Industry Regulatory Authority (a "***FINRA Dealer***") whereby you irrevocably elect to sell a portion of the shares to be delivered under the Agreement to satisfy the Withholding Taxes and whereby the FINRA Dealer irrevocably commits to forward the proceeds necessary to satisfy the Withholding Taxes directly to the Company; or (iv) withholding shares of Company Stock from the shares of Company Stock issued or otherwise issuable to you in connection with the RSUs with a Fair Market Value (measured as of the date shares of Company Stock are issued to you pursuant to Section 5) equal to the amount of such Withholding Taxes; provided, however, that the number of such shares of Company Stock so withheld shall not exceed the amount necessary to satisfy the Company's required tax withholding obligations using the minimum statutory withholding rates for federal, state, local and foreign tax purposes, including payroll taxes, that are applicable to supplemental taxable income. Unless the tax withholding obligations of the Company are satisfied, the Company shall have no obligation to deliver to you any Company Stock. In the event the Company's obligation to withhold arises prior to the delivery to you of Company Stock or it is determined after the delivery of Company Stock to you that the amount of the Company's withholding obligation was greater than the amount withheld by the Company, you agree to indemnify and hold the Company harmless from any failure by the Company to withhold the proper amount.

7. Adjustments for Corporate Transactions and Other Events.

(a) Stock Dividend, Stock Split and Reverse Stock Split. Upon a stock dividend of, or stock split or reverse stock split or other event described in Section 4(d) of the Plan affecting, the Company Stock, the number of outstanding RSUs shall, without further action of the Administrator, be adjusted to reflect such event; provided, however, that any fractional RSUs resulting from any such adjustment shall be eliminated. Adjustments under this paragraph will be made by the Administrator, whose determination as to what adjustments, if any, will be made and the extent thereof will be final, binding and conclusive.

(b) Merger, Consolidation and Other Events. If the Company shall be the surviving or resulting corporation in any merger or consolidation and the Company Stock shall be converted into other securities, the RSUs shall pertain to and apply to the securities to which a holder of the number of shares of Company Stock subject to the RSUs would have been entitled. If the stockholders of the Company receive by reason of any distribution in total or partial liquidation or pursuant to any merger of the Company or acquisition of its assets, securities of another entity or other property (including cash), then the rights of the Company under this Agreement shall inure to the benefit of the Company's successor, and this Agreement shall apply to the securities or other property (including cash) to which a holder of the number of shares of Company Stock subject to the RSUs would have been entitled, in the same manner and to the same extent as the RSUs.

8. Non-Guarantee of Employment or Service Relationship. Nothing in the Plan or this Agreement shall alter your at-will or other employment status or other service relationship with the Company, nor be construed as a contract of employment or service relationship between the Company and you, or as a contractual right of you to continue in the employ of, or in a service relationship with, the Company for any period of time, or as a limitation of the right of the Company to discharge you at any time with or without cause or notice and whether or not such discharge results in the forfeiture of any nonvested and forfeitable RSUs or any other adverse effect on your interests under the Plan.

9. Rights as Stockholder. You shall not have any of the rights of a stockholder with respect to any shares of Company Stock that may be issued in settlement of the RSUs until such shares of Company Stock have been issued to you.

10. The Company's Rights. The existence of the RSUs shall not affect in any way the right or power of the Company or its stockholders to make or authorize any or all adjustments, recapitalizations, reorganizations, or other changes in the Company's capital structure or its business, or any merger or consolidation of the Company, or any issue of bonds, debentures, preferred or other stocks with preference ahead of or convertible into, or otherwise affecting the Company Stock or the rights thereof, or the dissolution or liquidation of the Company, or any sale or transfer of all or any part of the Company's assets or business, or any other corporate act or proceeding, whether of a similar character or otherwise.

11. Restrictions on Issuance of Shares. The issuance of shares of Company Stock upon settlement of the RSUs shall be subject to and in compliance with all applicable requirements of federal, state, or foreign law with respect to such securities. No shares of Company Stock may be issued hereunder if the issuance of such shares would constitute a violation of any applicable federal, state, or foreign securities laws or other law or regulations or the requirements of any stock exchange or market system upon which the Company Stock may then be listed. The inability of the Company to obtain from any regulatory body having jurisdiction the authority, if any, deemed by the Company's legal counsel to be necessary to the lawful issuance of any shares subject to the RSUs shall relieve the Company of any liability in respect of the failure to issue such shares as to which such requisite authority shall not have been obtained. As a condition to the settlement of the RSUs, the Company may require you to satisfy any qualifications that may be necessary or appropriate, to evidence compliance with any applicable law or regulation, and to make any representation or warranty with respect thereto as may be requested by the Company.

