UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K
Current Report

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (date of earliest event reported): May 15, 2019

IOVANCE BIOTHERAPEUTICS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware	
(State of Incorporation)	
001-36860	**75-3254381**
Commission File Number	**(I.R.S. Employer Identification No.)**
999 Skyway Road, Suite 150 **San Carlos, California**	**94070**
(Address of Principal Executive Offices)	**(Zip Code)**

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

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c)).

Indicate by check mark whether the registrant is an emerging growth company as defined in as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter). 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. ☐

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 share	IOVA	The Nasdaq Stock Market, LLC

Item 8.01. Other Events.

On May 15, 2019, Iovance Biotherapeutics, Inc. (the "Company") issued a press release announcing updates from ongoing clinical trials including new interim data from studies of tumor infiltrating lymphocyte ("TIL") therapy LN-145 in patients with advanced cervical cancer and with TIL therapy lifileucel in advanced melanoma. In addition, the Company announced that the first PD-1/PD-L1 naive patient has been dosed with TIL therapy and that it has entered into a collaboration with Genocea Biosciences, Inc., to evaluate the potential for an improved TIL product. The full text of the press release is attached hereto as Exhibit 99.1 and incorporated herein by reference.

On May 15, 2019, the Company also updated its corporate presentation that it uses for presentations at healthcare conferences and to analysts, current stockholders, and others. A copy of the Company's presentation that it intends to use at such events is attached as Exhibit 99.2 and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release dated May 15, 2019.
99.2	Iovance Biotherapeutics, Inc., Corporate Presentation - May 2019.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this Report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: May 16, 2019

IOVANCE BIOTHERAPEUTICS, INC.

By: /s/ MARIA FARDIS
Maria Fardis, Chief Executive Officer

Exhibit 99.1

Iovance Biotherapeutics Announces Updates to Tumor Infiltrating Lymphocyte (TIL) Therapy Clinical Programs

Patients with advanced cervical cancer treated with LN-145 had an objective response rate of 44 percent

Patients in Cohort 2 with advanced melanoma treated with lifileucel following failure of checkpoint inhibitors had objective response rate of 38 percent

First patient dosed in IOV-COM-202; the first time that Iovance TIL therapy has been administered in a PD-1/PD-L1 naive patient population

SAN CARLOS, Calif., May 15, 2019 -- Iovance Biotherapeutics, Inc. (NASDAQ: IOVA), a late-stage biotechnology company developing novel cancer immunotherapies based on tumor-infiltrating lymphocyte (TIL) technology, today announced updates from ongoing clinical trials including new interim data from studies of TIL therapy LN-145 in patients with advanced cervical cancer and with TIL therapy lifileucel in advanced melanoma. These data will be presented at the 55th Annual Meeting of the American Society of Clinical Oncology (ASCO) taking place May 31 to June 4, 2019, in Chicago. In addition, the company announced that the first PD-1/PD-L1 naive patient has been dosed with TIL therapy and that it has entered into a collaboration with Genocea to evaluate the potential for an improved TIL product.

Data from the innovaTIL-04 study in patients with recurrent, metastatic or persistent cervical cancer showed an ORR of 44 percent (1 complete response, 9 partial responses and 2 unconfirmed partial responses) and a disease control rate of 89 percent. At 3.5-month median study follow-up, 11 out of 12 patients maintained a response. The mean patient age was 47 years and study participants had experienced a mean of 2.6 prior lines of therapy. The adverse event profile was generally consistent with the underlying advanced disease and the profile of the lymphodepletion and IL-2 regimens. These data will be presented on Saturday, June 1 (Abstract #2538). As a reference, ORR for Keytruda used in second line cervical cancer patients is 14 percent.[1]

“As advanced cervical cancer is typically diagnosed at a relatively young age and efficacy of existing treatment options is extremely low, there is potential to significantly impact care with an option that can bring about long-term remission and complete responses,” said Amir Jazaeri, M.D., innovaTIL-04 study investigator and associate professor of Gynecological Oncology and Reproductive Medicine at the MD Anderson Cancer Center. “The interim data from LN-145 present compelling evidence that TIL therapy, provided as a single administration, could improve upon current treatments.”

Updated results from Cohort 2 in the ongoing innovaTIL-01 study demonstrated an ORR of 38 percent (2 complete responses, 18 partial responses and 1 unconfirmed partial response) in 55 consecutively dosed post-PD-1 patients with Stage IIIC/IV unresectable melanoma. In this study, patients were heavily pretreated, with a mean of 3.1 lines of prior therapy including anti-PD1, and had high baseline tumor burden. The disease control rate was 76 percent. At 7.4-month median follow-up, responses were maintained in the majority of patients (only 4 out of 21 responders had progressed at the time of data analysis for the abstract). These data are consistent with prior results from Cohort 2, presented at the Society for Immunotherapy of Cancer (SITC) 2018 Annual Meeting, which demonstrated a 38 percent ORR in a subset of 47 of the 55 patients in Cohort 2. Adverse events resolved to baseline 2 weeks post TIL infusion. These data will be presented on Saturday, June 1 (Abstract #2518).

“We are pleased to be sharing our broader melanoma data and now Gen-2 cervical data at ASCO. The data are indicative of the efficacy of TIL therapy in multiple indications. Further, we believe that TIL therapy is a platform which may offer patients with different advanced cancers a potential therapy,” said Maria Fardis, Ph.D., president and chief executive officer of Iovance Biotherapeutics. “We will provide further updates, including duration of response data, at the ASCO meeting.”

The company today also announced that first melanoma patient has been dosed in its Phase 2 IOV-COM-202 study. This represents the first instance of a patient naive to checkpoint inhibitor treatment receiving Iovance’s TIL therapy in combination with Keytruda.

“TIL therapy represents a promising approach to further advance on the gains that have been made in cancer treatment thanks to immunotherapy and combination approaches,” commented Sajeve Thomas, M.D., Iovance study investigator and oncologist at the Orlando Heath UF Health Cancer Center. “We are encouraged to be part of evaluating new applications of Iovance TIL therapy with combinations and additional tumor types and look forward to the results in these areas.”

IOV-COM-202 is a Phase 2 global multicenter study evaluating the safety and efficacy of Iovance autologous TIL therapy in combination with pembrolizumab in patients who have not received prior immunotherapy for treatment. The study is currently enrolling in the U.S. and Europe. Additional information on this study is available at https://clinicaltrials.gov/ct2/show/NCT03645928.

To support efforts to improve the potency of TIL, Iovance has entered into a collaboration with Genocea to evaluate its ATLAS™ platform. As reported by the company at the American Association for Cancer Research (AACR) 2019 Annual Meeting, melanoma patients receiving lifileucel have a unique mutational landscape, suggesting that high mutational load solid tumors such as melanoma may benefit from treatment with a patient specific, polyclonal product such as the Iovance TIL product. The company plans to utilize the ATLAS platform to evaluate the potential for an improved TIL product.

Conference call

Management will host a conference call and live audio webcast to discuss these results on Thursday, May 16 at 8:00 a.m. EDT. To participate in the conference call, please dial 1-844-646-4465 (U.S.) or 1-615-247-0257 (international) and reference the access code 9291799. A live webcast can be accessed under “News & Events: Investor Calendar” in the Investors section of the Company’s website at www.iovance.com or at the link: https://edge.media-server.com/m6/p/wgjz5xa7. An archived webcast will be available in the Investors section of www.iovance.com for thirty days following the call.

