IOVANCE BIOTHERAPEUTICS

Corporate Overview

November 2024

ADVANCING IMMUNO-ONCOLOGY

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 (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,” “can,” “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 presentation are made as of the date of this presentation, 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 U.S. 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: the risks related to our ability to successfully commercialize our products, including Amtagvi, for which we have obtained U.S. Food and Drug Administration (“FDA”) approval, and Proleukin, for which we have obtained FDA and European Medicines Agency (“EMA”) approval; the risk that the EMA or other ex-U.S. regulatory authorities may not approve or may delay approval for our marketing authorization application submission for lifileucel in metastatic melanoma; the acceptance by the market of our products, including Amtagvi and Proleukin, and their potential pricing and/or reimbursement by payors, if approved (in the case of our product candidates), in the U.S. and other international markets and whether such acceptance is sufficient to support continued commercialization or development of our products, including Amtagvi and Proleukin, or product candidates, respectively; future competitive or other market factors may adversely affect the commercial potential for Amtagvi or Proleukin; the risk regarding our ability or inability to manufacture our therapies using third party manufacturers or at our own facility, including our ability to increase manufacturing capacity at such third party manufacturers and our own facility, may adversely affect our 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, including Amtagvi and Proleukin, may not generate sufficient revenue from product sales, and we may not become profitable in the near term, or at all; the risks related to the timing of and our ability to successfully develop, submit, obtain, or maintain FDA, EMA, or other regulatory authority approval of, or other action with respect to, our product candidates; whether clinical trial results from our pivotal studies and cohorts, and meetings with the FDA, EMA, or other regulatory authorities may support registrational studies and subsequent approvals by the FDA, EMA, or other regulatory authorities, including the risk that the planned single arm Phase 2 IOV-LUN-202 trial may not support registration; preliminary and interim clinical results, which may include efficacy and safety results, from ongoing clinical trials or cohorts 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; 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 the changing landscape of care for cervical cancer patients may impact our clinical trials in this indication; 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, EMA, or other regulatory authorities; the risk that our interpretation of the results of our clinical trials or communications with the FDA, EMA, or other regulatory authorities may differ from the interpretation of such results or communications by such regulatory authorities (including from our prior meetings with the FDA regarding our non-small cell lung cancer clinical trials); the risk that clinical data from ongoing clinical trials of Amtagvi will not continue or be repeated in ongoing or planned clinical trials or may not support regulatory approval or renewal of authorization; the risk that unanticipated expenses may decrease our estimated cash balances and forecasts and increase our estimated capital requirements; the risk that we may not be able to recognize revenue for our products; the risk that Proleukin revenues may not continue to serve as a leading indicator for Amtagvi revenues; the risks regarding our anticipated operating and financial performance, including our financial guidance and projections; the effects of global pandemic; the effects of global and domestic geopolitical factors; and other factors, including general economic conditions and regulatory developments, not within our control. Any financial guidance provided in this presentation assumes the following: no material change in our ability to manufacture our products; no material change in payor coverage; no material change in revenue recognition policies; no new business development transactions not completed as of the period covered by this presentation; and no material fluctuation in exchange rates.

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

2
Approved Products

AMTAGVI™ (lifileucel) Suspension for IV infusion

PROLEUKIN® (aldesleukin)

Commercial Launch

>140 Amtagvi Patients Treated as of 11/7/24

>250M U.S. patient lives covered under payer policies/plans

56 Authorized Treatment Centers as of 11/7/24

>70K Global Advanced Melanoma Treatment Opportunity

Pipeline

2 Ex-U.S. Regulatory Filings Submitted[1]

>700 Patients Treated in Clinical Studies

10 Clinical Trials[2]

DESIGNATIONS:

3 Fast Track **1** BTD **1** RMAT

People & Assets

~$404M
Cash as of 9/30/24

$58.6M
3Q24 Revenue

$160 - $165M
FY24 Product Revenue Guidance

>750
Employees

1. EU & UK 2. Iovance sponsored clinical trials, does not include expanded access or investigator sponsored studies.
Abbreviations: BTD=Breakthrough Therapy Designation; FDA=U.S. Food and Drug Administration; RMAT=Regenerative Medicine Advanced Therapy Designation

Iovance Solid Tumor Portfolio Highlights

		INDICATION & TREATMENT SETTING	PHASE 1	PHASE 2	PHASE 3	APPROVED
Commercial	AMTAGVI™ (lifileucel) Suspension for IV infusion	Post-anti-PD-1 advanced melanoma (U.S.) EMA & UK submitted; Canada submission planned 2H24				
	PROLEUKIN® (aldesleukin) Recombinant IL-2	Amtagvi treatment regimen (U.S.) Advanced melanoma, renal cell carcinoma (U.S., ex-U.S.)				
Label Expansion Opportunities						
Registration-Directed	Lifileucel + pembrolizumab	Frontline advanced melanoma	**TILVANCE-301 Phase 3 (FTD, Confirmatory)**			
	Lifileucel	Post-chemo & anti-PD-1 advanced NSCLC	**IOV-LUN-202: Cohorts 1&2**			
Lifileucel Pipeline	Lifileucel	Post-chemo & anti-PD-1 endometrial cancer	**IOV-END-201: Cohorts 1&2**			
	Lifileucel, Lifileucel + ICI	1-4L ICI-naïve & post-anti-PD1 advanced NSCLC	**IOV-COM-202: Cohorts 3A-3D***			
	Lifileucel + ICI	ICI-naïve advanced melanoma	**IOV-COM-202: Cohorts 1A, 1D***			
	Lifileucel core biopsy	2L post-chemo & post-anti-PD-1 advanced NSCLC	**IOV-LUN-202: Cohort 3**			
Next-Generation Products	PD-1 Inactivated TIL (IOV-4001)	Post anti-PD1 advanced melanoma	**IOV-GM1-201: Cohort 1**			
	PD-1 Inactivated TIL (IOV-4001)	2-4L incl. post-anti-PD-1 advanced NSCLC	**IOV-GM1-201: Cohort 2**			
	IL-2 analog (IOV-3001)	TIL treatment regimen	**IOV-IL2-101**			
	IL-12 tethered TIL (IOV-5001)	Basket trial (planned pre-IND in 2025)	***Planned***			

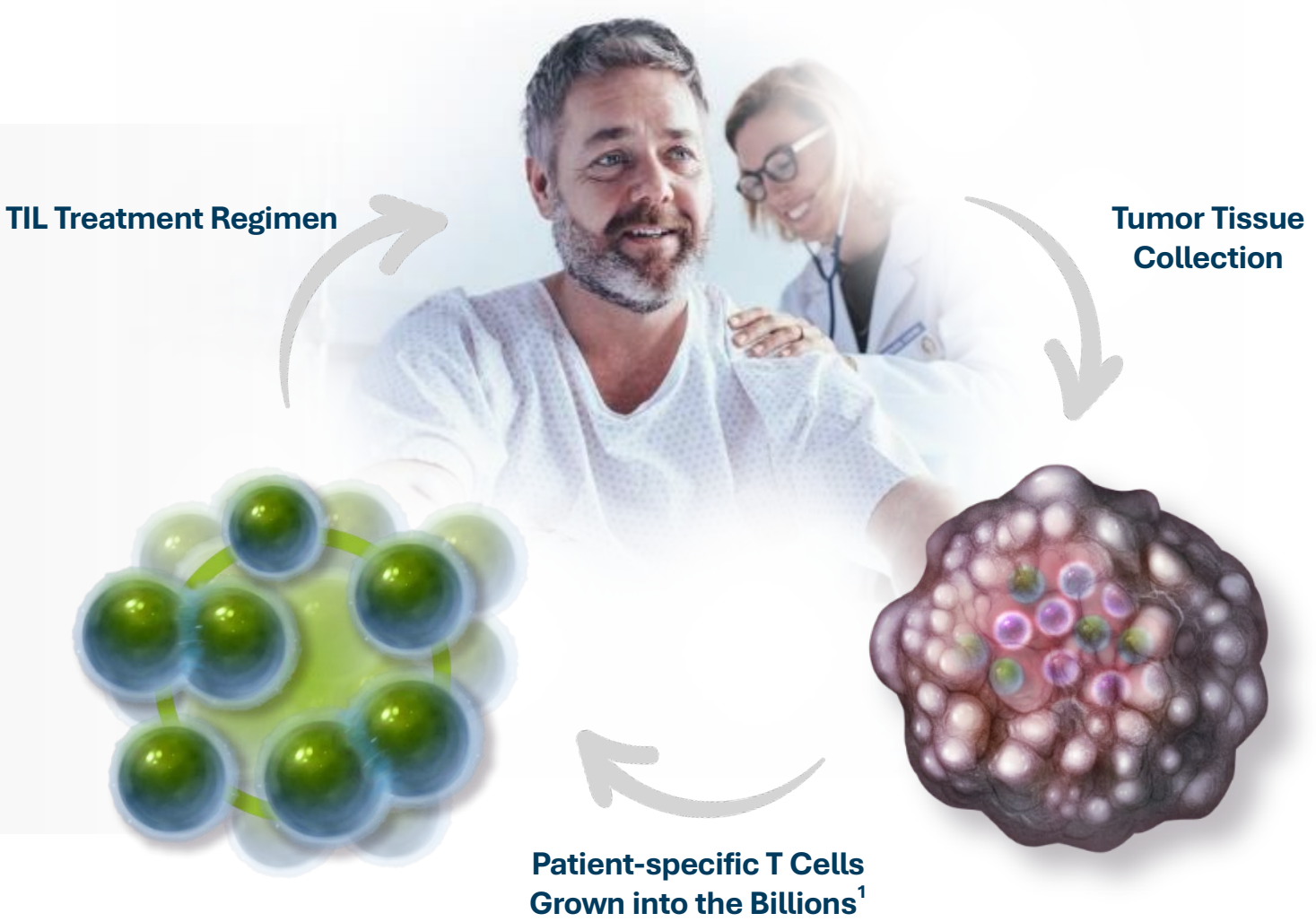
*Enrollment complete in Cohort 3B; Cohorts 1A and 3D are new planned cohorts

