

Corporate Overview

August 16, 2023

ADVANCING IMMUNO-ONCOLOGY

© 2023, Iovance Biotherapeutics, Inc.

# **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") within the meaning of the Private Securities Litigation Reform Act of 1995 (the "PSLRA"). All such written or oral statements made in this press release, other than statements of historical fact, are forward-looking statements and are intended to be covered by the safe harbor for forward-looking statements provided by the PSLRA. Without limiting the foregoing, we may, in some cases, use terms such as "predicts," "believes," "potential," "continue," "estimates," "anticipates," "expects," "plans," "intends," "forecast," "guidance," "outlook," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes and are intended to identify forward-looking statements. Forward-looking statements are based on assumptions and assessments made in light of management's experience and perception of historical trends, current conditions, expected future developments and other factors believed to be appropriate. Forward-looking statements in this press release are made as of the date of this press release, and we undertake no duty to update or revise any such statements, whether as a result of new information, future events or otherwise. Forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and other factors, many of which are outside of our control, that may cause actual results, levels of activity, performance, achievements and developments to be materially different from those expressed in or implied by these forward-looking statements. Important factors that could cause actual results, developments and business decisions to differ materially from forward-looking statements are described in the sections titled "Risk Factors" in our filings with the Securities and Exchange Commission, including our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, and include, but are not limited to, the following substantial known and unknown risks and uncertainties inherent in our business; preliminary and interim clinical results, which may include efficacy and safety results, from ongoing clinical trials or cohorts, including but not limited to our IOV-LUN-202 trial, may not be reflected in the final analyses of our ongoing clinical trials or subgroups within these trials or in other prior trials or cohorts; risks related to the timing of and our ability to successfully develop, submit, 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, and our ability to successfully commercialize any product candidates for which we obtain FDA approval; whether clinical trial results from our pivotal studies and cohorts, and meetings with the FDA, may support registrational studies and subsequent approvals by the FDA, including the risk that the planned single-arm Phase 2 IOV-LUN-202 trial may not support registration; the risk that enrollment may need to be adjusted for our trials and cohorts within those trials based on FDA and other regulatory agency input; the risk that we may be required to conduct additional clinical trials or modify ongoing or future clinical trials based on feedback from the FDA or other regulatory authorities; the risk that our interpretation of the results of our clinical trials or communications with the FDA may differ from the interpretation of such results or communications by the FDA (including from the prior pre-BLA meeting with the FDA and/or regarding our prior meetings with the FDA regarding our NSCLC clinical trials); the risk that the FDA may not approve our BLA submission for lifileucel in metastatic melanoma; the acceptance by the market of our product candidates and their potential reimbursement by payors, if approved; our ability or inability to manufacture our therapies using third party manufacturers or our own facility may adversely affect our potential commercial launch; the results of clinical trials with collaborators using different manufacturing processes may not be reflected in our sponsored trials; the risk regarding the successful integration of the recent Proleukin acquisition; the risk that the successful development or commercialization of our products may not generate sufficient revenue from product sales, and we may not become profitable in the near term or, if at all; the risk that unanticipated expenses may decrease our estimated cash balances and forecasts and increase our estimated capital requirements; and other factors, including general economic conditions and regulatory developments, not within our control.

# Global Leadership in Innovating, Developing and **Delivering TIL Therapy for Patients with Cancer**

# **Platform Pipeline**

600+

Patients Treated with Iovance TIL

90%+

Manufacturing Success Rate

**22-day** 

**Proprietary Manufacturing Process** 



**Active Clinical Trials** 

Tumor Types in Clinic

Designations

#### **People & Assets**



Cash Position as of 6/30/23

**US and International Patents** 

**Employees** 

### **Partners & Collaborators**



The University of Texas MD Anderson Cancer Center





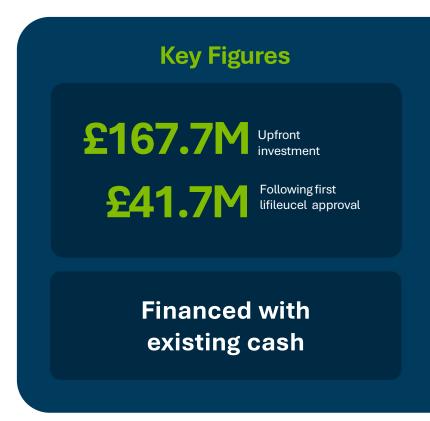


Abbreviations: BLA=Biologics License Application; BTD=Breakthrough Therapy Designation; RMAT=Regenerative Medicine Advanced Therapy Designation \*Includes net proceeds from an at-the market (ATM) equity financing facility of approximately \$260 million raised during the first quarter 2023. Cash position, including estimated net proceeds of approximately \$161 million from lovance's public offering of 23,000,000 shares of common stock at a price of \$7.50 per share which closed July 13, 2023, is expected to fund lovance's operating plan into the end of 2024.

### **Proleukin® Transaction Strategic Benefits**

Acquisition completed May 18, 2023

- Global rights to Proleukin® (aldesleukin, human recombinant IL-2) and associated revenue
- Secure IL-2 supply chain for lifileucel regimen
- Lower clinical trial costs and future COGS
- Significant additional revenue expected with TIL commercialization



# **Iovance Solid Tumor Pipeline Highlights**

	PRODUCT CANDIDATE	INDICATION(S)	PHASE 1 PHASE 2		PIVOTAL	
Advanced Melanoma	TIL (Lifileucel/LN-144)	Post-anti-PD-1	C-144-01, Cohorts 2 & 4		BLA Filed, ODD, RMAT	
(Metastatic or	Lifileucel + pembro	Frontline	TILVANCE-301 Phase 3		Confirmatory, FTD	
Unresectable)	Lifileucel + pembro	Anti-PD-1 naïve	IOV-COM-202, Cohort 1A			
Next Generation	PD-1 Inactivated TIL (IOV-4001)	Post-anti-PD-1	IOV-GM1-201, Coho			
Metastatic NSCLC	LN-145	2L post-chemo & post-anti-PD-1	IOV-LUN-202, Coho	rts 1 & 2		
NSCLC	LN-145 + pembro	Anti-PD-1 naïve IOV-COM-202, Cohort 3A		ort 3A		
	LN-145	2-4L incl. post-anti-PD-1	IOV-COM-202, Coho	ort 3B*		
	LN-145 + ipi/nivo	Post-anti-PD-1	Post-anti-PD-1 IOV-COM-202, Cohort 3C			
Next Generation	LN-145 Gen 3 + core biopsy	2L post-chemo & post-anti-PD-1	IOV-LUN-202, Cohort 3			
	PD-1 Inactivated TIL (IOV-4001)	2-4L incl. post-anti-PD-1	IOV-GM1-201, Cohort 2			
Cervical	Lifileucel	Post-chemo & post-anti-PD-1	C-145-04, Cohort 2		BTD, ODD	
	LN-145 + pembro	1L chemo and anti-PD-1 naïve	C-145-04, Cohort 3*			

<sup>\*</sup>Enrollment comple

Abbreviations: 1 = first line; 2L=second line; 4L=fourth line; BTD=Breakthrough Therapy Designation; FTD=Fast Track Designation; pi/nivo=ipilimumab/nivolumab; NSCLC=non-small cell lung cancer; ODD=Orphan Drug Designation; PD-1=programmed cell death protein-1; RMAT=Regenerative Medicines Advanced Therapy; TIL=tumor infiltrating lymphocytes

