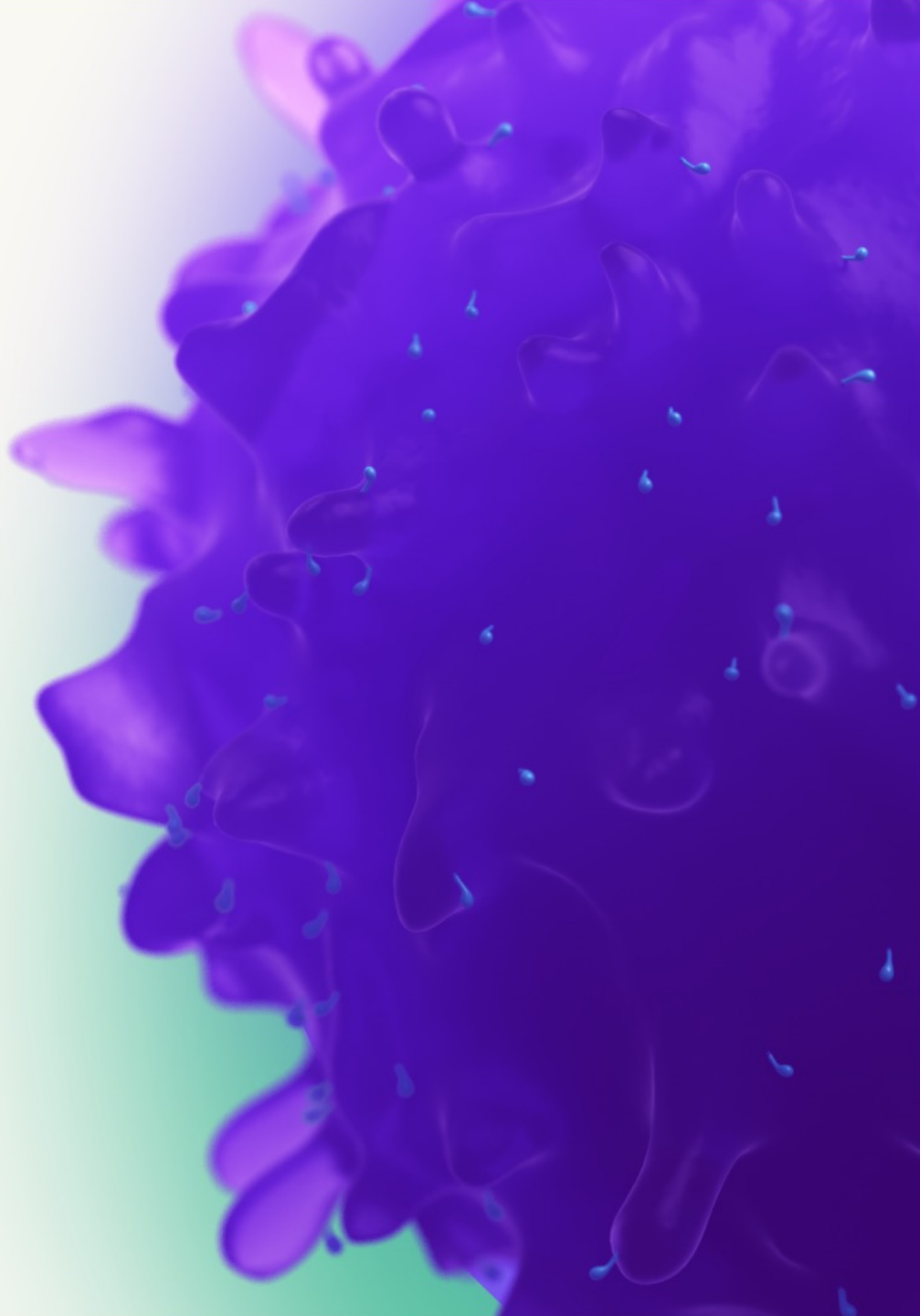
Lyell

Enhancing the Extraordinary

TCELL



Lyell Immunopharma — June 26, 2024

Forward Looking Statements

Certain matters discussed in this presentation are "forward-looking statements" of Lyell Immunopharma, 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 presentation are forward-looking statements, including expansion of clinical trials, plans for dose escalation, Lyell's plans to submit an IND for LYL797 and the timing thereof, the ability of Lyell's reprogramming technologies to infiltrate and persist in the solid tumor microenvironments, indicative milestones and other statements that are not statements of historical fact, 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 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, timelines 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 (the "SEC"), and include, but are not limited to, the following substantial known and unknown risks and uncertainties inherent in our business related to: the effects of geopolitical instability; macroeconomic conditions, including the effects of geopolitical instability and actual or perceived changes in interest rates and economic inflation; our ability to initiate or progress our current and planned clinical trials or to submit planned INDs on the anticipated timelines, if at all; the potential for results from clinical trials to differ from nonclinical, early clinical, preliminary or expected results; our limited experience as a company in enrolling, conducting or completing clinical trials; our ability to manufacture and supply our product candidates for our clinical trials; significant adverse events, toxicities or other undesirable side effects associated with our product candidates; the significant uncertainty associated with our product candidates ever receiving any regulatory approvals; our ability to obtain, maintain, or protect intellectual property rights related to our product candidates; implementation of our strategic plans for our business and product candidates; the sufficiency of our capital resources and the need for additional capital to achieve our goals; other risks, including general economic conditions and regulatory developments, not within our control; and those risks described under the heading "Risk Factors" in our SEC filings, including our Quarterly Report on Form 10-Q for the quarter ended March 31, 2024 and subsequent filings with the SEC.

This presentation concerns product candidates and technologies that are under clinical investigation, and which have not yet been approved for marketing by the U.S. Food and Drug Administration. These are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

Advancing T-cell Therapies Enhanced with Anti-exhaustion Technology

Wholly-owned product candidates addressing large patient populations

Expanding clinical pipeline; data from three programs over next 18 months

LYL797

ROR1-targeted CAR T cells

Initial Ph 1 data: dose-dependent clinical activity; 40% ORR and 60% CBR at 150M cells, expanding Ph 1 program from two to six tumor types

LYL845

Tumor Infiltrating Lymphocytes (TIL) for melanoma, NSCLC, and CRC

Initial Ph 1 clinical & translational data in advanced melanoma in 2H24

LYL119

Next-generation ROR1-targeted CAR T cells

IND filed in 1H24, awaiting clearance to initiate Ph 1 trial

Scientific expertise, capabilities and capital to drive continuous innovation and ability to scale

Multiple proprietary technologies to improve T-cell function

- Designed to generate T cells that resist exhaustion and have durable stemness

Scalable manufacturing strategy

- Capacity to produce all clinical supply at Lyell's LyFE center (capacity for ~500 doses/year depending on product mix)
- Shortening TIL manufacturing time in 2024

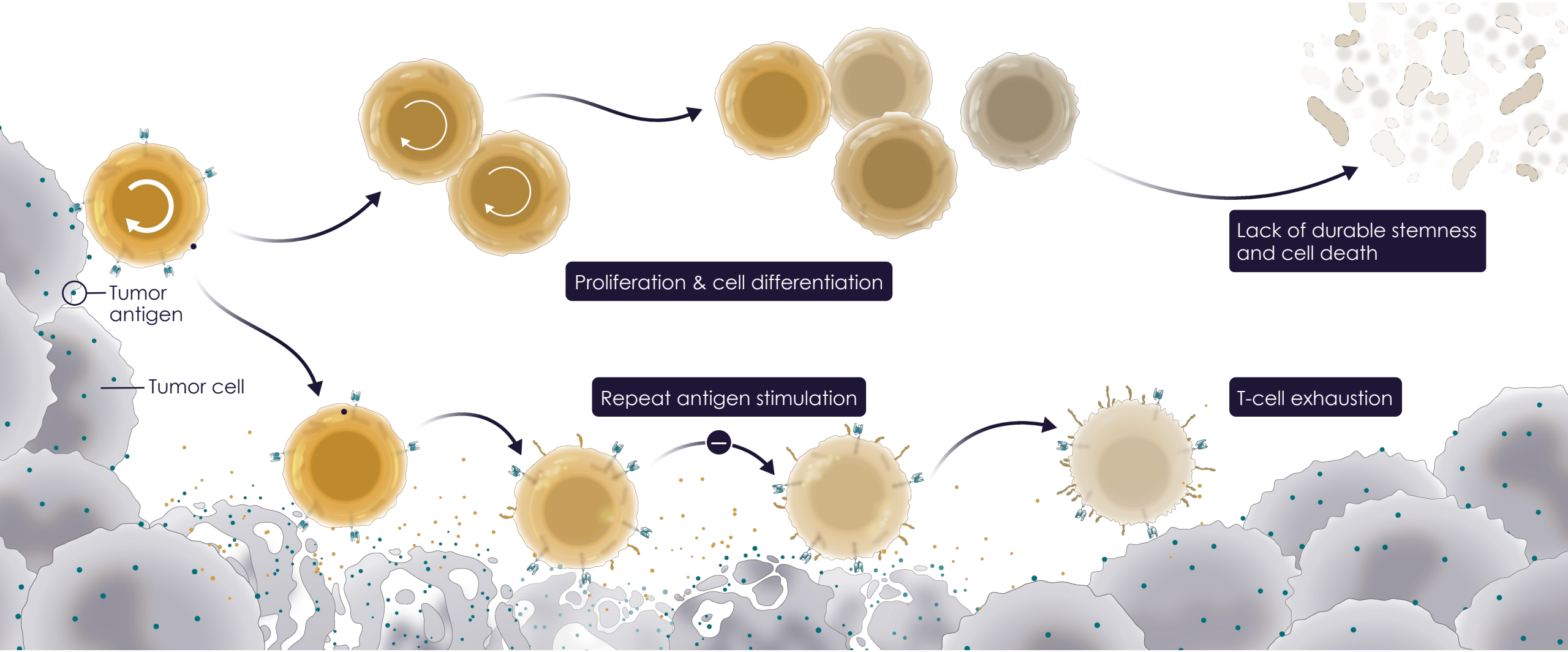
Strong balance sheet

- ~$526 million of cash*
- Runway into 2027 through multiple clinical readouts

*Cash, cash equivalents and marketable securities as of 3/31/2024

ORR, overall response rate; CBR, clinical benefit rate: CAR, chimeric antigen receptor; CRC, colorectal cancer; IND, investigational new drug; NSCLC, non-small cell lung cancer; ROR1, receptor tyrosine kinase-like orphan receptor 1; TIL, tumor-infiltrating lymphocytes; TNBC, triple-negative breast cancer.