Abbreviations: 1L=first line; 2L=second line; 4L=fourth line; FTD=Fast Track Designation; ICI=immune checkpoint inhibitor; IL-2=interleukin 2; IL-12=interleukin 12; IND=investigational new drug application; NSCLC=non-small cell lung cancer; PD-1=programmed cell death protein-1; TIL=tumor infiltrating lymphocytes

Tumor Infiltrating Lymphocytes (TIL): Leading Cell Therapy Platform for Solid Tumors

TIL – Unique Proposed Mechanism of Action

- Individualized
- One-time therapy
- Deploys the patient's own T cells to fight cancer



1. Amtagvi USPI

Significant Market Potential in Solid Tumors and our Key Programs

91%

of all cancer cases are solid tumors[1]

1.8M

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

Expand into other indications

	U.S. Deaths[1]	Global Deaths[2]
Melanoma	8,000	59,000
Lung & Bronchus	125,000	1,800,000
Endometrial	13,000	97,000

1. National Cancer Institute Surveillance, Epidemiology and End Results (SEER) Program. 2024 Estimates. https://seer.cancer.gov (accessed May 2024)
2. World Health Organization International Agency for Research on Cancer (IARC). GLOBOCAN 2022

Significant Opportunity to Expand Advanced Melanoma Market

Annual US & Ex-US Addressable Patient Opportunity in Previously Treated Advanced Melanoma[3]

~30,000

Advanced Melanoma Overall Patient Opportunity[3]

>70,000

Earlier Treatment Settings

Geographic Footprint

	Annual Deaths[1,2]	Frontline Addressable Patients[3]
U.S.	8K	14K
Ex-U.S. Anticipated Markets	22K	27K
Total	30K	41K

Initial Ex-U.S. Regulatory Submissions:

■ Submitted ■ Planned

EU: 2Q 2024[4]

UK: 2H 2024

Canada: 2H 2024

Australia: 1H 2025

Switzerland: 2025

1H	2H	1H	2H

1. National Cancer Institute Surveillance, Epidemiology and End Results (SEER) Program. 2024 Estimates. https://seer.cancer.gov (accessed May 2024)
2. World Health Organization International Agency for Research on Cancer (IARC). GLOBOCAN 2022
3. Data on file as of September 30, 2004. Includes more than 20,000 patients initial target markets plus additional potential markets.
4. Validated August 2024

AMTAGVI™
(lifileucel) Suspension for IV infusion

First FDA-approved One-time, Individualized T cell Therapy for a Solid Tumor Cancer

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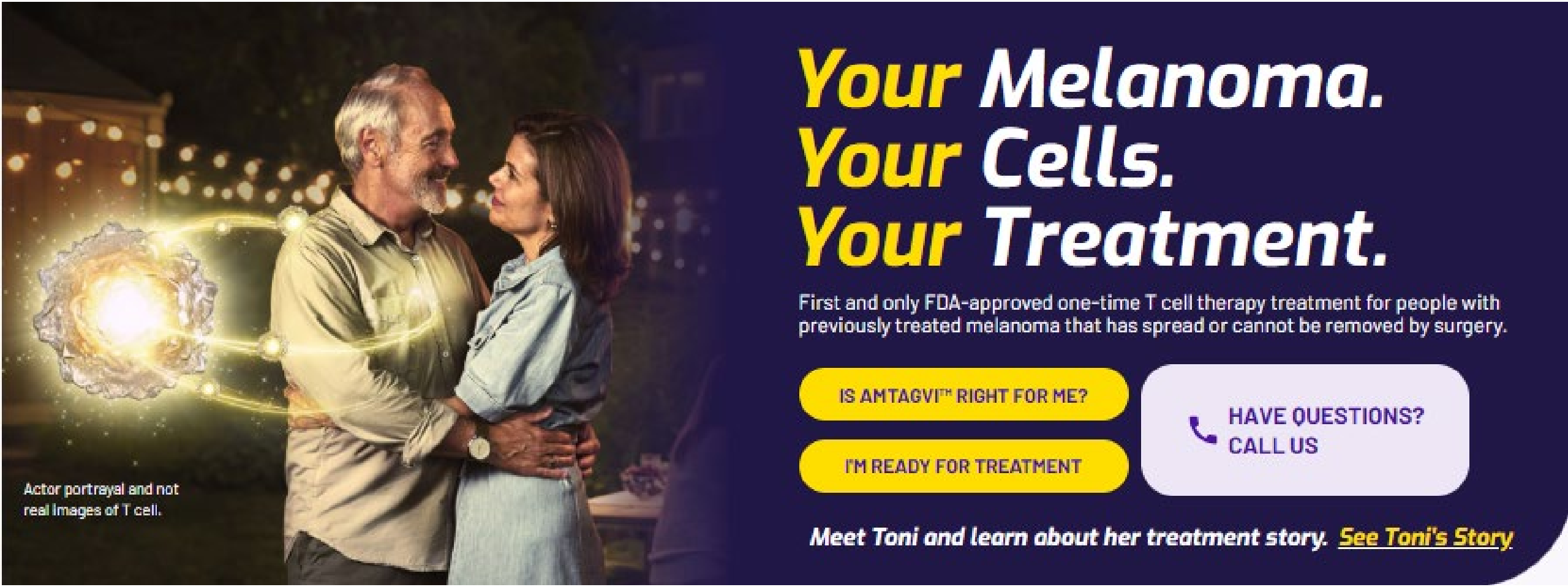
AMTAGVI™ (lifileucel) Suspension for IV infusion

Preferred second-line+ therapy in NCCN guidelines[1]



1.National Comprehensive Cancer Network® Guidelines, Melanoma: Cutaneous, Version 2.24

Amtagvi™ Delivered Deep and Durable Responses

Cohort 4 Pivotal[1] (n=73)

ORR 31.5%

(95% CI: 21.1, 43.4)

mDOR Not Reached

18.6 months follow up

(Range: 1.4+, 26.3+; 95% CI: 4.1, NR)

Supportive Pooled Data[1] (n=153)

ORR 31.4%

(95% CI: 24.1, 39.4)

mDOR Not Reached

21.5 months follow up[2]

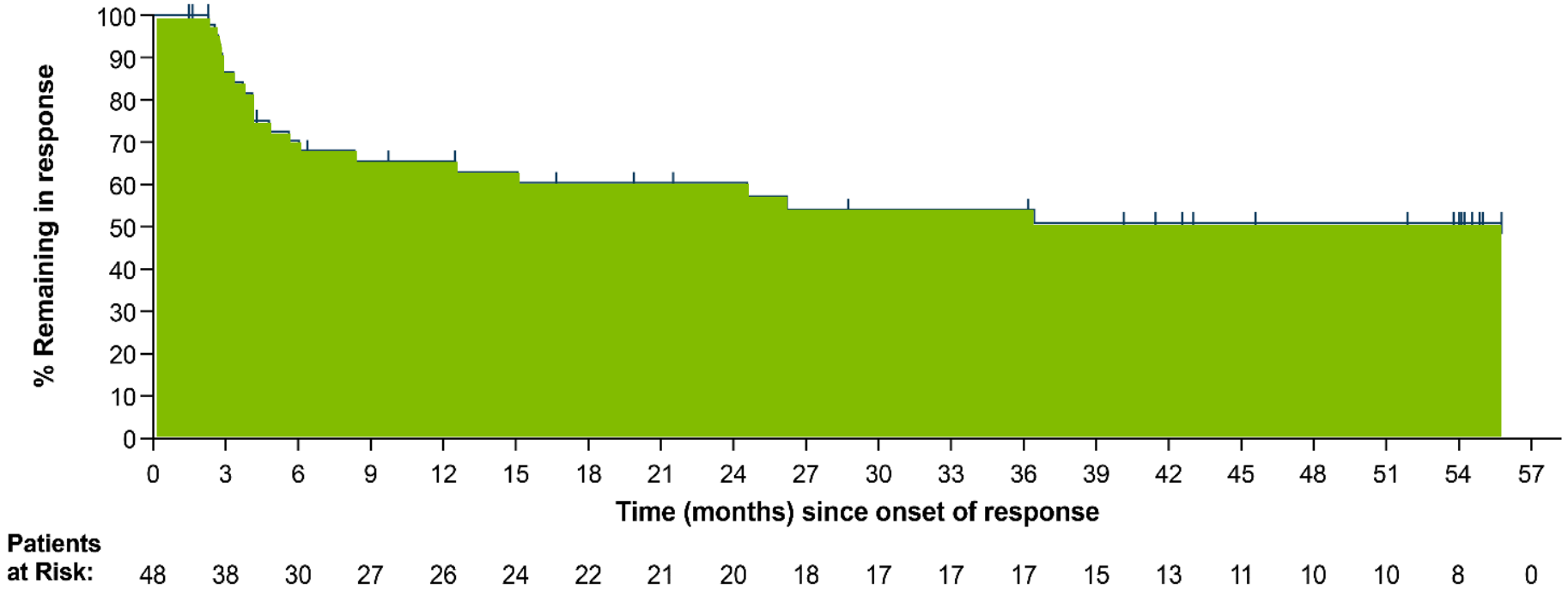
(Range: 1.4+, 45.0+)