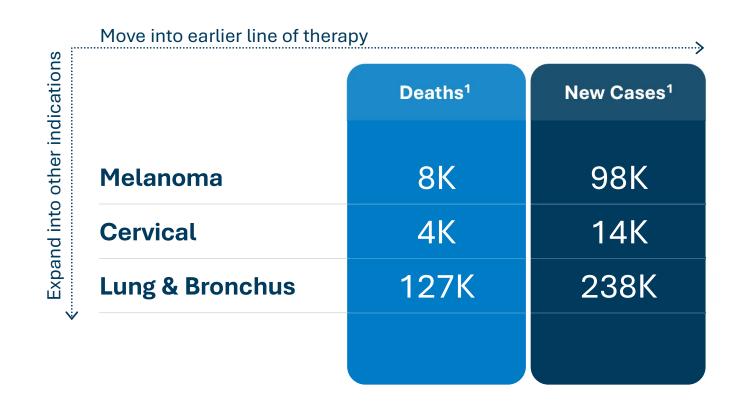
# Significant Market Potential in Solid Tumors and our Key Programs

91%

of all cancer cases are solid tumors<sup>1</sup>

**1.8M** 

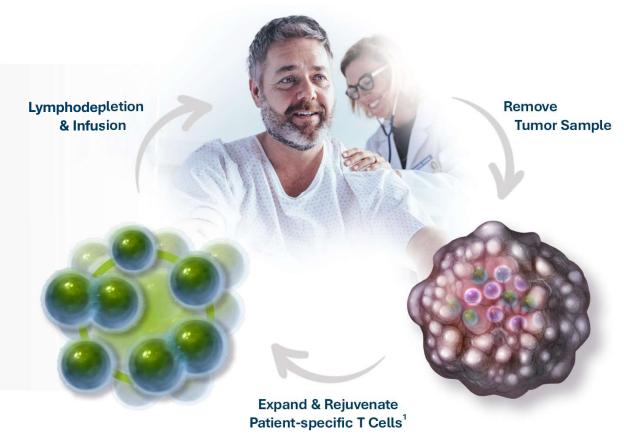
New cases of solid tumors in the U.S.<sup>1</sup>



# **Tumor Infiltrating Lymphocytes (TIL): Leading Platform for Treatment of Solid Tumors**

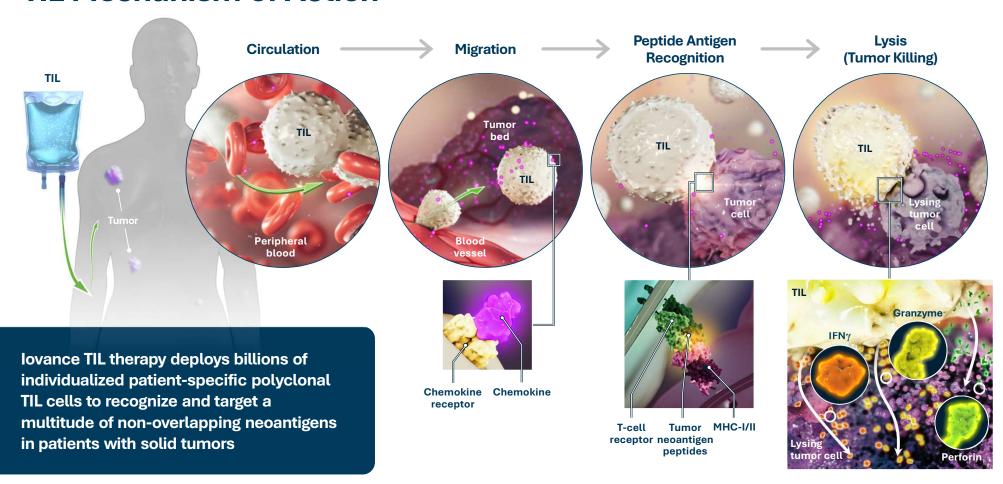
### TIL - Unique **Mechanism of Action**

- Individualized
- Patient's own immune system amplified and rejuvenated
- One-time therapy

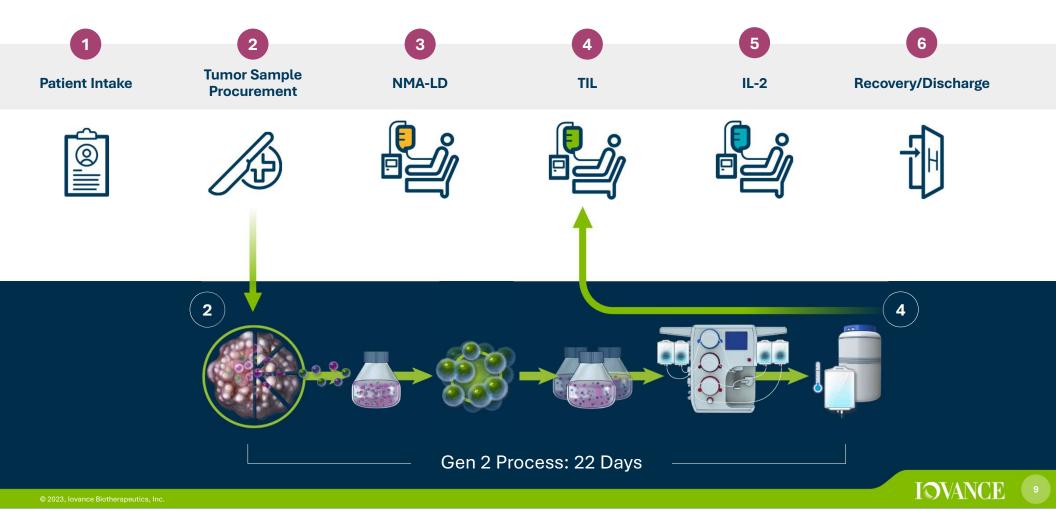


1. Simpson-Abelson et al., ESMO 2020

### **TIL Mechanism of Action**



# **Iovance Streamlined 22-Day GMP Manufacturing Process**



# Iovance Cell Therapy Center: iCTC

Built-to-suit custom facility in Navy Yard Philadelphia

136,000 ft<sup>2</sup>, \$85M investment

LEED gold certification for core and shell building

Honorable Mention Winner: 2022 ISPE Facility of the Year Awards

Clinical supply initiated 3Q21

Commercial manufacturing expected with BLA approval

Control to optimize capacity, quality & COGS

### **Leading Cell Therapy Manufacturing Facility**









Honorable Mention

**Iovance Cell Therapy Center (iCTC): Building Annual Capacity for Thousands** of Cancer Patients

Phase 1 iCTC **Today** 

100s

of patients/year

# **BLA Prep**

in core suites for commercial

4 separate flex suites for clinical

Phase 2 iCTC **Ongoing Staffing** 

2,000+

patients/year

**12** 

core suites for commercial

4

separate flex suites for clinical

Phase 3 iCTC Expansion<sup>1</sup>

5,000+

patients/year

24

core suites for commercial

separate flex suites for clinical

Phase 4 iCTC+ Additional Site(s)

10,000+

patients/year

*i*CTC

**Adjacent and** new sites<sup>2</sup>

**Automation** 

1. Expansion within existing shell 2. Option to build on adjacent parcel

# **Iovance TIL Therapy in Advanced Melanoma**



# **Unmet Medical Need for Metastatic Melanoma Therapy**

No FDA Approved Treatment Options After Progression on ICI (Anti-PD-1) Therapy and BRAF/MEK inhibitors

Annual new cases of advanced melanoma in U.S.¹

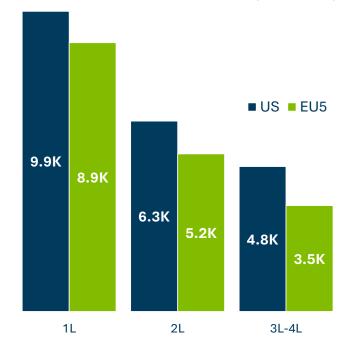
**8** Annual deaths in U.S.<sup>2</sup>

**57** Annual deaths worldwide<sup>3</sup>

- Estimate of US incidence (2021) of unresectable or metastatic melanoma based on secondary and primary market research
- 2. National Cancer Institute Surveillance, Epidemiology and End Results (SEER) Program. 2023 Estimates. https://seer.cancer.gov/accessed/May/2023
- Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries, CA Cancer J Clin., May 2021
- 4. Clarivate DRG Disease Landscape (2021)
- Keytruda USPI
- 6. Keytruda USPI (4%) and Weber et al., Lancet Oncol 2015 (ICC 10%)
- 7. Kirchburger et al., Eur J Cancer 2016 and Goldinger et al., J Clin Oncol 2018