Details of ASCO Abstracts

- Abstract #2538. Amir Jazaeri *et al.* Safety and efficacy of adoptive cell transfer using autologous tumor infiltrating lymphocytes (LN-145) for treatment of recurrent, metastatic, or persistent cervical carcinoma. Poster display Saturday, June 1, 8:00 a.m. - 11:00 a.m. CDT.
- Abstract #2518. Amod Sarnaik *et al.* Safety and efficacy of cryopreserved autologous tumor infiltrating lymphocyte therapy (LN-144, lifileucel) in advanced metastatic melanoma patients who progressed on multiple prior therapies including anti-PD-1. Poster display Saturday, June 1, 8:00 a.m. - 11:00 a.m. CDT; poster discussion 1:15 p.m. - 2:45 p.m. CDT.

Additional information is available at the ASCO website and at https://meetinglibrary.asco.org/.

[1]https://www.keytruda.com/hcp/advanced-cervical-cancer/

About Iovance Biotherapeutics, Inc.

Iovance Biotherapeutics intends to commercialize lifileucel, an autologous cell therapy product using TIL technology that amplifies the body's own immune response to eradicate solid tumors or attack blood cancers. The company is currently conducting the pivotal study innovaTIL-01 in patients with metastatic melanoma. In addition, the company's TIL therapies are being investigated for the treatment of patients with locally advanced, recurrent or metastatic cancers including cervical, head and neck, and non-small cell lung cancer. For more information, please visit www.iovance.com.

Forward-Looking Statements

Certain matters discussed in this press release are "forward-looking statements" of Iovance Biotherapeutics, Inc. (hereinafter referred to as the "Company," "we," "us," or "our"). We may, in some cases, use terms such as "predicts," "believes," "potential," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. The forward-looking statements include, but are not limited to, risks and uncertainties relating to the success, timing, projected enrollment, manufacturing capabilities, and cost of our ongoing clinical trials and anticipated clinical trials for our current product candidates (including both Company-sponsored and collaborator-sponsored trials in both the U.S. and Europe), such as statements regarding the timing of initiation and completion of these trials; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration ("FDA") or other regulatory authority approval of, or other action with respect to, our product candidates; the strength of Company's product pipeline; the successful implementation of the Company's research and development programs and collaborations; the success of the Company's manufacturing, license or development agreements; the acceptance by the market of the Company's product candidates, if approved; and other factors, including general economic conditions and regulatory developments, not within the Company's control. The factors discussed herein could cause actual results and developments to be materially different from those expressed in or implied by such statements. Actual results may differ from those set forth in this press release due to the risks and uncertainties inherent in the Company's business, including, without limitation; the preliminary clinical results, including efficacy and safety results, from ongoing Phase 2 studies, including the Company's studies in advanced melanoma and advanced cervical cancer, may not be reflected or maintained in the final analyses of these trials, including new cohorts within these trials, and may not be supportive of product approval; the FDA or other regulatory authorities may potentially delay the timing of their approval of, or other action with respect to, the Company's product candidates; the Company's ability to address FDA or other regulatory authority requirements relating to its clinical programs and registrational plans, such requirements including, but not limited to, clinical and safety requirements as well as manufacturing and control requirements; risks related to the Company's accelerated FDA review designations; and the ability of the Company to manufacture its therapies using third party manufacturers. A further list and description of the Company's risks, uncertainties and other factors can be found in the Company's most recent Annual Report on Form 10-K and the Company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov or www.iovance.com. The forward-looking statements are made only as of the date of this press release and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstances.

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Exhibit 99.2

IOVANCE BIOTHERAPEUTICS

ADVANCING IMMUNO-ONCOLOGY

Corporate Presentation

May 2019

Forward Looking Statements

This presentation contains "forward-looking statements" of Iovance Biotherapeutics, Inc. (hereinafter referred to as the "Company," "we," "us," or "our"). We may, in some cases, use terms such as "predicts," "believes," "potential," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. The forward-looking statements include, but are not limited to, risks and uncertainties relating to the success, timing, projected enrollment, manufacturing capabilities, and cost of our ongoing clinical trials and anticipated clinical trials for our current product candidates (including both Company-sponsored and collaborator-sponsored trials in the U.S. and Europe), such as statements regarding the timing of initiation and completion of these trials or cohorts within these trials; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration ("FDA") or other regulatory authority approval of, or other action with respect to, our product candidates; the strength of Company's product pipeline; the successful implementation of the Company's research and development programs and collaborations; the success of the Company's manufacturing, license or development agreements; the acceptance by the market of the Company's product candidates, if approved; and other factors, including general economic conditions and regulatory developments, not within the Company's control. The factors discussed herein could cause actual results and developments to be materially different from those expressed in or implied by such statements. Actual results may differ from those set forth in this presentation due to the risks and uncertainties inherent in the Company's business, including, without limitation: the FDA may not agree with the Company's interpretation of the results of its clinical trials; later developments with the FDA that may be inconsistent with already completed FDA meetings; the preliminary clinical results, including efficacy and safety results, from ongoing Phase 2 studies described above may not be reflected in the final analyses of these trials including new cohorts within these trials; the results obtained in the Company's ongoing clinical trials, such as the studies and trials referred to in this presentation, may not be indicative of results obtained in future clinical trials or supportive of product approval; regulatory authorities may potentially delay the timing of FDA or other regulatory authority approval of, or other action with respect to, the Company's product candidates (specifically, the Company's description of FDA interactions are subject to FDA's interpretation, as well as FDA's authority to request new or additional information); the Company may not be able to obtain or maintain FDA or other regulatory authority approval of its product candidates; the Company's ability to address FDA or other regulatory authority requirements relating to its clinical programs and registrational plans, such requirements including, but not limited to, clinical and safety requirements as well as manufacturing and control requirements; risks related to the Company's accelerated FDA review designations; the ability of the Company to obtain and maintain intellectual property rights relating to its product pipeline; and the acceptance by the market of the Company's product candidates and their potential reimbursement by payors, if approved.

For more detailed information about the risks and uncertainties that could cause actual results to differ materially from those implied by, or anticipated in, these forward-looking statements, please refer to the Risk Factors section of the Company's Annual Report on Form 10-K and subsequent updates that may be contained in the Company's Quarterly Reports on Form 10-Q and current reports on Form 8-K on file with the SEC. Forward-looking statements speak only as to the date they are made. Except as required by law, the Company does not undertake to update forward-looking statements to reflect circumstances or events that occur after the date the forward looking statements are made. This presentation does not constitute an offer to sell or buy securities, and no offer or sale will be made in any state or jurisdiction in which such offer or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

Leveraging Tumor Infiltrating Lymphocyte (TIL) to Address Unmet Need

Discovery | **Manufacturing Development, Clinical Program Establishment** | **Commercialization**

2011

TIL therapy conducted by Steven Rosenberg/NCI published results showing: 56% ORR[1] and 24% CR rate in melanoma patients, with durable CRs as an early line therapy[2]

2015

FDA Orphan Drug Designation for lifileucel in malignant melanoma

2016

First patient dosed for Gen 1 lifileucel in melanoma

Gen 2 manufacturing developed and transferred to CMOs

2017

Efficacy data from Gen 2 proprietary, centralized and commercial process presented