1. C-144-01 Clinical Trial, Amtagvi USPI
2. Data on file.

Abbreviations: CI=confidence interval; mDOR=median duration of response; NR=not reached; ORR=objective response rate

Amtagvi™ Durability at 4-Years Follow Up (Pooled Analysis, n=153)

21.9% of patients were alive at 4-year follow-up



ORR

31.4%

(95% CI: 24.1, 39.4)

mDOR

Not Reached

(95% CI: 8.3, NR)

48.1 months follow-up

1. Medina et al, ESMO IO 2023

Abbreviations: CI=confidence interval; mDOR=median duration of response; NR=not reached; ORR=objective response rate

Patient

Community Practice

Primary Oncologist

ATC Medical Oncologist

Post-Regimen Follow-Up & Return to Primary Oncologist

TREATMENT

PROLEUKIN® (aldesleukin) Recombinant IL-2

Short-Course

Amtagvi™ Patient Journey

AMTAGVI™

ENROLLMENT

3-4 WEEKS

~34 DAYS

7 DAYS

Lymphodepletion

Reimbursement Approval
~3 Weeks

Scheduling Tumor Procurement
Goal: <2 weeks

Manufacturing, Release & Shipment

*Turnaround times will be reduced**

*Earlier time to treatment driven by faster reimbursement and scheduling, earlier lymphodepletion, and shorter turnaround for manufacturing/release as the launch continues

Iovance Cell Therapy Center: *i*CTC

- Built-to-suit custom facility in Navy Yard Philadelphia
- Commercial and clinical TIL therapy supply
- Expanding headcount in alignment with expected growth in demand
- Control to optimize capacity, quality & COGS

FDA-Approved Cell Therapy Manufacturing Facility Dedicated to Commercial and Clinical TIL Cell Therapies

IOVANCE BIOTHERAPEUTICS CELL THERAPY CENTER

FOYA 2022 ISPE Facility of the Year Awards
CATEGORY WINNER
Honorable Mention

COGS= cost of goods sold

Iovance Cell Therapy Center (iCTC): Capacity Expansion Plans

Pre-Approval (Complete)

100s
of patients/year

Launch Prep
in core suites for commercial

4
separate flex suites for clinical

Today (As built)

up to **2,000+**
patients/year[1]

12
core suites for commercial

4
separate flex suites for clinical

Site Expansion (In progress)[2]

5,000+
patients/year

24
core suites for commercial

4
separate flex suites for clinical

***i*CTC Campus Expansion**

10,000+
patients/year

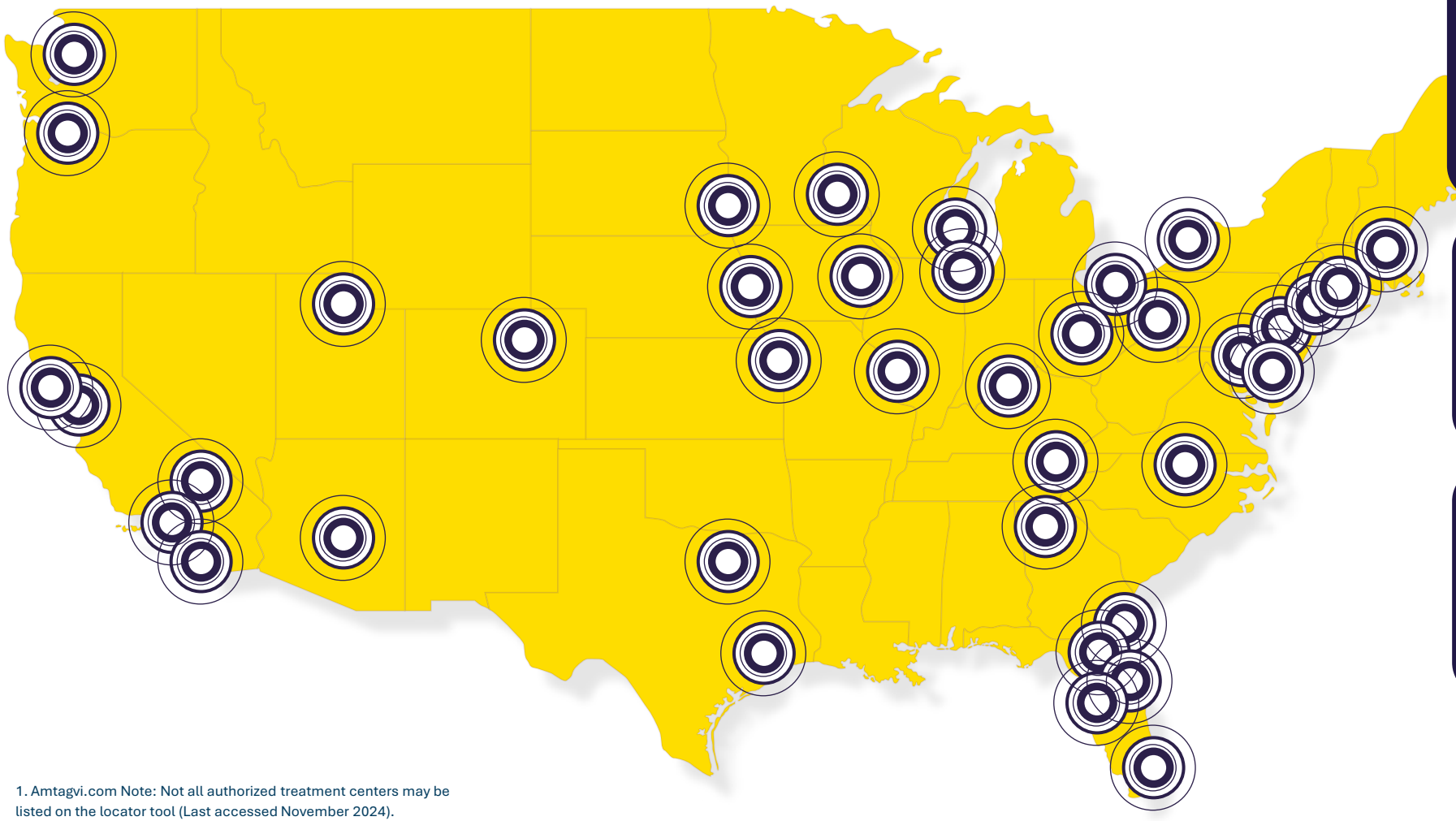
***i*CTC building expansion[3]**

Automation

1. Ongoing staffing, contract manufacturer provides flexibility for incremental additional capacity 2. Expansion within existing shell 3. Option to build on adjacent parcel

Amtagvi™ Authorized Treatment Centers (ATCs)[1]

Goal to ensure patients have geographic accessibility to ATCs



>90%

of Addressable Patients within 200 miles of an ATC

56

ATCs in November 2024

~70

ATCs by Year End

1. Amtagvi.com Note: Not all authorized treatment centers may be listed on the locator tool (Last accessed November 2024).
Abbreviations: ATC=Authorized Treatment Centers

Broad Market Access

Payer medical coverage policies consistent with Amtagvi label, clinical trials and NCCN guidelines

Data on file as of October 31, 2024.
*Plans or policies that cover Amtagvi, including pharmacy benefit managers (PBMs)
Abbreviations: NCCN = National Comprehensive Cancer Network

Amtagvi™ Expansion Plans in Advanced Melanoma

Unprecedented Rate, Depth & Durability of Responses in Frontline Advanced Melanoma

Data support rationale for TILVANCE frontline study:[1]