We are Applying our **Proprietary Anti-exhaustion Technology** to Generate **T cells Designed to Overcome Two Key Barriers to Cell Therapy in Solid Tumors: Lack of T-cell Expansion and Tumor Infiltration and Rapid T-cell Exhaustion**

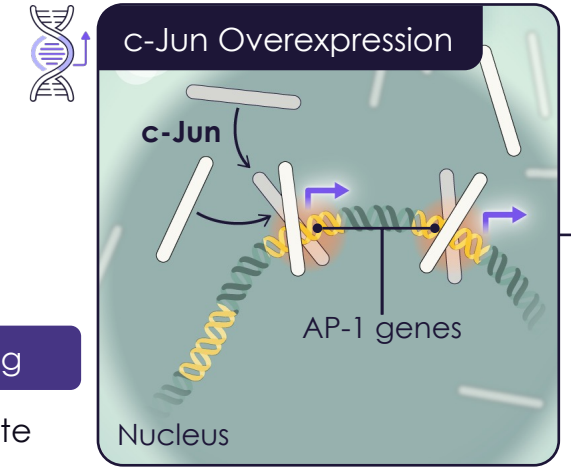


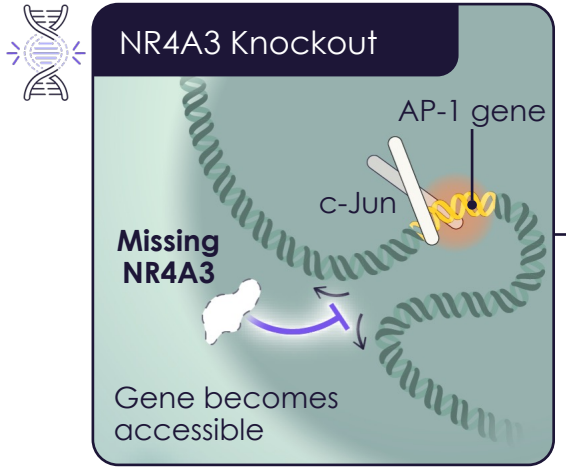
Lyell's T-cell Reprogramming Technologies

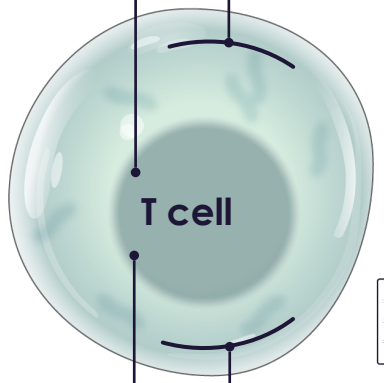
Designed to maintain cancer cell killing in the immunosuppressive tumor microenvironment while increasing ability to self-renew and persist to drive durable tumor cytotoxicity

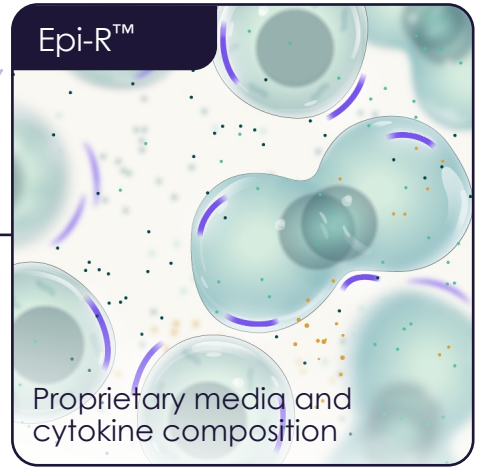
Genetic Reprogramming

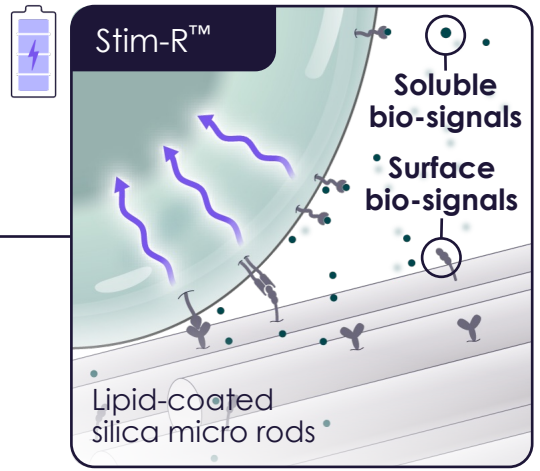
c-Jun and NR4A3 regulate the AP-1 transcription factor pathway, which plays a key role in T-cell effector function











Epigenetic Reprogramming

Manufacturing protocols that generate more stem-like cells that self renew and persist despite repeat antigen stimulation

Lynn, R. et al., *Nature*, 2019; Chen, J. et al., *Nature*, 2019.
Abbreviations: AP-1, activator protein 1; NR4A3, Nuclear receptor 4A3; TME, tumor microenvironment.

A Robust Pipeline of Novel T-cell Therapies

Product	Target	Reprogramming				Target Indications	Preclinical	Phase 1	Phase 2/ Pivotal	Next Milestone
		Genetic		Epigenetic						
		c-Jun	NR4A3	Epi-R™	Stim-R™					
LYL797 **CAR T cell**	ROR1	✓		✓		ROR1+ TNBC, NSCLC, Ovarian, Endometrial				• Initiate dose expansion and provide data update in late 24 - early 25 • Updated Ph 1 data - 1H25
LYL797 **CAR T cell**	ROR1	✓		✓		ROR1+ Multiple Myeloma, CLL				• Submit IND - 2H24
LYL119 **CAR T cell**	ROR1	✓	✓	✓	✓	ROR1+ Ovarian, Endometrial TNBC, NSCLC, CRC				• IND clearance in 2H24 • Initial data - 2H25
LYL845 **TIL**	Multiple antigens			✓		Melanoma (Orphan Drug Designation), NSCLC, CRC				• Initial data - 2H24
Next Gen **TIL**	Multiple antigens	Genetic and Epigenetic Reprogramming				Solid tumors				

Abbreviations: CAR, chimeric antigen receptor; CRC, colorectal cancer; IND, investigational new drug; NSCLC, non-small cell lung cancer; ROR1, receptor tyrosine kinase-like orphan receptor 1; TIL, tumor-infiltrating lymphocytes; TNBC, triple-negative breast cancer. CLL, chronic lymphocytic leukemia

Reprogramming T Cells to Target Aggressive Cancers

LYL797

ROR1 CAR T-cell product candidate enhanced with anti-exhaustion technology designed for improved tumor infiltration and tumor cell killing

LYL119

Next-generation ROR1 CAR T-cell product candidate designed to have even more powerful anti-exhaustion technology

Abbreviations: CAR, chimeric antigen receptor; ROR1, receptor tyrosine kinase-like orphan receptor 1.