Head & Neck and Cervical studies began

FDA Fast Track designation for lifileucel in melanoma received

Partnership with MD Anderson on multiple solid tumors

Partnership with Ohio State University for PBL in hematological malignancies

2018

European sites activated for Melanoma & Cervical

FDA RMAT designation for lifileucel in advanced melanoma received

FDA End-of-Phase 2 meeting for lifileucel held

Lifileucel Cohort 2 clinical data showed 38% ORR in 47 patients, Median DOR: 6.4 months, DCR: 77% in with average 3.3 prior lines of therapy

2019

First patient dosed for melanoma registrational trial

FDA Fast Track designation in cervical

Interim data at ASCO for melanoma showed 38% ORR and cervical 44% ORR

Determine registration path for cervical

Initiate building US manufacturing facility for commercial supply

File IND for PBL in CLL

2020

Complete enrollment for registrational Cohort 4 in melanoma

BLA submission for lifileucel

[1] Rosenberg, S. A., *et al.* Clinical Cancer Research, 2011, 17, 4550
[2] Goff, S. L. et al. *Journal of Clinical Oncology*, 2016, 34(20), 2389-2397

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Leveraging Tumor Infiltrating Lymphocyte (TIL) to Address Unmet Need

Key Highlights

2017: Efficacy data from **Gen 2 proprietary, centralized and commercial process** generated and presented

2018: Lifileucel Cohort 2 data showed **38% ORR in 47 patients,** Median DOR: 6.4 months, DCR: 77% in patients with average 3.3 prior lines of therapy

FDA End-of-Phase 2 meeting for lifileucel held
FDA agreed with the single arm registration plan

2019: Enrolling for **melanoma registrational Cohort 4** (fast to market registration plan)

Interim **data update at ASCO:**
Melanoma Cohort 4 showed **38% ORR** in 55 patients
Cervical showed **44% ORR** in 27 patients

Investment Highlights

Leading cell therapy company focused on treatment of solid tumors

Large market opportunity and strong unmet need

- Initial focus in post-checkpoint solid tumors
- Expansion into combinations and earlier lines of therapy
- Four company-sponsored programs in melanoma, cervical, head & neck, basket study in CPI naive

Potential to be the first cell therapy approved for solid tumors starting in melanoma

- Accelerated path to approval in melanoma
- First patient dosed in pivotal trial for melanoma and BLA filing expected 2H 2020
- RMAT, Orphan Drug, and Fast Track designations in melanoma
- Fast Track designation in cervical cancer

Efficient and scalable proprietary manufacturing

- Demonstrated U.S. and E.U. capacity with contract manufacturers
- Building Iovance manufacturing facility
- Rapid 22-day Gen 2 manufacturing with >90% success rate
- **100+ patients treated with Iovance proprietary process**

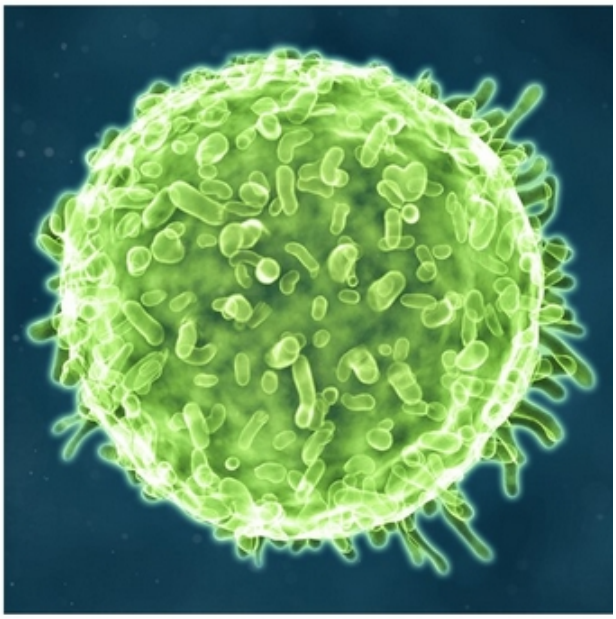
Broad platform and wide applications explored through partnerships

- Investigator-led programs to evaluate additional solid tumors or new combinations
- Touch points with institutions including NIH/NCI, Moffitt Cancer Center, MD Anderson, Roswell Park, and Ohio State University

Highly Individualized, Specific, and Potent Attack Against Cancer

Leverages and enhances the body's natural defense against cancer using a patient's own **Tumor Infiltrating Lymphocytes**, or **TIL**

- **Polyclonal**: Can recognize multiple neoantigens
  - Effective in solid tumors which are heterogeneous
  - Available data in melanoma, cervical, head & neck, and lung cancers
- **Individualized**: TIL of each patient is specific and private with almost no overlap of uCDR3 between patients [1]
- **Persistence**: 100% of patients had TIL persisting at Day 42[1]
- **Immunological memory**: Potentially no additional maintenance therapy after infusion
  - Responses seen in both treatment naïve and refractory melanoma patients, including checkpoint refractory
  - Complete responses observed in cervical cancer patients, maintained at 53 and 67 months[2]



[1] Gontcharova, *et al.*, Persistence of cryopreserved tumor-infiltrating lymphocyte product lifileucel (LN-144) in C-144-01 study of advanced metastatic melanoma, AACR 2019, Abstract #LB-069
[2] Stevanovic, *et al.*, Treatment of Metastatic Human Papiliomavirus-Associated Epithelial Cancers with Adoptive Transfer of Tumor-Infiltrating T Cells, ASCO 2018, Abstract #3004

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Competitive Advantages of TIL in Solid Tumors

CHECKPOINTS	TCR	CAR-T (LIQUID TUMORS)	TIL (SOLID TUMORS)
Target multiple tumor antigens	Target only single tumor antigen	Mainly target only single/ surface tumor antigen	**Target multiple tumor antigens**
Long maintenance period	One-time treatment	One-time treatment	**One-time treatment**
Utility in several solid tumors	Few solid tumors treated so far	No examples of successful utility in solid tumors	**Available data in: melanoma, cervical, head & neck and lung cancers**
Potential long-term irreversible toxicities	Potential on-target, off-tissue effects	Potentially immunogenic: cytokine release syndrome	**Minimal chance of unpredicted on-target, off-tissue effects found to date**
Off-the-shelf	Autologous	Autologous	**Autologous**

TIL target a diverse array of cancer antigens; we believe this approach represents a highly differentiated, customized, and targeted immunotherapy

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Developed Centralized, Scalable, and Efficient GMP Manufacturing

EXCISE: Patient's tumor is removed via surgical resection of a lesion

EXTRACT: Tumor is fragmented and placed in media for TIL to leave the tumor and enter media

EXPAND: TIL expanded via IL-2 + OKT3 exponentially *ex vivo* to yield $10^9 – 10^{11}$ TIL

PREPARE & INFUSE: Patient receives non-myeloablative lymphodepletion and is infused with their expanded TIL and IL-2

Process time: 22 days

- Courier from clinical site
- Co-culture TIL and feeder cells for expansion *ex vivo*
- Harvest and cryopreserved TIL infusion product
- Courier to clinical site for infusion

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Broad, Iovance-Owned IP Around TIL Therapy

Manufacturing

Multiple layers of patent applications filed for Gen 2 TIL products

- Iovance is pursuing claims covering cryopreserved TIL products, manufacturing processes and methods of treatment
- Includes three recently granted U.S. patents for methods of treatment in a broad range of cancers, including combinations with PD-1 antibodies and one additional patent relating to Gen 2 recently allowed
  - U.S. Patent No. 10,166,257
  - U.S. Patent No. 10,130,659
  - U.S. Patent No. 10,272,113