12. Notices. All notices and other communications made or given pursuant to this Agreement shall be given in writing and shall be deemed effectively given upon receipt or, in the case of notices delivered by the Company to you, five (5) days after deposit in the United States mail, postage prepaid, addressed to you at the last address you provided to the Company, or in the case of notices delivered to the Company by you, addressed to the Administrator, care of the Company for the attention of its Secretary at its principal executive office or, in either case, if the receiving party consents in advance, transmitted and received via telecopy or via such other electronic transmission mechanism as may be available to the parties. Notwithstanding the foregoing, the Company may, in its sole discretion, decide to deliver any documents related to participation in the Plan and this award of RSUs by electronic means or to request your consent to participate in the Plan or accept this award of RSUs by electronic means. You hereby consent to receive such documents by electronic delivery and, if requested, to agree to participate in the Plan through an on-line or electronic system established and maintained by the Company or another third party designated by the Company.

13. Entire Agreement. This Agreement, together with the relevant Notice and the Plan, contains the entire agreement between the parties with respect to the RSUs granted hereunder. Any oral or written agreements, representations, warranties, written inducements, or other communications made prior to the execution of this Agreement with respect to the RSUs granted hereunder shall be void and ineffective for all purposes.

14. Amendment. This Agreement may be amended from time to time by the Administrator in its discretion; provided, however, that this Agreement may not be modified in any manner that would have a materially adverse effect on the RSUs as determined in the discretion of the Administrator, except as provided in the Plan or in a written document signed by each of the parties hereto.

15. Recoupment Policy. You agree that, subject to the requirements of applicable law, if you breach any restrictive covenant agreement between you and the Company or you otherwise engage in activities that constitute Cause either while employed by, or providing service to, the Company or within two years thereafter, the RSU shall terminate, and the Company may rescind any delivery of shares upon vesting or settlement, as applicable on such terms as the Committee shall determine, including the right to require that in the event of any such rescission, (a) you shall return to the Company the shares received upon settlement of the RSU or, (b) if you no longer owns the shares, you shall pay to the Company the amount of any gain realized or payment received as a result of any sale or other disposition of the shares (or, in the event you transfer the shares by gift or otherwise without consideration, the Fair Market Value of the shares on the date of the breach of any restrictive covenant agreement or activity constituting Cause). You agree that payment shall be made in such manner and on such terms and conditions as may be required by the Committee and you shall be entitled to set off against the amount of any such payment any amounts otherwise owed to you by the Company. In addition, you agree that the RSU shall be subject to any applicable clawback or recoupment policies, share trading policies and other policies that may be implemented by the Board from time to time.

409A Savings Clause. This Agreement and the RSUs granted hereunder are intended to either fit within the "short-term deferral" exemption from Section 409A of the Code as set forth in Treasury Regulation Section 1.409A-1(b)(4) or comply with Section 409A. Notwithstanding the foregoing, if it is determined that the RSUs fail to satisfy the requirements of the short-term deferral rule and are otherwise deferred compensation subject to Section 409A, and if you are a "Specified Employee" (within the meaning set forth Section 409A(a)(2)(B)(i) of the Code) as of the date of your separation from service (within the meaning of Treasury Regulation Section 1.409A-1(h)), then the issuance of any shares that would otherwise be made upon the date of the separation from service or within the first six (6) months thereafter will not be made on the originally scheduled date(s) and will instead be issued in a lump sum on the date that is six (6) months and one day after the date of the separation from service, but if and only if such delay in the issuance of the shares is necessary to avoid the imposition of additional taxation on you in respect of the shares under Section 409A of the Code. Each installment of shares that vests is intended to constitute a "separate payment" for purposes of Section 409A of the Code and Treasury Regulation Section 1.409A-2(b)(2).

16. No Obligation to Minimize Taxes. The Company has no duty or obligation to minimize the tax consequences to you of this award of RSUs and shall not be liable to you for any adverse tax consequences to you arising in connection with this award. You are hereby advised to consult with your own personal tax, financial and/or legal advisors regarding the tax consequences of this award and by signing the Notice, you have agreed that you have done so or knowingly and voluntarily declined to do so.

17. Conformity with Plan. This Agreement is intended to conform in all respects with, and is subject to all applicable provisions of, the Plan. Inconsistencies between this Agreement and the Plan shall be resolved in accordance with the terms of the Plan. In the event of any ambiguity in this Agreement or any matters as to which this Agreement is silent, the Plan shall govern. A copy of the Plan is available upon request to the Administrator.