Melanoma Drug-Treated Population in 2021<sup>4</sup>

Unresectable / Metastatic (US and EU5)



#### **Available Care:**

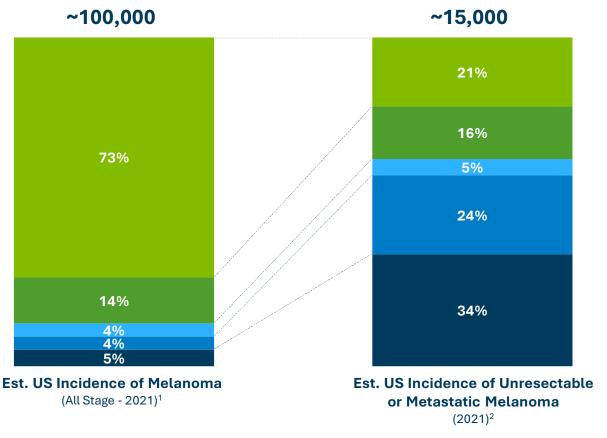
Anti-PD-1 Immunotherapy 21%-33% ORR<sup>5</sup>

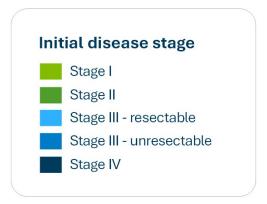
BRAF/MEK inhibitors if BRAF mutation +

Chemotherapy
ORR 4-10%6
mOS ~7-8 months<sup>7</sup>

Abbreviations: EU5=France, Germany, Italy, Spain and United Kingdom; 1L=first line therapy, 2L=second line therapy, 3L=third line therapy, 4L=fourth line therapy; ICI=immune checkpoint inhibitor; ORR=objective response rate; mOS=median overall survival; PD-1=programmed cell death protein-1

# Estimated total incidence and incidence of unresectable or metastatic melanoma by initial disease stage (US)





<sup>1.</sup> Estimate of US incidence from Epiphany Health with stage III resectability status informed by market research

<sup>2.</sup> Estimate of US incidence of unresectable or metastatic melanoma based on secondary and primary market research

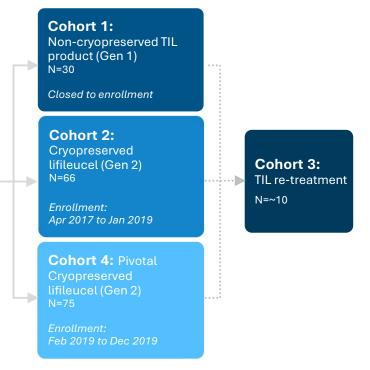
### C-144-01 Phase 2 Study Design

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

Identical
Eligibility and
Treatment for
Cohorts 2
and 4

# Patient Population

Unresectable or metastatic melanoma treated with ≥1 prior systemic therapy including a PD-1–blocking antibody and, if BRAF V600 mutation positive, a BRAF inhibitor ± MEK inhibitor



### **Key Endpoints**

- Primary: ORR (IRC-assessed using RECIST v1.1)
- · Secondary: DOR, PFS, OS, TEAE incidence and severity

### **Key Eligibility Criteria**

- Tumor lesion/s for TIL generation & response assessment
- No limit on number of prior therapies or markers of tumor burden (including size or LDH)

### **Treatment Regimen (Cohorts 2 and 4)**

- 22-day Gen 2 manufacturing process
- All patients received NMA-LD, a single lifileucel infusion, and up to 6 doses of high-dose IL-2

Data cutoff date: July 15, 2022

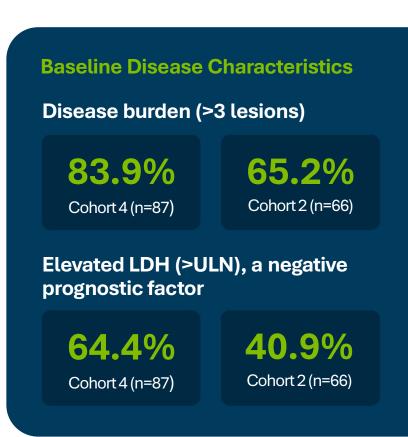
Abbreviations: DOR=duration of response; ECOG=Eastern Cooperative Oncology Group; IL-2=interleukin 2; IRC=Independent Review Committee; NMA-LD=nonmyeloablative lymphodepletion; ORR=objective response rate; OS=overall survival; PD-1=programmed cell death protein 1; RECIST=Response Evaluation Criteria in Solid Tumors; TEAE=treatment-emergent adverse events; TIL=tumor-infiltrating lymphocytes

# **Highlighted Prior Therapy and Baseline Disease Characteristics\***

Cohorts 2 and 4 Heavily Pre-Treated and Mostly Similar; Cohort 4 had Higher Disease Burden and LDH Elevation

### **Prior Therapy Experience (Cohorts 2+4)**

- Median of 3 lines of therapy (range, 1-9)<sup>1</sup>
- Median of 2 lines (range, 1-7) of ICI-containing therapy
- 113 (73.9%) retreated with ICI-containing therapy
- 125 (81.7%) received anti–CTLA-4
- 82 (53.6%) received anti–PD-1 + anti–CTLA-4 combination



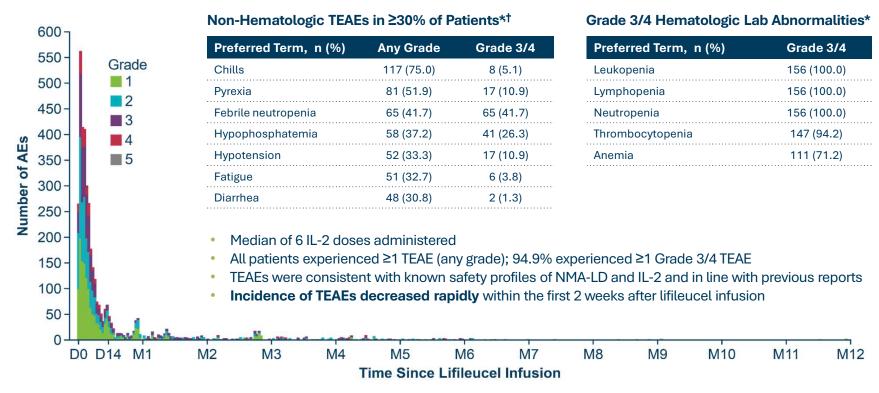
\*Refer to SITC 2022 presentation for full baseline characteristics

1. All patients received prior anti-PD1 therapy

Abbreviations: CTLA-4=cytotoxic T-lymphocyte antigen 4; ICI=immune checkpoint inhibitor; LDH=lactate dehydrogenase; PD-1=programmed cell death protein 1; ULN=upper limit of normal

# **Safety**

#### Transient and Manageable Nature of AEs Support the Potential Benefit of One-Time Treatment with Lifileucel



\*Per CTCAE v4.03; Safety Analysis Set (N=156).

