



ADVANCING IMMUNO-ONCOLOGY

Investigating the Power of Tumor Infiltrating Lymphocytes for Treatment of Cancer

May 2020



Forward Looking Statements

Certain matters discussed in this presentation are “forward-looking statements” of Iovance Biotherapeutics, Inc. (hereinafter referred to as the “Company,” “we,” “us,” or “our”) within the meaning of the Private Securities Litigation Reform Act of 1995. 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 and production 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 successfully submit, obtain and maintain 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 and new product candidates in both solid tumor and blood cancers; the strength of the Company’s product pipeline; the successful implementation of the Company’s research and development programs and collaborations; the Company’s ability to obtain tax incentives and credits; the guidance provided for the Company’s future cash, cash equivalents, short term investment and restricted cash balances; 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 COVID-19 pandemic may have an adverse effect on the Company and its clinical trials, including potential slower patient recruitment, inability of clinical trial sites to collect data, inability of the Company or its contract research organizations to monitor patients, as well as FDA availability due to competing priorities; the preliminary clinical results, which may include efficacy and safety results, from ongoing Phase 2 studies may not be reflected in the final analyses of these trials or subgroups within these trials; a slower rate of enrollment may impact the Company’s clinical trial timelines; enrollment may need to be adjusted for the Company’s trials and cohorts within those trials based on FDA and other regulatory agency input; the new version of the protocol which further defines the patient population to include more advanced patients in the Company’s cervical cancer trial may have an adverse effect on the results reported to date; the data within these trials may not be supportive of product approval; changes in patient populations may result in changes in preliminary clinical results; the Company’s ability or inability to address FDA or other regulatory authority requirements relating to its clinical programs and registrational plans, such requirements including, but not limited to, clinical, safety, manufacturing and control requirements; the Company’s interpretation of communications with the FDA may differ from the interpretation of such communications by the FDA; risks related to the Company’s ability to maintain and benefit from accelerated FDA review designations, including BTD and RMAT, which may not result in a faster development process or review of the Company’s product candidates (and which may later be rescinded by the FDA), and does not assure approval of such product candidates by the FDA or the ability of the Company to obtain FDA approval in time to benefit from commercial opportunities; the ability or inability of the Company to manufacture its therapies using third party manufacturers or its own facility may adversely affect the Company’s potential commercial launch; the results of clinical trials with collaborators using different manufacturing processes may not be reflected in the Company’s sponsored trials; and additional expenses may decrease our estimated cash balances and increase our estimated capital requirements. 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 presentation and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstances.

2020 Recent Updates



Last patient dosed in Cohort 4 pivotal melanoma program: supporting a BLA in melanoma in 2020



90%+ manufacturing success rate in > 300 patients



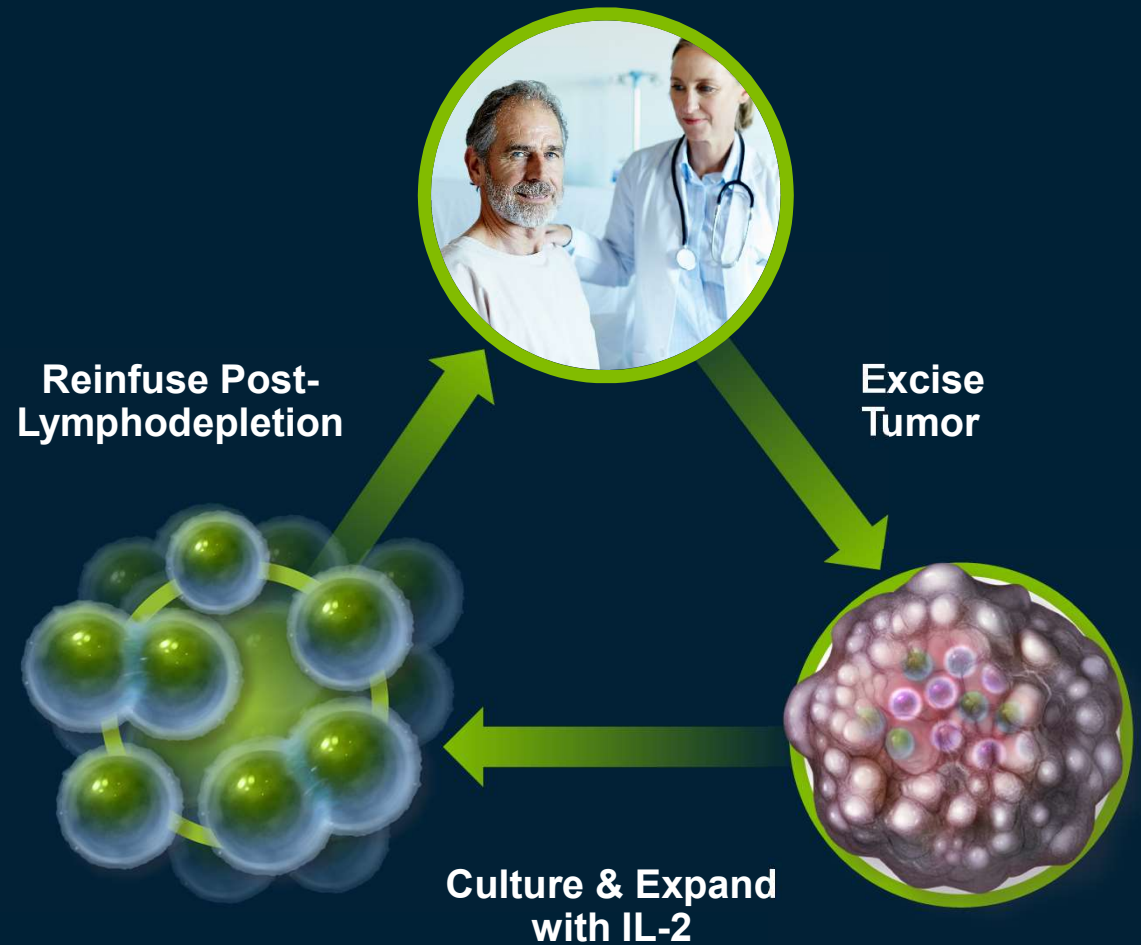
Data showing effect of Moffitt TIL in NSCLC presented at AACR 2020



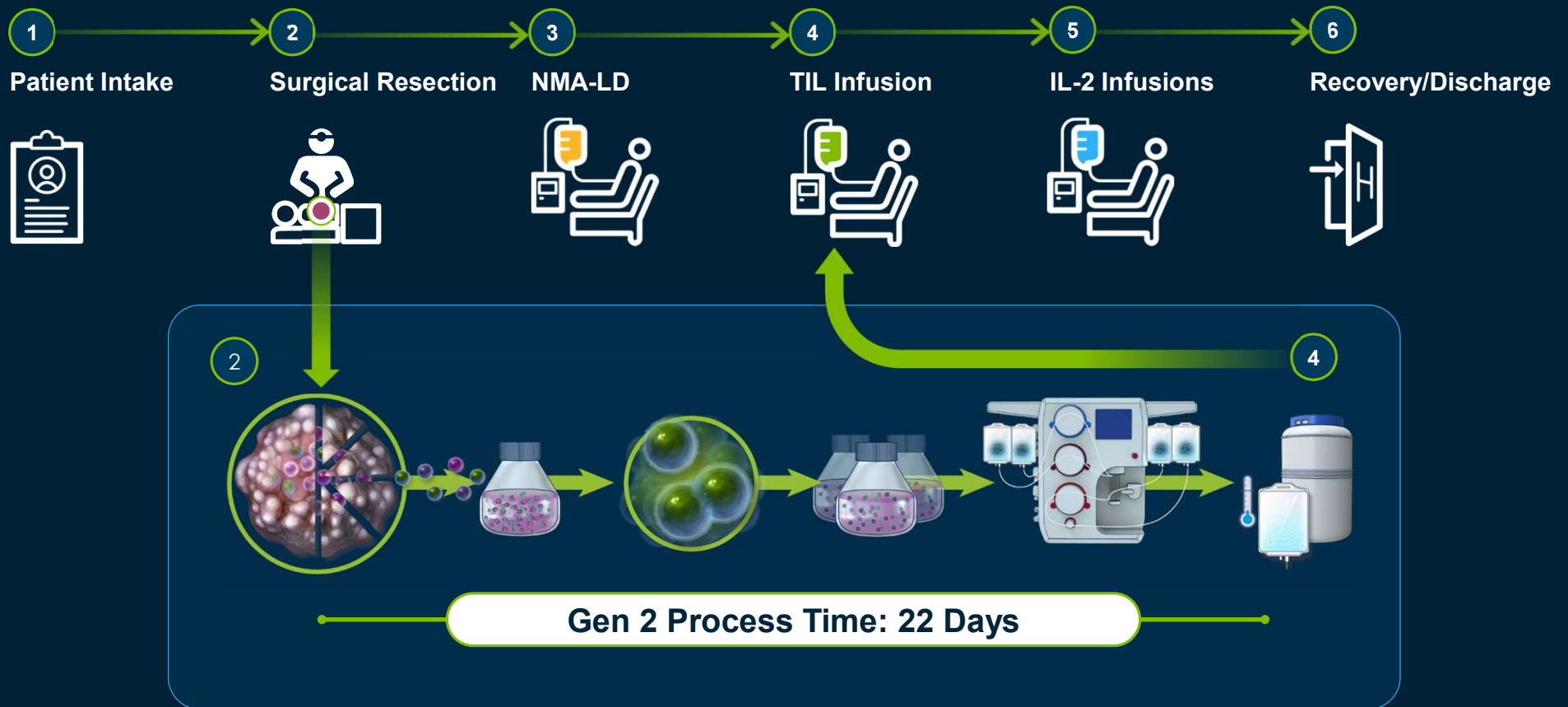
Oral presentation from Cohort 2 melanoma program at ASCO20