18. No Funding. This Agreement constitutes an unfunded and unsecured promise by the Company to issue shares of Company Stock in the future in accordance with its terms. You have the status of a general unsecured creditor of the Company as a result of receiving the grant of RSUs.

19. Effect on Other Employee Benefit Plans. The value of the RSUs subject to this Agreement shall not be included as compensation, earnings, salaries, or other similar terms used when calculating your benefits under any employee benefit plan sponsored by the Company, except as such plan otherwise expressly provides. The Company expressly reserves its rights to amend, modify, or terminate any of the Company's employee benefit plans.

20. Governing Law. The validity, construction and effect of this Agreement, and of any determinations or decisions made by the Administrator relating to this Agreement, and the rights of any and all persons having or claiming to have any interest under this Agreement, shall be determined exclusively in accordance with the laws of the State of Delaware, without regard to its provisions concerning the applicability of laws of other jurisdictions. As a condition of this Agreement, you agree that you will not bring any action arising under, as a result of, pursuant to or relating to, this Agreement in any court other than a federal or state court in the districts which include Delaware, and you hereby agree and submit to the personal jurisdiction of any federal court located in the district which includes Delaware or any state court in the district which includes Delaware. You further agree that you will not deny or attempt to defeat such personal jurisdiction or object to venue by motion or other request for leave from any such court.

21. Resolution of Disputes. Any dispute or disagreement which shall arise under, or as a result of, or pursuant to or relating to, this Agreement shall be determined by the Administrator in good faith in its absolute and uncontrolled discretion, and any such determination or any other determination by the Administrator under or pursuant to this Agreement and any interpretation by the Administrator of the terms of this Agreement, will be final, binding and conclusive on all persons affected thereby. You agree that before you may bring any legal action arising under, as a result of, pursuant to or relating to, this Agreement you will first exhaust your administrative remedies before the Administrator. You further agree that in the event that the Administrator does not resolve any dispute or disagreement arising under, as a result of, pursuant to or relating to, this Agreement to your satisfaction, no legal action may be commenced or maintained relating to this Agreement more than twenty-four (24) months after the Administrator's decision.

22. Headings. The headings in this Agreement are for reference purposes only and shall not affect the meaning or interpretation of this Agreement.

23. Electronic Delivery of Documents. By your signing the Notice, you (i) consent to the electronic delivery of this Agreement, all information with respect to the Plan and the RSUs, and any reports of the Company provided generally to the Company's stockholders; (ii) acknowledge that you may receive from the Company a paper copy of any documents delivered electronically at no cost to you by contacting the Company by telephone or in writing; (iii) further acknowledge that you may revoke your consent to the electronic delivery of documents at any time by notifying the Company of such revoked consent by telephone, postal service or electronic mail; and (iv) further acknowledge that you understand that you are not required to consent to electronic delivery of documents.

24. No Future Entitlement. By your signing the Notice, you acknowledge and agree that: (i) the grant of a restricted stock unit award is a one-time benefit which does not create any contractual or other right to receive future grants of restricted stock units, or compensation in lieu of restricted stock units, even if restricted stock units have been granted repeatedly in the past; (ii) all determinations with respect to any such future grants and the terms thereof will be at the sole discretion of the Committee; (iii) the value of the restricted stock units is an extraordinary item of compensation which is outside the scope of your employment contract, if any; (iv) the value of the restricted stock units is not part of normal or expected compensation or salary for any purpose, including, but not limited to, calculating any termination, severance, resignation, redundancy, end of service payments or similar payments, or bonuses, long-service awards, pension or retirement benefits; (v) the vesting of the restricted stock units ceases upon termination of Service with the Company or transfer of employment from the Company, or other cessation of eligibility for any reason, except as may otherwise be explicitly provided in this Agreement; (vi) the Company does not guarantee any future value of the restricted stock units; and (vii) no claim or entitlement to compensation or damages arises if the restricted stock units decrease or do not increase in value and you irrevocably release the Company from any such claim that does arise.