ROR1 is Highly Expressed in Many Malignancies

Expression associated with a poor prognosis in solid tumors

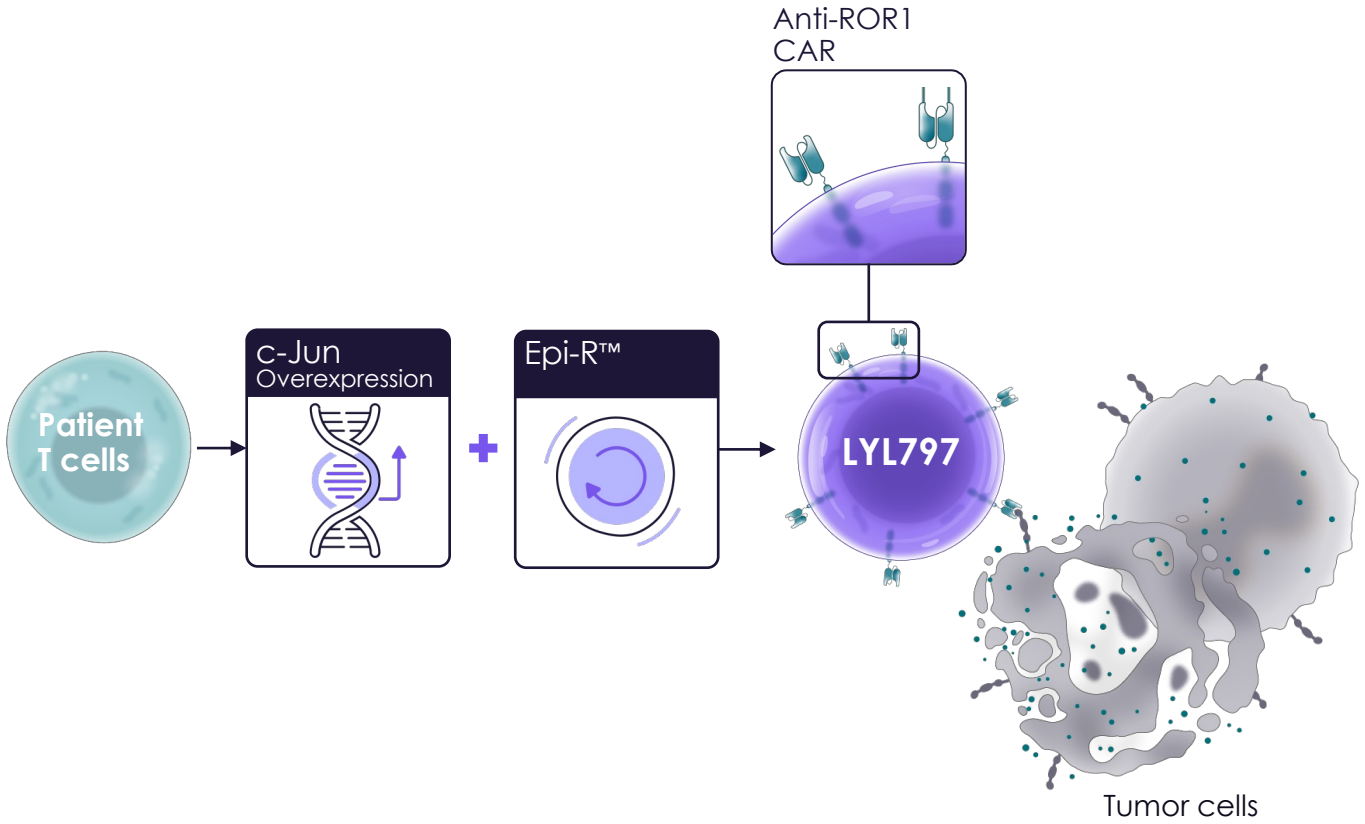
Solid Tumor Indications in Development				
	TNBC	NSCLC	Endometrial	Ovarian
ROR1 Expression	**51%***	**35%***	**~50%**	**~50%**
US Incidences	~40K new cases ~10K deaths	~200K new cases ~110K deaths	~68K new cases ~13K deaths	~20K new cases ~13K deaths

Hematologic Indications in Development		
	Multiple Myeloma	CLL
ROR1 Expression	**~60%**	**~95%**
US Incidences	~36K new cases ~13K deaths	~ 21K new cases ~ 4.4K deaths

*Data from Lyell's LYL797 clinical trial (TNBC N=259, NSCLC, N=104)
CLL, chronic lymphocytic leukemia; NSCLC, non-small cell lung cancer; TNBC, triple-negative breast cancer
American Cancer Society (cancer.org); Balakrishnan et al., *Clin Cancer Res* 2017; Liu et al., Sci Reports, 2020; Mosaad et al., *Asian Pac J Cancer Prev*, 2023; Zhang et al., *Am J Pathol,* 2012.; Daneshmanesh, et al., *Leuk Lymphoma*, 2013

LYL797: Clinical Program Supported by Robust Preclinical Data

ROR1 CAR T cell + c-Jun + Epi-R



Key Differentiators

Tumor reduction, enhanced cytokine production, and tumor infiltration in aggressive NSCLC syngeneic model with c-Jun CAR T cells

Stem-like phenotype, durability, and enhanced cytotoxicity with Epi-R technology

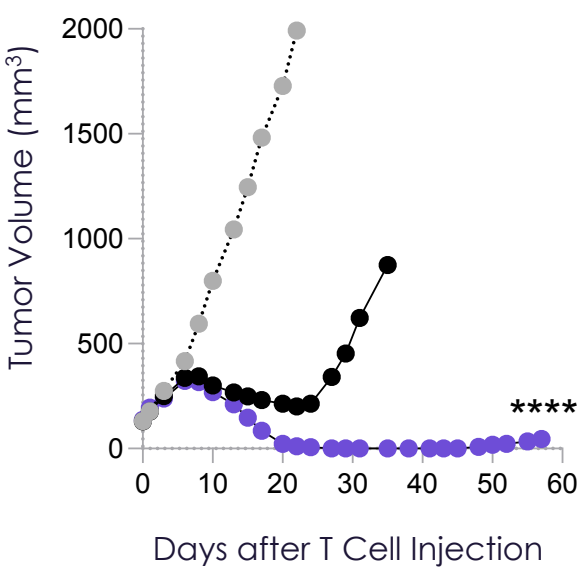
Prolonged survival by combining c-Jun and Epi-R technologies (LYL797) in xenograft NSCLC animal model

Abbreviations: CAR, chimeric antigen receptor; NSCLC, non-small cell lung cancer; ROR1, receptor tyrosine kinase-like orphan receptor 1.

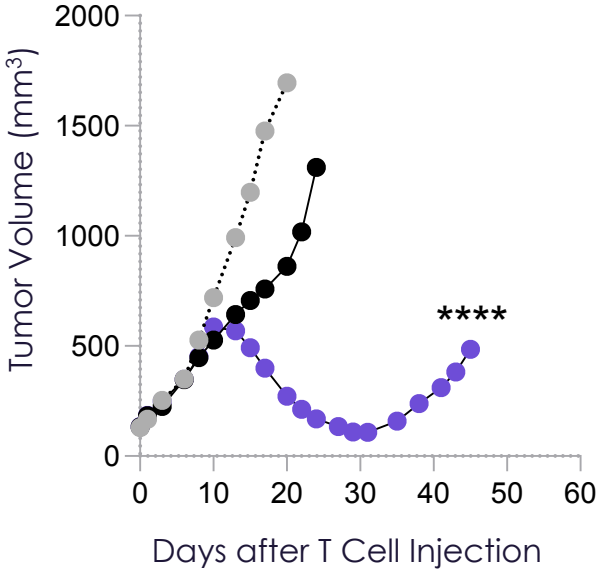
LYL797: Combining c-Jun and Epi-R Reprogramming Technologies Prolonged Survival in NSCLC (H1975) Xenograft Model

LYL797 Reduced Tumor Burden

High Dose
5 x 10^6 CAR T cells

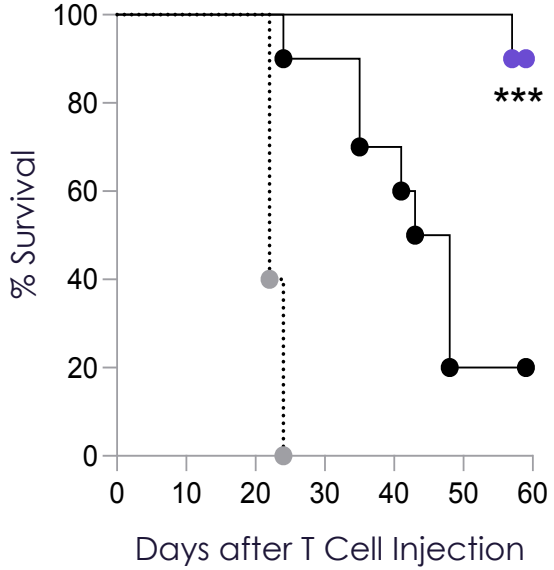


Low Dose
2.5 x 10^6 CAR T cells

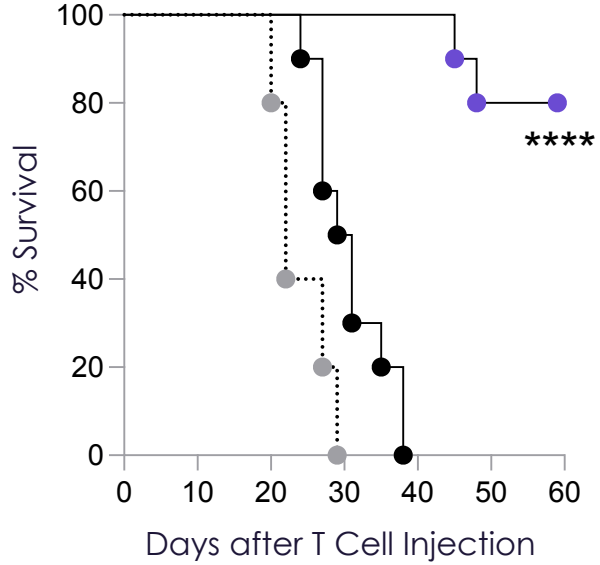


LYL797 Prolonged Survival

High Dose
5 x 10^6 CAR T cells



Low Dose
2.5 x 10^6 CAR T cells



Mock Control ROR1 CAR T LYL797

Park et al., ASGCT 2022. *P<0.05, ***P<0.001, ****P<0.0001
Abbreviations: CAR, chimeric antigen receptor; NSCLC, non-small cell lung cancer; ROR1, receptor tyrosine kinase-like orphan receptor 1.