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

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

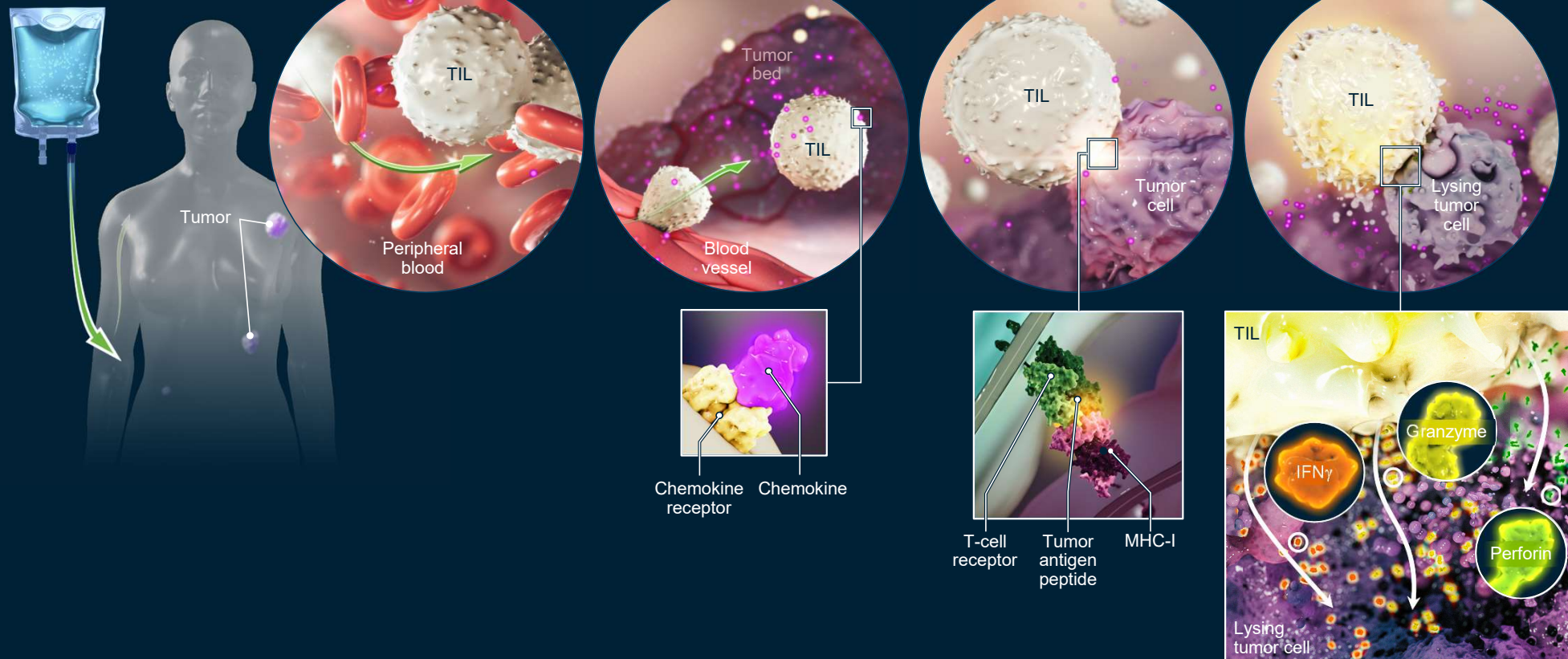


Iovance Proprietary Centralized, Scalable, and Efficient GMP Manufacturing



TIL Mechanism of Action

Infusion of
tumor-infiltrating
lymphocytes (TIL)



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

Head & Neck and Cervical studies began

FDA Fast Track designation for lifileucel in melanoma received

2018

FDA RMAT designation for lifileucel in advanced melanoma received

FDA EOP2 meeting for lifileucel held

Lifileucel Cohort 2 clinical data showed **38% ORR in 47 patients**, patients 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

FDA EOP 2 held for LN-145 for cervical

File IND for PBL in chronic lymphocytic leukemia (CLL), IND cleared and first patient dosed

Clinical IRC data from Cohort 2 of melanoma at SITC shows **35% ORR**

Pre-Commercialization

2020

Dosed last patient in Cohort 4 pivotal melanoma program

TIL manufactured by Moffitt shows **2 durable CRs** in post-PD1 NSCLC

Oral ASCO presentation of updated Cohort 2 melanoma data

Complete enrollment for registrational program in cervical

Hold pre-BLA meeting with FDA

Submit BLA for lifileucel for melanoma

Plan for **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

Key Highlights

2019: Melanoma Data update at SITC (8 Nov 2019)⁽¹⁾

Melanoma Cohort 2 showed

36.4% ORR

by investigator and

34.8% ORR

as read by independent
review committee (IRC)
(N=66)

2020: Updated Melanoma Data cut (Feb 2020-ASCO Abstract)

**Median DOR not reached
at 17.0 months of median
study follow up**

(investigator assessed)

**ASCO 2020: Oral
Presentation of Updated
Melanoma Cohort 2 Data**

(29 May 2020)⁽²⁾

⁽¹⁾Sarnaik *et al.*, SITC 2019, P865
⁽²⁾Sarnaik *et al.*, ASCO 2020, 10006


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
- Five company-sponsored programs in melanoma, cervical, head & neck, non-small cell lung cancer (NSCLC), and CLL indications




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

- Accelerated path to approval in melanoma and cervical cancer
- Last patient dosed in pivotal trial for melanoma and BLA filing expected 2H 2020
- Melanoma: RMAT, Orphan Drug, and Fast Track
- Cervical: BTM, Orphan Drug and Fast Track



Efficient and scalable proprietary manufacturing

- 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
- **300+ patients treated with Iovance proprietary process**
- Faster 16-day Gen 3 manufacturing in clinic



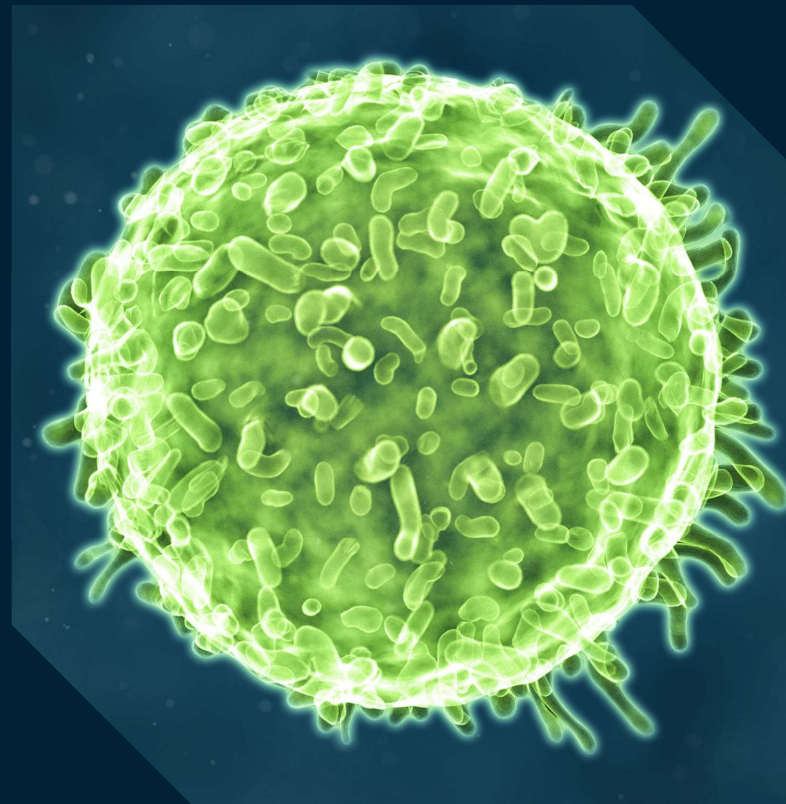
Broad platform and wide applications explored through partnerships

- Investigator-led programs to evaluate additional solid tumors or new combinations
- Data from Moffitt TIL in NSCLC as a new indication for Iovance
- Touch points with institutions including NIH/NCI, Moffitt Cancer Center, MD Anderson, Yale, 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 TIL

- **Polyclonal:** Can recognize multiple neoantigens:
 - Effective in solid tumors which are heterogeneous
- **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 (CRs) observed in cervical cancer patients, maintained at 53 and 67 months⁽²⁾
 - Durable CRs observed in NSCLC patients beyond one year post-TIL⁽³⁾



⁽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

⁽³⁾ Creelan, et. al., Durable complete responses to adoptive cell transfer using tumor infiltrating lymphocytes (TIL) in non-small cell lung cancer (NSCLC): a phase I trial, AACR 2020, Abstract #20-LB-10617

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

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

Advanced Technologies

Patent applications filed for a wide range of TIL technologies including:

- Marrow infiltrating (MIL) and peripheral blood lymphocyte therapies (PBL)
- Novel manufacturing processes including selected TIL process
- 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, \$85 mil investment
- Clean room build initiated April 2020
- Commercial GMP production is expected to commence in 2022
- Significant reduction in COGS expected



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	7,230	96,480
Cervix Uteri	4,250	13,170
Lung & Bronchus	142,670	228,150
Oral Cavity, Pharynx & Larynx	10,860	53,000
Breast	41,760	268,600
Pancreatic	45,750	56,770
Brain & Other Nervous System	17,760	23,820
	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>

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	178	—	<div></div>		
	LN-145	C-145-04	Cervical cancer	138	—	<div></div>		
	LN-145/ LN-145-S1	C-145-03	Head & neck cancer	55	—	<div></div>		
	Lifileucel + pembrolizumab LN-145-S1 LN-145 + pembrolizumab LN-145 + pembrolizumab LN-145	IOV-COM-202	Melanoma Melanoma Head & neck Non-small cell lung Non-small cell lung	~75	—	<div></div>		
	IOV-2001	IOV-CLL-01	Chronic lymphocytic leukemia	~70	—	<div></div>		
Select investigator sponsored proof-of-concept studies	MDA TIL	NCT03610490	Ovarian, colorectal, pancreatic	~54	MDAnderson Cancer Network	<div></div>		
	LN-145	NCT03449108	Ovarian, sarcomas	~54	MDAnderson Cancer Network	<div></div>		
	Moffitt TIL + nivolumab	NCT03215810	Non-small cell lung	20	MOFFITT CANCER CENTER	<div></div>		

Metastatic Melanoma

Potential Market for Metastatic Melanoma

- Estimated 7,230⁽¹⁾ U.S. patients' deaths due to melanoma
- Limited options after progression on checkpoint and BRAF/MEK inhibitors

“Nature has selected TIL to recognize features unique to the tumor not present on normal tissues, which helps make a TIL therapy approach effective compared to other cell therapy strategies for solid tumors. Iovance TIL treatment has a novel mechanism of action, completely separate from those of other treatment options, and has resulted in highly durable responses in patients that have progressed on prior FDA-approved treatment for their metastatic melanoma.”