25. Personal Data. For purposes of the implementation, administration and management of the restricted stock units or the effectuation of any acquisition, equity or debt financing, joint venture, merger, reorganization, consolidation, recapitalization, business combination, liquidation, dissolution, share exchange, sale of stock, sale of material assets or other similar corporate transaction involving the Company (a "***Corporate Transaction***"), you consent, by execution of the Notice, to the collection, receipt, use, retention and transfer, in electronic or other form, of your personal data by and among the Company and its third party vendors or any potential party to a potential Corporate Transaction. You understand that personal data (including but not limited to, name, home address, telephone number, employee number, employment status, social security number, tax identification number, date of birth, nationality, job and payroll location, data for tax withholding purposes and shares awarded, cancelled, vested and unvested) may be transferred to third parties assisting in the implementation, administration and management of the restricted stock units or the effectuation of a Corporate Transaction and you expressly authorize such transfer as well as the retention, use, and the subsequent transfer of the data by the recipient(s). You understand that these recipients may be located in your country or elsewhere, and that the recipient's country may have different data privacy laws and protections than your country. You understand that data will be held only as long as is necessary to implement, administer and manage the restricted stock units or effect a Corporate Transaction. You understand that you may, at any time, request a list with the names and addresses of any potential recipients of the personal data, view data, request additional information about the storage and processing of data, require any necessary amendments to data or refuse or withdraw the consents herein, in any case without cost, by contacting in writing the Company's Secretary. You understand, however, that refusing or withdrawing your consent may affect your ability to accept a restricted stock unit award.

{*Glossary begins on next page*}

(a) “***Administrator***” means the Committee as defined in the Plan.

(b) “***Agreement***” means this document, as amended from time to time, together with the Plan which is incorporated herein by reference.

(c) ***“Cause”*** has the meaning set forth in the Plan.

(d) *“**Change in Control**”* shall have the meaning set forth in the Plan.

(e) “**Code**” means the Internal Revenue Code of 1986, as amended, and the Treasury regulations and other guidance promulgated thereunder.

(f) “**Company Stock**” shall mean common stock of the Company.

(g) “***Company***” means Iovance Biotherapeutics, Inc., and shall include all its successors except where the context otherwise requires. For purposes of determining whether a Change in Control has occurred, Company shall mean only Iovance Biotherapeutics, Inc.

(h) “***Fair Market Value***” has the meaning set forth in the Plan.

(i) “***Grant Date***” means the effective date of a grant of RSUs made to you as set forth in the relevant Notice.

(j) “***Notice***” means the statement, letter or other written notification provided to you by the Company setting forth the terms of a grant of RSUs made to you.

(k) “***Plan***” means the Iovance Biotherapeutics, Inc. 2018 Equity Incentive Plan, as amended, as in effect from time to time.

(l) “***RSU***” means the Company’s commitment to issue one share of Company Stock at a future date, subject to the terms of the Agreement and the Plan.

(m) “***You***” or “***Your***” means the recipient of the RSUs as reflected on the applicable Notice. Whenever the word “you” or “your” is used in any provision of this Agreement under circumstances where the provision should logically be construed, as determined by the Administrator, to apply to the estate, personal representative, or beneficiary to whom the RSUs may be transferred by will or by the laws of descent and distribution, the words “you” and “your” shall be deemed to include such person.

{*End of Agreement*}

IOVANCE BIOTHERAPEUTICS, INC.
2018 EQUITY INCENTIVE PLAN

NONQUALIFIED STOCK OPTION AWARD AGREEMENT

THIS NONQUALIFIED STOCK OPTION AWARD AGREEMENT (this "Agreement"), is entered into as of [ ] (the "Date of Grant"), by and between Iovance Biotherapeutics, Inc., a Delaware corporation (the "Company") on behalf of itself and its Affiliates, and [ ] (the "Participant"). Capitalized terms used in this Agreement and not otherwise defined herein have the meanings ascribed to such terms in the Iovance Biotherapeutics, Inc. 2018 Equity Incentive Plan, as amended, restated or otherwise modified from time to time in accordance with its terms (the "Plan").

WHEREAS, the Compensation Committee of the board of directors (the "Committee"), through its own action or through the action of the full board of directors, has determined that it is in the best interests of the Company and its stockholders to grant the award provided for herein to the Participant on the terms and subject to the conditions set forth herein.

NOW, THEREFORE, for and in consideration of the premises and the covenants of the parties contained in this Agreement, and for other good and valuable consideration, the receipt of which is hereby acknowledged, the parties hereto, for themselves, their successors and assigns, hereby agree as follows:

1. Grant of Option.

(a) Grant. The Company hereby grants to the Participant an option (the "Option") to purchase [ ] shares of Common Stock (the "Option Shares") on the terms and subject to the conditions set forth in this Agreement and as otherwise provided in the Plan. The Option is a Nonqualifed Stock Option. The Option shall vest in accordance with Section 2. The Exercise Price shall be [ ] per Option Share.