LYL797 Initial Phase 1 Clinical and Translational Data

June 26, 2024

LYL797 Initial Clinical Data and ROR1 Program Status

Dose-Dependent Clinical Activity Observed

- **40% Objective Response Rate, including 2 confirmed partial responses,** at 150M CAR T cell dose (n=5), the highest dose level cleared to date
  - **Clinical Benefit Rate of 60%** at 150M CAR T cell dose and 38% across all dose levels
- **LYL797 CAR T cells successfully expanded, infiltrated solid tumors and killed cancer cells**
  - First clinical demonstration of robust CAR T cell solid tumor infiltration

Dose Escalation Ongoing Separately in Patients With or Without Lung Involvement

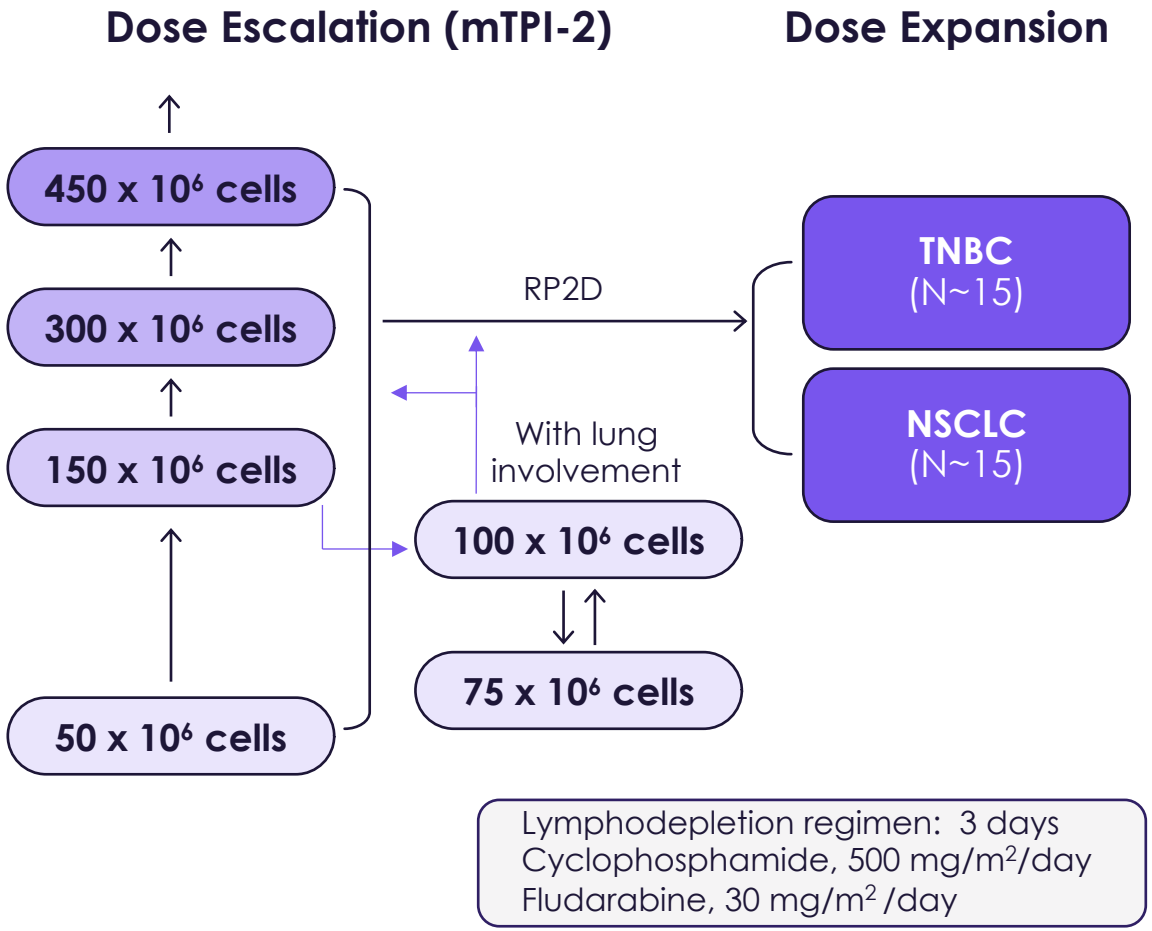
- **No DLTs in patients without lung involvement;** 300M cell dose under evaluation
- **Pneumonitis observed in patients with lung involvement;** dose escalation continuing with dexamethasone prophylaxis; treatable with steroids; 75M cell dose under evaluation

Expanding into Additional ROR1-expressing Tumor Types Given Clinical Activity

- **Expanding into ovarian and endometrial cancers**
- Initiating a new clinical trial of **LYL797 in multiple myeloma and chronic lymphocytic leukemia**
- **IND submitted for LYL119,** a next-generation ROR1-targeted product candidate

Data cutoff of 29 May 2024; CAR, chimeric antigen receptor; DLTs, dose-limiting toxicities; ROR1, receptor tyrosine kinase-like orphan receptor

LYL797: Phase 1 Trial



Patient Population

- Patients with relapsed/refractory TNBC
- Patients with relapsed/refractory NSCLC
- ROR1 positive tumors

Study Objectives

- Safety and tolerability
- Objective response rate and durability
- Recommended Ph2 dose
- CAR T-cell PK
- Assessment of T-cell phenotype and infiltration

As of May 29, 2024 data cutoff:

- No DLTs in patients without lung metastases
- Pneumonitis observed in some patients with lung metastases
  - Separately escalating cohorts of patients based on lung involvement
  - Dexamethasone prophylaxis for all patients
- Dexamethasone prophylaxis regimen intended to enable dose expansion regardless of lung involvement

NCT05274451; DLTs, dose-limiting toxicities; m-TPI-2, Modified Toxicity Probability Interval; NSCLC, non-small cell lung cancer; PK, pharmacokinetics; RP2D, recommended phase 2 dose; TNBC, triple-negative breast cancer

Patient Characteristics
Predominantly TNBC with Multiple Lines of Prior Therapy

	50 x 10^6 cells n = 8	75 x 10^6 cells n = 2	100 x 10^6 cells n = 4	150 x 10^6 cells n = 5	300 x 10^6 cells n = 1	Total N = 20
Age, mean	54	59	48	48	58	52
Indication, n (%)						
TNBC	6 (75%)	1 (50%)	3 (75%)	5 (100%)	1 (100%)	16 (80%)
NSCLC	2 (25%)	1 (50%)	1 (25%)	0	0	4 (20%)
Prior lines of treatment*, mean (range)	5 (3 – 9)	8 (4 – 12)	5 (4 – 7)	5 (2 – 8)	8	6 (2 – 12)
ECOG at Screening, n (%)						
0	3 (38%)	1 (50%)	2 (50%)	3 (60%)	1 (100%)	10 (50%)
1	5 (62%)	1 (50%)	2 (50%)	2 (40%)	0	10 (50%)

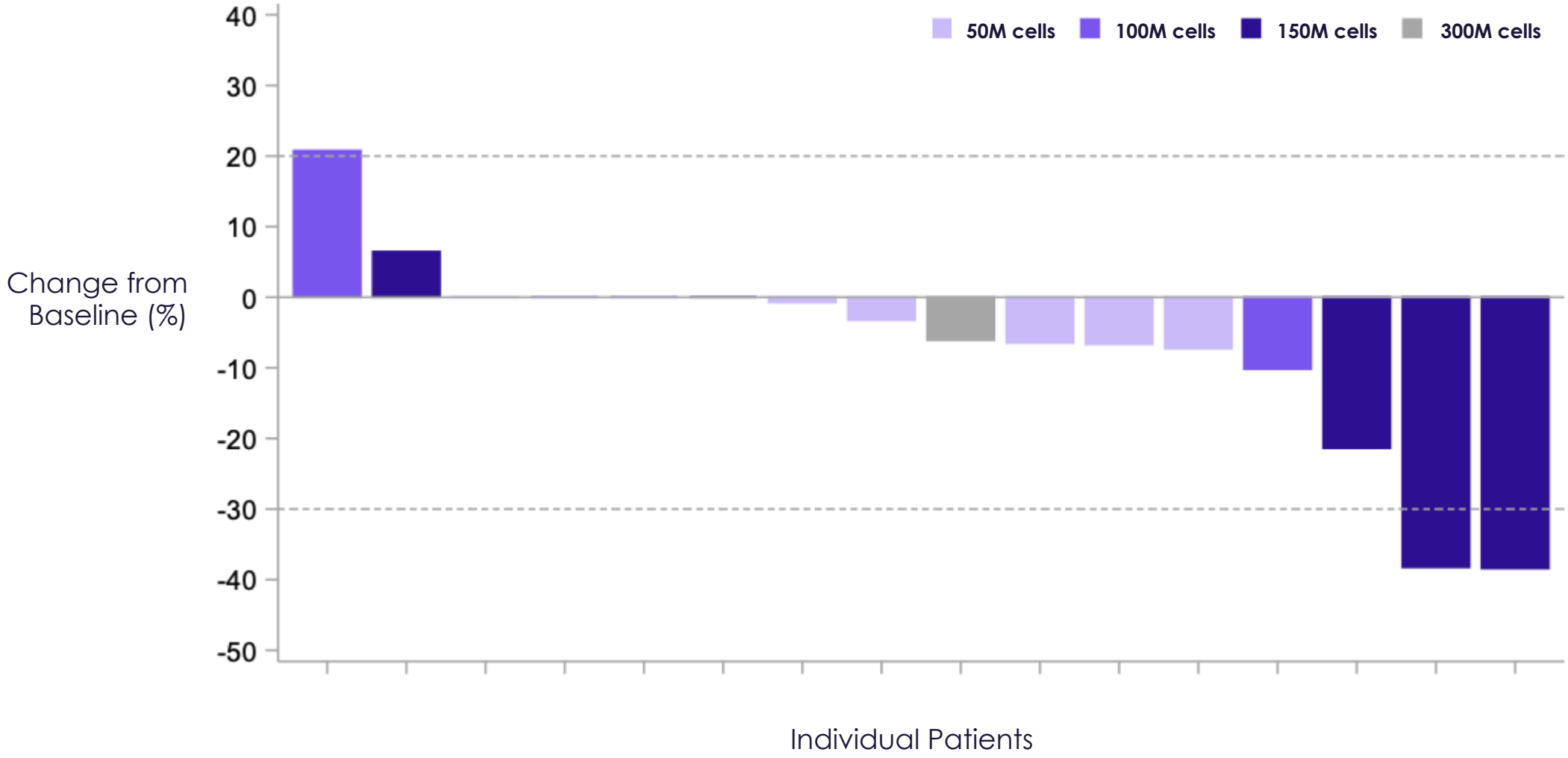
*In the metastatic setting; Data Cutoff of 14 June 2024
ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small cell lung cancer, TNBC, triple-negative breast cancer