— Dr. Amod Sarnaik
Department of Cutaneous Oncology,
the Immunology Program and the Melanoma
Center of Excellence at Moffitt Cancer Center

Metastatic Melanoma Facts

309k

New Cases WW
each year⁽³⁾

62k

Deaths WW
each year⁽³⁾

96k

Diagnoses in U.S.
each year⁽¹⁾

7k

Deaths in U.S.
each year⁽¹⁾

1st line:

Immuno-therapy

BRAF/MEK
inhibitors for
**BRAF
positive**

Chemotherapy

ORR 4-10%⁽²⁾
OS ~7-8 mons⁽⁴⁾

⁽¹⁾ in 2019, <https://seer.cancer.gov>;

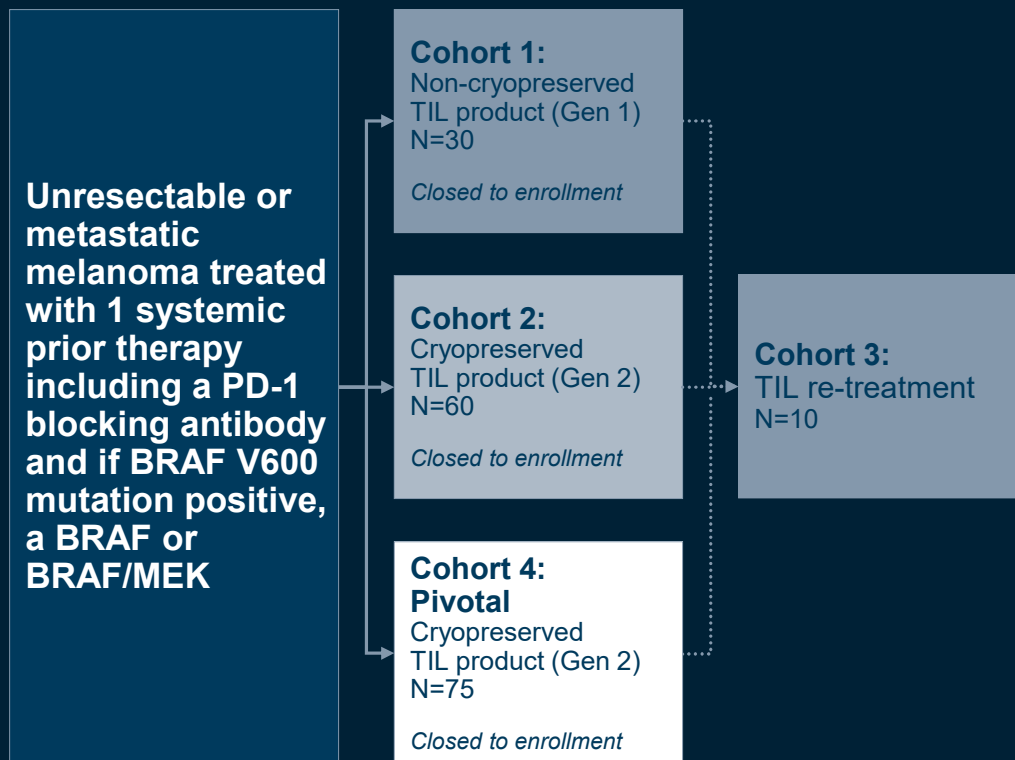
⁽²⁾ CheckMate-37 Trial Results (ICC 10%), Keytruda label (4%);

⁽³⁾ JAMA Oncol. 2019; 5(12):1749-1768. doi:10.1001/jamaoncol.2019.2996;

⁽⁴⁾ Eur J Cancer. 2016; 65:182-184. J Clin Oncol. 2018; 36 (suppl: abstr e21588)

C-144-01: Phase 2 Study Design

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



Endpoints

- Primary: Efficacy defined as IRC ORR

Study Updates

- March 2019: Cohort 4 (pivotal trial) FPI
- June 2019: Full Cohort 2 data on 66 patients presented at ASCO
- November 2019: IRC Cohort 2 data presented at SITC
- November 2019: Investigator read of Cohort 2 sub-analysis for primary refractory to PD-1 presented
- Jan 2020: last patient dosed
- May 2020 ASCO abstract: at 17.0 months of study follow up, median DOR not reached.

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 and a BRAF or BRAF/MEK if indicated
- Age ≥ 18
- ECOG PS 0-1

Endpoints

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

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)
Progressive Disease (PD) for at least 1 prior therapy	
Anti-CTLA-4	41 (77)
Anti-PD-1	65 (99)
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)

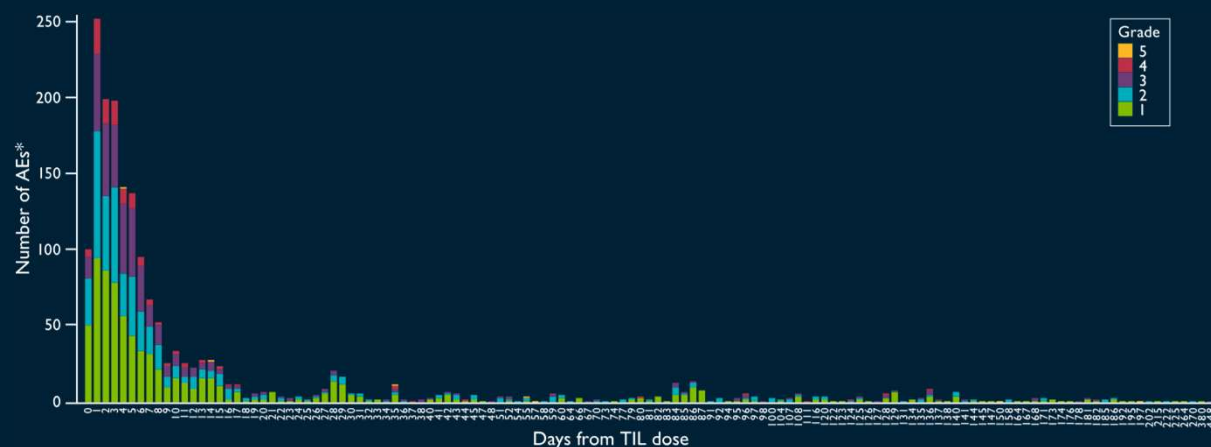
Adverse Events Tend to be Expected, Early and Transient

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

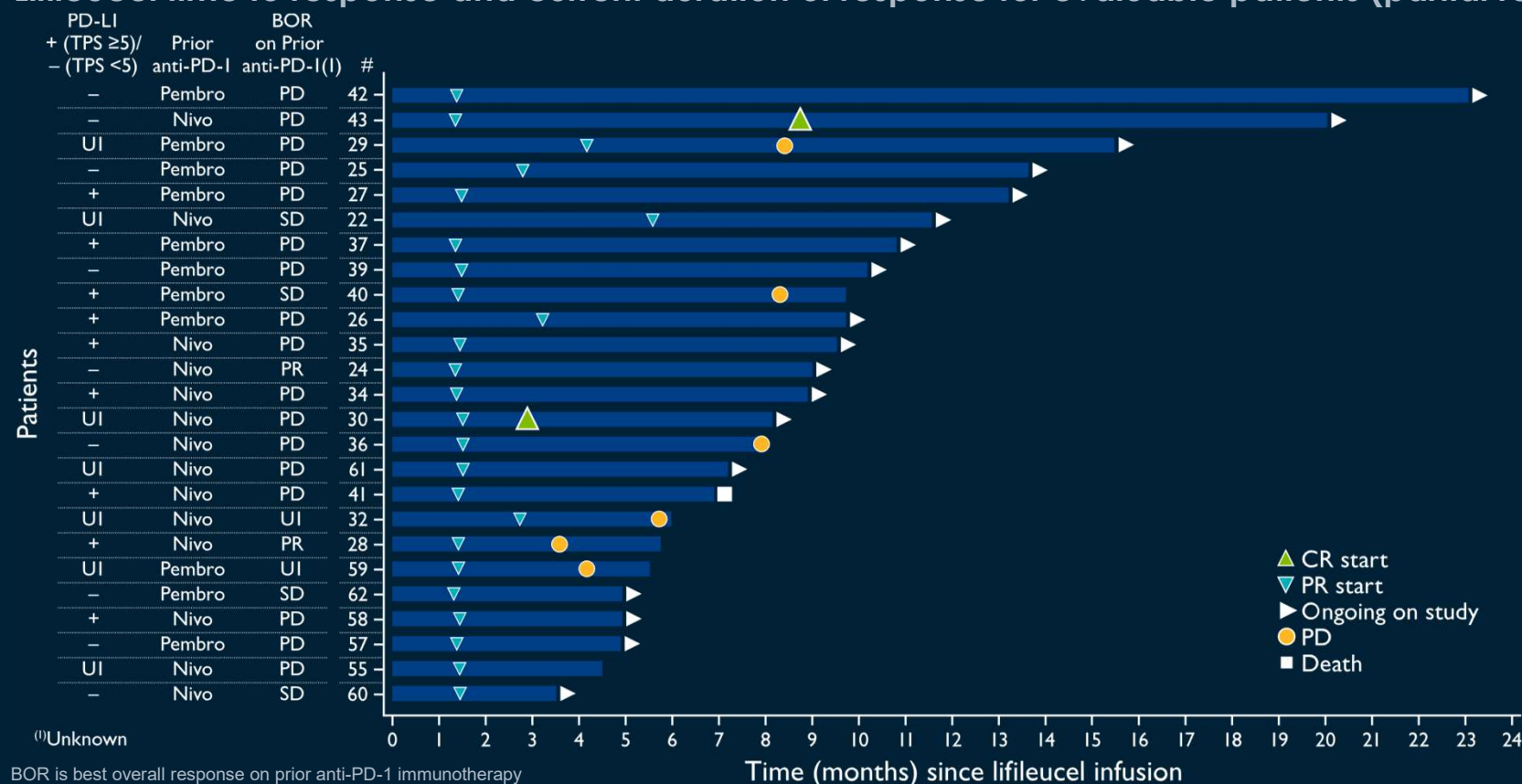
In heavily pretreated metastatic melanoma patients (3.3 mean prior therapies)