(b) Incorporation by Reference. The provisions of the Plan are incorporated herein by reference. Except as otherwise expressly set forth herein, this Agreement shall be construed in accordance with the provisions of the Plan and any interpretations, rules and regulations and additional terms adopted by the Committee from time to time pursuant to the Plan. The Committee shall have final authority to interpret and construe the Plan and this Agreement and to make any and all determinations under them, and its decision shall be binding and conclusive upon the Participant and the Participant's beneficiary in respect of any questions arising under the Plan or this Agreement. The Participant acknowledges that the Participant has received a copy of the Plan and has had an opportunity to review the Plan and agrees to be bound by all the terms and provisions of the Plan.

2. Vesting. Except as may otherwise be provided herein, the Option shall vest and become exercisable [ ] (each such date, a "Vesting Date"), subject to the Participant's continued employment with, appointment as a director of, or engagement to provide services to, the Company or any of its Affiliates through the applicable Vesting Date. Any fractional Option Share resulting from the application of the vesting schedule shall be aggregated and the Option Share resulting from such aggregation shall vest on the final Vesting Date.

3. Termination of Employment or Services.

(a) Generally. Except as otherwise provided herein, if the Participant's employment with, membership on the board of directors, or engagement to provide services to the Company or any of its Affiliates terminates for any reason, the unvested portion of the Option shall be canceled immediately and the Participant shall have no rights with respect to the Option Shares subject to such unvested portion.

(b) Death or Disability. Notwithstanding anything to the contrary in Section 3, if the Participant's employment with, membership on the board of directors, or engagement to provide services to the Company or any of its Affiliates terminates due to the Participant's death or Disability, any unvested portion of the Option shall become fully vested as of the date of such termination, which shall be the final Vesting Date.

(c) The term "Retirement" shall mean, unless otherwise defined in a Superseding Agreement or in a Resolution, the termination of a Participant's employment with the Company or its Affiliates after the Participant has attained the age of 55 years and the Participant has stated at the time of resignation, in writing, his or her intention to leave the Company's industry or to leave the general workforce. Notwithstanding the foregoing, the term "Retirement" shall not apply to any Participant whose employment is terminated with Cause or to any Participant who is solely a director or consultant. In the event that the Participant accepts full-time or part-time employment during the one-year period following the Participant's employment termination date, the Participant's termination will be deemed, for all purposes hereunder, to have been a voluntary resignation, and not a termination upon Retirement.

4. Expiration.

(a) In no event shall all or any portion of the Option be exercisable after the tenth annual anniversary of the Date of Grant (such ten-year period, the "Option Period"); provided, that if the Option Period would expire at a time when trading in the shares of Common Stock is prohibited by the Company's securities trading policy (or Company-imposed "blackout period"), the Option Period shall be automatically extended until the 30th day following the expiration of such prohibition (but not to the extent that any such extension would otherwise violate Section 409A of the Code).

(b) If, prior to the end of the Option Period, the Participant's employment with, or engagement to provide services to, the Company and all Affiliates is terminated without Cause or by the Participant for any reason, then the Option shall expire on the earlier of the last day of the Option Period and the date that is 90 days after the date of such termination; provided, however, that if the Participant's employment or engagement to provide services to the Company and its Affiliates is terminated and the Participant is subsequently rehired or reengaged by the Company or any Affiliate within 90 days following such termination and prior to the expiration of the Option, the Participant shall not be considered to have undergone a termination of employment or service, as applicable. In the event of a termination described in this subsection (b), the Option shall remain exercisable by the Participant until its expiration only to the extent that the Option was exercisable at the time of such termination.

(c) If (i) the Participant's employment with or engagement to provide services to, the Company is terminated prior to the end of the Option Period on account of the Participant's Disability, (ii) the Participant dies while still in the employ or engagement of the Company or an Affiliate, (iii) the Participant dies following a termination described in subsection (b) above but prior to the expiration of an Option, or (iv) the Participant's employment with, or engagement to provide services to, the Company is terminated prior to the end of the Option Period on account of his or her Retirement, the Option shall expire on the earlier of the last day of the Option Period and the date that is one (1) year after the date of death or termination on account of Disability of or Retirement by the Participant, as applicable. In such event, the Option shall remain exercisable by the Participant or Participant's beneficiary, as applicable, until its expiration only to the extent that the Option was exercisable by the Participant at the time of such event.

(d) If the Participant's Option Shares were awarded pursuant to a directorship, and prior to the end of the Option Period, the Participant's directorship with the Company is terminated without Cause or by the Participant for any reason, then the Option shall expire on the earlier of the last day of the Option Period and the date that is two years after the date of such termination.