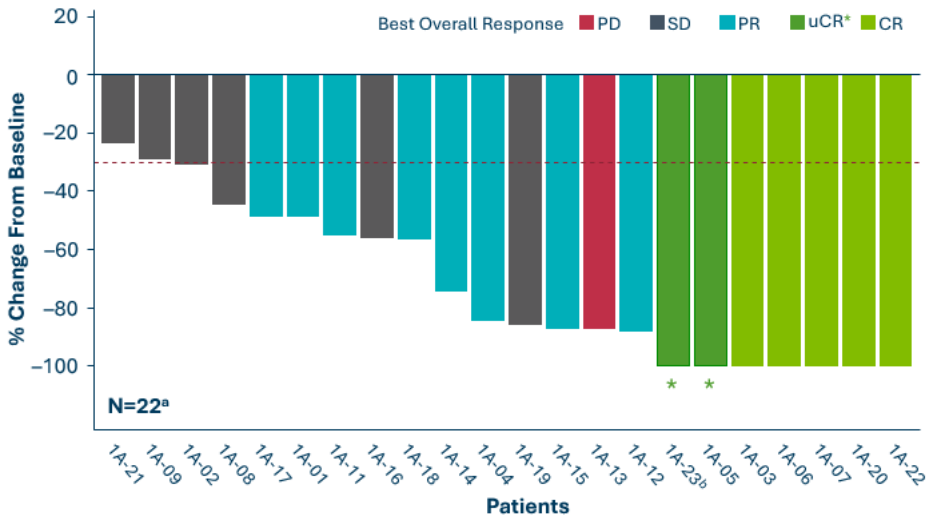
65.2%
ORR via RECIST v 1.1

30.4%
CR

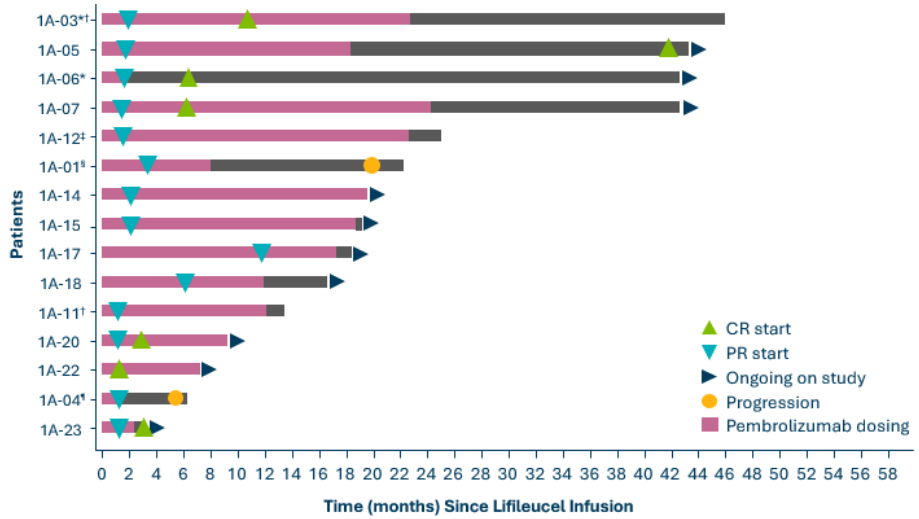
64.7%
PFS at 6 & 12 months

- Median PFS and median DOR not reached at nearly 2 years of median follow-up (median follow-up 21.7 months)
- All response-evaluable patients demonstrated regression of target lesions
- Safety consistent with underlying disease and known safety profiles of pembrolizumab, NMA-LD, lifileucel, and IL-2
- Late AEs consistent with anti-PD-1 monotherapy, differentiated from ICI combination therapies

Best Percentage Change from Baseline in Target Lesion SOD



Time to Response and Time of Efficacy Assessment for Confirmed Responders (PR or Better)



1. Thomas et al, ASCO 2024; Data on file as of May 31, 2024.

* Unconfirmed CRs, confirmed following data cut.

[A] One patient without a postdose tumor response assessment was not included. [b]Target lesion lymph node at baseline decreased by 50% is no longer pathological, and thus is shown here as -100% representing uCR. CI, confidence interval; CR, complete response; DOR, duration of response; ICI, immune checkpoint inhibitor; ORR, objective response rate; PD, progressive disease; PFS, progression free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SOD, sum of diameters; AE, adverse event; IL-2, interleukin-2; NMA-LD, nonmyeloablative lymphodepletion

TILVANCE-301 Global Phase 3 and Confirmatory Trial

Randomized, multicenter study with optional crossover to lifileucel (NCT05727904)

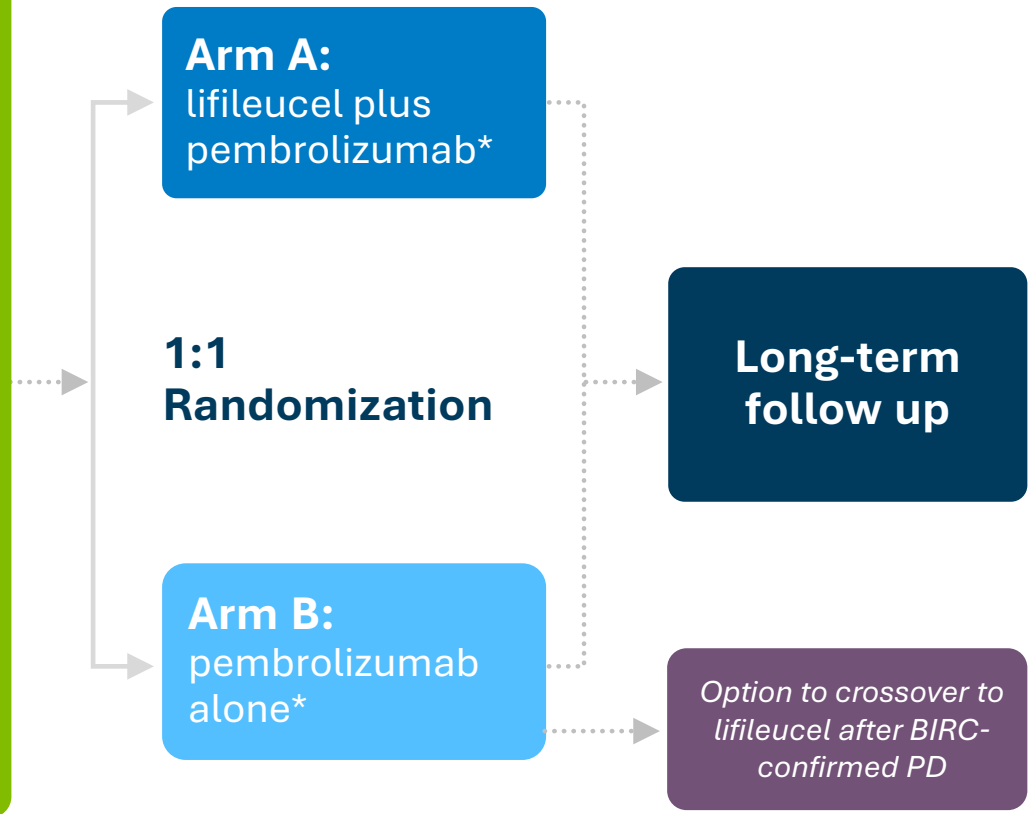
Patient Population

Unresectable or metastatic melanoma; no prior therapy for metastatic disease

N=670

48 active sites in U.S., Europe, Australia, Canada

>50 additional sites committed



Study Design with FDA Agreement

- Dual primary endpoints: ORR & PFS
- Interim analysis on ORR
- Final analysis on PFS
- Registrational for frontline melanoma
- Confirmatory for full approval of Amtagvi™ in post-anti-PD-1 melanoma
- Enrollment on track with internal projections

*Pembrolizumab in both arms is started at the same time after randomization.
Abbreviations: BIRC=blinded independent review committee; ORR=objective response rate; PD=progressive disease; PD-1=programmed cell death protein-1; PFS=progression free survival

TIL Therapy Pipeline

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Large Domestic and Global Addressable Market in Non-Small Cell Lung Cancer (NSCLC)

Cohorts investigating multiple treatment regimens and patient populations in 3 Iovance clinical trials

2L+ NSCLC Addressable Patient Population[1,2]

US: 50K

Target EU Markets: 50K

Globally (2L+): 100K

210K+ Frontline NSCLC addressable patient population in U.S. & globally[1,2]

Leading cause of U.S. cancer deaths, accounting for approx. **1 in 5** cancer-related deaths[3]

< 6 mo. Real-world overall survival (US)[4]

9% 5-yr survival rate[3]

1. Clarivate DRG Disease Landscape (2021), figures approximate
2. Data on file as of September 30, 2024, figures approximate
3. American Cancer Society, Lung Cancer. https://www.cancer.org/cancer/types/lung-cancer/about.html accessed July 2023
4. 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.