- **ORR 36%**
- **DCR 80%**
- ***Median DOR has not been reached***
 - ***Median study follow-up 15.5 months (as of 2 Jan 2020) – data update***
- Patients with PD-L1 negative status (TPS<5%) were among responders
- Mean TIL cells infused: 27.3×10^9
- Median number of IL-2 doses: 5.5

Responses	N=66 (%)
Objective Response Rate	24 (36.4%)
Complete Response	2 (3%)
Partial Response	22 (33.3%)
Stable Disease	29 (43.9%)
Progressive Disease	9 (13.6%)
Non-Evaluable	4 (6.1%)
Disease Control Rate	53 (80.3%)

Responders Previously Progressed on Checkpoint Inhibitors

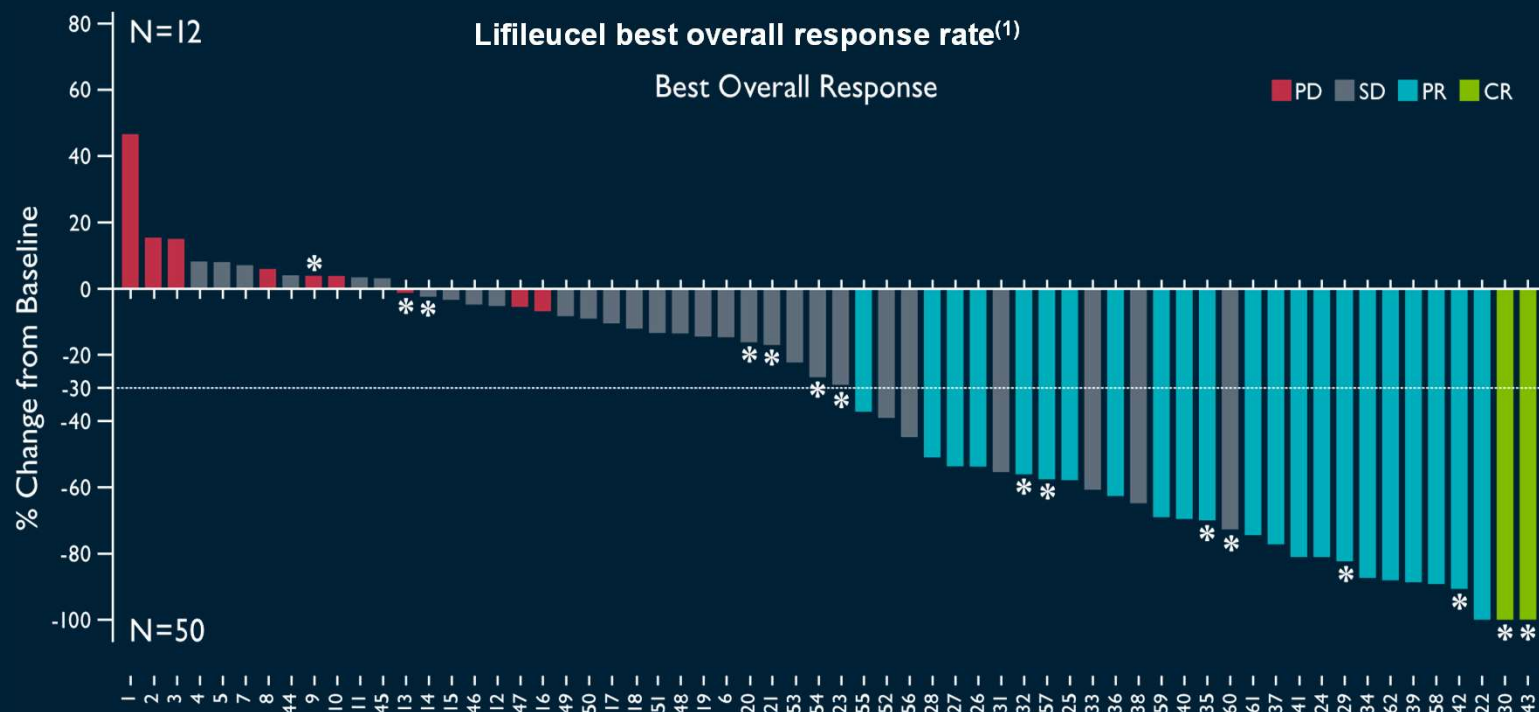
Lifileucel time to response and current duration of response for evaluable patients (partial response or better)



TIL Therapy Provides Deep Responses

- 81% of evaluable 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 >30%

* BRAF mutant patients



SMR Annual Meeting | November 20-23, 2019 | Salt Lake City, UT, USA

Lifileucel, a Potential Therapy for Metastatic Melanoma Patients who are Primary Refractory to Prior Anti-PD1 Therapy

ClinicalTrials.gov identifier: NCT02360579

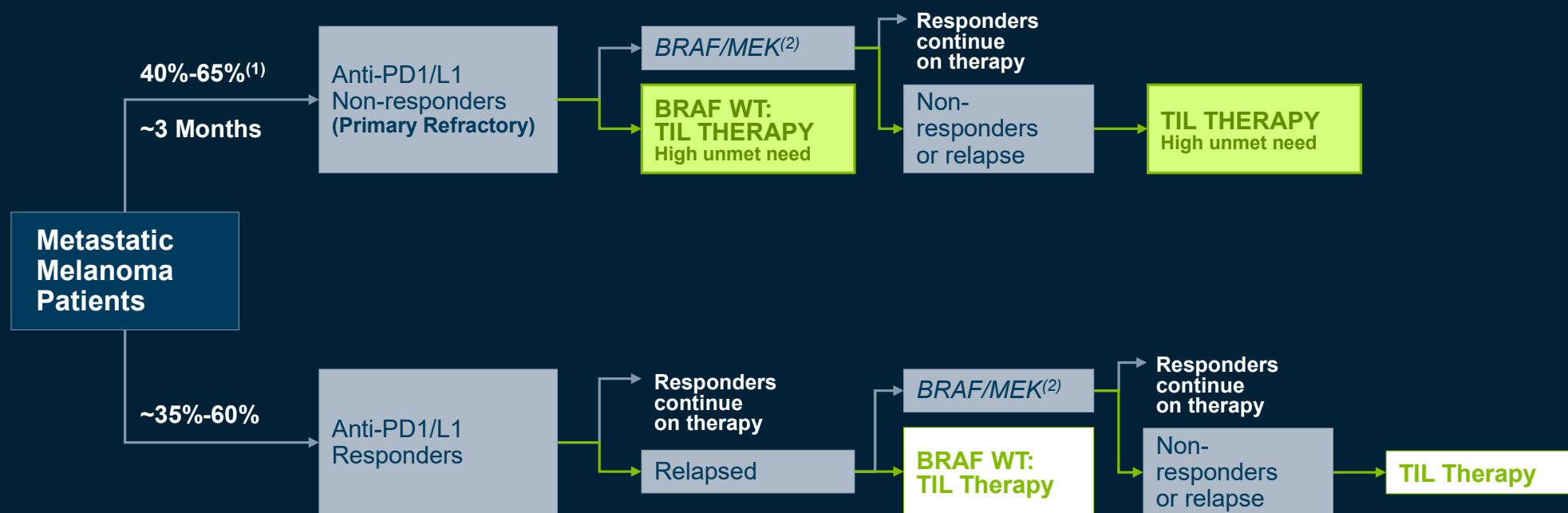
Metastatic Melanoma Patients who are Primary Refractory to Anti-PD1/L1

- High unmet medical need for patients with advanced melanoma who have a BOR of PD to checkpoint therapy, known as primary refractory or primary resistance
- 40-65% of all metastatic melanoma patients are primary refractory to initial immune Anti-PD1/L1 therapy⁽¹⁾
- TIL therapy offers a potential therapeutic option in primary refractory metastatic melanoma patients
- A subset analysis of data from Cohort 2 of C-144-01 study focused on primary refractory patients was presented at Society for Melanoma Research (SMR) 2019 conference

⁽¹⁾ Gide T.N., et al. Primary and Acquired Resistance to Immune Checkpoint Inhibitors in Metastatic Melanoma. *Clin. Cancer Res.* 2018;24:1260–1270

Subset Analysis of Metastatic Melanoma Cohort 2 C-144-01 Patients Primary Refractory to Anti-PD1/L1

A subset analysis of data from Cohort 2 of C-144-01 study focused on primary refractory patients was presented at SMR 2019 conference



⁽¹⁾ Gide T.N., et al. Primary and Acquired Resistance to Immune Checkpoint Inhibitors in Metastatic Melanoma. *Clin. Cancer Res.* 2018;24:1260–1270. ⁽²⁾ Patients with BRAF V600E

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

Characteristic	Cohort 2, n=42 (%)
Gender, n (%)	
Male	26 (62)
Female	16 (38)
Age	
Median	56
Min, Max	20, 77
Prior therapies, n (%)	
Mean # prior therapies	3.3
Anti-CTLA-4	33 (79)
Anti-PD-1	42 (100)
BRAF/MEK	9 (21)
Progressive Disease (PD) for at least 1 prior therapy	
Anti-CTLA-4	29 (88)*
Anti-PD-1	42 (100)
Baseline ECOG score, n (%)	
0	25 (60)
1	17 (40)

*% is calculated based on number of patients received prior anti-CTLA4.