Advanced technologies

Patent applications filed for a wide range of TIL technologies including

- Marrow infiltrating and peripheral blood lymphocyte therapies
- Use of costimulatory molecules in TIL therapy
- Stable and transient genetically-modified TIL therapies
- Patient subpopulations for TIL therapies

Significant Market Potential in Solid Tumors

90%

of all cancer cases are solid tumors

1.6M

New cases of solid tumors in the U.S.[1]

Move into earlier line of therapy →

Expand into other indications ↓

Solid Tumor Indication	Deaths[1]	New Cases[1]
Melanoma	9,320	91,270
Cervix Uteri	4,170	13,240
Oral Cavity, Pharynx & Larynx	13,740	64,690
Lung & Bronchus	154,050	234,030
Bladder	17,240	81,190
Breast	41,400	268,670
Pancreatic	44,330	55,440
Brain & Other Nervous System	16,830	23,880
	Potential to address unmet need in late lines of treatment	Potential market for early lines in combo with standard of care

[1] https://seer.cancer.gov

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Current Clinical Pipeline and Select Collaboration Studies

	Regimen	Trial	Indication	N	Partner	Phase 1	Phase 2	Pivotal
Company sponsored studies	Lifileucel	innovaTIL-01	Melanoma	164	—			
	LN-145	innovaTIL-04	Cervical cancer	59	—			
	LN-145	C-145-03	Head & neck cancer	47	—			
	Lifileucel + pembrolizumab LN-145 + pembrolizumab LN-145	IOV-COM-202	Melanoma Head & neck Non-small cell lung	36	—			
Select investigator sponsored proof-of-concept studies	MDA TIL	NCT03610490	Ovarian, sarcomas, pancreatic	~54	MD Anderson Cancer Network			
	LN-145	NCT03449108	Ovarian, sarcomas	~54	MD Anderson Cancer Network			
	LN-145 + pembrolizumab	NCT03935347	Bladder cancer	12	Roswell Park			

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ASCO Abstract Interim Update (May 2019)

InnovaTIL-01: Lifileucel in Patients with Advanced Melanoma

- Patient demographics:
  - N=55
  - Mean of 3.1 prior therapies including anti-PD1
- Adverse events resolved to baseline 2 weeks post TIL infusion
- Efficacy
  - **ORR: 38% (2 CR, 18 PR, 1 uPR)**
  - **DCR: 76%**

Authors: Amod Sarnaik *et al.*
Abstract Number: 2518
Date/Time: Poster display Saturday, June 1, 8:00 a.m. - 11:00 a.m.; poster discussion 1:15 p.m. - 2:45 p.m.

InnovaTIL-04: LN-145 in Patients with Advanced Cervical Cancer

- Patient demographics:
  - N=27, patients all treated with **Gen 2 TIL product**
  - Mean of 2.6 prior therapies
- Adverse events consistent with the underlying disease and lymphodepletion and IL-2 regimens
- Efficacy
  - **ORR: 44% (1 CR, 9 PR, 2 uPR)**
  - **DCR: 89%**

Authors: Amir Jazaeri *et al.*
Abstract Number: 2538
Date/Time: Saturday, June 1, 8:00 a.m. - 11:00 a.m.


Metastatic Melanoma
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Potential Market for Metastatic Melanoma

- **Estimated 9,320** U.S. patients deaths due to melanoma in 2018[1]
- **Limited options** after progression on checkpoint and BRAF/MEK inhibitors:
  - **6,282** U.S. patients are on 2nd line therapy[2]
  - **4,950** U.S. patients are on 3rd and 4th line of therapy[2]
  - **TIL is available as a 2nd line** for those who are BRAF WT (3rd line if BRAF mutant)

Metastatic Melanoma Facts

282k New Cases WW each year[4]	**62k** Deaths WW each year[4]
91k Diagnoses in U.S. each year[1]	**9k** Deaths in U.S. each year[1]

Available care: **immuno-therapy** as first line option	**BRAF positive** patients treated with BRAF/MEK inhibitors	**ORR 4-10%** Retreatment with checkpoint inhibitors or chemotherapy post progression on anti-PD1 and BRAF/MEK[3]

[1] https://seer.cancer.gov
[2] Decision Resources Group – Disease Landscape and Forecast for Malignant Melanoma- Reprinted with permission. ©2018 DR/Decision Resources, LLC
[3] Keynote-37 Trial Results
[4] Global Burden of Disease Cancer Collaboration, Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 29 Cancer Groups, 1990 to 2016: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol. 2018 Nov 1;4(11):1553-1568. doi: 10.1001/jamaoncol.2018.2706

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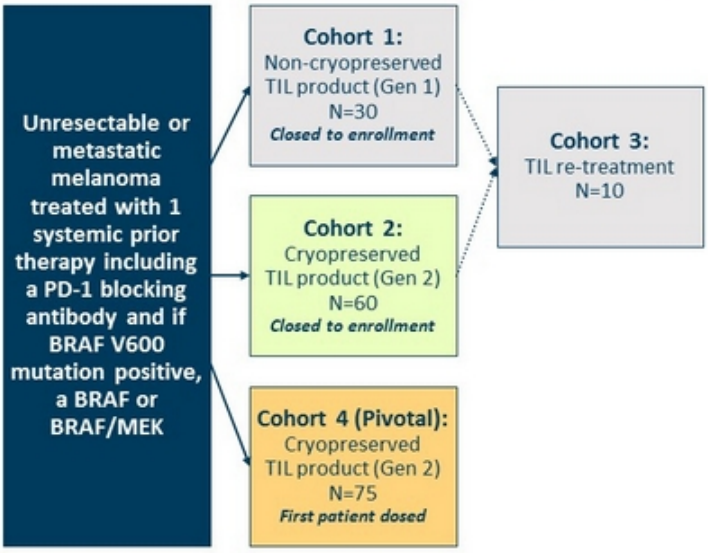
InnovaTIL-01: Phase 2 Study Design

Phase 2, multicenter study to assess the efficacy and safety of autologous **Tumor Infiltrating Lymphocytes (lifileucel)** for treatment of patients with **metastatic melanoma** (NCT02360579)



Endpoints:

- Primary: Efficacy defined as investigator ORR
- Secondary: Safety and efficacy

Study Updates:

- October 2018: Cohort 2 data for 47 patients at SITC
- March 2019: Cohort 4 (pivotal trial) first patient dosed
- May 2019: Topline data on 55 patients in ASCO abstract
- June 2019: Full Cohort 2 data will be presented at ASCO

InnovaTIL-01: Cohort 2 Interim Update at SITC 2018

COHORT 2

Key inclusion criteria:

- Measurable metastatic melanoma and ≥ 1 lesion resectable for TIL generation
- Progression on at least one prior line of systemic therapy including immune checkpoint inhibitor or a BRAF or BRAF/MEK
- Age ≥ 18
- ECOG PS 0-1

Endpoints:

- Primary: efficacy defined as ORR by investigator per RECIST 1.1
- Secondary: safety and efficacy

Study updates:

- Cohort 2 fully enrolled
- Data readout on 47 patients at SITC
- Data readout on full Cohort 2 patients at ASCO

Baseline Demographics	N=47 (%)
Prior therapies	
Mean # prior therapies (min, max)	3.3 (1-9)
Anti-PD-1	47 (100)
Anti-CTLA-4	37 (79)
BRAF/MEK	12 (26)
Target lesions sum of diameter (mm)	
Mean (SD)	112 (73)
Min, Max	17, 343
Baseline LDH (U/L)	
Median	246
1-2 times ULN	12 (26)
> 2 times ULN	7 (15)
Number of target & non-target lesions (at baseline)	
>3	37 (79)
Mean	6

"This is a heavily pre-treated cohort. There are usually pre-treated patients with only 1 line of therapy, but these patients in cohort 2 have on average 3.3 prior lines. Given there are no 2L/3L standard of care treatments, these patients got every treatment, and then some."