Dose-Dependent Clinical Activity with 40% Objective Response Rate at Highest Completed Dose Level

Efficacy evaluable patients, n	50 x 10^6 cells n = 6	100 x 10^6 cells n = 4	150 x 10^6 cells n = 5*	300 x 10^6 cells n = 1	Total N = 16
Patients with CR/PR, n	0	0	2	0	2
Patients with SD, n	1	1	1	1	4
ORR %	0%	0%	**40%**	0%	13%
Duration of Response			2 cPRs to Day 90		
Clinical Benefit Rate	17%	25%	**60%**	100%	**38%**

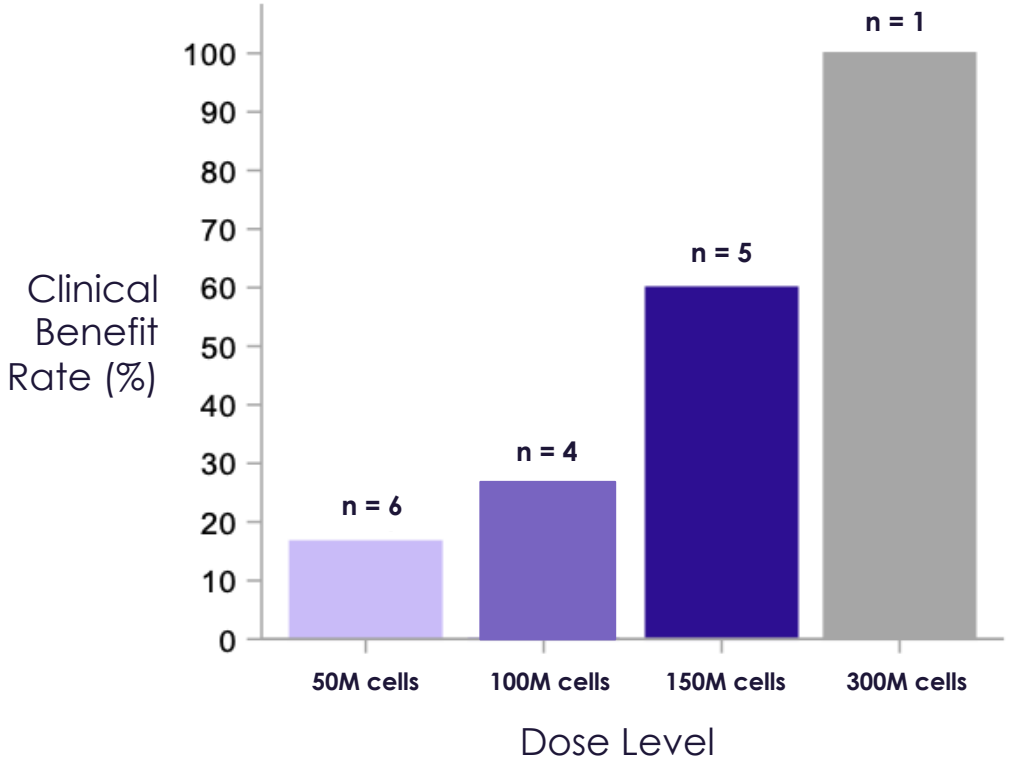
* 5 patients with TNBC; Data cutoff of 29 May 2024
cPR, confirmed partial response; CR, complete response; ORR, objective response rate; PR, partial response; SD, stable disease

Best Response for Target Lesions Demonstrating Clinical Activity



Data cutoff of 29 May 2024

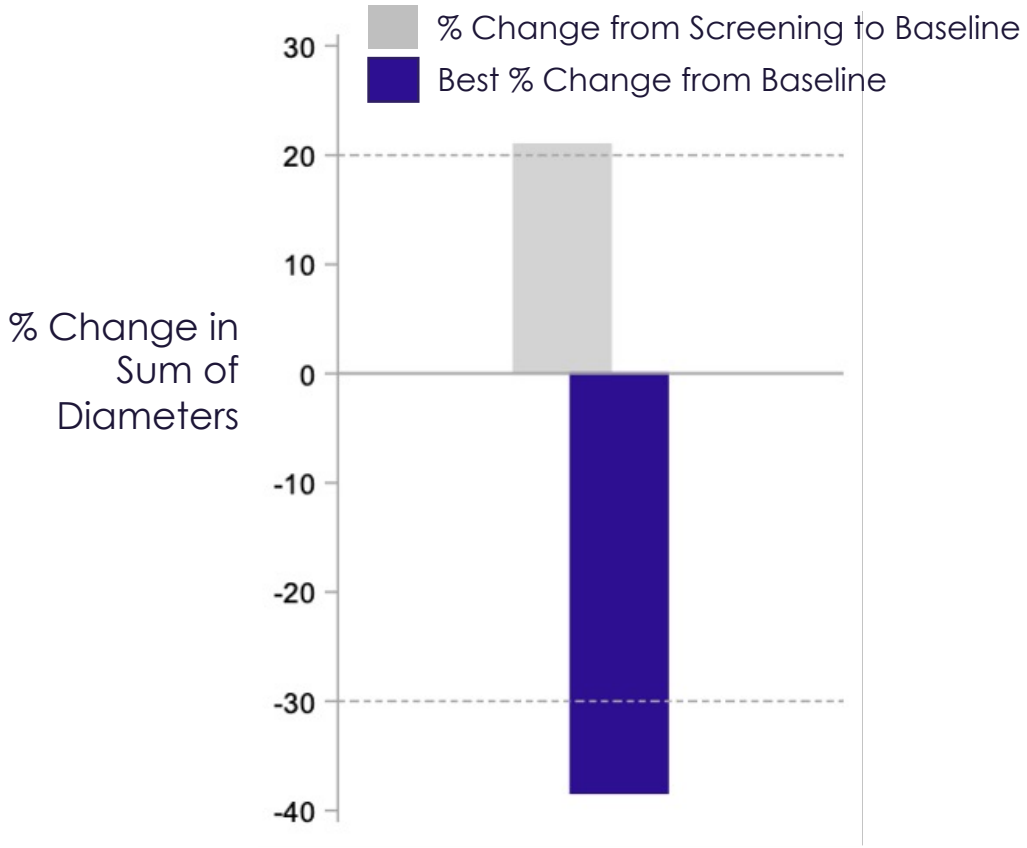
Clinical Benefit Rate was Dose Dependent



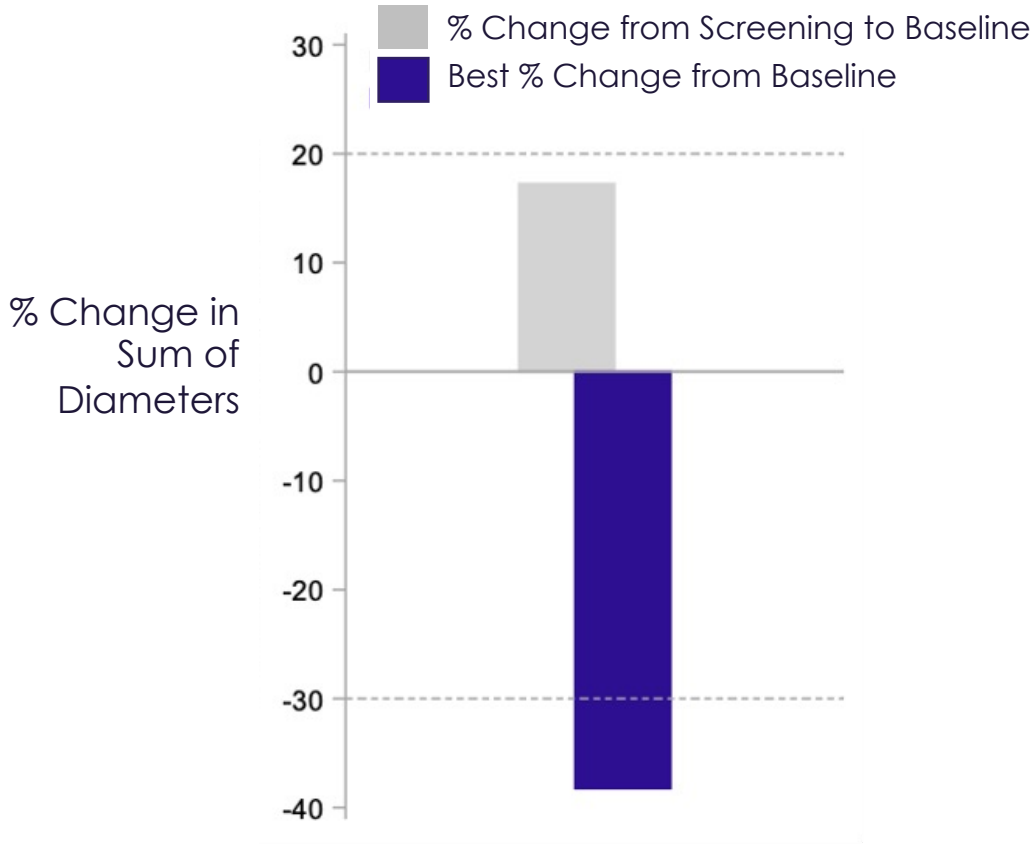
- Clinical benefit rate is defined as SD, PR or CR as best response
- Several patients had additional observations of clinical benefit including weight gain, decreased pain and improved liver function tests