Characteristic	Cohort 2, n=42 (%)
BRAF Status, n (%)	
Mutated V600	11 (26)
Wild Type	29 (69)
Unknown	2 (5)
Baseline LDH (U/L)	
Median	259
1-2 times ULN	10 (24)
> 2 times ULN	5 (12)
Target Lesion Sum of Diameter (mm)	
Mean (SD)	114 (78)
Min, Max	17, 343
Number of Target & Non-Target Lesions (at Baseline)	
>3	35 (83)
Mean	6
Patients with Baseline Liver and/or Brain Lesions	21 (50)

➤ In n=42 patients primary refractory to anti-PD-1/L1, defined as BOR of PD to the earliest anti-PD-1/L1 treatment:

- Mean duration on first anti-PD-1/L1 was 3.1 months
- 57% PD-L1 High/Positive (TPS \geq 1%)

Treatment Emergent Adverse Events (≥30%) Subset Analysis⁽¹⁾

Patients Primary Refractory to Anti-PD1/L1

Cohort 2 Patients Primary Refractory to Anti-PD1/PDL1, (N=42)

Preferred Term	Any Grade, n (%)	Grade ≥3, n (%)	Grade 5, n (%)
Number of subjects reporting at least one TEAE	42 (100)	41 (97.6)	2 (4.8)
Thrombocytopenia	38 (90.5)	33 (78.6)	0
Chills	32 (76.2)	3 (7.1)	0
Anemia	30 (71.4)	25 (59.5)	0
Pyrexia	25 (59.5)	7 (16.7)	0
Febrile neutropenia	23 (54.8)	23 (54.8)	0
Neutropenia	21 (50.0)	15 (35.7)	0
Hypophosphatemia	19 (45.2)	12 (28.6)	0
Leukopenia	18 (42.9)	15 (35.7)	0
Fatigue	18 (42.9)	1 (2.4)	0
Lymphopenia	15 (35.7)	13 (31.0)	0
Hypotension	14 (33.3)	5 (11.9)	0
Hypocalcemia	14 (33.3)	3 (7.1)	0
Aspartate aminotransferase increased	13 (31.0)	0	0
Diarrhea	13 (31.0)	1 (2.4)	0
Tachycardia	13 (31.0)	1 (2.4)	0

AEs are consistent with prior reports on the full Cohort 2 analysis set

- Patients with multiple events for a given preferred term are counted only once using the maximum grade under each preferred term
- Treatment-Emergent Adverse Events refer to all AEs starting on or after the first dose date of TIL up to 30 days

Potentially Efficacious Treatment for Metastatic Melanoma⁽¹⁾

Patients Primary Refractory to Anti-PD1/L1

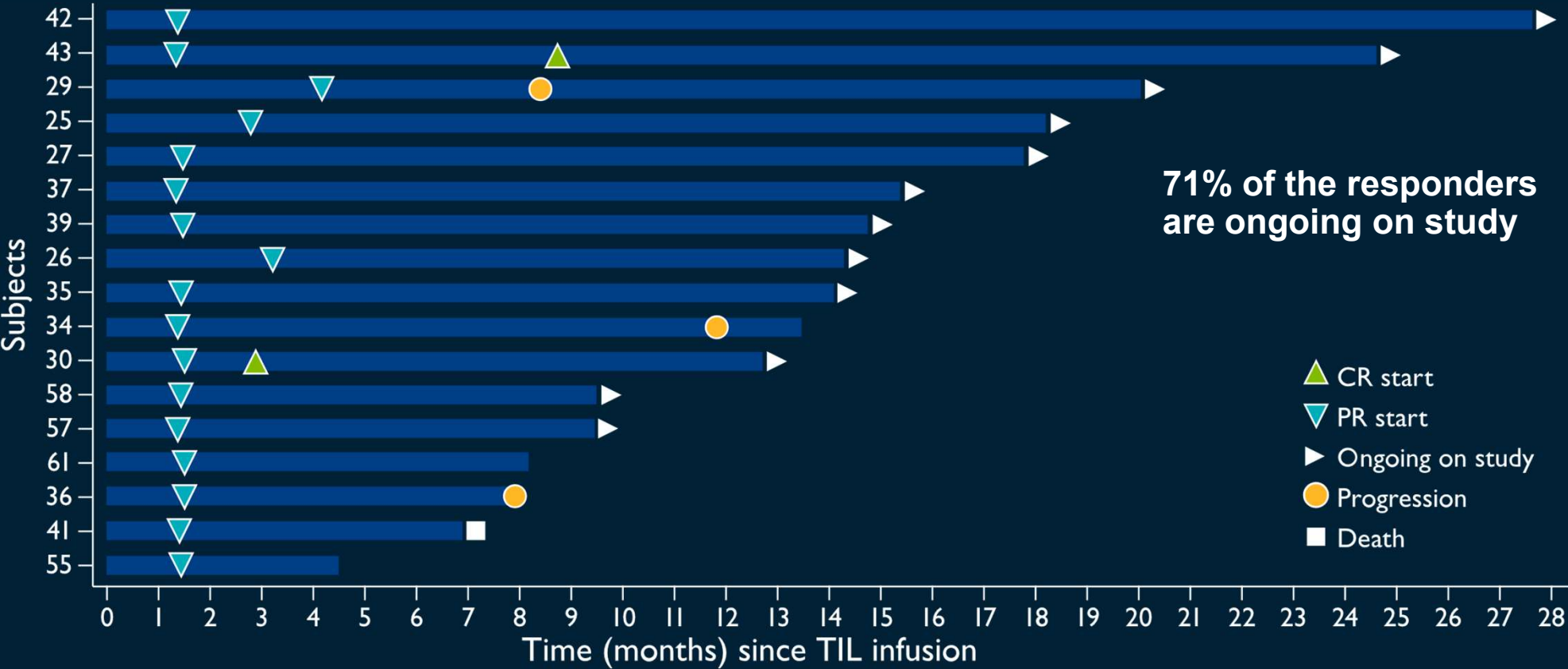
Response (Recist v1.1)	Cohort 2	
	Full analysis set, N=66 (%)	Patients Primary Refractory to Anti-PD1/L1, n=42 (%)
Objective Response Rate (ORR)	24 (36.4)	17 (40.5)
Complete Response (CR)	2 (3.0)	2 (4.8)
Partial Response (PR)	22 (33.3)	15 (35.7)
Stable Disease (SD)	29 (43.9)	17 (40.5)
Progressive Disease (PD)	9 (13.6)	5 (11.9)
Non-Evaluable	4 (6.1)	3 (7.1)
Disease Control Rate (DCR)	53 (80.3)	34 (81.0)
Median Duration of Response (DOR)	Not Reached	Not Reached
Min, Max	2.2, 21.2+	2.8+, 21.2+

➤ In 42 patients primary refractory to anti-PD1/L1:

- Median DOR has not been reached at median 12.0 months study follow up
- ORR was notable in this sub-group at 40.5%

Time to Response for Evaluable Patients with PR or Better⁽¹⁾

Patients Primary Refractory to Anti-PD1/L1



Lifileucel in Metastatic Melanoma Primary Refractory to Anti-PD1/L1

40-65% of all metastatic melanoma patients are primary refractory to initial ICI therapy⁽¹⁾

Lifileucel offers a highly efficacious therapy in patients who were primary refractory to prior anti-PD1/L1 ICI therapy⁽²⁾

- 40.5% ORR in patients who were primary refractory to anti-PD1/L1, which is a better response than Cohort 2
- 71% of responders who were primary refractory to anti-PD1/L1 remain on study
- At 12 months of study follow up, median DOR has not been reached for primary refractory subset

⁽¹⁾ Gide T.N., et al. Primary and Acquired Resistance to Immune Checkpoint Inhibitors in Metastatic Melanoma. *Clin. Cancer Res.* 2018;24:1260–1270.

⁽²⁾ Sarnaik, et al. SMR 2019.