Dr. Diwakar Davar
Assistant Professor, Hillman Cancer Center

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Adverse Events Tend to be Early and Transient

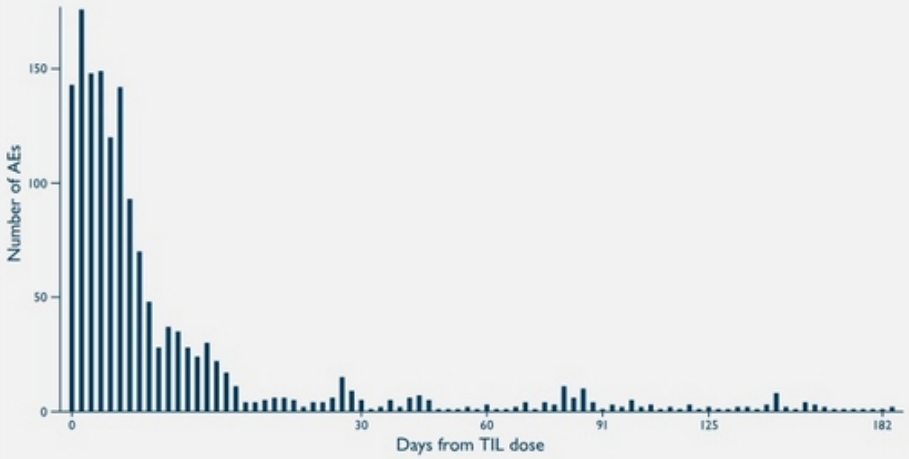
COHORT 2

Frequency of AEs over time is reflective of potential benefit of one time treatment with TIL (lifileucel)

Lifileucel Treatment-Emergent Adverse Events (≥ 30%)

PREFERRED TERM	Cohort 2 (N=47) Any Grade n (%)	Grade 3/4 n (%)	Grade 5 n (%)
Patients reporting at least one Treatment-Emergent Adverse Events[1]	47(100)	45 (95.7)	2 (4.3)
Thrombocytopenia	42 (89.4)	38 (80.9)	0
Chills	36 (76.6)	3 (6.4)	0
Neutropenia	29 (61.7)	25 (53.2)	0
Febrile neutropenia	28 (59.6)	25 (53.2)	0
Anemia	27 (57.4)	22 (46.8)	0
Pyrexia	25 (53.2)	7 (14.9)	0
Hypophosphatemia	23 (48.9)	17 (36.2)	0
Leukopenia	21 (44.7)	20 (42.6)	0
Fatigue	17 (36.2)	0	0
Hypotension	17 (36.2)	4 (8.5)	0
Lymphopenia	17 (36.2)	17 (36.2)	0
Tachycardia	15 (31.9)	1 (2.1)	0

Adverse Events Over Time



[1] Treatment-Emergent Adverse Events refer to all AEs starting on or after the first dose date of TIL up to 30 days
Patients with multiple events for a given preferred term are counted only once using the maximum grade under each preferred term. Safety terms which describe the same medical condition were combined.

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Potentially Efficacious Treatment for Patients with Limited Options

COHORT 2

- In heavily pretreated metastatic melanoma patients, preliminary efficacy is notable for:
  - **ORR 38%** (3.3 prior lines of therapy) vs. standard of care chemotherapy has ~10% ORR (in 2nd line)
  - **Median DOR is 6.4 months**, range 1.3+ to 14+
  - **Single treatment of TIL led to DCR of 77%** in late stage metastatic patients
  - Mean number of TIL cells infused: **26×10^9**
  - Median number of IL-2 doses administered was 6.0 as per protocol

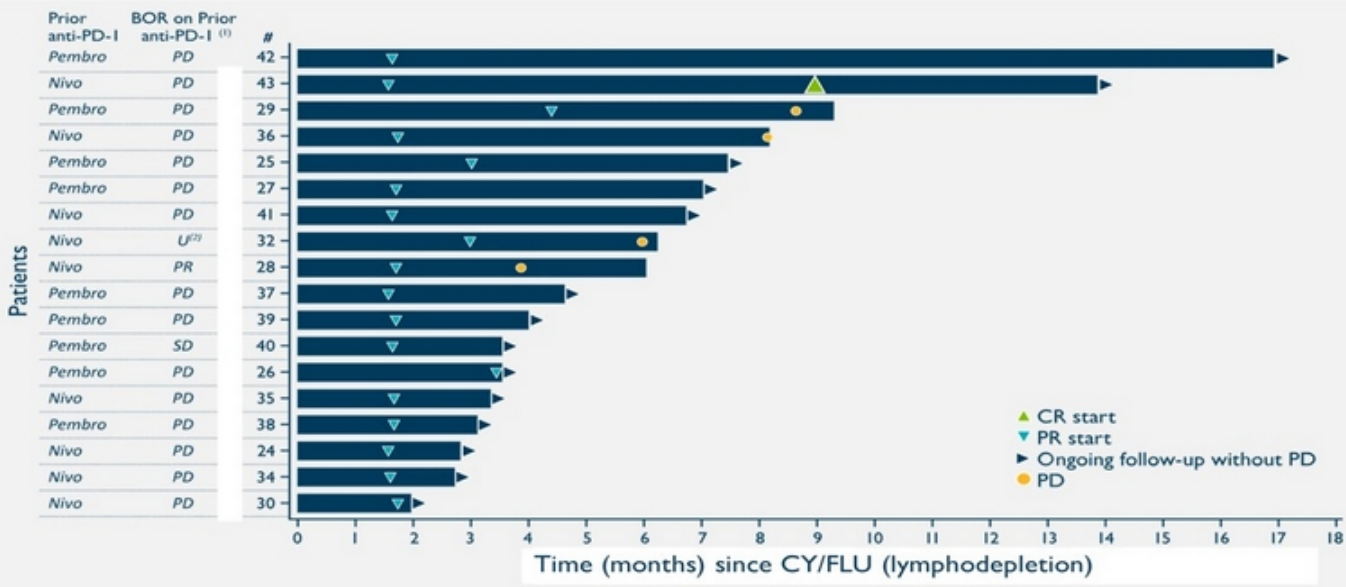
Responses	**N=47 (%)**
Objective Response Rate	**18 (38%)**
Complete Response	1 (2%)
Partial Response (PR + uPR[1])	17 (36%)
Stable Disease	18 (38%)
Progressive Disease	7 (15%)
Non-Evaluable	4 (9%)
Disease Control Rate	36 (77%)

[1] Only one patient is uPR due to not having reached the follow on assessment as of end Dec 2018

Responders Previously Progressed on Checkpoint Inhibitors

COHORT 2

Lifileucel time to response and current duration of for evaluable patients (partial response or better)