All occurrences of AEs were counted if a patient experienced a new onset of the same AE at different timepoints. If multiple records were reported on the electronic case report form because of toxicity grade decrease of the same AE that had not resolved, then the event was counted once with the highest grade reported 15 events were reported after Month 12 (Grade 1, n=7; Grade 2, n=6; Grade 3, n=1; Grade 5, n=1)

Abbreviations: AE=adverse event; D=day; IL-2=interleukin 2; M, month; NMA-LD=nonmyeloablative lymphodepletion; TEAE=treatment-emergent adverse event

<sup>†</sup>Grade 5 TEAEs included pneumonia (n=1), acute respiratory failure (n=1), arrhythmia (n=1), and intra-abdominal hemorrhage (n=1)

# Objective Response Rate (ORR) of 31.4% by IRC

91% Concordance Rate between IRC- and Investigator-assessed ORR

	<b>Cohort 2</b> (n=66)	<b>Cohort 4</b> (n=87)	<b>Cohort 2+4</b> (n=153)	
ORR, n (%)	23 (34.8)	25 (28.7)	48 (31.4)	
(95% CI)	(23.5, 47.6)	(19.5, 39.4)	(24.1, 39.4)	
Best overall response,				
CR	5 (7.6)	4 (4.6)	9 (5.9)	
PR	18 (27.3)	21 (24.1)	39 (25.5)	
SD	24 (36.4)	47 (54.0)	71 (46.4)	
Non-CR/Non-PD*	1 (1.5)	0	1 (0.7)	
PD	15 (22.7)	12 (13.8)	27 (17.6)	
Nonevaluable <sup>†</sup>	3 (4.5)	3 (3.4)	6 (3.9)	

- 33 days median time from resection to lifileucel infusion
- Lifileucel manufactured within specification in 94.7% of patients
- Median number of TIL cells infused was  $21.1 \times 10^9$  (range,  $1.2 \times 10^9$  to  $99.5 \times 10^9$ )

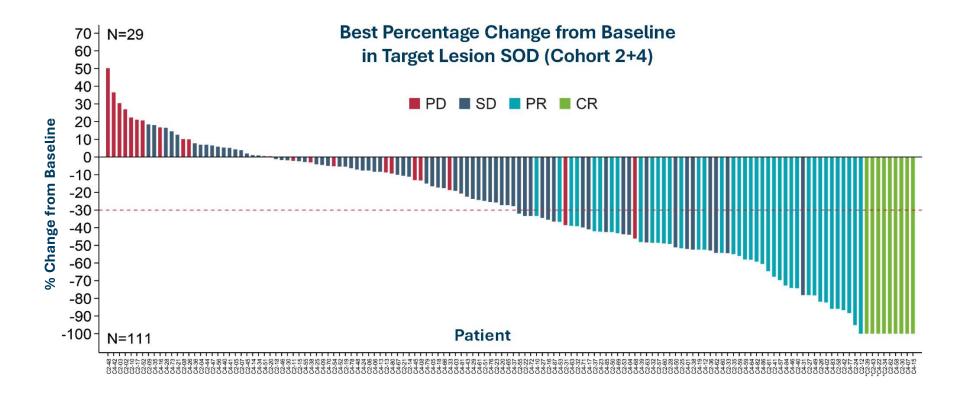
<sup>\*</sup>Patient did not have acceptable target lesions and had best overall response of non-CR/non-PD per IRC assessment

<sup>†</sup>Six patients were nonevaluable for response (5 due to early death; 1 due to new anticancer therapy)

Abbreviations: CR,=complete response; IRC=independent review committee; ORR=objective response rate; PD=progressive disease; PR=partial response; SD=stable disease

# Tumor Burden Reduction and Best Response to Lifileucel

Reduction of Tumor Burden in 79.3% (111/140) of Patients



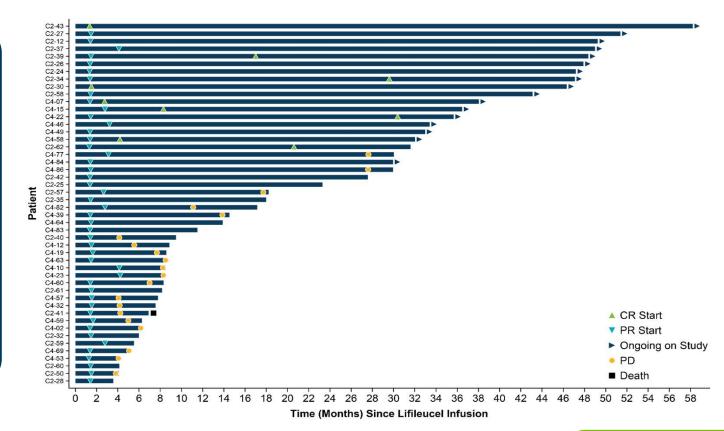
<sup>13</sup> patients in the full analysis set are not included (9 had no post lifileucel target lesion SOD measurements, and 4 had no acceptable target lesions by IRC).

Abbreviations: CR=complete response; PD=progressive disease; PR=partial response; SD=stable disease; SOD=sum of diameters

<sup>\*-100%</sup> change from baseline is presented for CR assessment that includes lymph node lesions.

# Time to Response, Duration of Response, and Time on Efficacy Assessment for Confirmed Responders (PR or Better)

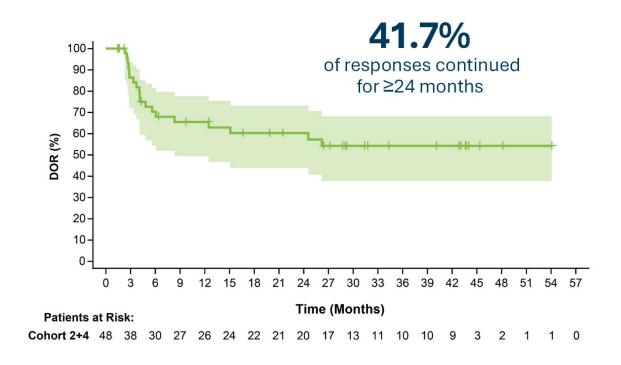
- Median time from lifileucel infusion to best response was 1.5 months
- Responses deepened over time
  - 7 patients (14.6%) initially assessed as PR were later confirmed CR
  - 4 patients (8.3%) converted to CR
     >1yr post-lifileucel infusion; 2 (4.2%) of 4 patients converted after 2 years
  - 10 patients (20.8%) improved from best response of SD to PR
- 35.4% of responses ongoing as of data cutoff



Abbreviations: CR=complete response; PD=progressive disease; PR=partial response; SD=stable disease

# **Duration of Response\***

Median DOR Not Reached at Median Study Follow Up of 36.5 Months



	Cohort 2 (n=23)	Cohort 4 (n=25)	Cohort 2+4 (N=48)		
Median follow- up, months	45.1	33.0	36.5		
95% CI	(44.2, 51.4)	(30.4, 35.2)	(34.7, 44.2)		
Median DOR <sup>†</sup> , months	NR	10.4	NR		
95% CI	(NR, NR)	(4.1, NR)	(8.3, NR)		
Min, max (months)	1.4+, 54.1+	1.4+, 34.3+	1.4+, 54.1+		
DOR ≥12 months, n (%)	15 (65.2)	11 (44.0)	26 (54.2)		
DOR ≥24 months, n (%)	11 (47.8)	9 (36.0)	20 (41.7)		

\*Patients not experiencing PD or who did not die prior to the time of data cut had their event times censored at the last adequate tumor assessment. For patients who received new anticancer therapies, DOR was censored at the date of last tumor response assessment prior to the start of new anticancer therapies. For patients with PD or death immediately after ≥2 consecutive missing tumor assessment visits, DOR was censored at the last adequate tumor assessment prior to the missing tumor assessments.