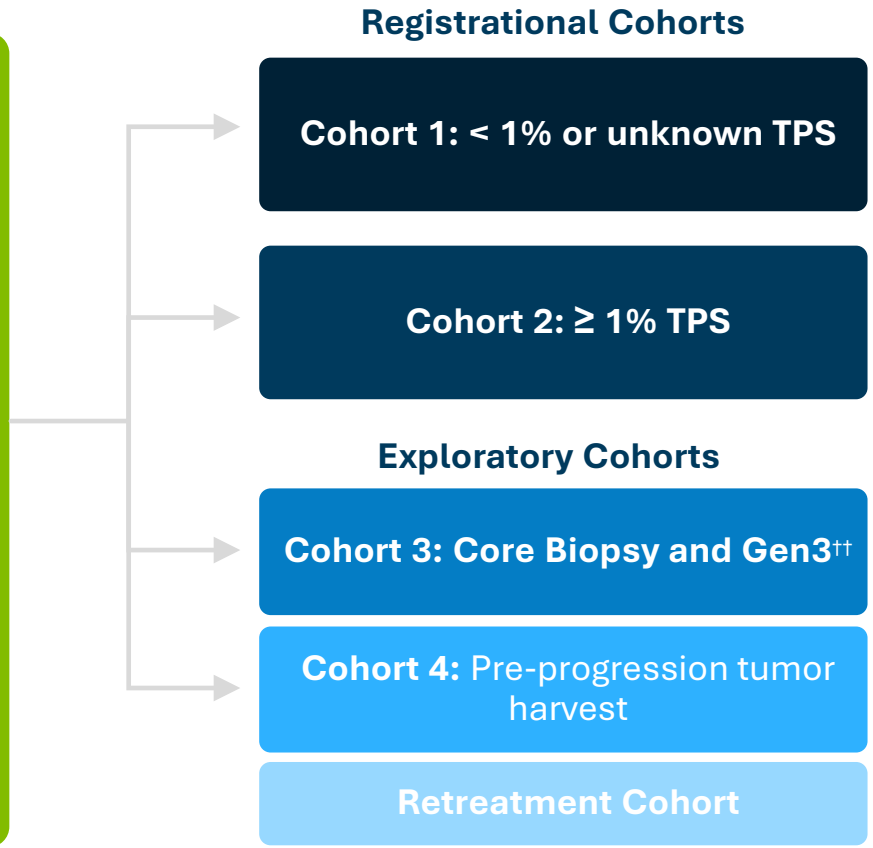
IOV-LUN-202 Registrational Trial Design

Phase 2 Multicenter Study of Lifileucel† 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

~35 sites and expanding in U.S., Canada, Europe, APAC



IOV-LUN-202 is designed to enroll patients with advanced NSCLC with a high unmet medical need, post anti-PD-1 treatment

Endpoints

- Primary: ORR by IRC
- Secondary: Safety

Data for registrational cohorts anticipated in 2025

†Gen 2 TIL product †† Cohort 3 patients unable to undergo surgical harvest, TIL grown from core biopsy
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

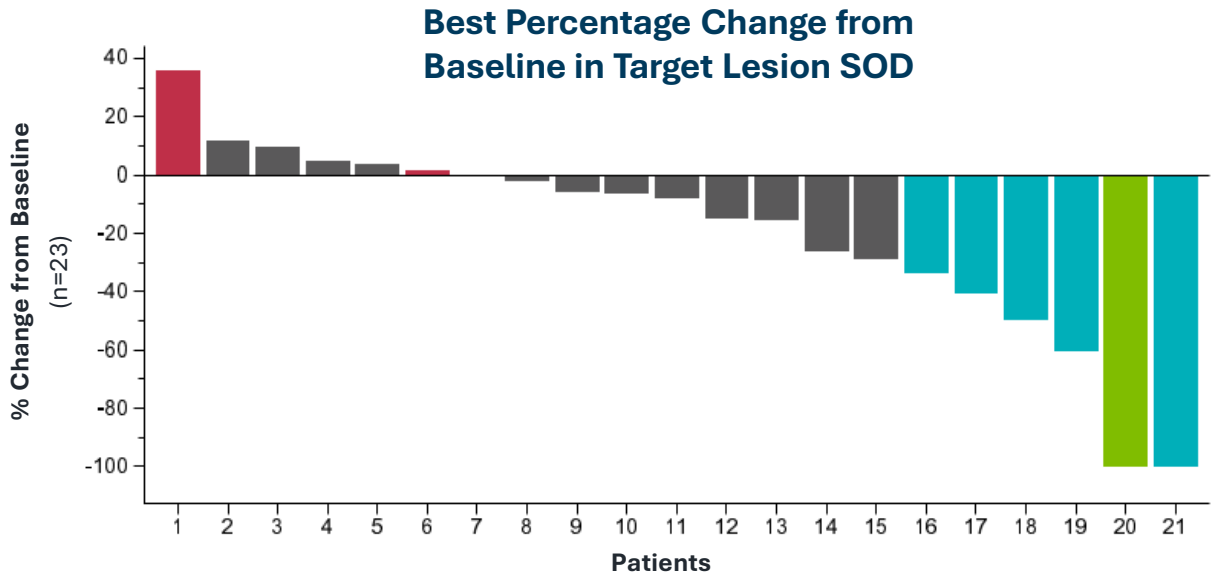
Strong Preliminary Clinical Results in Second-Line mNSCLC

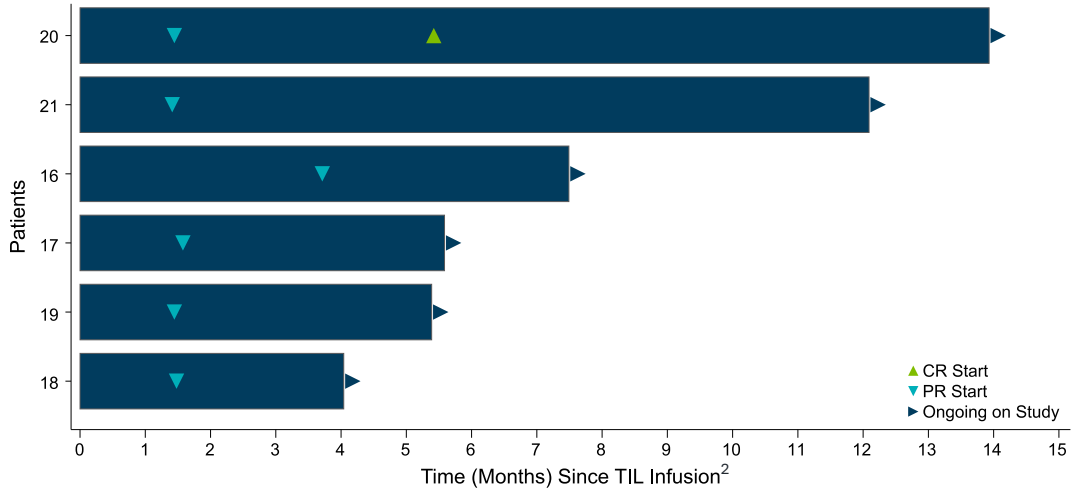
Tumor Reduction and Deep, Durable Responses in Previously Treated NSCLC, Regardless of PD-L1 Status[1]

26.1% ORR

by RECIST 1.1, Regardless of PD-L1 Status*

Duration of response >6 months for 71% of confirmed responders in the trial**





*Data cut: July 6, 2023. 21 evaluable patients for response. Responses were assessed by investigator; **Updated analysis in November 2023 showed additional ongoing responses (not indicated in above charts)
1. 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.
2. A bar is presented for each patient starting from date of Lifileucel infusion up to date of new anti-cancer therapy, end of assessment, death, or data cutoff date, whichever occurs earlier.
Abbreviations: AE, adverse event; CI, confidence interval; CR, complete response; DOR, duration of response; ICI, immune checkpoint inhibitor; NE, not evaluable; NMA-LD, non-myeloablative lymphodepletion; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; SOD, sum of diameters; TEAE, treatment-emergent AE; TPS, tumor proportion score.

Cohort 3A Results Support Adding TIL Therapy to Frontline NSCLC[1]

PD-L1 negative, EGFR^{WT} subgroup has a high unmet need[2]