(1) BOR is best overall response on prior anti-PD-1 immunotherapy
(2) U: unknown best overall response on prior anti-PD-1 immunotherapy

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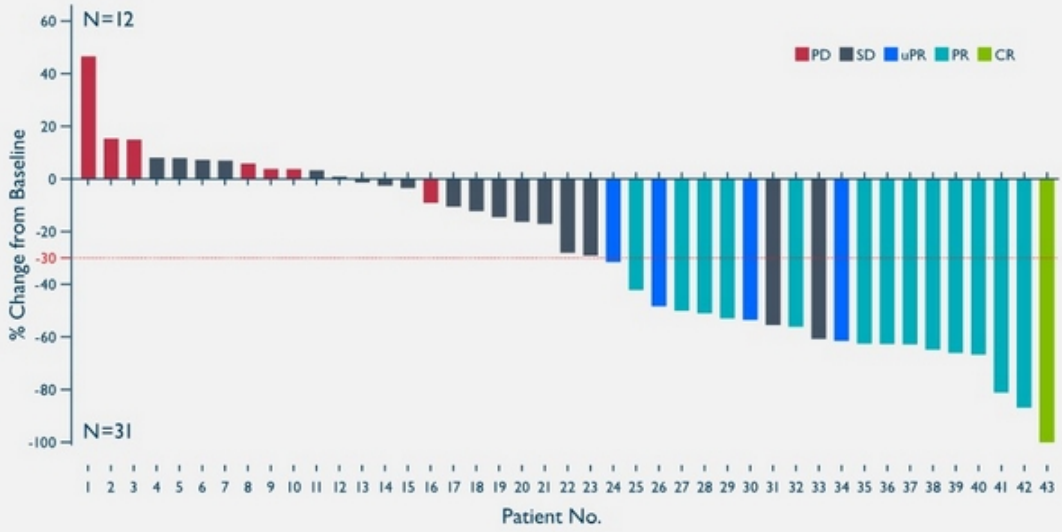
TIL Therapy Provides Deep Responses

COHORT 2

- 72% of patients had a reduction in tumor burden
- Median study follow up is 6.0 months
- All assessments are by RECIST 1.1
- Responses are deep – nearly all responders are greater than 30%

Lifileucel best overall response rate[1]



[1] Per RECIST 1.1, two patients (31,33) had BOR of SD: met PR criteria at Day 42 and PD at Day 84 due to new lesions

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Cohort 4 is a Pivotal Single-Arm Registrational Trial

COHORT 4

Key inclusion criteria:

- Measurable metastatic melanoma and ≥ 1 lesion resectable for TIL generation
- Progression on at least one prior line of systemic therapy including immune checkpoint inhibitor and if BRAF V600 mutation positive, BRAF or BRAF/MEK targeted therapy

Endpoints:

- Primary: efficacy defined as ORR by BIRC
- Secondary: safety and efficacy

Study updates:

- Confirmed with FDA that a randomized Phase 3 study is not feasible in advanced melanoma post-CPI
- FDA has acknowledged acceptability of single-arm data for registration
- March 2019: **First patient dosed**

Cohort 4 (Pivotal):

Cryopreserved TIL product (Gen 2)
N=75

Per FDA interaction

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Late Stage (2L/3L) Melanoma Treatment Development Efforts

2L/3L melanoma treatment has no current standard of care

	Agent	ORR % (N)	Current Development Status	Prior Lines of Tx	Patient Characteristics
Combination with anti-PD-1	**Checkpoints**				
	LAG-3 +nivo (BMS)	12% (N=61)[1]	Multiple 1L studies	1+	All comers, ECOG ≤2 • LAG-3 expression ≥1% (N=33) ORR=18%; • LAG-3 expression <1% (N=22) ORR=5%
	TLR9 agonists, HDAC				
	IMO-2125 (Idera) + ipi	29% (N=34)[2]	Phase 3, post-PD-1 melanoma ILLUMINATE 204	1-3	ECOG ≤1, intratumoral injection
	CMP-001 (CheckMate) + pembro	22% (N=69)[3]	Phase 1b	1+	ECOG ≤1, intratumoral injection
	SD-101 (Dynavax) + pembro	21% (N=29)[4]	Phase 1b/2	1+	ECOG ≤1
	Entinostat (Syndax) + pembro	19% (N=53)[5]	ENCORE 601	1+	ECOG ≤1
Single Agent	**Checkpoints**				
	TIGIT, TIM-3	Unknown	Phase 1/2		
	Cytokines				
	HD IL-2	8% (N=9)[6]		1+	HD IL-2 post PD-1
	Other				
	TIL	**38% (N=55)**	**Phase 2, continuing to enroll pivotal trial**	**3**	**All post-anti-PD1**

(1) Ascierto P *et al.*, ESMO 2017
(2) Idera Pharmaceuticals Results Dec 14, 2018
(3) Milhem M *et al.*, AACR 2018
(4) DVAX Corp Pres, Jan 10, 2019
(5) Ramalingam *et al.*, AACR 2019
(6) Buchbinder EI *et al.*, JCO 2017

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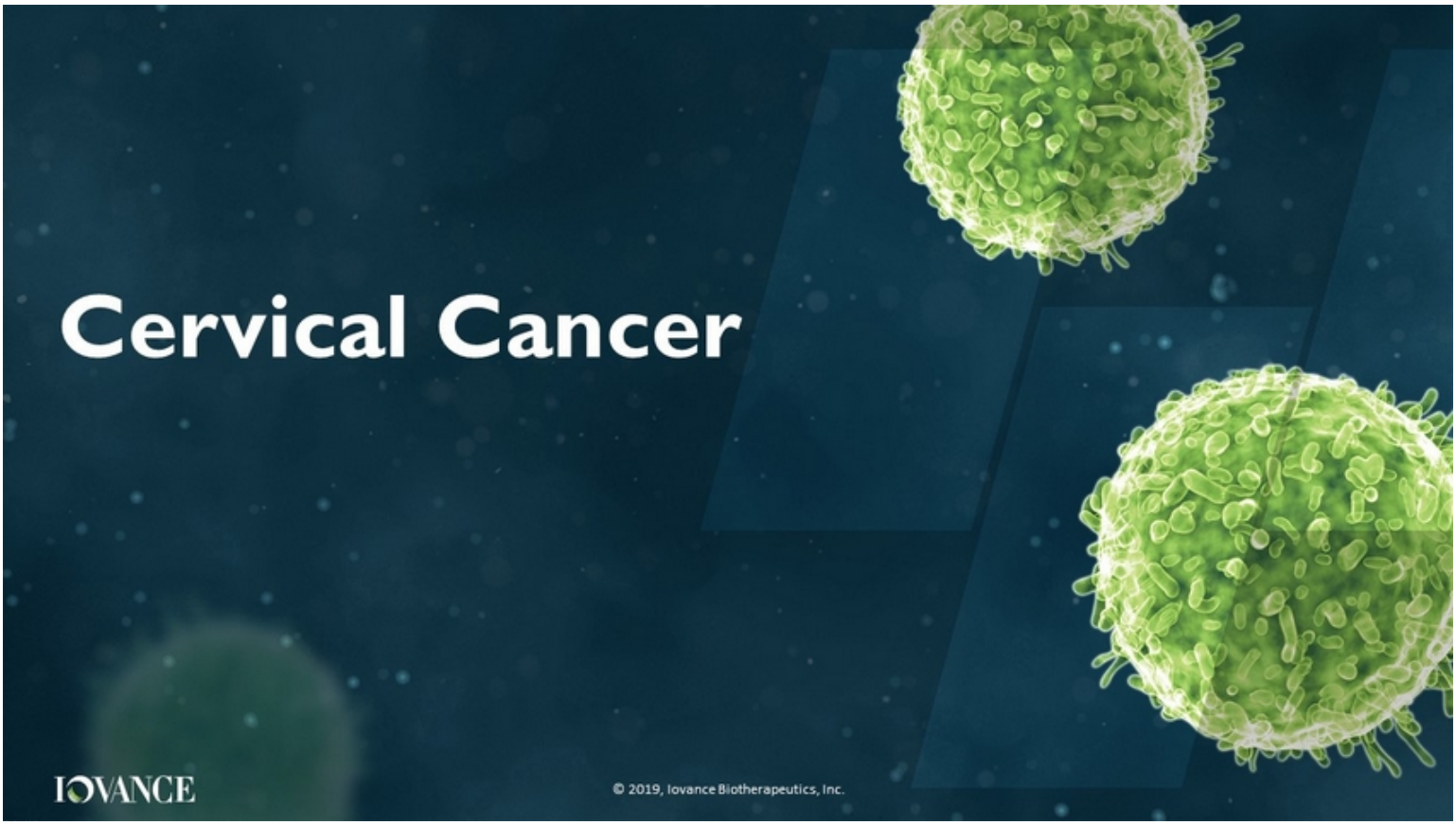
Cervical Cancer
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Potential Market for Cervical Cancer