Shaded area indicates 95% CI

Abbreviations: DOR=duration of response; NR=not reached; PD=progressive disease

<sup>†</sup>Based on Kaplan-Meier estimate

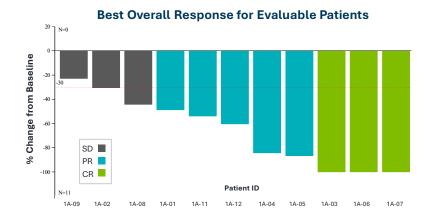
IOV-COM-202 COHORT 1A MELANOMA COMBINATION (TIL+PEMBROLIZUMAB)

# Iovance TIL Clinical Highlights in Combination with Pembrolizumab in Metastatic Melanoma

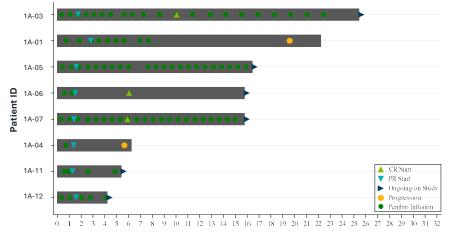
Lifileucel in combination with anti-PD-1/PD-L1 therapy in ICI-naïve patients (IOV-COM-202 Cohort 1A, N=12)<sup>1</sup>

# 66.7% ORR

- 8 / 12 patients had a confirmed objective response per RECIST v1.1 (3 CRs & 5 PRs)
- 6 / 8 responders had ongoing response
- 5 responders had DOR >1 year
- FDA Fast Track Designation



#### Time to Response for Responders<sup>2</sup>



1. As assessed by investigator using RECIST 1.1 (January 20, 2022 data cutoff)

Each bar is presented for each patient starting from date of TIL infusion up to date of new anti-cancer therapy, end of assessment, death, or data cutoff date, whichever occurs earlier.
 Abbreviations: CR=complete response; ICI=immune checkpoint inhibitor; ORR=objective response rate; PR=partial response; SD=stable disease; pembro=pembrolizumab; RECIST=Response Evaluation Criteria in Solid Tumors

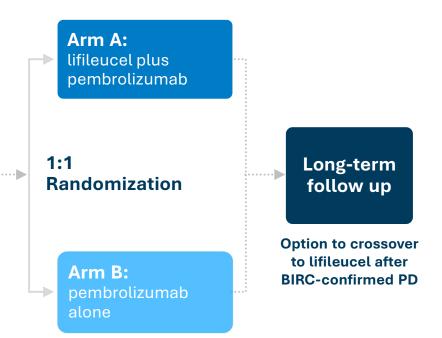
Time (months) since TIL Infusion

# **TILVANCE-301 Global Phase 3 and Confirmatory Trial**

Randomized, multicenter study with optional crossover to offer all patients potential to receive lifileucel (NCT05727904)

# Patient Population

Unresectable or metastatic melanoma; no prior therapy for metastatic disease N=670



# Study Design with FDA Agreement

- Dual Primary Endpoints: ORR & PFS
- Registrational for frontline melanoma
- Confirmatory for full approval in postanti-PD-1 melanoma
- First patient randomized 2Q23

Abbreviations: BIRC, blinded independent review committee; ORR=objective response rate; PD=progressive disease; PD-1, programmed cell death protein-1; PFS=progression free survival

# Iovance TIL Therapy in Non-Small Cell Lung Cancer



# Potential Market for Advanced Non-Small Cell Lung Cancer (NSCLC)

Addressing a Substantial Unmet Need in Metastatic NSCLC

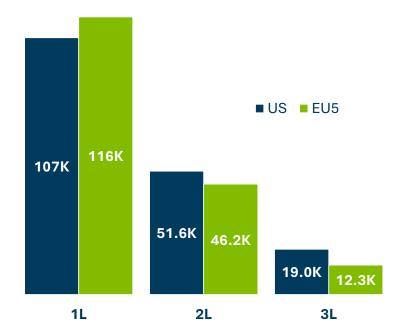
### **Iovance TIL clinical program:**

- 6 cohorts across 3 trials
- Multiple treatment regimens
- Various populations and stages of disease

127,000 annual deaths in U.S.1

Leading cause of U.S. cancer deaths, accounting for ~1 in 5 cancer-related deaths<sup>2</sup> 9% 5-year survival rate<sup>2</sup> and real-world overall survival <6 months<sup>3</sup> in U.S.

### **NSCLC Drug-Treated Population in 2022** Stage IV (US and EU5)4



Abbreviations: EU5=France, Germany, Italy, Spain and United Kingdom; 1L=first line therapy, 2L=second line therapy, 3L=third line therapy, 4L=fourth line therapy; mOS=median overall survival

<sup>1.</sup> National Cancer Institute Surveillance, Epidemiology and End Results (SEER) Program. 2023 Estimates. https://seer.cancer.gov/accessed May 2023

<sup>3.</sup> National Cancer Database, NSCLC survival from >1 million patients assessed. Lou Y et al. Survival trends among non-small-cell lung cancer patients over a decade: impact of initial therapy at academic centers. Cancer Med. 2018.

<sup>4.</sup> Clarivate DRG Disease Landscape (2021)

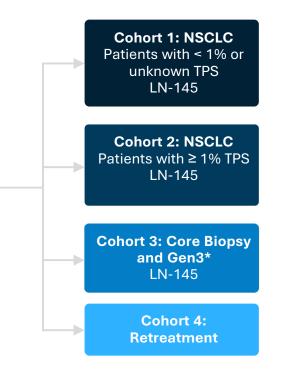
### **IOV-LUN-202 Trial Design**

Phase 2 Multicenter Study of LN-145<sup>†</sup> in Patients Post-Anti-PD-1 NSCLC (NCT04614103)

### **Patient Population**

Unresectable or metastatic NSCLC with progression on or after prior anti-PD-1 treatment and chemotherapy

40+ sites active in US, Canada, Europe



IOV-LUN-202 is designed to enroll patients with advanced NSCLC with a high unmet medical need, but limited prior lines of therapy post anti-PD-1 treatment

### **Endpoints**

- Primary: ORR by IRC
- Secondary: Safety

<sup>\*</sup>Cohort 3 patients unable to undergo surgical harvest, TIL grown from core biopsy. †Gen 2 TIL product.

Abbreviations: Anti-PD-1, anti-programmed cell death inhibitor; IRC, independent review committee; NSCLC, non-small-cell lung cancer; ORR, objective response rate; TPS, tumor proportion score.

# Preliminary Clinical Results for IOV-LUN-202 Cohorts 1 and 2

All Patients Progressed on or After Anti-PD-1 Therapy and Chemotherapy

	<b>Cohort 1 + 2</b> (n=23) <sup>2</sup>
Objective Response Rate, n (%) <sup>1</sup>	6 (26.1)
(95% CI)	(10.2, 48.4)
Best overall response, n (%)	
CR	1 (4.3)
PR	5 (21.7)
SD	13 (56.5)
PD	2 (8.7)
NE	2 (8.7)

TEAEs were consistent with the underlying disease and known AE profiles of NMA-LD and IL-2

**IOVANCE** (

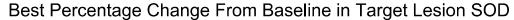
<sup>1.</sup> Data cut: July 6, 2023. Responses were assessed by investigator.

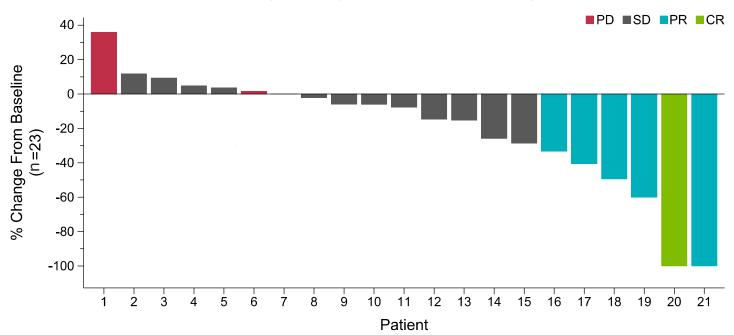
<sup>2.</sup> Patients who have progressed on or after chemotherapy and anti-PD-1 therapy for advanced (unresectable or metastatic) NSCLC without EGFR, ROS or ALK genomic mutations and had received at least one line of an FDA-approved targeted therapy if indicated by other actionable tumor mutations.

Abbreviations: AE, adverse event; CI, confidence interval; CR, complete response; ICI, immune checkpoint inhibitor; NE, not evaluable; NMA-LD, non-myeloablative lymphodepletion; NSCLC, non-smallcell lung cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; TEAE, treatment-emergent AE.