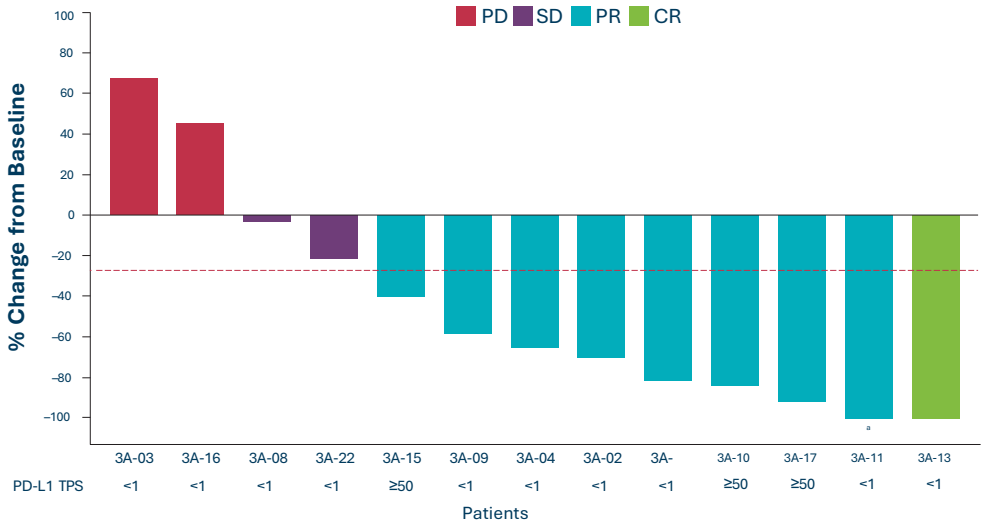
64.3% ORR EGFR^{WT}

→ **54.5% ORR** EGFR ^{WT} PD-L1 Negative
by RECIST 1.1

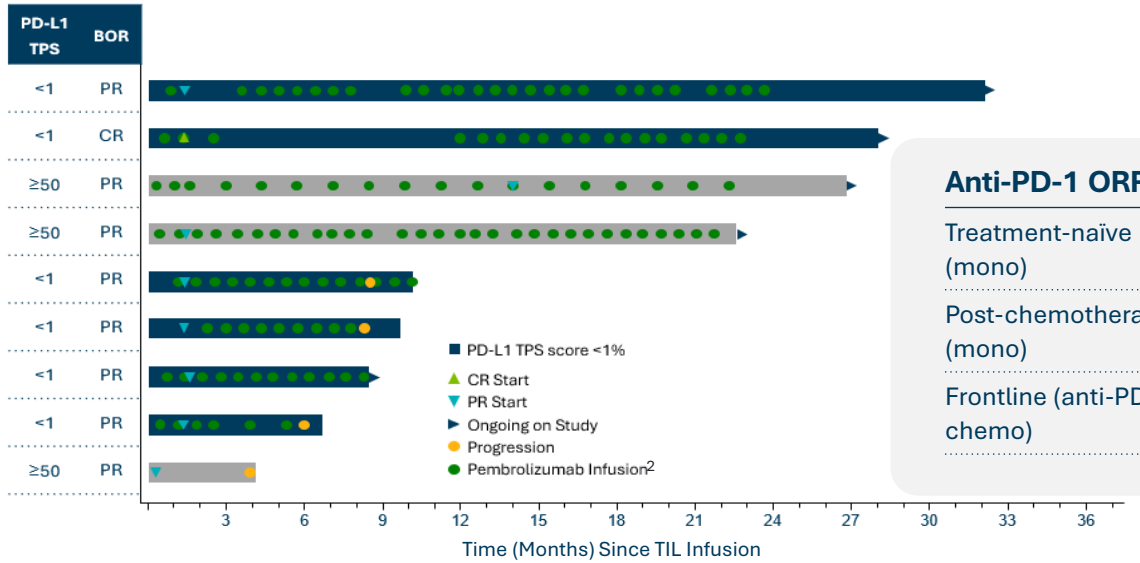
mDOR not reached (median follow-up 26.5 months)

- Safety consistent with Iovance TIL combination studies
- Supports adding TIL therapy to pembrolizumab plus chemotherapy for frontline NSCLC in new IOV-COM-202 cohort

Best Percentage Change from Baseline in Target Lesion SOD



Time to Response for Confirmed Responders (PR or Better, EGFR^{WT} Patients)



Anti-PD-1 ORR Benchmarks[2]

Treatment-naïve (mono)	27% (TPS ≥ 1%); 39 - 45% (TPS ≥ 50%)
Post-chemotherapy (mono)	18 - 20%
Frontline (anti-PD-1 + chemo)	48-58%

1. Creelan et al,SITC 2024
2. KEYTRUDA USPI; OPDIVO USPI

*PR response based on target lesion reduction of 100% with the persistence of nontarget lesions.

Abbreviations: CR, complete response; EGFR, epidermal growth factor receptor; ICI, immune checkpoint inhibitor; NSCLC, non-small-cell lung cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SOD, sum of diameter; TPS, tumor proportion score; WT, wild-type

Potential Market for Advanced Endometrial Cancer

Immunosensitive Tumor Type with Significant Unmet Need in 2L+

90%+
of Uterine Cancers are Endometrial

13,300 US annual uterine cancer deaths [1]

97,000 Global deaths[2]

18.9% 5-yr survival (distant metastases)[1]

Anti-PD-(L)1 moving into front-line therapy setting[3]

No standard of care for 2L+ post-anti-PD-1

- Molecularly defined subgroups with available targeted therapies are small
- ORR with mono-chemotherapy after front-line chemo doublet: ~15%[5,6]
- Limited data on treatments after anti-PD-(L)1

Endometrial Cancer Biomarkers[4]

dMMR: 27%
pMMR: 73%

1. National Cancer Institute Surveillance, Epidemiology and End Results (SEER) Program. 2024 Estimates. https://seer.cancer.gov (accessed May 2024); 2. World Health Organization International Agency for Research on Cancer (IARC). GLOBOCAN 2022
3. NCCN Guidelines Version 2.2024 Endometrial Carcinoma; 4. Kang et al, Nature Portfolio, Scientific Reports, 2022; 5. Makker V, et al. N Engl J Med. 2022; 6. McMeekin S, et al. Gynecol Oncol. 2015.
Abbreviations: Anti-PD-1=anti-programmed cell death inhibitor; pMMR = proficient DNA mismatch repair; dMMR = deficient DNA mismatch repair; SOC=standard of care; TMB-H = tumor mutational burden high; ORR = objective response rate

IOV-END-201 Phase 2 Proof of Concept Study

Proof-of-Concept Trial in Patients with Mismatch Repair (MMR) Proficient and Deficient Tumors (NCT06481592)

Endometrial Cancer Patient Population*

Recurrent, metastatic or primary unresectable disease after chemo and anti-PD-1 therapy

≤3 lines of prior systemic therapy with no more than 1 line of chemotherapy

- **pMMR Subgroup**
- **dMMR Subgroup**

Endpoints

- **Primary**: ORR per RECIST v1.1 by investigator
- **Secondary**: CR rate, DOR, DCR, PFS, OS, safety and tolerability
- Subgroup analyses specified in protocol
- Potential to expand / convert to registrational trial
- First patient enrolled Q4 2024

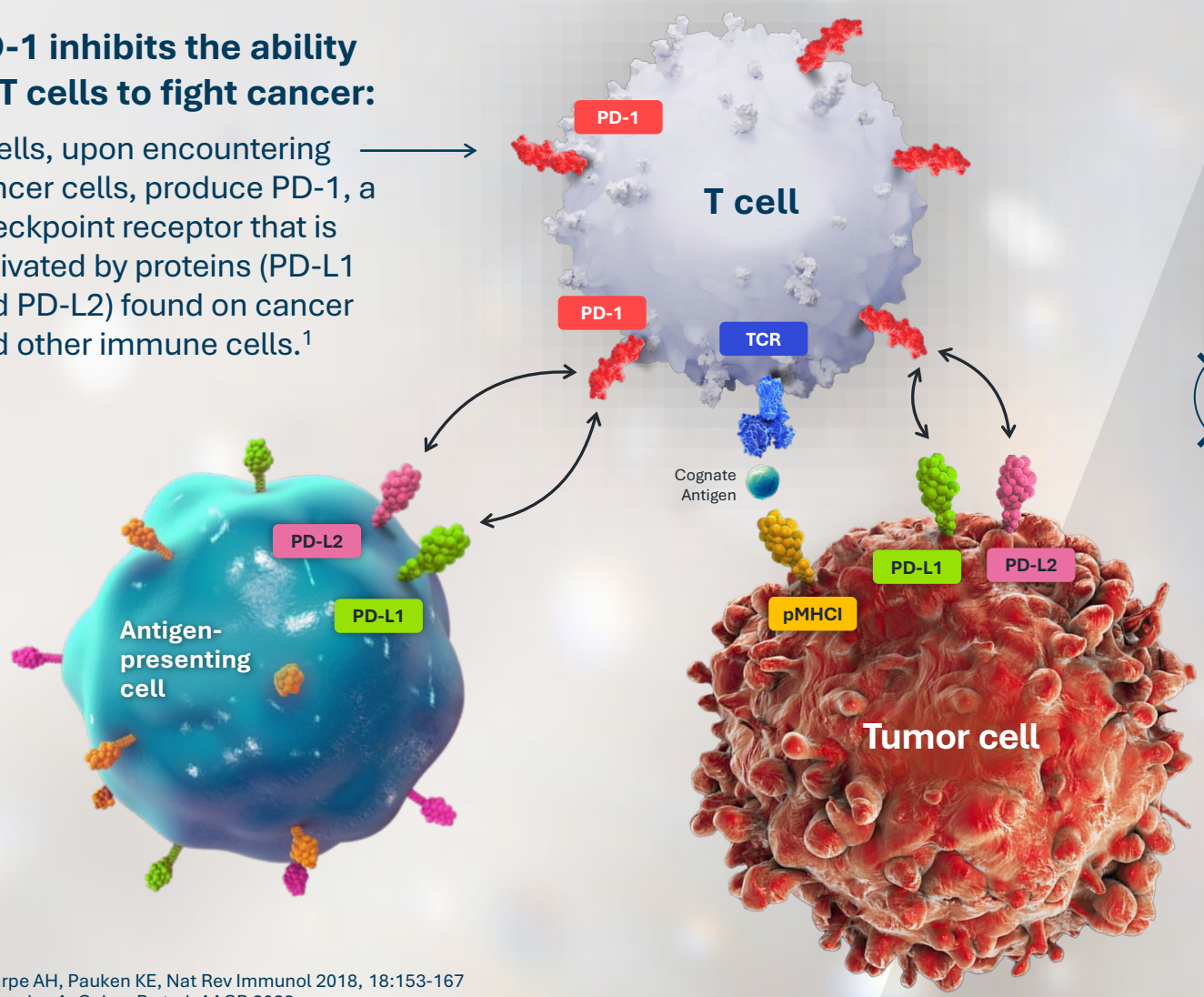
*Sample size and study population of registrational ph2 study will be determined after PoC final analysis

