

IOVANCE

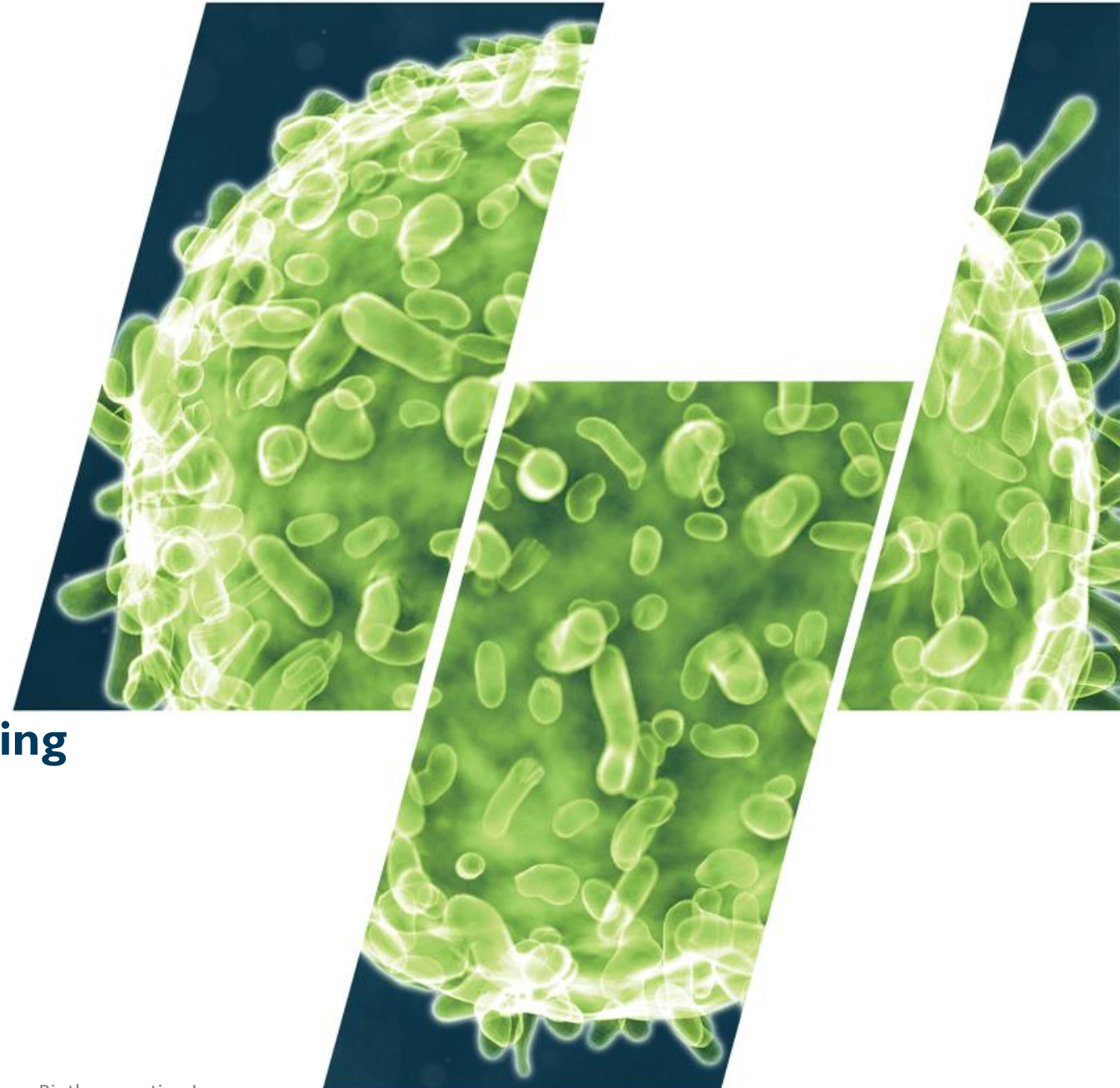
BIO THERAPEUTICS

ADVANCING IMMUNO-ONCOLOGY

**Investigating the Power of Tumor Infiltrating
Lymphocytes for Treatment of Cancer**

Maria Fardis, PhD
CEO and President

October 2019

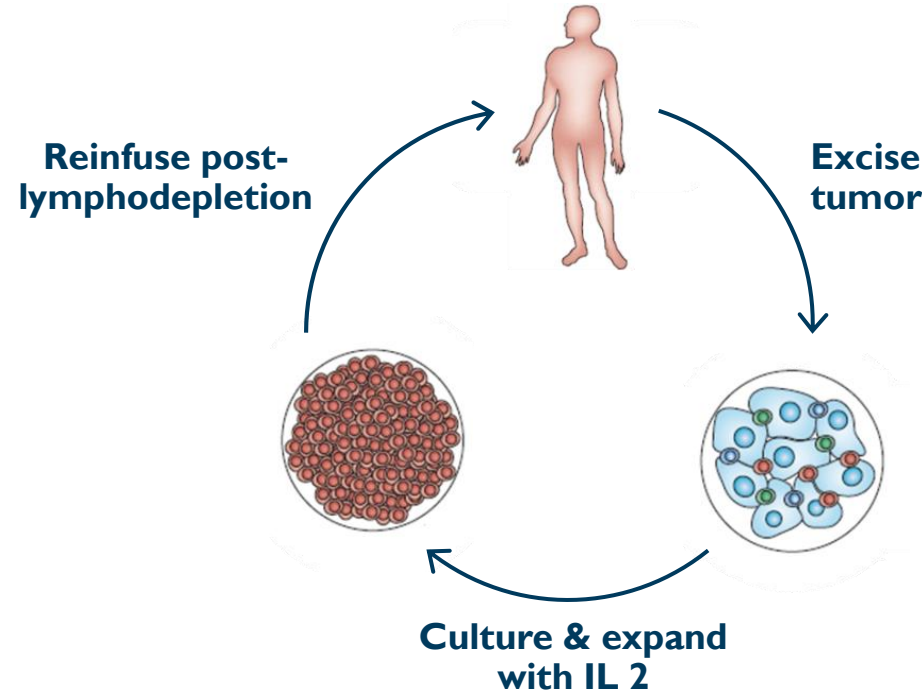


Forward Looking Statements

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, including those product candidates that have been granted breakthrough therapy designation (“BTD”) or regenerative medicine advanced therapy designation (“RMAT”) by the FDA; the strength of our product pipeline; the successful implementation of our research and development programs and collaborations; the success of our manufacturing, license or development agreements; the acceptance by the market of the our product candidates, if approved; our ability to obtain tax incentives and credits; and other factors, including general economic conditions and regulatory developments, not within the our 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 our business, including, without limitation: the FDA may not agree with our interpretation of the results of its clinical trials; later