# Preliminary Clinical Results for IOV-LUN-202 Cohorts 1 and 2

Objective Response Rate of 26.1% by RECIST 1.1, Regardless of PD-L1 Status

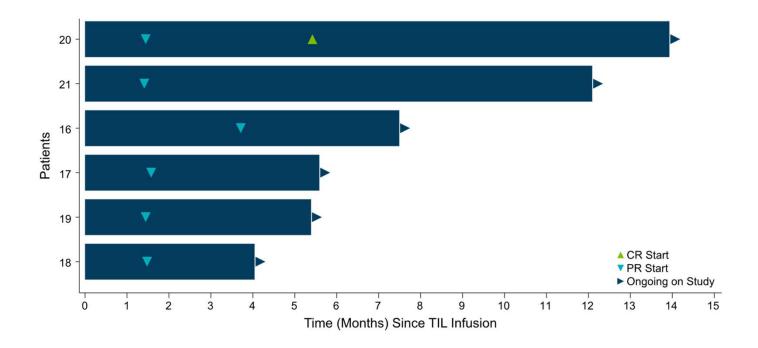




Data cut: July 6, 2023. 21 evaluable patients for response. Abbreviations: CR, complete response; NSCLC, non-small-cell lung cancer; PR, partial response; SD=stable disease; SOD, sum of diameters; TPS, tumor proportion score.

# Preliminary Clinical Results for IOV-LUN-202 Cohorts 1 and 2

All Responses Remain Ongoing at Time of Data Cut



Data cut: July 6, 2023.

A bar is presented for each patient starting from date of LN-145 infusion up to date of new anti-cancer therapy, end of assessment, death, or data cutoff date, whichever occurs earlier. Abbreviations: CR, complete response; DOR, duration of response; NSCLC, non-small-cell lung cancer; PR, partial response.

### Preliminary Clinical Results in ICI Naïve NSCLC

IOV-COM-202 Cohort 3A (TIL+pembrolizumab, n=17)

Clinical Subset	ORR, n (%)
Treatment Naïve	4/5 (80)
Post-Chemotherapy	3/7 (43)
Treatment Naïve OR Post- Chemotherapy	7/12 (58)
EGFR <sup>WT</sup> , PD-L1 Negative	4/8 (50)
EGFR-Mutant, after prior EGFR-TKI	1/5 (20)

### **Clinical Activity**

- 8/17 patients had a confirmed objective response per RECIST 1.1 (2 CRs and 6 PRs)
- Responses observed regardless of PD-L1 status
- Safety consistent with lovance TIL combination studies
- Results support the design of a subsequent potential registrational trial

### **Regulatory Strategy**

- Meet with FDA to discuss a frontline registration trial in treatment naïve EGFR<sup>WT</sup> NSCLC patients:
  - Goal to improve frontline NSCLC therapy by adding TIL maintenance therapy to standard-of-care pembrolizumab and chemotherapy, administered after completion of the initial chemo/immunotherapy
  - Seek regulatory alignment regarding the frontline NSCLC trial as the confirmatory study for accelerated approval in post anti-PD-1 NSCLC

Abbreviations: CR, complete response; EGFR<sup>WT</sup>, wild-type epidermal growth factor receptor; ICI, immune checkpoint inhibitor; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD-1, Programmed cell death protein 1; PD-L1, Programmed death-ligand 1; pembro, pembrolizumab; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; TIL, tumor infiltrating lymphocytes; TKI, tyrosine kinase inhibitor; WT, wild-type

IOV-COM-202 COHORT 3A NSCLC COMBINATION (TIL+PEMBROLIZUMAB), WCLC ORAL PRESENTATION (JUNE 26, 2023 DATA CUT)

# Time to Response for Confirmed Responders (n=8)

Durable Responses Observed, Including 3 Ongoing Responders with EGFRWT Disease, at a Median Study Follow up of 18.2 Months

Subgroup	Pt	PD-L1 TPS (%) <sup>a</sup>	Mutation Status <sup>b</sup>	BOR on Study	
	3A-02 <sup>c</sup>	<1	None detected	PR	▲ CR start
Treatment-	3A-04	≥50	KRAS G12V mutated	PR	PR start Ongoing on Study
naïve	3A-17	≥50	KRAS G12V mutated	PR	Progression  Pembrolizumab
	3A-10	≥50	None detected	PR	
	3A-11	<1	None detected <sup>d</sup>	PR	•
Post- chemotherapy	3A-13	<1	None detected <sup>e</sup>	CR	• • • •
500 50	3A-09	<1	NTRK gene fusion	PR	• • • • •
EGFR-mutated post-TKI	3A-14	1-49	EGFR mutated	CR	• 🗥 • • • • • • • • • • • • • • • • • •
					0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
					Time (Months) Since LN-145 Infusion

#### Pembrolizumab + platinum doublet benchmarks<sup>f</sup>

#### **NSQ NSCLC**

- mDOR 11.2 months
- ORR 48%
- (KEYNOTE-189)

#### SO NSCLC

- mDOR 7.2 months
- ORR 58%
- (KEYNOTE-407)

Data cut: June 26, 2023.

A bar is presented for each patient starting from date of LN-145 infusion up to date of new anti-cancer therapy, end of assessment, death, or data cutoff date, whichever occurs earlier. a. As adjudicated between site-reported and central-laboratory data; b. The following genes were tested: BRAF, EGFR, ALK, ROS1, KRAS, and NTRK; c. Patient received prior neoadjuvant chemoradiotherapy; d. ROS1, NTRK not assessed; e. NTRK not assessed; f.Kevtruda USPI

Abbreviations: BOR, best overall response; CR, complete response; mDOR, median duration of response; NSCLC, non-small-cell lung cancer; NSO, nonsquamous; platinum doublet, pemetrexed and cisplatin or carboplatin; ORR, objective response rate; PD-L1, programmed death ligand 1; PR, partial response; Pt, patient; SQ, squamous; TKI, tyrosine kinase inhibitor; TPS, tumor proportion score; WT, wild-type

# **Moving TIL Therapy into Relevant Lines of Therapy in NSCLC**

COM-202 Cohort 3A (TIL+pembrolizumab)

COM-202 Cohort 3C (TIL+nivolumab/ipilimumab)

GM1-201 Cohort 2 IOV-4001 (PD1-KO TIL)

(TIL mono)

**Current Standard of Care** 

			1L Th	erapy	2L Therapy		3L Therapy		4L Therapy			
SOC IOVA Trial SOC		SOC	IOVA	Trial	SOC	IOVA Trial		soc	IOVA Trial			
Advanced or metastatic NSCLC, no prior systemic therapy	ıtation (-)	PD-L1 ≥50%	Anti-PD-1 Mono <i>ORR</i> 39-45% <sup>1</sup>	COM-202 Cohort 3A	Chemo Doublet		1-202 ort 3C	Docetaxel or Docetaxel + Ramucirumab <i>ORR</i> 9-23% <sup>2</sup>	LUN-202 Cohorts 1-3	GM1-201		GM1-201 Cohort 2*
	Driver mutation (-)	PD-L1 0-49%	Anti-PD-1 + Chemo ORR 48-58% <sup>1</sup>		Docetaxel or Docetaxel + Ramucirumab ORR 9-23% <sup>2</sup>	LUN-202 Cohorts 1-3	GM1-201 Cohort 2*					
	rtation (+)	Other actionable mutations	TKI		Anti-PD-1 +Chemo <i>ORR 48-58%</i> <sup>1</sup>	COM	COM-202	Docetaxel or Docetaxel +		Cohort 2*		
	Driver mutation (+)	EGFR ALK ROS	1(-3) L TKI		Chemo ORR 17-32% <sup>3</sup>	Cohort 3.	ort 3A	Ramucirumab ORR 9-23% <sup>2</sup>	COM-202 Cohort 3A			