Data cutoff of 29 May 2024
CR, complete response, DL, dose level; PR, partial response, SD, stable disease

Confirmed Partial Responses in Patients Who had Progression in their Target Lesions Between Screening and Baseline



Patient 5
(150 x 10^6 cells)



Patient 8
(150 x 10^6 cells)

Data cutoff of 29 May 2024

Treatment Related Adverse Events:

All Dose-Limiting Toxicities in Patients with Lung Involvement and Prior to Implementing Dexamethasone Prophylaxis

Safety Evaluable Patients With:	50 x 10^6 cells n = 7	75 x 10^6 cells n = 1	100 x 10^6 cells n = 4	150 x 10^6 cells n = 5	300 x 10^6 cells n = 1
TRAEs Grade ≥ 3	2	0	2	3	0
DLTs (pneumonitis, hypoxia)	0	0	2	2	0
CRS	4 (G1, 2)	0	3 (G1, 2)	3 (G1, 2)	1 (G1)
ICANS	0	0	0	0	0

- The most frequently reported related adverse events of any grade were CRS, pneumonitis and headache, and the expected cytopenia from lymphodepletion
- CRS was generally mild (Grade 1 or 2), characterized by fever, and treated with tocilizumab and steroids
- The most frequently reported Grade ≥ 3 related adverse events were pneumonitis and hypoxia, and the expected cytopenia from lymphodepletion; the first patient with pneumonitis had acute Grade 5 respiratory failure on Day 41. Subsequently, all patients were treated early for any sign of pneumonitis

Data cutoff of 29 May 2024; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; ICANS, immune-effector cell-associated neurotoxicity syndrome; TRAE, treatment-related adverse event

Pneumonitis has a Predictable Onset and is Treatable

- Pneumonitis does not appear to be related to on-target, off-tumor toxicity; we believe it is related to local cytokine production due to underlying lung disease
- The onset is predictable(generally 4 – 10 days after treatment)
- It has been effectively treated with early high-dose steroids
- All patients now treated prophylactically with dexamethasone
  - Dexamethasone use has resulted in decreased CRS without diminished efficacy in hematological malignancies and CD19 CAR therapy*
- Dose escalation is moving forward separately in patients with or without NSCLC or lung metastatic disease
  - Dosing at 300 x 10^6 cells for patients without lung involvement
  - Dosing at 75 x 10^6 cells for patients with lung involvement

Data cutoff of 29 May 2024
CAR, chimeric antigen receptor; CRS, cytokine release syndrome; NSCLC, non-small cell lung cancer
*Oluwole, OO, et al, *Bone Marrow Transplant*, 59, 2024

LYL797 Translational Data: Key Findings

Expansion

- LYL797 **CAR T-cell expansion observed in the peripheral blood** from all patients (n=11)

CAR T Cell Phenotype

- LYL797 cells had **low exhaustion markers** and a significant proportion of cells with the **desired stem-like and effector-memory phenotype** (n=6)

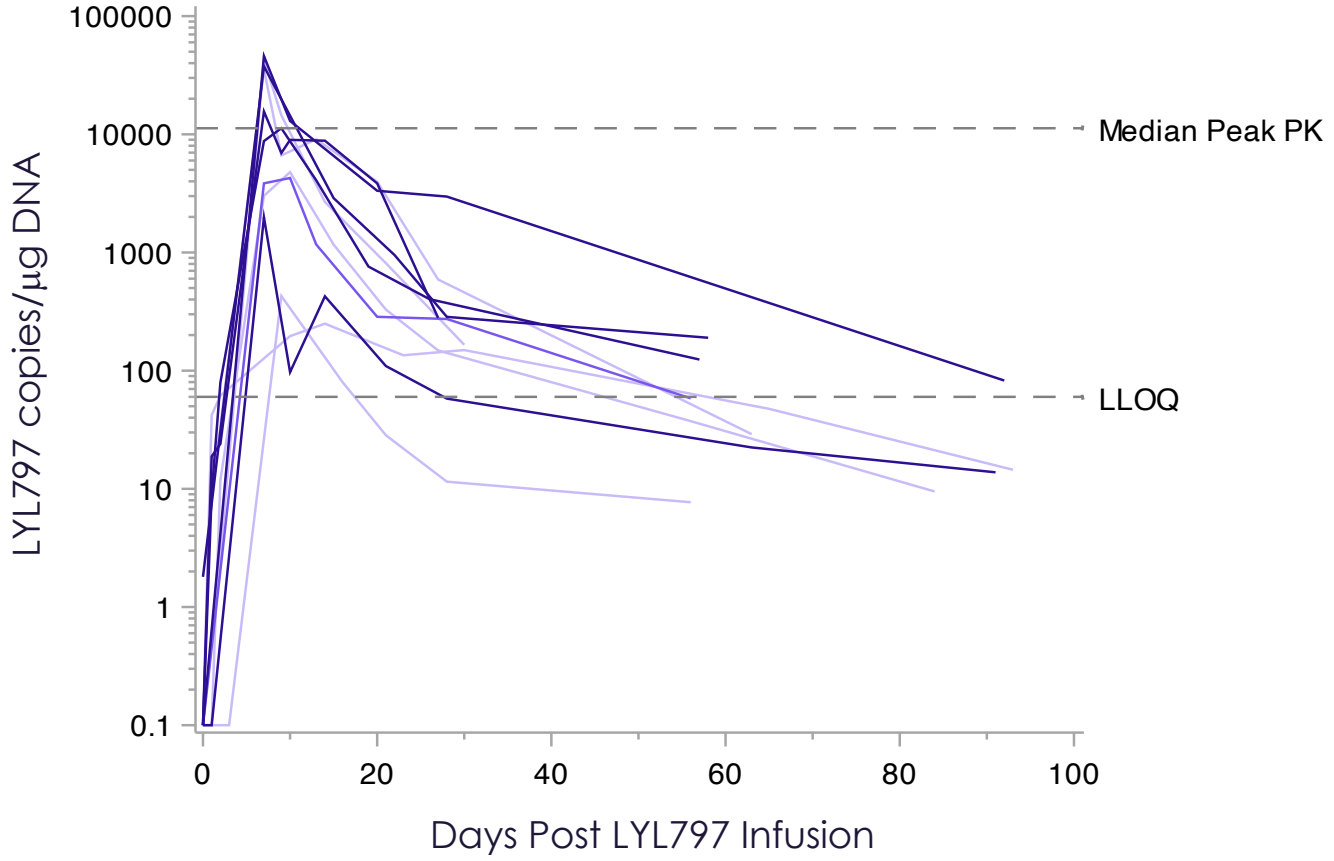
Infiltration and Tumor Lysis

- Persistent **LYL797 CAR T cell infiltration present in all evaluable on-study tumor biopsies** (n=9) with histologic evidence of tumor lysis in some samples

Data cutoff of 29 May 2024
CAR, chimeric antigen receptor

LYL797 CAR T-cell Expansion Observed in Peripheral Blood Samples from All Treated Patients

Peak Expansion Between Days 8 and 11



- 50 x 10^6 cells (n = 5)
- 100 x 10^6 cells (n = 1)
- 150 x 10^6 cells (n = 5)

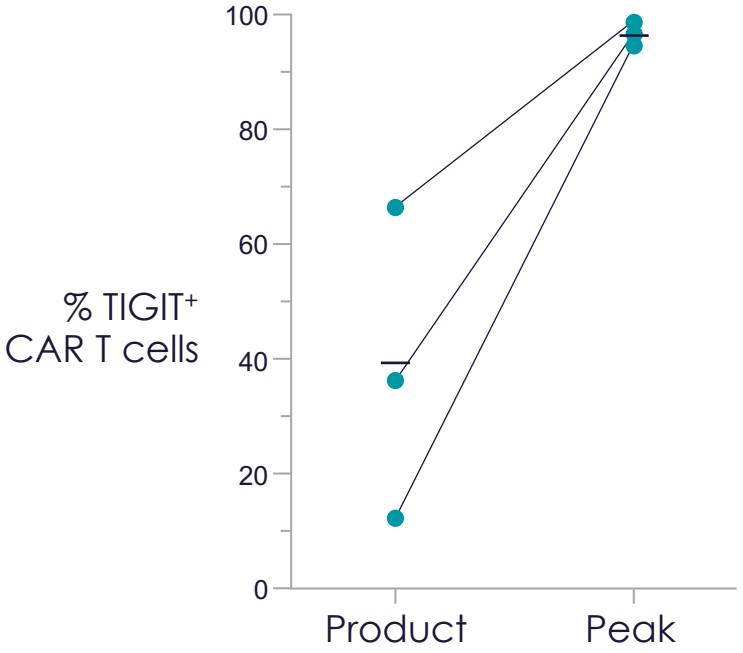
Median peak PK = 11,251 copies/µg DNA

- 50 x 10^6: 4,783 copies/µg DNA
- 150 x 10^6: 15,598 copies/µg DNA

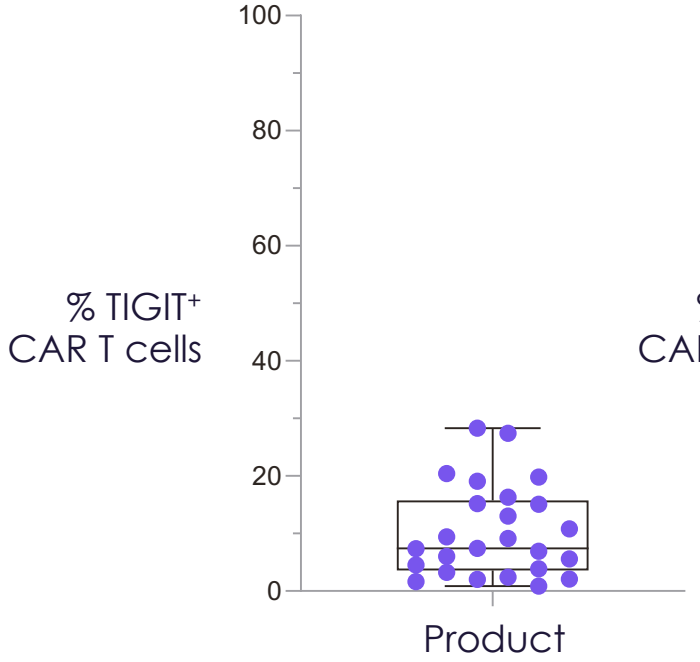
Data cutoff of 29 May 2024; CAR, chimeric antigen receptor; cPR, confirmed partial response; PK, pharmacokinetics; DNA, deoxyribonucleic acid