developments with the FDA that may be inconsistent with already completed FDA interactions; preliminary clinical results, including efficacy and safety results, from ongoing clinical trials may not be reflected in the final analyses of these trials, including new cohorts within these trials; the results obtained in our ongoing clinical trials, such as the studies and trials referred to in this 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, our product candidates (specifically, our description of FDA interactions are subject to FDA’s interpretation, as well as FDA’s authority to request new or additional information); our 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 our accelerated FDA review designations, including BTD and RMAT and our ability to benefit from such designations; our ability to obtain and maintain intellectual property rights relating to its product pipeline; and the potential reimbursement of our product candidates by payors, if approved.

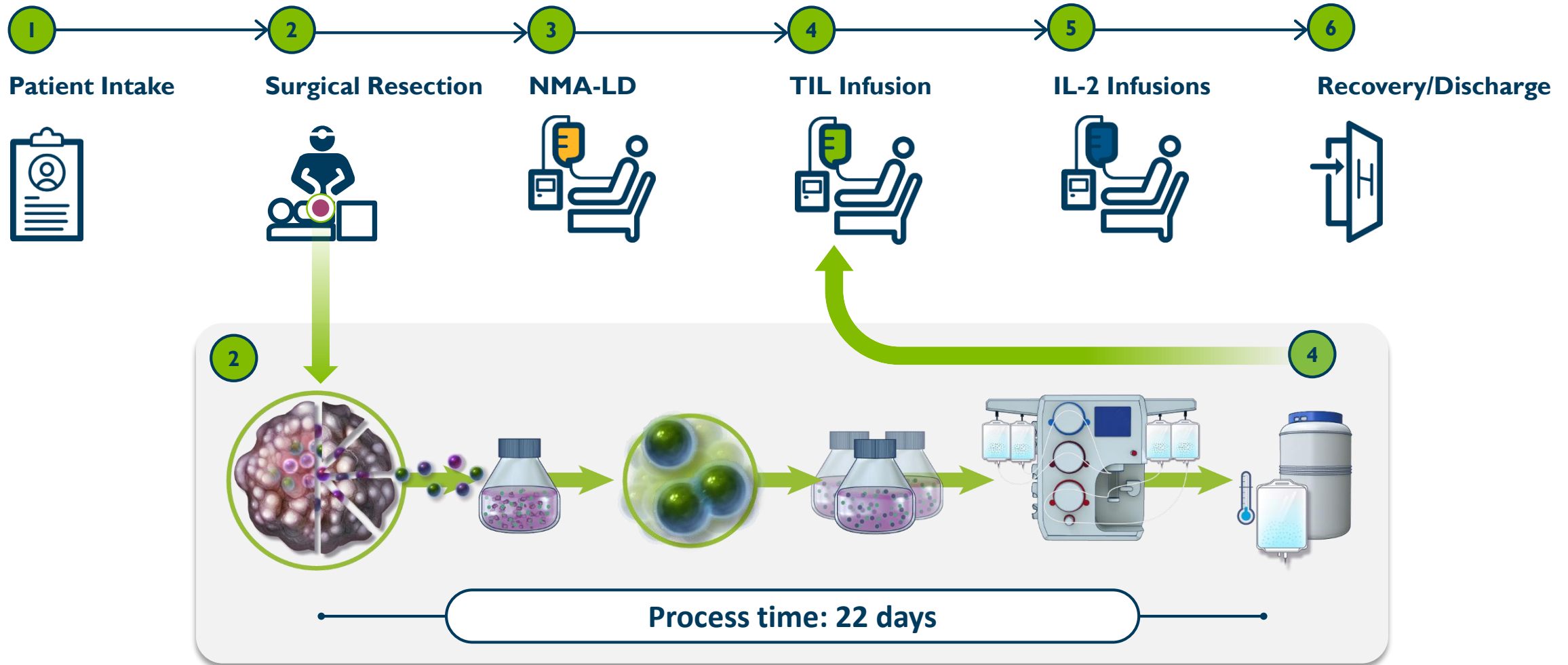
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Tumor-Infiltrating Lymphocytes (TILs) – Unique Mechanism in Immuno-oncology