(e) If the Participant ceases employment with or engagement to provide services to the Company or any Affiliates or is removed as a director due to a termination for Cause, the Option (whether vested or unvested) shall be cancelled immediately and the Participant shall have no rights with respect to the Option Shares.

5. Method of Exercise and Form of Payment.

(a) No Option Shares shall be delivered pursuant to any exercise of the Option until the Participant has paid in full to the Company the Exercise Price and an amount equal to any U.S. federal, state, local and non-U.S. income and employment taxes required to be withheld. The Option may be exercised by delivery of written or electronic notice of exercise to the Company or its designee (including a third-party-administrator) in accordance with the terms hereof. The Exercise Price and all applicable required withholding taxes shall be payable (i) in cash, check or cash equivalent; or (ii) by such other method as the Committee may permit, including without limitation: (A) shares of Common Stock valued at the Fair Market Value at the time the Option is exercised (including, pursuant to procedures approved by the Committee, by means of attestation of ownership of a sufficient number of shares of Common Stock in lieu of actual delivery of such shares to the Company), provided that such shares of Common Stock are not subject to any pledge or other security interest; (B) in other property having a Fair Market Value equal to the Exercise Price and all applicable required withholding taxes; or (C) if there is a public market for the shares of Common Stock at such time, by means of a broker-assisted "cashless exercise" pursuant to which the Company is delivered a copy of irrevocable instructions to a stockbroker to sell the shares of Common Stock otherwise deliverable upon the exercise of the Option and to deliver promptly to the Company an amount equal to the Exercise

Price and all applicable required withholding taxes. Any fractional shares of Common Stock resulting from the application of this Section 5 shall be settled in cash.

6. Rights as a Stockholder. The Participant shall not be deemed for any purpose to be the owner of any shares of Common Stock subject to this Option unless, until and to the extent that (i) this Option shall have been exercised pursuant to its terms, (ii) the Company shall have issued and delivered to the Participant the Option Shares and (iii) the Participant's name shall have been entered as a stockholder of record with respect to such Option Shares on the books of the Company. The Company shall cause the actions described in clauses (ii) and (iii) of the preceding sentence to occur promptly following settlement as contemplated by this Agreement, subject to compliance with applicable laws.

7. Compliance with Legal Requirements.

(a) Generally. The granting and exercising of the Option, and any other obligations of the Company under this Agreement, shall be subject to all applicable U.S. federal, state and local laws, rules and regulations, all applicable non-U.S. laws, rules and regulations and to such approvals by any regulatory or governmental agency as may be required. The Participant agrees to take all steps that the Committee or the Company determines are reasonably necessary to comply with all applicable provisions of U.S. federal and state securities law and non-U.S. securities law in exercising the Participant's rights under this Agreement.

(b) Tax Withholding. Any exercise of the Option shall be subject to the Participant's satisfying any applicable U.S. federal, state and local tax withholding obligations and non-U.S. tax withholding obligations. The Company shall have the right and is hereby authorized to withhold from any amounts payable to the Participant in connection with the Option or otherwise the amount of any required withholding taxes in respect of the Option, its exercise or any payment or transfer of the Option or under the Plan and to take any such other action as the Committee or the Company deem necessary to satisfy all obligations for the payment of such withholding taxes (up to the maximum permissible withholding amounts), including the right to use a broker-assisted "cashless exercise" as described in Section 5(i)(C) hereof. The Participant may elect to satisfy, and the Company may require the Participant to satisfy, in whole or in part, the tax obligations by withholding shares of Common Stock that would otherwise be received upon exercise of the Option with a Fair Market Value equal to such withholding liability. For exercises of the Option occurring during a blackout period under the Company's insider trading policy, the Company shall arrange for the sale of a number of shares of Common Stock to be delivered to the Participant to satisfy the applicable withholding obligations. Such shares of Common Stock shall be sold on behalf of the Participant through the Company's transfer agent on the facilities of any exchange on which the Common Stock is listed at the time of such sale.

8. Miscellaneous.

(a) Transferability. The Option may not be assigned, alienated, pledged, attached, sold or otherwise transferred or encumbered (a "Transfer") by the Participant other than by will or by the laws of descent and distribution, pursuant to a qualified domestic relations order or as otherwise permitted under Section 14(b) of the Plan. Any attempted Transfer of the Option contrary to the provisions hereof, and the levy of any execution, attachment or similar process upon the Option, shall be null and void and without effect.