Cohort 4 is a Pivotal Single-Arm Registrational Trial

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 IRC
- Secondary: safety and efficacy

Study Updates

- Confirmed with FDA that a randomized Phase 3 study is not feasible in advanced melanoma post-CPI
- Jan 2020: Last patient dosed

**Cohort 4
(Pivotal):**
Cryopreserved TIL
product (Gen 2)
N=75

Per FDA interaction

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	22% (N=49) ⁽²⁾	Phase 3, post-PD-1 melanoma ILLUMINATE 204	1-3	ECOG ≤1, intratumoral injection
	CMP-001 (CheckMate) + pembro	25% (N=82) ⁽³⁾	Phase 1b	1+	ECOG ≤1, intratumoral injection
	SD-101 (Dynavax) + pembro	19% (N=31) 13% (N=30) ⁽⁴⁾	Phase 1b/2 (abandoned) ⁽⁸⁾	1+	2mg, 1-4 lesions, 8 mg 1 lesion ECOG ≤1 intratumoral injection
Single Agent	Entinostat (Syndax) + pembro	19% (N=53) ⁽⁵⁾	ENCORE 601	1+	ECOG ≤1
	Checkpoints				
	TIGIT, TIM-3	Unknown	Phase 1/2		
	Cytokines				
	HD IL-2	8% (N=9) ⁽⁶⁾		1+	HD IL-2 post anti-PD1
	Other				
	TIL	36.4% (N=66)⁽⁷⁾	Phase 2, continuing to enroll pivotal trial	3.3	All post anti-PD1

⁽¹⁾ Ascierto P et al., ESMO 2017; ⁽²⁾ Idera Pharmaceuticals Press Release April 21, 2020; ⁽³⁾ Milhem M et al., SITC 2019; ⁽⁴⁾ Amin et al., ASCO 2019, Abstract 9555;

⁽⁵⁾ Ramalingam et al., AACR 2019; ⁽⁶⁾ Buchbinder EI et al., JCO 2017; ⁽⁷⁾ Sarnaik et al., SITC 2019; ⁽⁸⁾ DVAX press release May 23, 2019

Cervical Cancer

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

601k

New Cases WW
each year⁽¹⁾

260k

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 metastatic
cervical patients
4.5-13%⁽⁴⁾⁽⁵⁾

⁽¹⁾ JAMA Oncol. 2019;5(12):1749-1768. doi:10.1001/jamaoncol.2019.2996;

⁽²⁾ <https://seer.cancer.gov/>

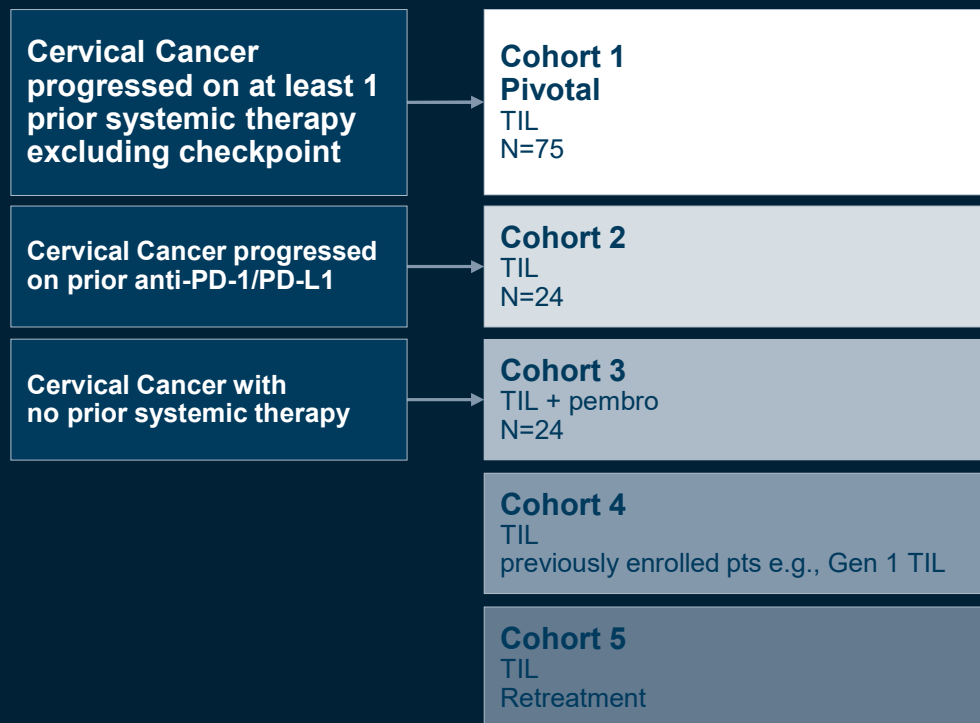
⁽³⁾ https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf

⁽⁴⁾ Schilder et al., Gynecologic Oncology, 2005;

⁽⁵⁾ Weiss, et al., A phase II trial of carboplatin for recurrent or metastatic squamous carcinoma of the uterine cervix: A Southwest Oncology Group Study

C-145-04: Pivotal 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 IRC
- Secondary: safety and efficacy

Study Updates

- March 2019: Fast Track designation
- May 2019: Breakthrough Therapy Designation
- June 2019: ASCO data presentation
- June 2019: FDA EOP2 held-existing study may be sufficient to support registration of LN-145
- July 2019: Study expanded to enroll a total of 75 patients
- November 2019: Additional cohorts added (Cohorts 2-5)

LN-145 in Cervical Cancer Interim Update at ASCO 2019

Key Inclusion Criteria

- Recurrent, metastatic or persistent cervical carcinoma with at least 1 prior therapy
- Age ≥ 18

Endpoints

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

Study Updates

- Protocol amended to increase total to 75 patients
- ORR as determined by IRC
- Fast Track and BTB received
- EOP2 meeting held with FDA

Baseline Demographics

N=27 (%)

Prior therapies

Mean # prior therapies	2.4
Platinum-based	27 (100)
Taxane	26 (96)
Anti-VEGF	22 (82)
PD-1/PD-L1	4 (15%)

Target lesions sum of diameter (mm)

Mean (SD)	61 (38)
Min, Max	10, 165

Histologic Cell Type, n (%)

Squamous Cell Carcinoma	12 (44)
Adenocarcinoma	12 (44)
Adenosquamous Carcinoma	3 (11)

Number of target & non-target lesions (at baseline)

>3	17 (63)
Mean (min,max)	4 (1,9)

Adverse Events Tend to be Early and Transient

Frequency of AEs over time is reflective of potential benefit of one-time treatment with TIL (LN-145)

N=27			
Preferred Term	Any Grade, n (%)	Grade 3/4, n (%)	Grade 5, n (%)
Number of patients reporting at least one Treatment-Emergent AE**	27 (100)	26 (96.3)	0
Chills	21 (77.8)	0	0
Anemia	15 (55.6)	15 (55.6)	0
Diarrhea	14 (51.9)	2 (7.4)	0
Pyrexia	14 (51.9)	1 (3.7)	0
Thrombocytopenia	14 (51.9)	12 (44.4)	0
Neutropenia	11 (40.7)	8 (29.6)	0
Vomiting	11 (40.7)	1 (3.7)	0
Hypotension	10 (37.0)	4 (14.8)	0
Dyspnea	9 (33.3)	1 (3.7)	0
Febrile neutropenia	9 (33.3)	8 (29.6)	0
Hypoxia	9 (33.3)	3 (11.1)	0
Leukopenia	9 (33.3)	6 (22.2)	0
Hypomagnesemia	8 (29.6)	0	0
Sinus tachycardia	8 (29.6)	0	0



**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

Significant Response Observed in Patients with Limited Options

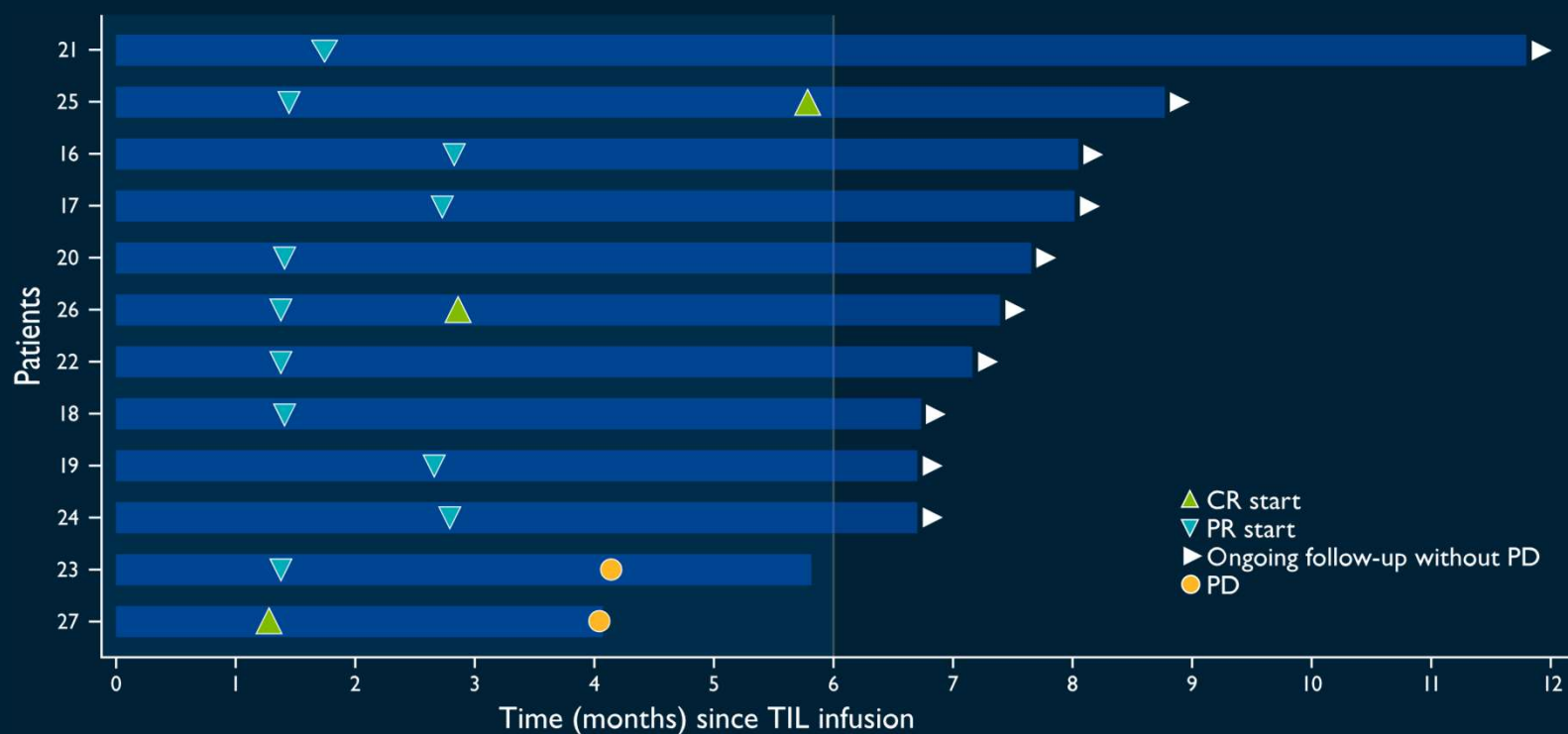
In heavily pretreated cervical cancer patients (2.4 mean prior therapies)