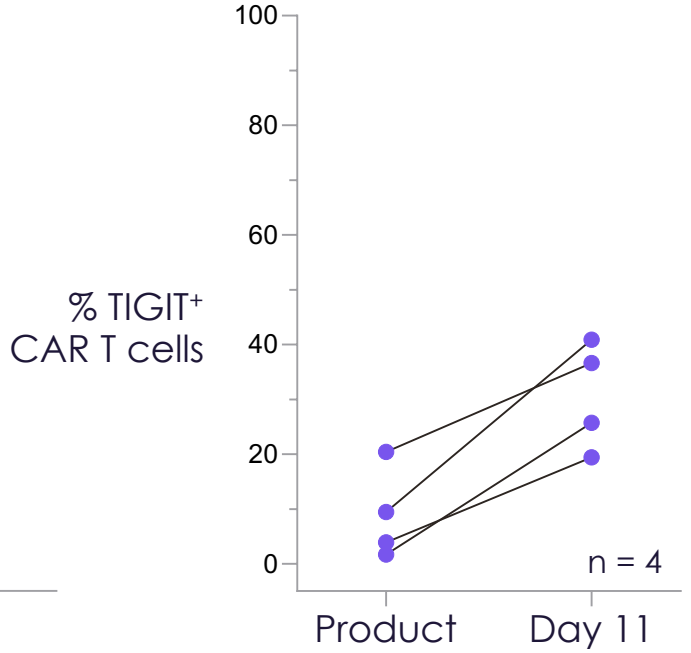
Infusion Products and LYL797 in Day 11 Peripheral Blood Samples Had Significantly Lower Percent TIGIT+ Cells (Exhaustion Marker)

Fred Hutch Cancer Center: Solid Tumor Patients



LYL797 CAR T Cell Data

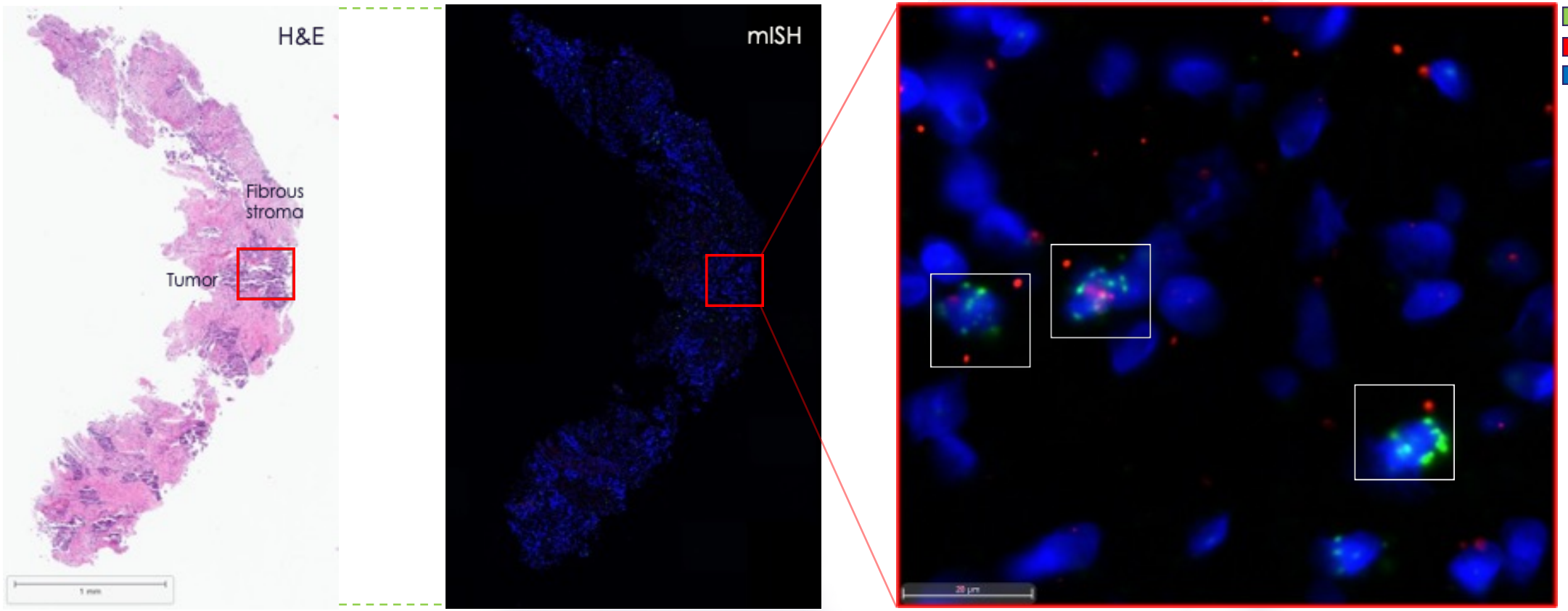




Data cutoff of 29 May 2024; CAR, chimeric antigen receptor; TIGIT, T cell immunoreceptor with immunoglobulin and ITIM domain
Specht J. Jan 31 2020, EHA
*LYL797 defined by CD8+ EGFR+

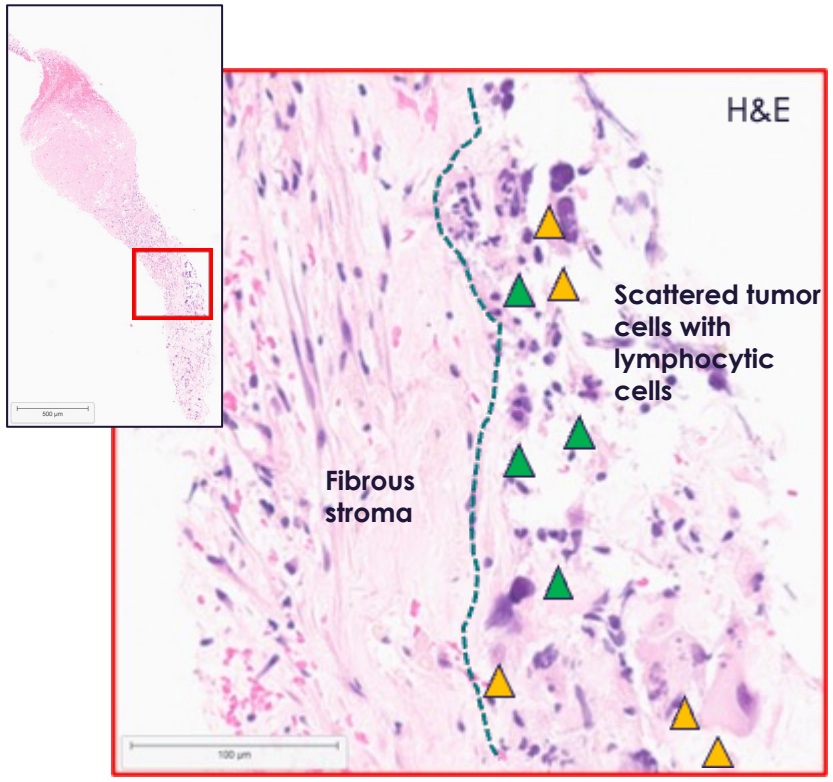
Detection of LYL797 CAR T Cell Infiltration in All Evaluable (N=9) On-study Tumor Biopsies (Days 21-30)

In situ detection of CAR-specific T cells using anti-ROR1 scFv mRNA in situ hybridization (ISH) assay