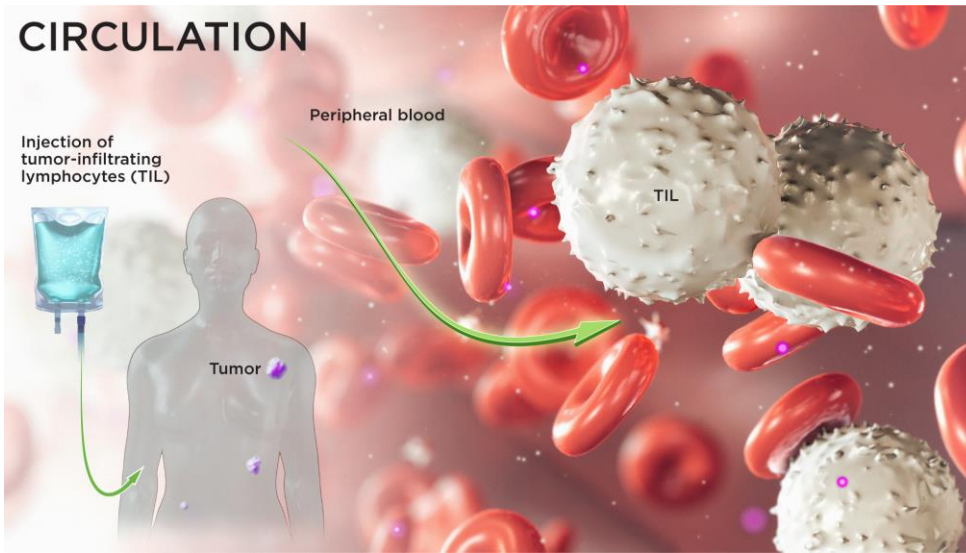
- Highly personalized therapy
- Our own immune system amplified and rejuvenated