(b) Waiver. Any right of the Company contained in this Agreement may be waived in writing by the Committee. No waiver of any right hereunder by any party shall operate as a waiver of any other right, or as a waiver of the same right with respect to any subsequent occasion for its exercise, or as a waiver of any right to damages. No waiver by any party of any breach of this Agreement shall be held to constitute a waiver of any other breach or a waiver of the continuation of the same breach.

(c) Section 409A. The Option is not intended to be subject to Section 409A of the Code. Notwithstanding the foregoing or any provision of the Plan or this Agreement, if any provision of the Plan or this Agreement contravenes Section 409A of the Code or could cause the Participant to incur any tax, interest or penalties under Section 409A of the Code, the Committee may, in its sole discretion and without the Participant's consent, modify such provision to (i) comply with, or avoid being subject to, Section 409A of the Code, or to avoid the incurrence of taxes, interest and penalties under Section 409A of the Code, and/or (ii) maintain, to the maximum extent practicable, the original intent and economic benefit to the Participant of the applicable provision without materially increasing the cost to the Company or contravening the provisions of Section 409A of the Code. This Section 8(c) does not create an obligation on the part of the Company to modify the Plan or this Agreement and does not guarantee that the Option or the Option Shares will not be subject to interest and penalties under Section 409A.

(d) Change in Control. Notwithstanding anything to the contrary in this Agreement or the Plan, provided the Participant is still employed by or providing services to the Company on the date of a Change in Control, any unvested portion of the Option shall become fully vested as of the date of the Change in Control, which shall be the final Vesting Date.

(e) Notices. Any notices provided for in this Agreement or the Plan shall be in writing and shall be deemed sufficiently given if either hand delivered or if sent by fax, pdf/email or overnight courier, or by postage-paid first-class mail. Notices sent by mail shall be deemed received three business days after mailing but in no event later than the date of actual receipt. Notices shall be directed, if to the Participant, at the Participant's address indicated by the Company's records, or if to the Company, to the attention of the General Counsel at the Company's principal executive office.

(f) Severability. The invalidity or unenforceability of any provision of this Agreement shall not affect the validity or enforceability of any other provision of this Agreement, and each other provision of this Agreement shall be severable and enforceable to the extent permitted by law.

(g) No Rights to Employment, Directorship or Service. Nothing contained in this Agreement shall be construed as giving the Participant any right to be retained, in any position, as an employee, consultant or director of the Company or any of its Affiliates or shall interfere with or restrict in any way the rights of the Company or any of its Affiliates, which are hereby expressly reserved, to remove, terminate or discharge the Participant at any time for any reason whatsoever.

(h) Fractional Shares. In lieu of issuing a fraction of a share of Common Stock resulting from any exercise of the Option or an adjustment of the Option pursuant to Section 11 of the Plan or otherwise, the Company shall be entitled to pay to the Participant an amount in cash equal to the Fair Market Value of such fractional share.

(i) Beneficiary. The Participant may file with the Committee a written designation of a beneficiary on such form as may be prescribed by the Committee and may, from time to time, amend or revoke such designation.

(j) Successors. The terms of this Agreement shall be binding upon and inure to the benefit of the Company and its successors and assigns, and of the Participant and the beneficiaries, executors, administrators, heirs and successors of the Participant.

(k) Entire Agreement. This Agreement and the Plan contain the entire agreement and understanding of the parties hereto with respect to the subject matter contained herein and supersede all prior communications, representations and negotiations in respect thereto. Notwithstanding the foregoing or anything to the contrary herein, if the Participant is a party to an employment, consulting, change-in-control, severance or other applicable written agreement with the Company that modifies or supplements the terms of this Agreement (each, a "Superseding Agreement"), or is the subject of a resolution by the Committee or the board of directors of the Company evidencing the grant of an award that modifies or supplements the terms of this Agreement (a "Resolution"), such modified or supplemented terms shall control in the event of any conflict between such terms and the terms of this Agreement, provided that in the event that the Superseding Agreement or Resolution is silent on a matter addressed in this Agreement, then such silence is not a conflict. No change, modification or waiver of any provision of this Agreement shall be valid unless the same be in writing and signed by the parties hereto, except for any changes permitted without consent under Section 11 or 13 of the Plan.

(l) Governing Law and Venue. This Agreement shall be construed and interpreted in accordance with the laws of the State of Delaware, without regard to principles of conflicts of laws thereof, or principles of conflicts of laws of any other jurisdiction that could cause the application of the laws of any jurisdiction other than the State of Delaware.