Abbreviations: L=line; NSCLC=non-small cell lung cancer PD-1=programmed cell death protein-1; TIL=tumor infiltrating lymphocytes; TKI=tyrosine kinase inhibitor \* GM1-201 Cohort 2 population is comparable to completed COM-202 Cohort 3B 1. KEYTRUDA USPI; 2. CYRAMZA USPI; Brahmer et al., NEJM 2015; Borghaei et al., NEJM 2015; Herbst et al., Lancet 2016; Rittmeyer et al., Lancet 2017; 3. Park et al., Cancer Res Treat 2015; Yoshida et al., Lung Cancer 2017

IOVANCE 32

Patient Populations

# Phase 1/2 Open-Label First-in-Human Study: IOV-GM1-201

Genetically Modified, PD-1 Inactivated TIL Therapy IOV-4001 in Previously Treated Metastatic Melanoma and NSCLC (NCT05361174)

# Patient Population

Adults with unresectable or metastatic melanoma or advanced NSCLC

N = 53

Cohort 1: Unresectable or metastatic melanoma
Post-anti-PD-1/L1, post-BRAF/MEK inhibitor in patients with BRAF mutations

# Cohort 2: Stage III or IV NSCLC

Post-anti-PD-1/L1 or post targeted therapy and either chemotherapy or anti-PD-1/L1

### **Endpoints**

- Phase 1: Safety
- Phase 2: Objective Response Rate (ORR) per RECIST v1.1 as assessed by the investigator
- Secondary endpoints include complete response (CR) rate, duration of response (DOR), disease control rate (DCR), progression free survival (PFS), overall survival (OS), safety and tolerability, feasibility

### **Study Updates**

• 3Q22: first patient treated

# Launch Preparation



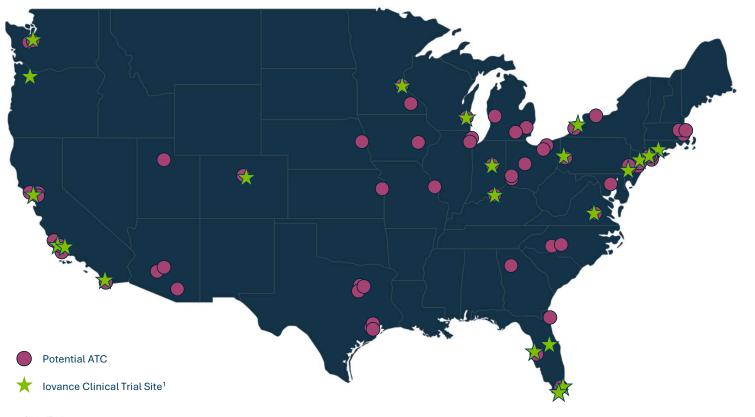
# *i*CTC Designed for High-Volume TIL Manufacturing and Flexibility

- Core suites: TIL commercial manufacturing
- Flexible suites: clinical supply, pipeline expansion and advanced manufacturing
- Integrated quality control, supply chain and IT systems
- 100+ employees with additional staffing into launch and beyond
- iCTC supplemented with external CDMO manufacturing capacity





# **Targeting Potential Authorized Treatment Centers (ATCs)**



### **Targeting Considerations**

- Patient volume
- NCCN status, KOLs
- Existing cell therapy / BMT
- Inpatient capacity
- Iovance clinical trial

#### **Drive Demand**

- Top account prioritization
- Community referrals

1. ClinicalTrials.gov

Abbreviations: NCCN=National Comprehensive Cancer Network; KOL=Key Opinion Leaders; BMT=Bone Marrow Transplant

# Hospital Bed Capacity Supports Broad Lifileucel Adoption at ATCs

HHS data and lovance onboarding assessments reinforce ample oncology beds

#### Average Beds per Target ATC<sup>1</sup>



#### **Hospital Bed Capacity**

- HHS data reinforce sufficient overall bed availability at target ATCs<sup>1</sup>
  - Average of ~ 91 available beds per target ATC
- Target ATCs report sufficient oncology bed availability for anticipated lifileucel demand<sup>2</sup>
  - Average of ~25 available beds per target ATC per month suitable for lifileucel patients
  - Multi-disciplinary teams of clinicians and hospital administrators invest significant resources to build TIL cell therapy service lines
- Over half of target ATCs report ongoing or planned investments that will increase inpatient capacity<sup>3</sup>

Note: Oncology/cell therapy beds are a subset of the total available hospital beds

Abbreviations: ATC=Authorized Treatment Center; HHS=U.S. Department of Health and Human Services; TIL=tumor infiltrating lymphocytes

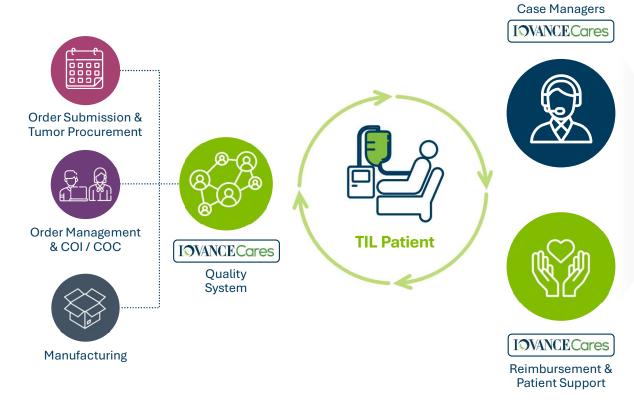
<sup>1.</sup> HHS, Daily avg bed capacity and utilization at target centers (all types of hospital beds): Jan 2022-Mar 2023, https://healthdata.gov/Hospital/COVID-19-Reported-Patient-Impact-and-Hospital-Capa/anag-cw7u

<sup>2.</sup> lovance primary market research, 2022-2023

<sup>3.</sup> lovance secondary market research, 2023

# **Supporting Providers & Patients: IovanceCares™**

Dedicated



#### **Customer-Centric**

- Patient management ecosystem
- Proprietary COI/COC
- Treatment center quality program

#### **Patient-Centric**

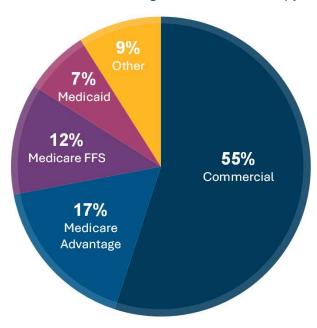
- Dedicated case managers
- Reimbursement support
- Patient support

## **Enabling Market Access**

Lifileucel is included in established cell therapy coverage and payment methodologies

#### Metastatic Melanoma Payer Mix<sup>1</sup>

All Treatment Settings and Lines of Therapy



#### **Anticipated Access**

- · Engagement with Commercial and Medicare payers responsible for ~90% of covered lives
- Payers reimburse hospitals through established inpatient payment methodologies

#### **Coding, Coverage and Payment**

- ICD-10 PCS codes issued
- Expect payer coverage expected to be similar to CARTs
- DRG-018 approved, NTAP in-process

<sup>1.</sup> Metastatic Melanoma Insurance Claims Analysis, TIL-eligible patients treated in the ATC setting(1/1/2018 -6/30/2021). Medicaid is 6% Medicaid Advantage and 1% Medicaid Fee-For-Service; For the 12% Medicare FFS lives, 11 PPS-exempt hospitals are reimbursed by Medicare FFS on a cost-basis (~4%), with the remaining Medicare FFS lives (~8%) reimbursed under DRG-018 payment methodology. Abbreviations: FFS=Fee-For-Service; ICD-10 PCS=International Classification of Diseases, 10th Revision, Procedure Coding System; NTAP = New Technology Add-on Payment