Developed Centralized, Scalable, and Efficient GMP Manufacturing

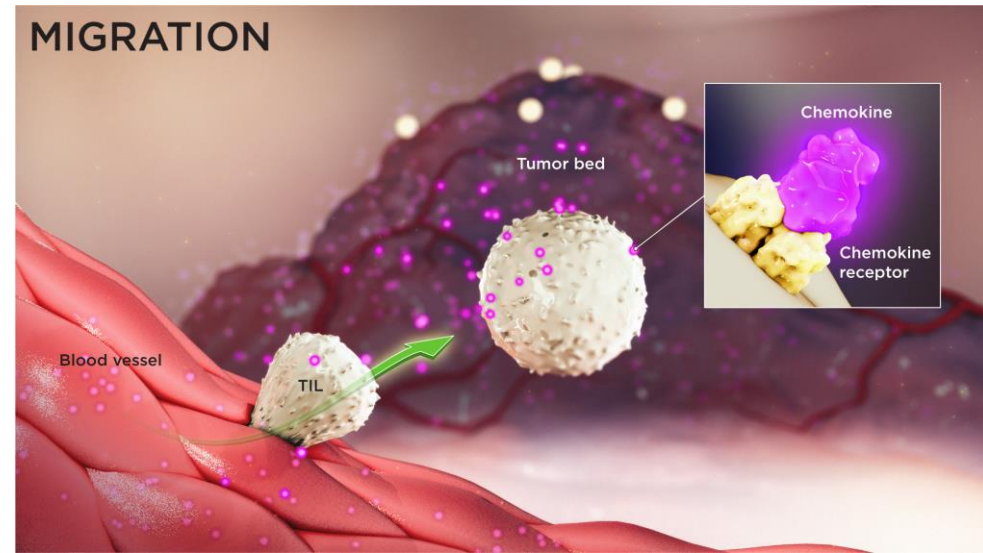


TIL Mechanism of Action

CIRCULATION



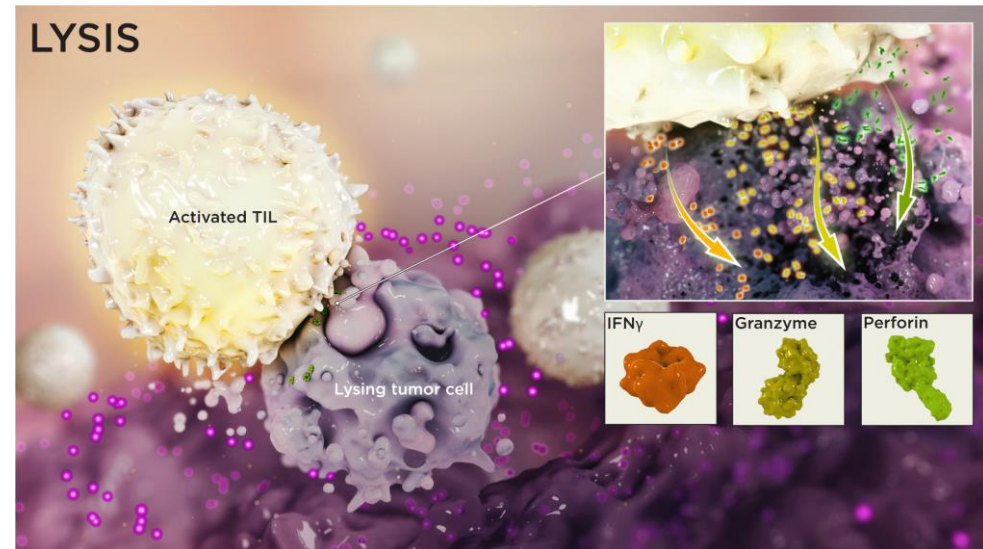
MIGRATION



RECOGNITION



LYSIS



Leveraging Tumor Infiltrating Lymphocyte (TIL) to Address Unmet Need

Discovery



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⁾

Manufacturing Development, Clinical Program Establishment



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

Two rounds of financing conducted: **over \$425 mil raised**



2019

First patient dosed for melanoma registrational trial

FDA Fast Track, BTD in cervical

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

Groundbreaking on **commercial production** facility in Philadelphia

FDA EOP 2 C for LN-145 for cervical

File IND for PBL in CLL

Nonclinical data at **SITC**

clinical IRC **data from Cohort 2 of melanoma in 4Q 2019**

Pre-Commercialization



2020

Complete enrollment for registrational Cohort 4 in melanoma

BLA submission for lifileucel for melanoma

BLA submission for LN-145 for cervical

⁽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

Leveraging Tumor Infiltrating Lymphocyte (TIL) to Address Unmet Need

Key Highlights

Discovery

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⁾

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⁽²⁾ Goff, S. L. et al. Journal of Clinical Oncology, 2016, 34(20), 2389-2397

Manufacturing Development, Clinical Program Establishment

2015

FDA Orphan Drug

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

FDA End-of-Phase 2 meeting for LN-145 for cervical held, FDA agreed that the ongoing single arm study may be sufficient to support registration of LN-145

Breakthrough Therapy designation received in Cervical cancer

Data update at ASCO:

Melanoma Cohort 2 showed **38% ORR** (N=66), **DOR not reached**

Cervical showed **44% ORR** (N=27), **DOR not reached**

Pre-Commercialization

2020

Complete enrollment for registrational Cohort 4 in melanoma

BLA submission for lifileucel for melanoma

BLA submission for LN-145 for cervical

Groundbreaking on commercial production facility in Philadelphia

FDA SUP 2 for LN-145 for cervical

File IND for PBL in CLL

Updated data from Cohort 2 of melanoma in 4Q 2019

Investment Highlights

Leading cell therapy company focused on treatment of solid tumors

Large market opportunity and strong unmet need

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

Efficient and scalable proprietary manufacturing

Broad platform and wide applications explored through partnerships

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

- Accelerated path to approval in melanoma and cervical cancer
- Enrollment on track for pivotal trial for melanoma and BLA filing expected 2H 2020
- Melanoma: RMAT, Orphan Drug, and Fast Track
- Cervical: Breakthrough Therapy designation, Orphan Drug and Fast Track

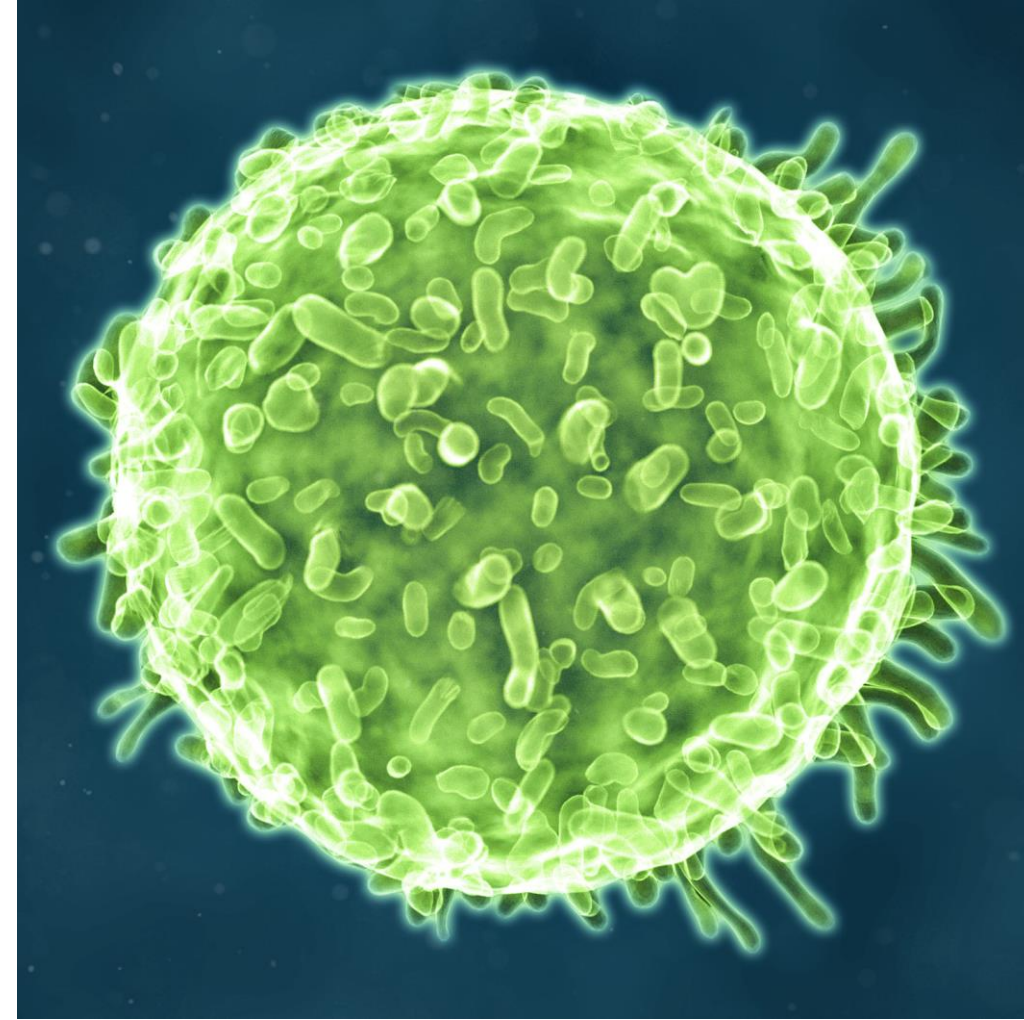
- U.S. and E.U. capacity with contract manufacturers
- Building Iovance 136,000 sq. ft. manufacturing facility in Philadelphia
- Rapid 22-day Gen 2 manufacturing with >90% success rate
- **200+ patients treated with Iovance proprietary process**