(m) Dispute Resolution; Consent to Jurisdiction. All disputes between or among any Persons arising out of or in any way connected with the Plan, this Agreement or the Option shall be solely and finally settled by the Committee, acting in good faith, the determination of which shall be final. Any matters not covered by the preceding sentence shall be solely and finally settled in accordance with the Plan, and the Participant and the Company consent to the personal jurisdiction of the United States federal and state courts sitting in Wilmington, Delaware, as the exclusive jurisdiction with respect to matters arising out of or related to the enforcement of the Committee's determinations and resolution of matters, if any, related to the Plan or this Agreement not required to be resolved by the Committee. Each such Person hereby irrevocably consents to the service of process of any of the aforementioned courts in any such suit, action or proceeding by the mailing of copies thereof by registered or certified mail, postage prepaid, to the last known address of such Person, such service to become effective ten (10) days after such mailing.

(n) Waiver of Jury Trial. Each party hereto hereby waives, to the fullest extent permitted by applicable law, any right it may have to a trial by jury in any legal proceeding directly or indirectly arising out of or relating to this Agreement or the transactions contemplated (whether based on contract, tort or any other theory). Each party hereto (A) certifies that no representative, agent or attorney of any other party has represented, expressly or otherwise, that such other party would not, in the event of litigation, seek to enforce the foregoing waiver and (B) acknowledges that it and the other parties hereto have been induced to enter into this Agreement by, among other things, the mutual waivers and certifications in this section.

(o) Headings. The headings of the Sections hereof are provided for convenience only and are not to serve as a basis for interpretation or construction, and shall not constitute a part, of this Agreement.

(p) Counterparts. This Agreement may be executed in counterparts (including via electronic signature or acceptance, facsimile, or electronic image scan (pdf)), each of which shall be deemed to be an original, but both of which together shall constitute one and the same instrument and shall become effective when one or more counterparts have been signed by each of the parties and delivered to the other parties.

(q) Electronic Delivery. By accepting this Agreement, the Participant consents to the electronic delivery of prospectuses, annual reports and other information required to be delivered by U.S. Securities and Exchange Commission rules (which consent may be revoked in writing by the Participant at any time upon three business days' notice to the Company, in which case subsequent prospectuses, annual reports and other information will be delivered in hard copy to the Participant).

(r) Electronic Participation in Plan. The Company may, in its sole discretion, decide to deliver any documents related to current or future participation in the Plan by electronic means. The Participant hereby consents to receive such documents by electronic delivery and agrees to participate in the Plan through an on-line or electronic system established and maintained by the Company or a third party designated by the Company.

[Signature page follows]

IN WITNESS WHEREOF, this Agreement has been executed by the Company and the Participant as of the day first written above.

IOVANCE BIOTHERAPEUTICS, INC.

By: ______________________________
Name: ______________________________
Title: ______________________________

PARTICIPANT

____
[Insert Name]

Exhibit 31.1

CERTIFICATION

I, Frederick G. Vogt, PhD., Esq., Interim Chief Executive Officer and President, and General Counsel of Iovance Biotherapeutics, Inc., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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. I am 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 my 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 my 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 my 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 that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting; and

5. I have disclosed, based on my 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.

Dated: August 5, 2021

By: /s/ Frederick G. Vogt, PhD., Esq
Frederick G. Vogt, PhD., Esq
Interim Chief Executive Officer and President, and General Counsel (Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Jean-Marc Bellemin, Chief Financial Officer of Iovance Biotherapeutics, Inc., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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. I am 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 my 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 my 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 my 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 that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. I have disclosed, based on my 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.

Dated: August 5, 2021

By: /s/ Jean-Marc Bellemin
Jean-Marc Bellemin
Chief Financial Officer
(Principal Financial Officer & Principal Accounting Officer)

Exhibit 32.1

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Quarterly Report on Form 10-Q of Iovance Biotherapeutics, Inc. (the “Company”) for the quarter ended June 30, 2021, as filed with the Securities and Exchange Commission on the date hereof (the “Report”), Frederick G. Vogt, PhD., Esq, Interim Chief Executive Officer and President, and General Counsel, hereby certifies, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: August 5, 2021

By: /s/ Frederick G. Vogt, PhD., Esq
Frederick G. Vogt, PhD., Esq
Interim Chief Executive Officer and President, and General Counsel (Principal Executive Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Iovance Biotherapeutics, Inc. (the “Company”) for the quarter ended June 30, 2021 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), Jean-Marc Bellemin, Chief Financial Officer, hereby certifies, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: August 5, 2021

By: /s/ Jean-Marc Bellemin
Jean-Marc Bellemin
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.