"TIL immunotherapy with LN-145 is literally redefining what is treatable and potentially curable in advanced metastatic chemo-refractory cervical cancer. Patients who only two years ago would be facing hospice as their only alternative now have access to this potentially life extending new treatment. This is the most exciting news in this field in decades."

Amir Jazaeri, M.D.
Director of the Gynecologic Cancer Immunotherapy Program in the Department of Gynecologic Oncology and Reproductive Medicine at MD Anderson

Cervical Cancer Facts

511k New Cases WW each year[1]

247k Deaths WW each year[1]

13k Diagnoses in U.S. each year[2]

4k Deaths in U.S. each year[2]

Available care: **Chemo-therapy** as first line option

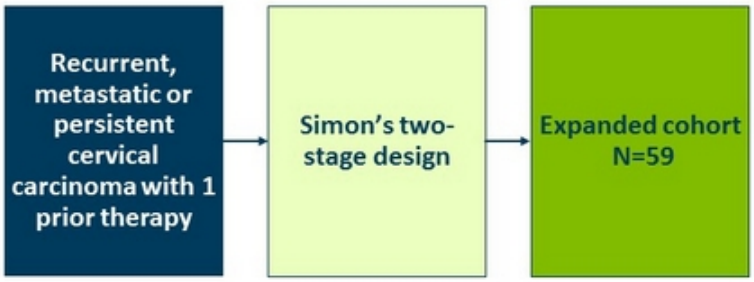
For PD-L1 + patients, post-chemo receiving Keytruda[3] **ORR 14.3%**

Available Care for chemotherapy in 2L cervical patients **13%**[4]

[1] Global Burden of Disease Cancer Collaboration, Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 29 Cancer Groups, 1990 to 2016: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol. 2018 Nov 1;4(11):1553-1568. doi: 10.1001/jamaoncol.2018.2706
[2] https://seer.cancer.gov/
[3] https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf
[4] Weiss, et al., A phase II trial of carboplatin for recurrent or metastatic squamous carcinoma of the uterine cervix: A Southwest Oncology Group Study

InnovaTIL-04: Phase 2 Trial in Cervical Cancer

Phase 2, multicenter study to evaluate the efficacy and safety of autologous **Tumor Infiltrating Lymphocytes (LN-145)** in patients with **recurrent, metastatic or persistent cervical carcinoma** (NCT03108495)



Endpoints:

- Primary: ORR as determined by BIRC
- Secondary: safety and efficacy

Study updates:

- March 2019: Protocol amended to 59 total patients and ORR determined by BIRC
- March 2019: Fast Track Designation
- May 2019: Topline ASCO abstract update on Gen 2 patients
- June 2019: Longer follow-up and additional analysis at ASCO presentation

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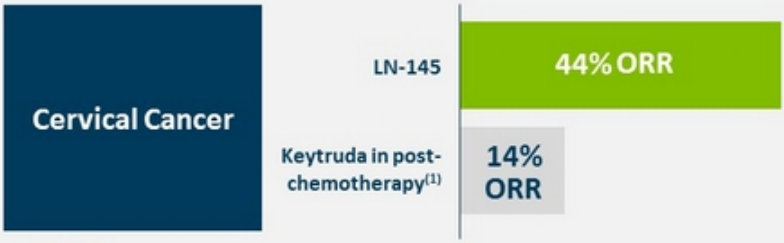
TIL Offers a Favorable Treatment for Cervical Cancer Patients

ASCO Abstract Interim Data Update (Data as of February 2019)



- N=27
- **44% ORR**
- **89% DCR at 3.5 months median study follow**
- **1 CR, 11 PRs** (2 unconfirmed)
- CR being seeing in cervical cancer, similar to melanoma

- Patients reported are exclusively **Gen 2 manufacturing**
- ASCO presentation to include longer follow up
- **2.6 mean prior therapies**
- Patient mean age 47 years old
- TIL infused **28 x 10^9**
- 6 median doses of IL-2 administered
- AE profile consistent with prior results

[1] The composition of the relevant patient population may differ between Iovance trials and published data for CPIs (USPI used) but serves as a point of reference for assessing the overall efficacy landscape for relevant therapies

Development Efforts in Recurrent, Metastatic or Persistent Cervical Carcinoma

Recurrent, metastatic or persistent cervical carcinoma has no current standard of care

Agent	ORR % (N)	Current Dev Status	Prior Line of Tx	Patient Characteristics
Antibody-drug conjugate				
tisotumab vedotin (TV) (Genmab/Seattle Genetics)	22% (N=35)[1]	Phase 2	1+	Recurrent or metastatic cervical cancer that progressed on standard therapy (most had received at least two prior therapies)
Anti-PD-1				
AGEN2034 (Agenus)	11% (N=9)[2]	Phase 2	1+	Patients must have relapsed after a platinum-containing doublet administered for treatment of advanced disease
cemiplimab (Regeneron)	10% (N=10)[3]	Phase 3	2+	Recurrent or metastatic cervical cancer resistant to, or intolerant of, platinum therapy
TKI				
neratinib (Puma Biotechnology)	27% (N=11)[4]	Phase 2	2	Metastatic HER2-positive cervical cancer (percentage of HER2+ in cervical cancer is ~3.9%)[5]
Cell therapies				
TIL (LN-145)	**44% (N=27)**	**Phase 2**	**2.6 (mean)**	**All patients progressed on or after chemotherapy**

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(1) Hong et al., SGO 2019
(2) Drescher, et al. ESMO 2018
(3) Rischin, D. et al. ESMO 2018
(4) D'Souza et al. SGO 2019
(5) Yan, et al. Cancer Metastasis Rev. 2015


Head & Neck Cancer
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Potential Market for Head & Neck Cancer

Head & Neck Cancer Facts

694k New Cases WW each year[1]	**303k** Deaths WW each year[1]
65k Diagnoses in U.S. each year[2]	**14k** Deaths in U.S. each year[2]