- **CR 11%**
- **ORR 44%**
- **DCR 85%**
- **Median DOR has not been reached**
 - Median follow-up 7.4 months
- Mean TIL cells infused: **28×10^9**
- Median number of IL-2 doses: 6.0

Responses		N=27 (%)
Objective Response Rate		12 (44%)
Complete Response		3 (11%)
Partial Response		9 (33%)
Stable Disease		11 (41%)
Progressive Disease		4 (15%)
Non-Evaluable		0
Disease Control Rate		23 (85%)

Responses Observed Early On and Consistent with Melanoma

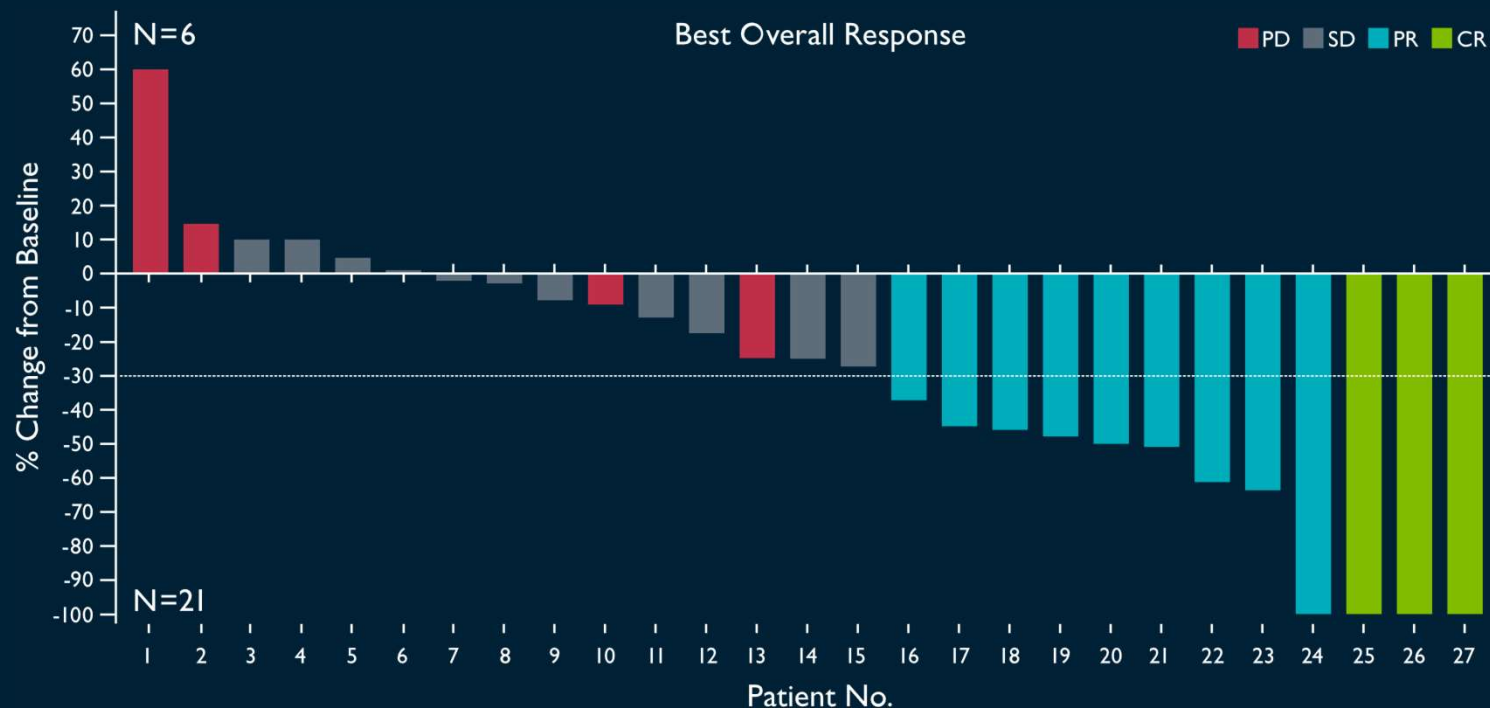
LN-145 time to response and current duration of for evaluable patients (partial response or better)



- Mean time to first response 1.9 months
- Mean time to best response 2.4 months

Three Complete Responses Observed with LN-145

LN-145 best overall response rate



- 78% of patients had a reduction in tumor burden
- Mean time to response 1.9 months
- All assessments are by RECIST 1.1
- Responses are deep with majority of responders are over 30%

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=55) ⁽¹⁾	Phase 2	1+	Recurrent or metastatic cervical cancer that progressed on standard therapy (most had received at least two prior therapies), median DOR= 6 months
Anti-PD-1				
AGEN2034 (Agenus)	11.4% (N=44) ⁽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	2.4 (mean)	All patients progressed on or after chemotherapy

⁽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

Additional Solid Tumor Studies

Non-Small Cell Lung Cancer (NSCLC)

Efficacy Data Post TIL Infusion

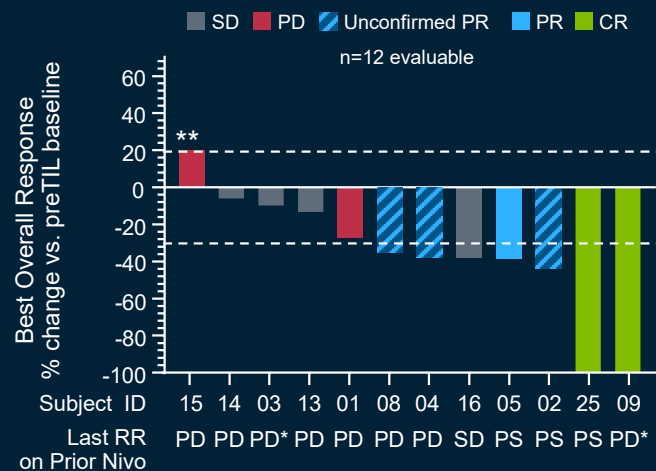
Responses	N=12 (%)
Objective Response Rate	3 (25%)
Complete Response	2 (17%)
Partial Response	1 (8%)

- **ORR 25%;**
 - 1 CR is noted in EGFR^{ΔEx19} post afatinib, osimertinib, nivolumab
- **Median DOR not reached;**
 - All 3 responders on TIL were relapsed or refractory to monotherapy Nivo
 - The TIL CR responses were ongoing
 - 2/3 responders were PD-L1 low (TPS<5%)

Moffitt TIL in Post-Nivolumab NSCLC

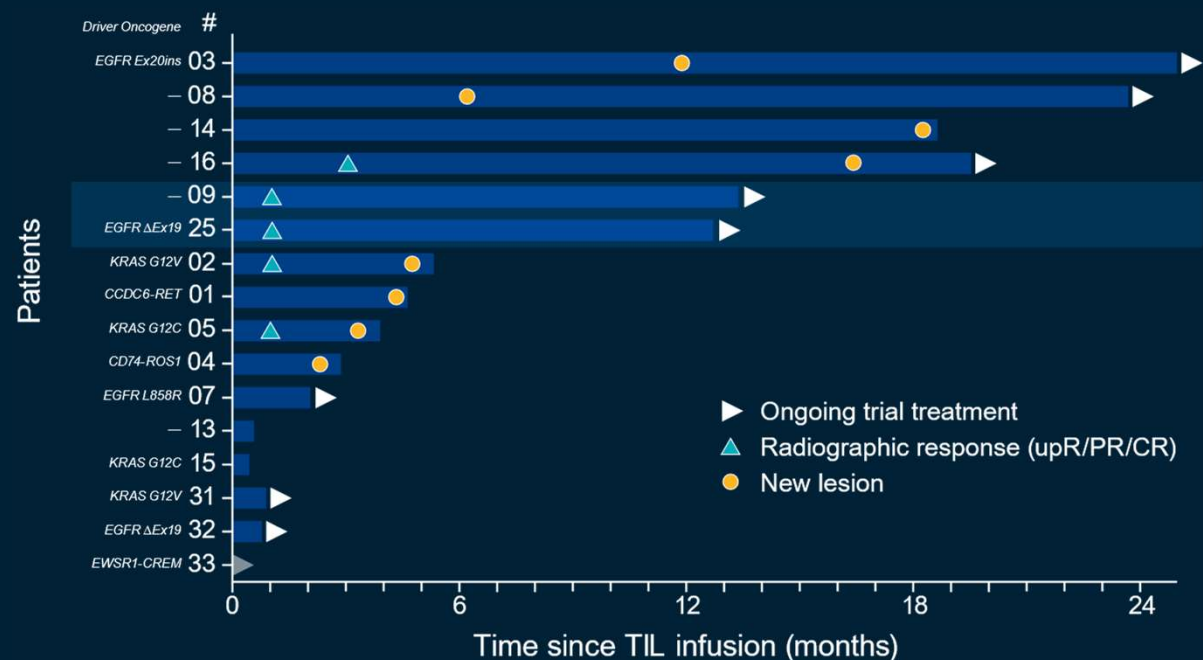
Nivolumab and Tumor Infiltrating Lymphocytes (TIL) in Advanced Non-Small Cell Lung Cancer (NCT03215810)