- 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, Ohio State University, and University of Montreal (CHUM)

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 Papillomavirus-Associated Epithelial Cancers with Adoptive Transfer of Tumor-Infiltrating T Cells, ASCO 2018, Abstract #3004

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	No unexpected 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**

Broad, Iovance-Owned IP Around TIL Therapy

Manufacturing

Seven granted or allowed U.S. patents for compositions and methods of treatment in a broad range of cancers relating to its Gen 2 manufacturing process including combinations with PD-1 antibodies:

- US Patent No. 10,130,659
- US Patent No. 10,166,257
- US Patent No. 10,272,113
- US Patent No. 10,363,273
- US Patent No. 10,398,734
- US Patent No. 10,420,799

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

Iovance Commercial Manufacturing Facility



- Build-to-suit custom facility located in the Navy Yard, Philadelphia, PA
- ~136,000 sq. feet
- GMP production is expected to commence in 2022
- IOVA investing \$75M over 3 years
- Significant reduction in COGS expected

Rendering by DIGSAU

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⁾

⁽¹⁾ <https://seer.cancer.gov>

	Move into earlier line of therapy	
	Deaths ⁽¹⁾	New Cases ⁽¹⁾
Expand into other indications	Melanoma	91,270
	Cervix Uteri	13,240
	Oral Cavity, Pharynx & Larynx	64,690
	Lung & Bronchus	234,030
	Bladder	81,190
	Breast	268,670
	Pancreatic	55,440
	Brain & Other Nervous System	23,880
	Potential to address unmet need in late lines of treatment	Potential market for early lines in combo with standard of care

Current Clinical Pipeline and Select Collaboration Studies

	Regimen	Trial	Indication	N	Partner	Phase 1	Phase 2	Pivotal
Company sponsored studies	Lifileucel	C-144-01	Melanoma	164	—	<div></div>		
	LN-145	C-145-04	Cervical cancer	75	—	<div></div>		
	LN-145	C-145-03	Head & neck cancer	47	—	<div></div>		
	Lifileucel + pembrolizumab	IOV-COM-202	Melanoma	48	—	<div></div>		
	LN-145 + pembrolizumab		Head & neck					
Select investigator sponsored proof-of-concept studies	LN-145 + pembrolizumab		Non-small cell lung					
	LN-145		Non-small cell lung					
	MDA TIL	NCT03610490	Ovarian, pancreatic, colorectal	~54	MD Anderson Cancer Network™	<div></div>		
	LN-145	NCT03449108	Ovarian, sarcomas	~54	MD Anderson Cancer Network™	<div></div>		
	LN-145 + pembrolizumab	NCT03935347	Bladder cancer	12		<div></div>		

Peripheral Blood Lymphocytes (PBL) for Hematological Indications

Expand the TIL platform into new indications



- IOV-2001 for post-ibrutinib CLL patients
- IOV-2001 is a non-genetically modified, polyclonal T cell product
- IOV-2001 shows cytotoxicity against autologous tumor cells in leukemia
- Ibrutinib has known to improve proliferative and effector functions of T cells
- Iovance has generated PBL from 50 mL blood of ibrutinib-treated patients with CLL
- A 9 day manufacturing process is optimized and is being transferred to a CMO
- IND filing is planned for 2019



Karyapudi et al., EHA 2019, PF 447

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⁾ CheckMate-37 Trial Results (ICC 10%), Keytruda label (4%)

⁽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

C-144-01: Cohort 2 Update at ASCO 2019

Key inclusion criteria:

- 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 66 patients at ASCO

Baseline Demographics	N=66 (%)
Prior therapies	
Mean # prior therapies	3.3
Anti-PD-1	66 (100)
Anti-CTLA-4	53 (80)
BRAF/MEK	15 (23)
Target lesions sum of diameter (mm)	
Mean (SD)	106 (71)
Min, Max	11, 343
Baseline LDH (U/L)	
Median	244
1-2 times ULN	19 (29)
> 2 times ULN	8 (12)
Number of target & non-target lesions (at baseline)	
>3	51 (77)
Mean	6

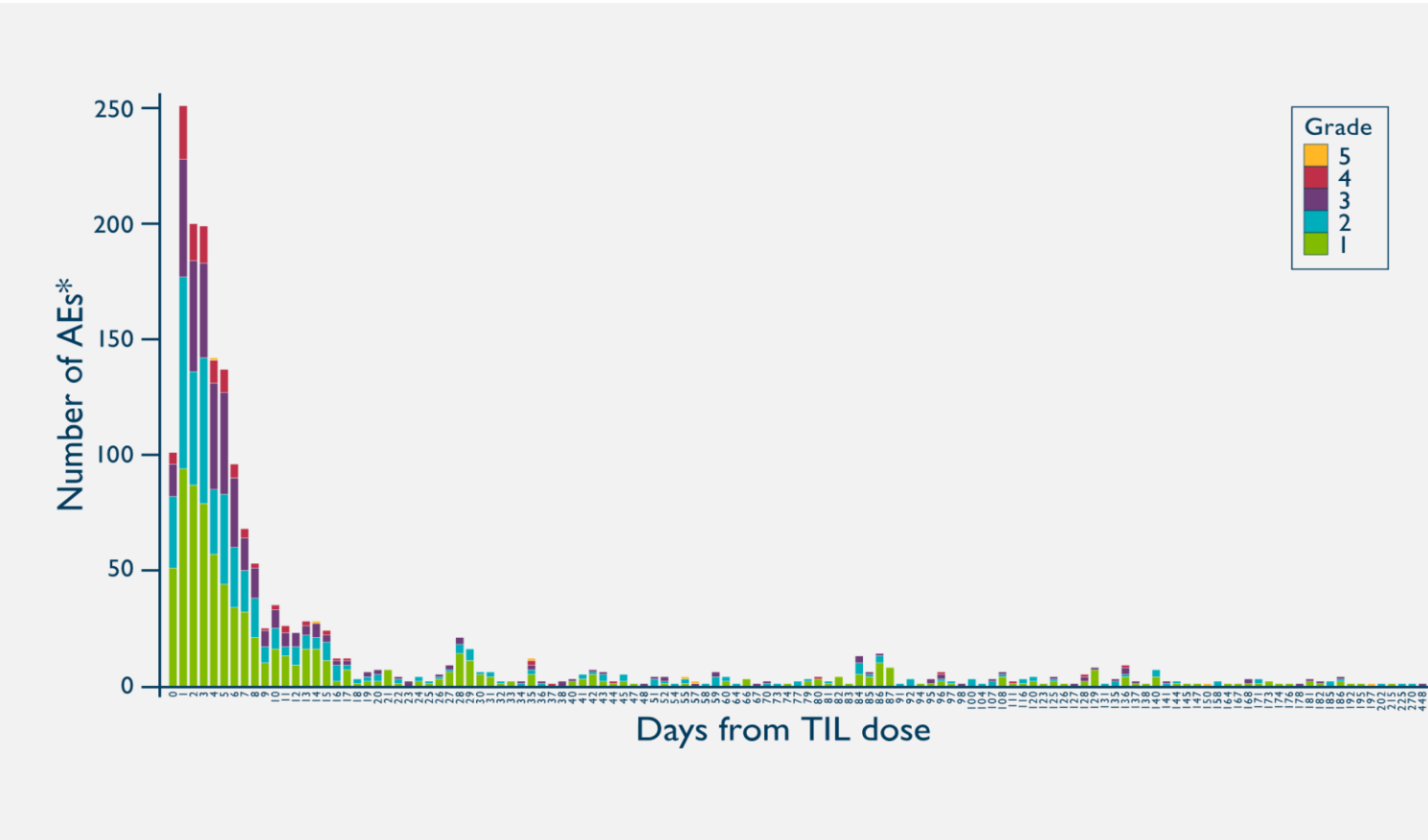
Adverse Events Tend to be Expected, Early and Transient

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

Lifileucel Treatment-Emergent Adverse Events (≥ 30%)

PREFERRED TERM	Cohort 2, N=66		
	Any Grade, n (%)	Grade 3/4, n (%)	Grade 5, n (%)
Number of patients reporting at least one Treatment-Emergent AE**	65 (98.5)	63 (95.5)	2 (3.0)
Thrombocytopenia	59 (89.4)	53 (80.3)	0
Chills	52 (78.8)	4 (6.1)	0
Anemia	44 (66.7)	36 (54.5)	0
Pyrexia	39 (59.1)	11 (16.7)	0
Febrile neutropenia	36 (54.5)	35 (53.0)	0
Neutropenia	36 (54.5)	25 (37.9)	0
Hypophosphatemia	29 (43.9)	22 (33.3)	0
Fatigue	27 (40.9)	1 (1.5)	0
Leukopenia	27 (40.9)	22 (33.3)	0
Hypotension	23 (34.8)	7 (10.6)	0
Tachycardia	22 (33.3)	1 (1.5)	0
Lymphopenia	21 (31.8)	19 (28.8)	0