### **Potential Market for Cervical Cancer**

Addressing a Defined Unmet Need in Cervical Cancer Following Chemo and Anti-PD-1

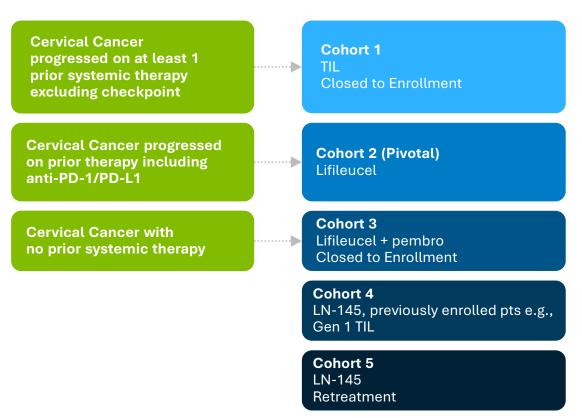


Available Care	ORR	Median DOR
Frontline:		
Combination chemotherapy + bevacizumab <sup>3</sup>	48%	Not reported
Pembrolizumab + chemo + bevacizumab (PD-L1+ patients) <sup>4</sup>	68.1%	18 months
Second Line/Third Line:		
Pembrolizumab post-chemo (PD-L1+ patients) <sup>5</sup>	14.3%	Not reached
Tisotumab vedotin-tftv post-chemo <sup>6</sup>	24%	8.3 months
Chemotherapy in second line/third line <sup>7,8</sup>	3.4%–15%	4.4 months <sup>8</sup>

<sup>1.</sup> Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries, CA Cancer J Clin., May 2021; 2. National Cancer Institute Surveillance, Epidemiology and End Results (SEER) Program. 2023 Estimates. https://seer.cancer.gov accessed May 2023; 3. Tewari, et al., NEJM 2014; 4. Colombo et al., NEJM 2021; 5. Keytruda USPI; 6. Coleman et al., Lancet Oncol 2021; 7. McLachlan et al., Clin Oncol 2017; 8. Miller et al., Gynecol Oncol 2008

# Pivotal Phase 2 Trial of Lifileucel in Recurrent, Metastatic or Persistent Cervical Carcinoma (NCT03108495)

Regulatory Strategy Focused on Significant Unmet Need in Cervical Cancer Following Chemo and Anti-PD-1 Therapy



#### **Endpoints (Pivotal Cohort 2)**

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

#### **Study Updates**

- 4021: initial Cohort 3 data at SITC<sup>1</sup>
- 3Q22: Expanded Cohort 2 to support regulatory submissions

1. O'Malley et al., SITC 2021





# **Trailblazing Next-Generation TIL Programs**









Genetically modify TIL

Optimize TIL composition

Next-generation processes

Expand TIL into new regimens

Cellectis gene-editing TALEN® collaboration<sup>1,2</sup>

PD-1 and other immune checkpoint targets (single and multiple knockouts)

Cytokine-tethered TILs

PD-1+ selected TIL

CD39/69 double negative TILs<sup>3</sup>

Gen 3 (16-day) process

Core biopsy

IOV-3001 IL-2 analog licensed from Novartis: IND enabling studies

<sup>1.</sup> Ritthipichai et al., ESMO 2020

<sup>2.</sup> Natarajan, et al., AACR 2022

<sup>3.</sup> Cubas et al., ESMO IO 2021

# Corporate Summary & Milestones



# Well-Capitalized in Pursuit of TIL Commercialization

June 30, 2023	(in millions)
Cash, cash equivalents, investments, restricted cash	\$317.3 <sup>1</sup>
Common shares outstanding	224.7
Preferred shares outstanding	2.9 <sup>2</sup>
Stock options and restricted stock units outstanding	23.6

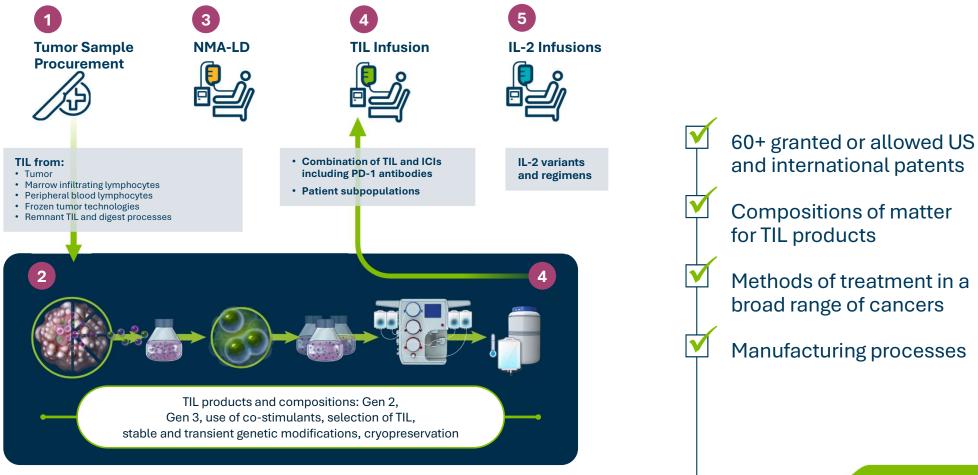
#### Cash runway is sufficient into the end of 2024\*

\*Includes estimated proceeds of lovance's public offering of 23,000,000 shares of common stock at a price of \$7.50 per share which closed July 13, 2023. The gross proceeds from the offering, before deducting the underwriting discounts and commissions and other estimated offering expenses payable by lovance, are \$172.5 million

Includes Restricted Cash of \$6.4 million as of March 31, 2023.

Preferred shares are shown on an as-converted basis

## **Broad, Iovance-Owned IP Around TIL Therapy**



## **Corporate Highlights**

Pioneering a Transformational Approach to Cure Cancer

# Large Market Opportunity in High Unmet Need Cancers

- Initial focus in post-ICI solid tumors
- Expansion into combinations, earlier lines of therapy and genetic modifications
- Key late-stage trials in melanoma, NSCLC and cervical cancer
- First-in-human trial of genetically modified TIL, PD-1 inactivated

Potential for First Cell Therapy Approved for Solid Tumors

- BLA filed, 25 Nov 2023
   PDUFA for lifileucel in advanced melanoma with Priority Review and RMAT
- TILVANCE-301 Phase 3 frontline advanced melanoma confirmatory trial with FTD
- Defined registration strategy in NSCLC and cervical cancer (BTD)

# Efficient and Scalable Proprietary Manufacturing Facility

- Iovance Cell Therapy Center (iCTC) in-house manufacturing
- Additional capacity with contract manufacturers
- Rapid 22-day Gen 2 manufacturing with 90%+ success rate
- >600 patients treated with lovance proprietary process



- Fully integrated company
- Experienced crossfunctional cell therapy team
- Partnering with leading U.S. cancer centers to develop TIL service-line capabilities
- lovanceCares<sup>™</sup> proprietary platform
- Proleukin® integration

# **Anticipated 2023 Milestones**

REGULATORY	BLA: Complete rolling BLA submission for lifileucel in post-anti-PD-1 advanced melanoma in Q1 2023
	BLA: Obtain FDA approval
PIPELINE	Melanoma: enroll patients in frontline advanced melanoma Phase 3 confirmatory trial
	NSCLC: report data and continue to enroll IOV-LUN-202, IOV-COM-202, IOV-GM1-201 trials
	Cervical: enroll additional patients in registrational Cohort 2
	PD-1 inactivated TIL (IOV-4001): complete Phase 1 safety and proceed to Phase 2 of IOV-GM1-201 trial
	Research: advance new products toward clinic, including additional genetically-modified TIL therapies
MANUFACTURING	Execute GMP commercial readiness activities to support BLA approval and supply lifileucel at launch
COMMERCIAL	Prepare for and execute commercial launch
	Close transaction and successfully integrate Proleukin® business



Thank You

ADVANCING IMMUNO-ONCOLOGY

© 2023 Jovance Biotheraneutics Inc