Post-TIL



In 12 evaluable patients with advanced NSCLC who received nivolumab and TIL:

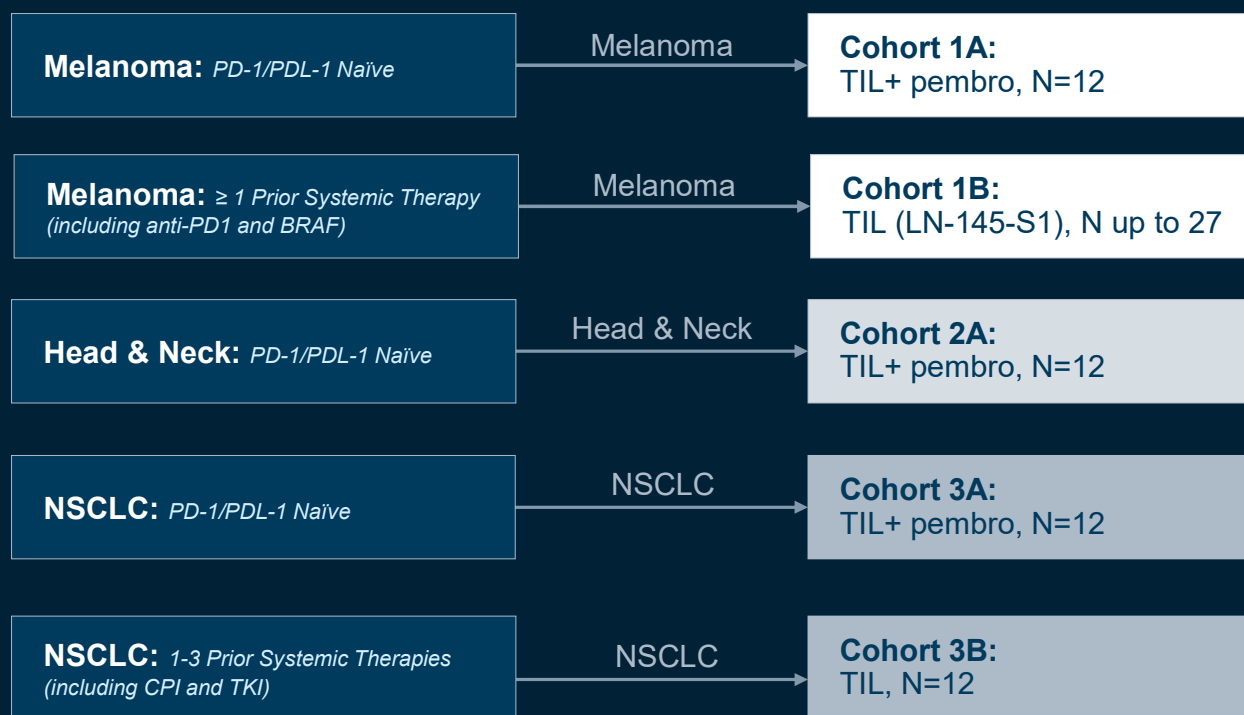
- Two CRs out to one year
 - (PD-L1 low=1, EGFR mutation=1)
- ORR 25% (or 33% if a uPR confirms)



(1) Creelan, et. al., Durable complete responses to adoptive cell transfer using tumor infiltrating lymphocytes (TIL) in non-small cell lung cancer (NSCLC): a phase I trial, AACR 2020, Abstract #20-LB-10617

TIL in Earlier Lines of Therapy in Combination with SOC

A prospective, open-label, multi-cohort, non-randomized, multicenter Phase 2 study evaluating adoptive cell therapy (ACT) with TIL LN-144 (Lifileucel)/LN-145 in combination with pembrolizumab or TIL LN-145/LN-145-S1 as a single therapy (NCT03645928)



Endpoints

- Primary: ORR and safety
- Secondary: CR rate

Study Updates

- 28 sites are activated globally
- Sites in the U.S., Canada and Europe

Research Focus into Next Generation TIL



Expand the TIL platform into new indications/regimens

- Triple Negative Breast Cancer (Yale)
- First patient dosed in Phase 1/2 study for PBL in CLL
- **IOV-3001 IL-2 analog licensed from Novartis**



Select more potent TIL

- PD-1 positive selected TIL by Iovance
- PD-1 positive selected TIL also through collaboration with CHUM



Genetically modify to make a more tumor-reactive TIL

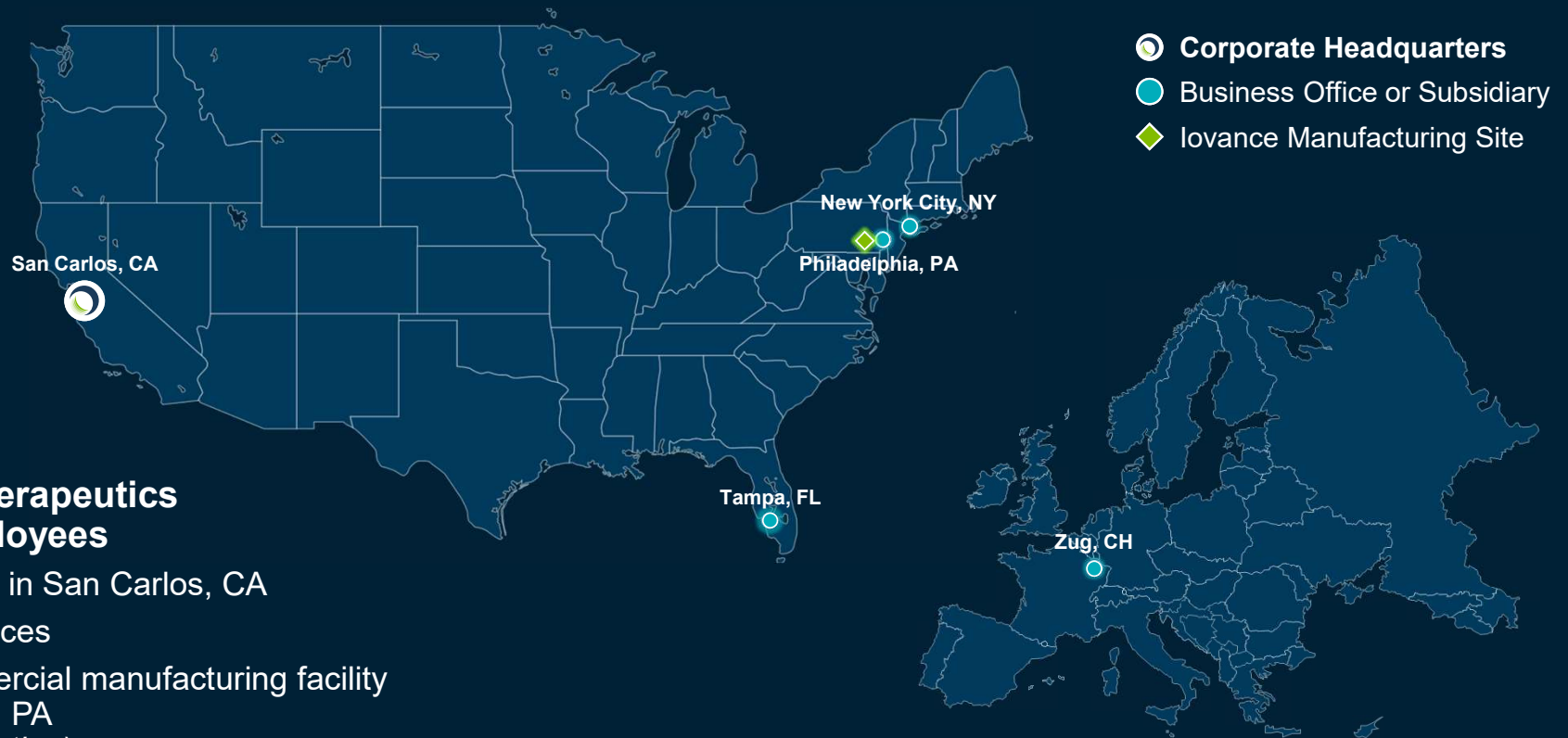
- Cellectis TALEN® collaboration agreement in place to support a clinical program



Process optimization

- Gen 3 (16-day) process
- Core biopsy

Iovance Biotherapeutics Global Reach and Scale



Iovance Biotherapeutics has ~190 employees

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

Well Capitalized in Pursuit of TIL Commercialization

March 31, 2020	In millions (unaudited)
Common shares outstanding	127
Preferred shares	4 ⁽¹⁾
Options	12
Cash, cash equivalents, short-term investments, restricted cash	\$251 ⁽²⁾
Debt	0

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

⁽²⁾ Includes Restricted Cash of \$5.5 million

Upcoming Milestones 2020

- ☒ Last patient dosed in Cohort 4 for lifileucel in support of registration in melanoma
- ☒ Data presentation at ASCO for long term follow up of melanoma Cohort 2
- ☐ Last patient dosed in pivotal program of LN-145 for cervical cancer
- ☐ Hold a pre-BLA meeting with FDA
- ☐ Top line data from melanoma
- ☐ Top line data from cervical
- ☐ File BLA



ADVANCING IMMUNO-ONCOLOGY

Thank You