Available care in first line: **Chemotherapy & Immunotherapy**	Anti-PD-1 immunotherapy as second line (Opdivo and Keytruda) **ORR 13-16%**[3]

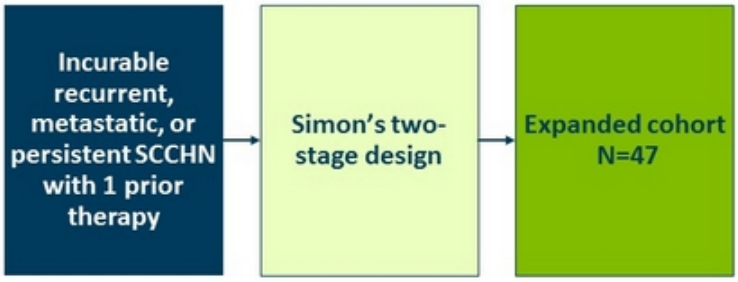
[1] Global Burden of Disease Cancer Collaboration, Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 29 Cancer Groups, 1990 to 2016: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol. 2018 Nov 1;4(11):1553-1568. doi: 10.1001/jamaoncol.2018.2706

[2] https://seer.cancer.gov/

[3] The composition of the relevant patient population may differ between Iovance trials and published data for CPIs (USPI used) but serves as a point of reference for assessing the overall efficacy landscape for relevant therapies

C-145-03: Phase 2 Trial in Head & Neck Cancer

Phase 2 study to evaluate the efficacy and safety of autologous **Tumor Infiltrating Lymphocytes (LN-145)** for the treatment of patients with **recurrent metastatic squamous cell carcinoma of the head and neck** (NCT03083873)

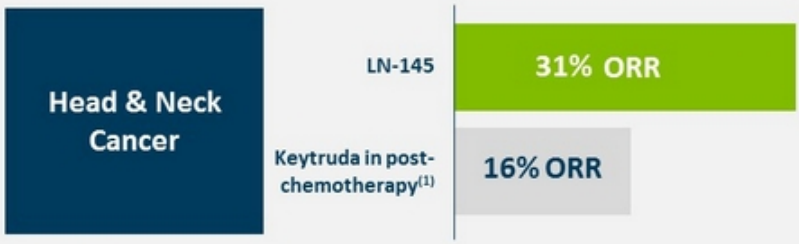


Endpoints:
- Primary: ORR
- Secondary: safety and efficacy

Study updates:
- Limited prior therapies to 1-3

TIL Offers a Favorable Treatment for Head & Neck Cancer Patients

October 2018 Interim Data Update



- N=13
- **31% ORR**
- **4 PRs**
- **DOR** (min, max): 2.8, 7.6 months
- Patients reported are a combination of Gen 1 and Gen 2 manufacturing process

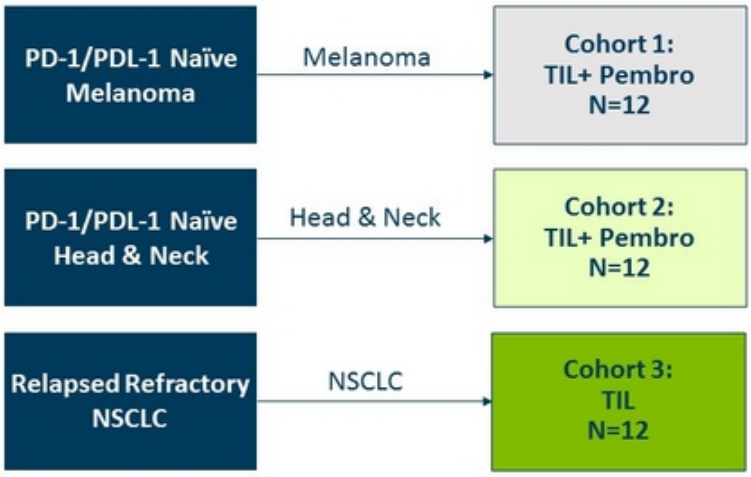
Baseline Demographics	N=13 (%)
Prior therapies	
Median prior therapies (min, max)	3 (1, 5)
Anti-PD-1	11 (85)
Anti-CTLA-4	3 (23)
Baseline number of target & non-target lesions	
>3	10 (77)

Treatment-Related Adverse Events(2) (≥40%), any grade	N=13 (%)
Chills	10 (77)
Hypotension	8 (62)
Hyponatremia	7 (54)
Pyrexia	7 (54)

(1) The composition of the relevant patient population may differ between Iovance trials and published data for CPIs (USPI used) but serves as a point of reference for assessing the overall efficacy landscape for relevant therapies
(2) Treatment-Emergent Adverse Events refer to all AEs starting on or after the first dose date of TIL up to 30 days

TIL in Earlier Lines of Therapy in Combination with SOC

A Phase 2, Multicenter Study of Autologous **Tumor Infiltrating Lymphocytes (lifileucel or LN-145)** in Patients with **Solid Tumors** (NCT03645928)



Endpoints:

- Primary: ORR and safety
- Secondary: CR rate

Study updates:

- 16+ sites are activated globally
- Sites in the U.S. and 5 additional countries
- Additional cohort for LN-145 in combination with pembro for NSCLC patients to be added

Research Focus into Next Generation TIL

Expand the TIL platform into new indications

- Bladder cancer (Roswell Park Cancer Institute)
- IND for PBL in CLL (OSU collaboration)

Prepare or select more potent TIL

- Use anti-4-1BB, anti-OX40, or other co-stimulants in cocktails in *ex vivo* growth of TIL
  - License to uses of 4-1BB agonists obtained from Moffitt Cancer Center
- Select more potent TIL

Genetically modify to make a more tumor-reactive TIL

- Cellectis TALEN® collaboration
- Phio RNAi collaboration

Identify biomarkers to find a better TIL product or better patient population

Iovance Biotherapeutics Global Reach and Scale

Iovance Biotherapeutics is headquartered in San Carlos, California and has >**110** global employees

- 4 corporate office locations
- 4 contract manufacturing locations
- 1 Iovance manufacturing location to be announced

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Well Capitalized in Pursuit of TIL Commercialization

	In millions
Common shares outstanding	123
Preferred shares	6[1]
Options	9
Cash, cash equivalents, short-term investments	$440
Debt	0

[1] Preferred shares are shown on an as-converted basis

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Achieved and Upcoming Milestones

2018

- [x] Demonstrate consistent, scalable, rapid proprietary manufacturing method
- [x] Secure new IP around TIL technology and manufacturing
- [x] Secure adequate financing providing 3 years of runway
- [x] Demonstrate activity in melanoma post-checkpoint inhibitor (difficult to treat patients)
- [x] Align on registration pathway for melanoma with FDA
- [x] Demonstrate activity in post-CPI cervical, head & neck tumors

2019

- [x] First patient dosed in Cohort 4 for lifileucel in support of registration
- [ ] Present updated data in Cohort 2 for melanoma **at ASCO**
- [ ] Present data from Gen 2 of cervical study **at ASCO**
- [ ] Initiate building Iovance manufacturing facility
- [ ] Define regulatory path for LN-145 in cervical cancer with FDA
- [ ] Explore therapeutic potential of TIL in other indications
- [ ] File new IND for new manufacturing process and/or new indications

IOVANCE BIOTHERAPEUTICS

ADVANCING IMMUNO-ONCOLOGY

Thank you