Adverse Events Over Time



**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.

*The number of AEs is cumulative and represent the total number of patients dosed

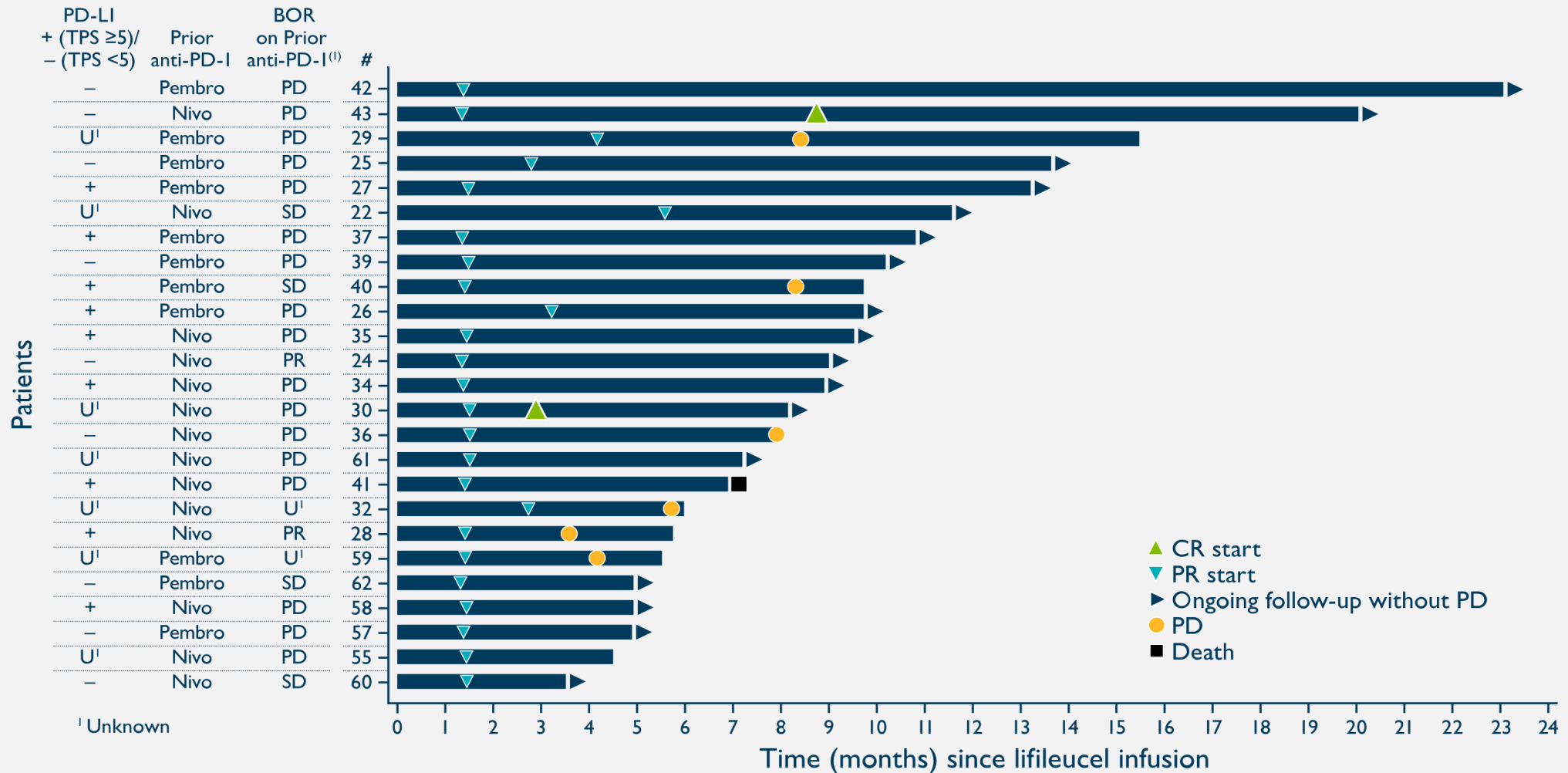
Potentially Efficacious Treatment for Patients with Limited Options

- In heavily pretreated metastatic melanoma patients (3.3 mean prior therapies)
 - **ORR 38%**
 - **DCR 80%**
 - **Median DOR has not been reached**
 - Median follow-up 8.8 months
 - Patients with PD-L1 negative status (TPS<5%) were among responders
 - Mean TIL cells infused: **27.3 x 10⁹**
 - Median number of IL-2 doses: 5.5

Responses	N=66 (%)
Objective Response Rate	25 (38%)
Complete Response	2 (3%)
Partial Response	23 (35%)
Stable Disease	28 (42%)
Progressive Disease	9 (14%)
Non-Evaluable	4 (6%)
Disease Control Rate	53 (80%)