Abbreviations: Anti-PD-1, anti-programmed cell death inhibitor; CR, complete response; dMMR, mismatch repair deficient; pMMR, mismatch repair proficient; DCR, disease control rate; DOR, duration of response; ORR, objective response rate; OS, overall survival; PFS, progression free survival

IOV-4001: PD-1 Inactivated TIL Therapy

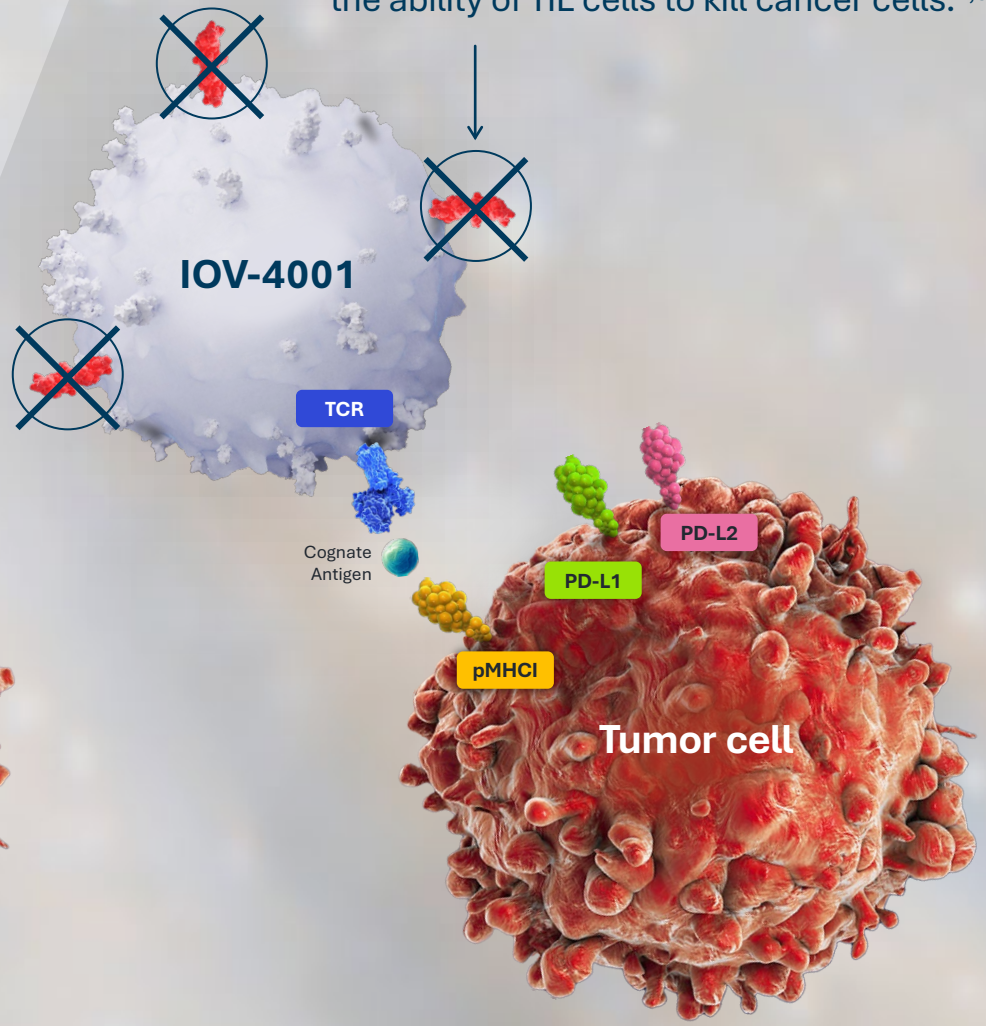
1 PD-1 inhibits the ability of T cells to fight cancer:

T cells, upon encountering cancer cells, produce PD-1, a checkpoint receptor that is activated by proteins (PD-L1 and PD-L2) found on cancer and other immune cells.[1]



2 PD-1 Inactivated T Cells Avoid Checkpoint Signals:

PD-1 is inactivated using TALEN, restoring the ability of TIL cells to kill cancer cells.[2,3]



1. Sharpe AH, Pauken KE, Nat Rev Immunol 2018, 18:153-167
2. Natarajan A, Cubas R et.al. AACR 2022
3. Licensed from Cellectis

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 (Complete)
- **Phase 2 Primary:** ORR per RECIST v1.1 by investigator
- **Secondary**: CR rate, DOR, DCR, PFS, OS, safety and tolerability

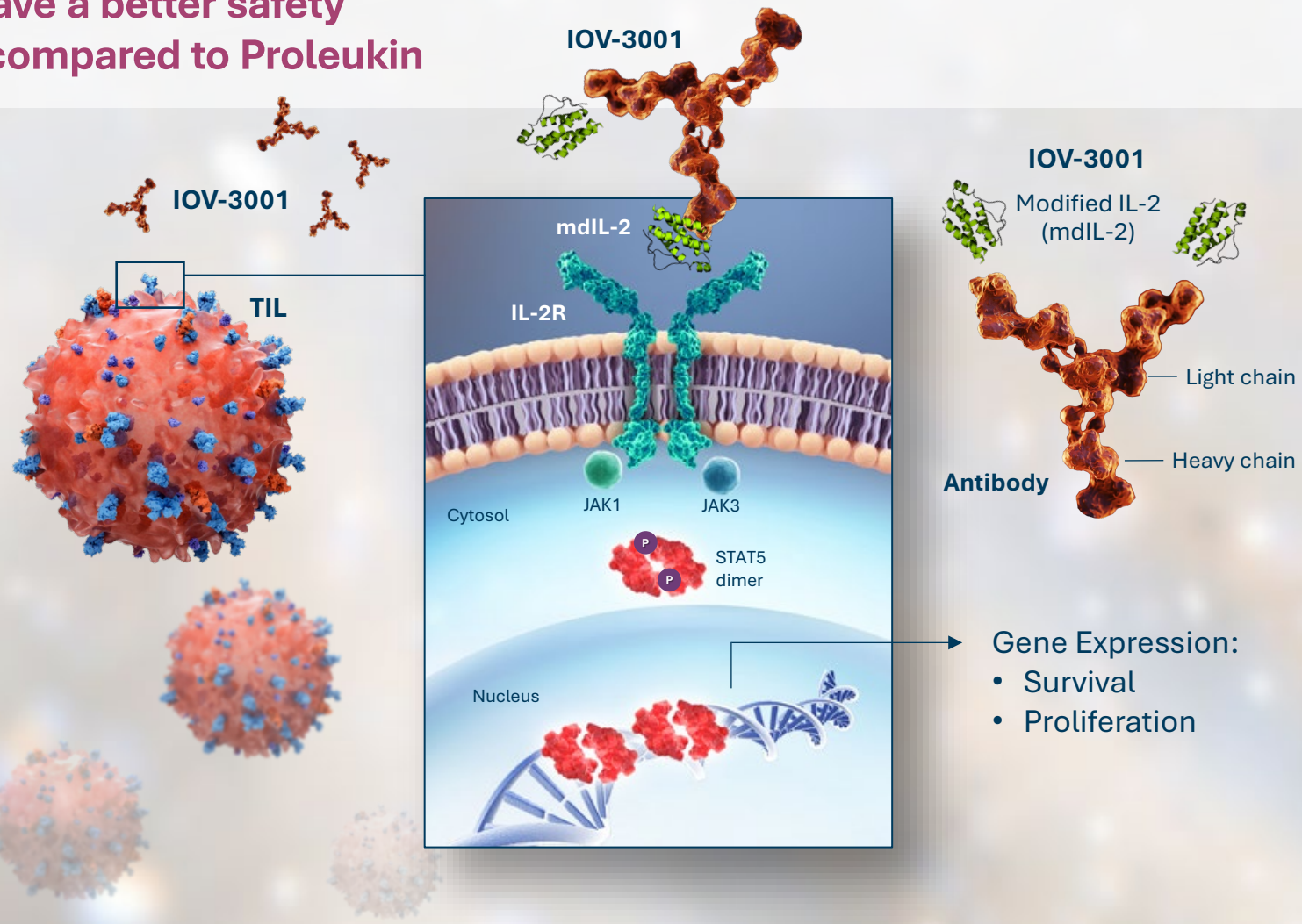
Abbreviations: Anti-PD-1=anti-programmed cell death inhibitor; CR=complete response;; DCR=disease control rate; DOR=duration of response; NSCLC=non-small cell lung cancer; ORR=objective response rate; OS=overall survival; PFS= progression free survival

IOV-3001: Next Generation IL-2 for TIL Supportive Regimen

Preclinical data suggest IOV-3001 may have a better safety profile and require less frequent dosing compared to Proleukin

Recombinant fusion protein designed to enhance TIL survival and cellular proliferation