Responders Previously Progressed on Checkpoint Inhibitors

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

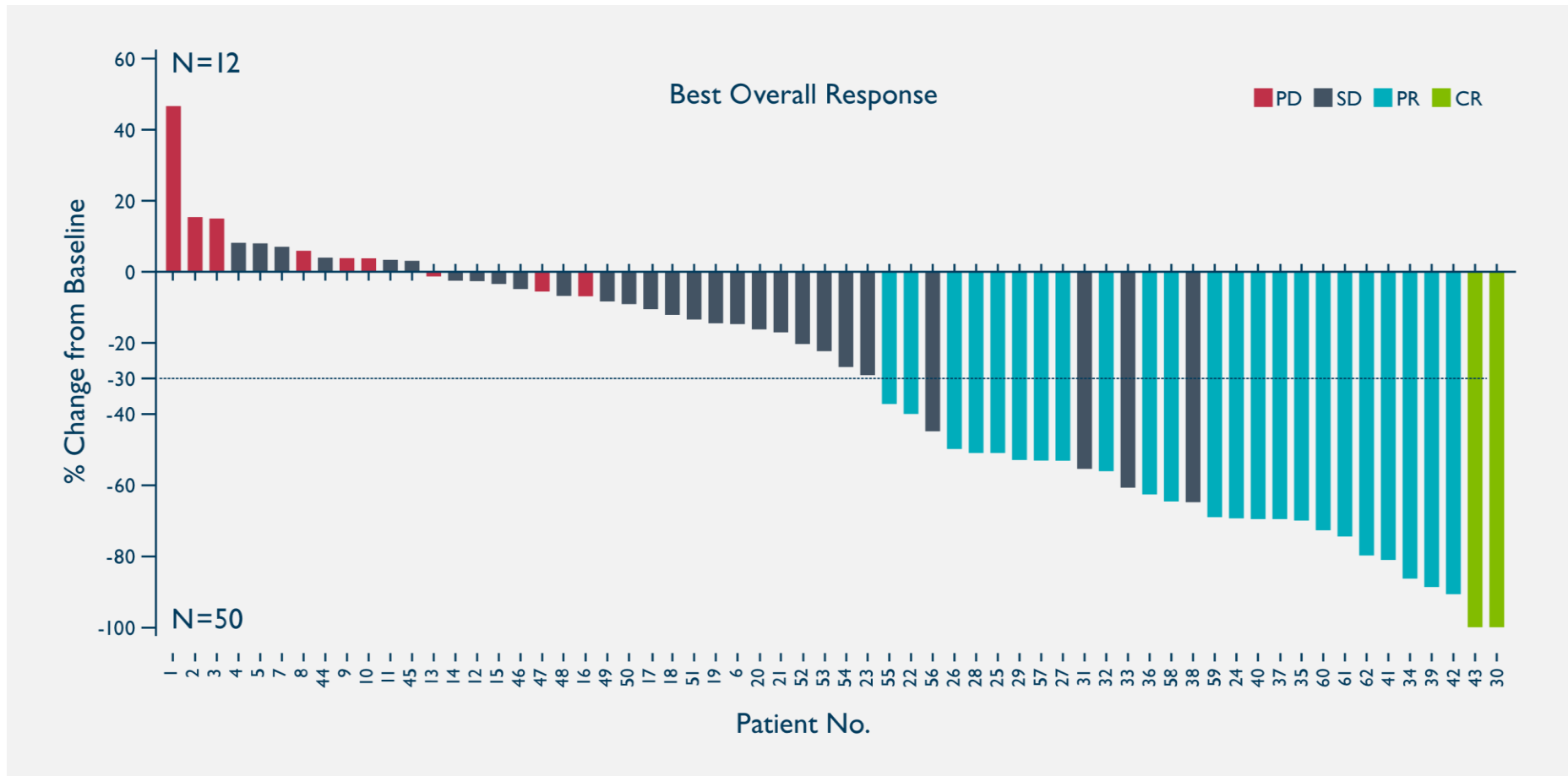


BOR is best overall response on prior anti-PD-1 immunotherapy

TIL Therapy Provides Deep Responses

- 81% of patients had a reduction in tumor burden
- Mean Time to response 1.9 months (range 1.3-5.6)
- All assessments are by RECIST 1.1
- Responses are deep – nearly all responders are greater than 30%

Lifileucel best overall response rate⁽¹⁾



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
- PD-1 positive select TIL collaboration with CHUM



Genetically modify to make a more tumor-reactive TIL

- Collectis TALEN® collaboration
- Phio RNAi collaboration



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

- Genocea ATLAS™ collaboration

Iovance Biotherapeutics Global Reach and Scale

Iovance Biotherapeutics has ~130 employees

- Headquartered in San Carlos, CA
- 4 additional offices
- Iovance commercial manufacturing facility in Philadelphia, PA (under construction)



Well Capitalized in Pursuit of TIL Commercialization

June 30, 2019

In millions (unaudited)

Common shares outstanding	124
Preferred shares	6 ⁽¹⁾
Options	9
Cash, cash equivalents, short-term investments, restricted cash	\$410 ⁽²⁾
Debt	0

(1) Preferred shares are shown on an as-converted basis

(2) Includes Restricted Cash of \$5.5 million

Achieved and Upcoming Milestones 2019

- ☒ 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 lovance 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
- ☐ Present Cohort 2 lifileucel Independent Review Committee results

IOVANCE

B I O T H E R A P E U T I C S

ADVANCING IMMUNO-ONCOLOGY

Thank you