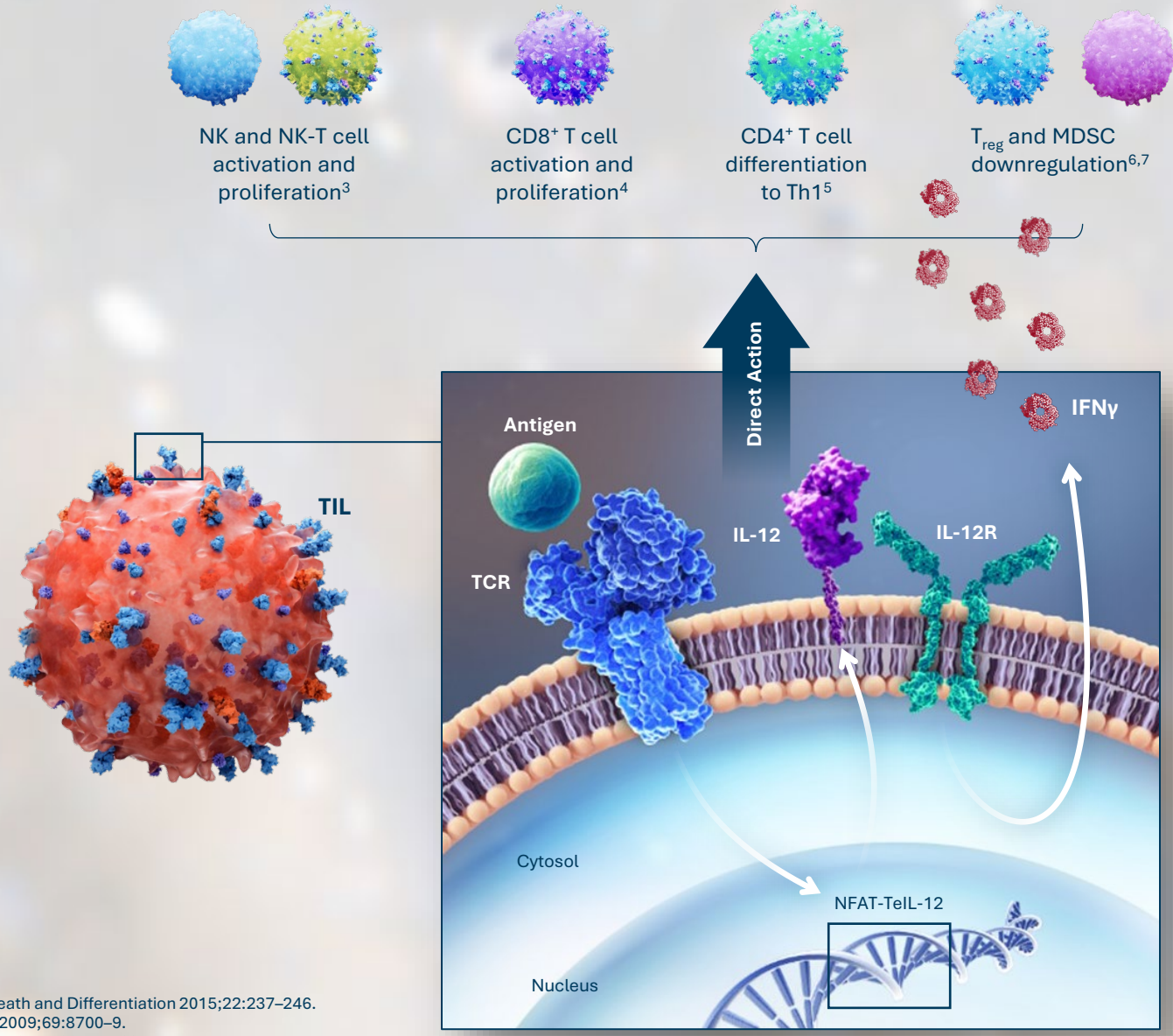
- A modified copy of the coding sequence for aldesleukin (mdIL-2) is fused to a humanized monoclonal immunoglobulin (Ig)G1κ antibody
- The mdIL-2 moiety of IOV-3001 binds to the IL-2-receptor (IL-2R) with subsequent phosphorylation of signal transducer and activator of transcription 5 (STAT5), resulting in enhanced performance



Mitra S, Leonard WJ, Journal of Leukocyte Biology 2018 103(4): 643-655
Simpson-Abelson et al, ASCO 2024
Simpson-Abelson MR, Johnson S et al, ASCO 2024.

IOV-5001: IL-12 TIL Therapy to Increase Efficacy

- Tethered IL-12 TIL cells can improve efficacy by remodeling the suppressive TME into an immuno-supportive state
  - In advanced melanoma patients, an ORR of 63% (n=16) was observed with prior generation IL-12 secreting TIL product at doses 10- to 100-fold lower than conventional TIL products[1]
- IL-12 shows independent clinical efficacy, with safe delivery to the TME being the primary challenge[1,2]
- Expression of IL-12 on IOV-5001 is induced upon antigen encounter in the TME[1,2]
- IOV-5001's expressed IL-12 is tethered to the membrane surface of TIL to avoid release into circulation (shedding) [2]
- Inducible IL-12 expression in the TME and lack of IL-12 shedding are expected to allow increased IOV-5001 cell doses and improved TIL efficacy in solid tumor cancers



1. Zhang L, Rosenberg SA, et al, Clin Cancer Res 2015;21(10):2278–2288
2. Zhang L, Davis JS, et al, J Immunother Cancer 2020;8:e000210
3. Kobayashi M, Fitz L, et al, J Exp Med 1989;170:827–845.
4. Zeh HJ, Hurd S et al, J Immunother 1993;14:155–61.
5. Tugues S, Burkhard SH, et al, Cell Death and Differentiation 2015;22:237–246.
6. Cao X, Leonard K, et al, Cancer Res 2009;69:8700–9.
7. Steding CE, Wu S, et al, Immunology 2011;133:221–38.

IL=12 = interleukin 12; MDSC = myeloid derived suppressor cell; NK = natural killer cell; NKT = natural killer T cell; ORR = objective response rate; TME = tumor microenvironment; Treg = regulatory T cell

Corporate Summary & Milestones

Strong Financial Position for Launch Success and Pipeline Growth

September 30, 2024	(in millions)
Cash position	$403.8[1]
Common shares outstanding	304.6
Preferred shares outstanding	2.9[2]
Stock options and restricted stock units outstanding	28.8

Cash runway is sufficient into early 2026[3]

Gross margins expected to increase to >70% over next several years[4]

1. Includes net proceeds of approximately $200.0 million raised from an at-the market (ATM) equity financing facility during the second and third quarter of 2024
2. Preferred shares are shown on an as-converted basis
3. Includes anticipated revenue from Amtagvi™ and Proleukin®
4. Q3 total product revenue of $58.6 million and cost of sales $39.8 million, primarily attributed to $8.3 million in period costs associated with patient drop off and manufacturing success rates, $5.5 million for non-cash amortization expense for intangible assets, and $3.9 million in royalties payable on product sales

Anticipated 2024 Milestones

REGULATORY

- ☑ Obtain FDA approval for lifileucel in advanced melanoma (approved on Feb. 16, 2024)
- ☑ Submit EMA regulatory dossier (1H24) (Validated by EMA)
- ☑ Submit additional ex-U.S. dossiers (2H24) (UK complete, Canada underway)
- ☐ Present data for NSCLC frontline and pursue registrational pathway

PIPELINE

- ☑ Report clinical and pre-clinical data
- ☑ Resume enrollment in IOV-LUN-202
- ☑ Initiate Phase 2 trial in endometrial cancer
- ☐ Continue to enroll patients in clinical trials for advanced melanoma, NSCLC and gynecological cancers
- ☑ Advance new products toward clinic, including additional genetically-modified TIL therapies

MANUFACTURING

- ☐ Fulfill patient demand for commercial launch and clinical trials
- ☐ Further expand capacity to meet U.S. and ex-U.S. demand

COMMERCIAL

- ☑ Execute commercial launch (1Q24)
- ☑ On-board 50 ATCs within 90 days of PDUFA date
- ☐ On-board ~70 ATCs by end of 2024

Abbreviations: ATC=Authorized Treatment Centers; EMA=European Medicines Agency; FDA=U.S. Food and Drug Association; NSCLC=non-small cell lung cancer; PDUFA=Prescription Drug User Fee Act

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, new tumor types, earlier lines of therapy and genetic modifications
- Key late-stage trials in melanoma, NSCLC
- First-in-human trial of genetically modified PD-1 inactivated TIL

First FDA Approved T Cell Therapy for a Solid Tumor Cancer

- FDA accelerated approval for Amtagvi™ in advanced melanoma
- TILVANCE-301 Phase 3 confirmatory trial in frontline advanced melanoma (FTD)
- Defined registration strategy in NSCLC
- Regulatory dossiers under review, submitted or planned across multiple international markets

Efficient and Scalable Proprietary Manufacturing Facility

- Iovance Cell Therapy Center (*i*CTC) in-house manufacturing
- Ample capacity for U.S. launch and global clinical trials
- Additional capacity with contract manufacturer

AMTAGVI™ (lifileucel) Suspension for IV infusion

Fully-Integrated for Commercial Success

- Experienced cross-functional cell therapy team
- TIL service-line capabilities established with leading U.S. cancer centers
- IovanceCares™ proprietary platform

Abbreviations: FTD, fast track designation; ICI, immune checkpoint inhibitor; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein-1

IOVANCE BIOTHERAPEUTICS

Thank You

ADVANCING IMMUNO-ONCOLOGY