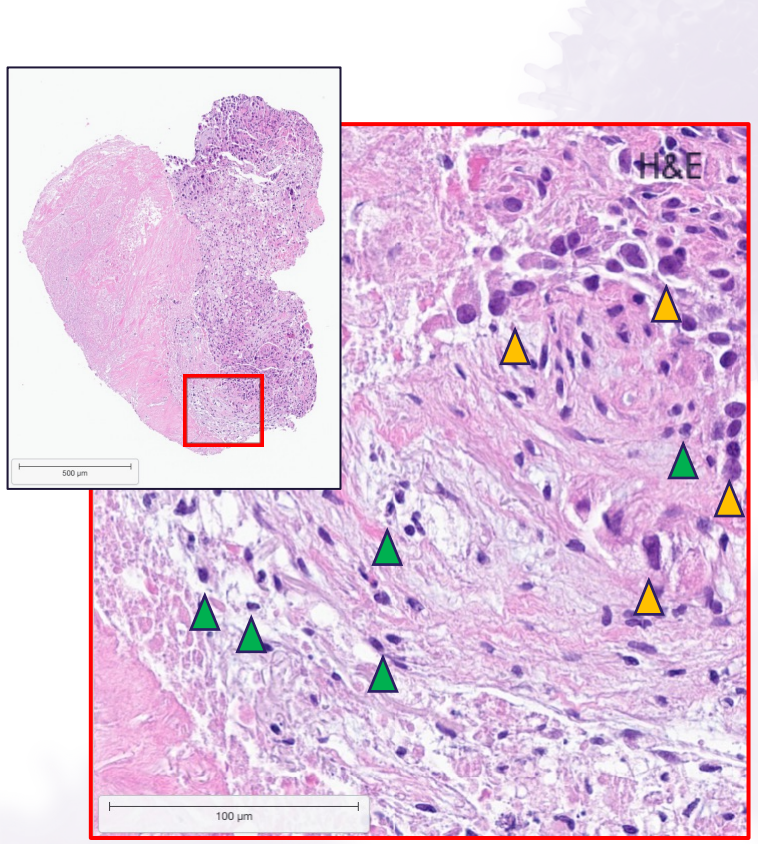


Data cutoff of 29 May 2024; Patient 18; TNBC; 100 x 10^6 cells; Day 29 tumor biopsy of abdominal mass
CAR, chimeric antigen receptor; H&E: Hematoxylin & Eosin; mISH: multiplex fluorescent in situ hybridization; mRNA, messenger RNA; ROR1, receptor tyrosine kinase-like orphan receptor 1

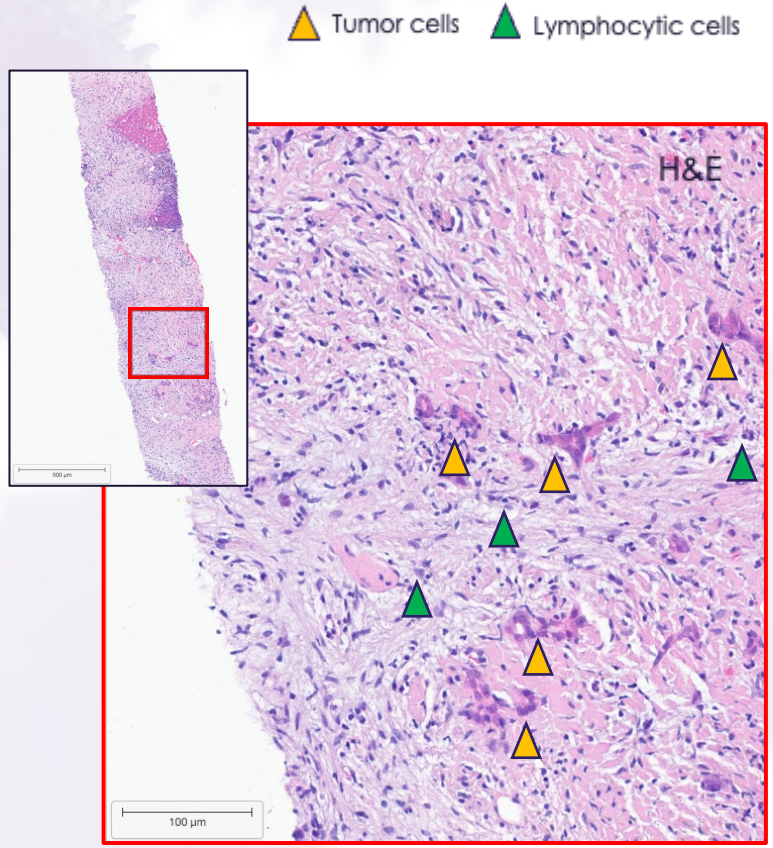
Multiple Tumor Biopsies Had Features Consistent with T Cell-mediated Tumor Lysis Including T Cell-rich Inflammation with Scattered Tumor Cells



Patient 3, TNBC
50 x 10^6 cells, Day 26 liver biopsy



Patient 5, TNBC
150 x 10^6 cells, Day 23 liver biopsy



Patient 8, TNBC
150 x 10^6 cells, Day 28 lung biopsy

Data cutoff of 29 May 2024; H&E: Hematoxylin & Eosin; TNBC, triple-negative breast cancer

LYL797 Clinical and Translational Data Summary

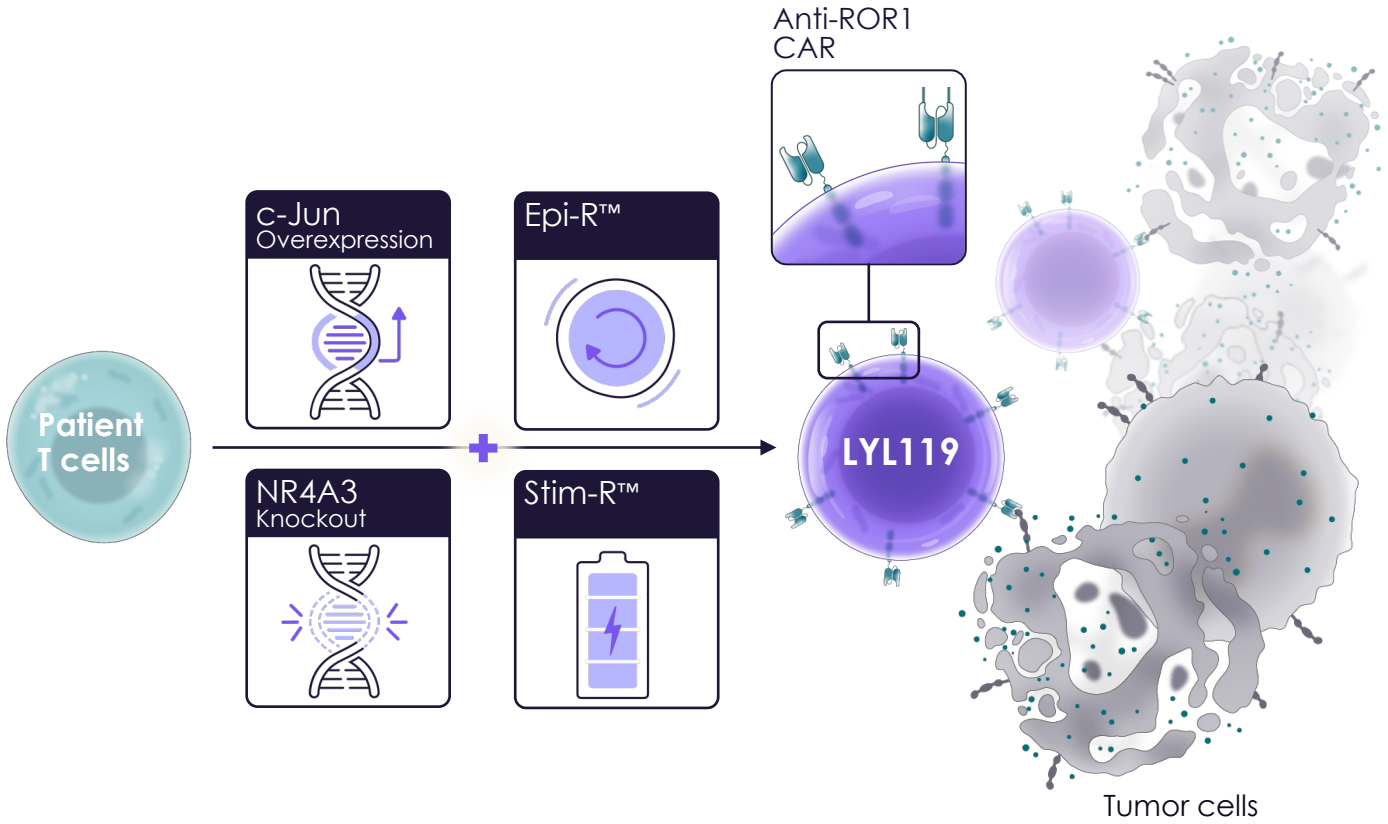
LYL797 CAR T cells had dose-dependent clinical activity and expanded, infiltrated, persisted and killed tumor cells in patients with TNBC

- ✓ 40% ORR and 60% CBR at 150M cells; dose escalation continuing
- ✓ No significant safety signal related to LYL797 observed in patients without lung involvement; steroid prophylaxis to mitigate pneumonitis in patients with lung involvement
- ✓ Persistent LYL797 CAR T cell infiltration (up to 4 months) present in all evaluable on-study tumor biopsies with histologic evidence of tumor lysis in some samples
- ✓ CAR T cell expansion observed in the peripheral blood, with low inhibitory markers of exhaustion and a significant proportion of cells with the desired stem-like and effector-memory phenotype
- ✓ Clinical data validate preclinical models that demonstrate benefit of LYL797 over ROR1 CAR T cells without c-Jun and Epi-R
- ✓ Translational and early clinical data validate hypothesis that c-Jun overexpression and Epi-R technologies can improve clinical benefit of LYL797 ROR1 CAR T cell activity
- ✓ 100% manufacturing success rate to date

Data cutoff of 29 May 2024; CAR, chimeric antigen receptor; CBR, clinical benefit rate; ORR, objective response rate; ROR1, receptor tyrosine kinase-like orphan receptor 1; TNBC, triple-negative breast cancer

LYL119: Incorporates Novel Stackable Technologies Designed to Improve Potency

ROR1 CAR T cell + c-Jun + NR4A3 KO + Epi-R + Stim-R



Key Differentiators

Combining NR4A3 knockout and c-Jun overexpression further reduces T-cell exhaustion and enhances cytotoxicity in preclinical models:

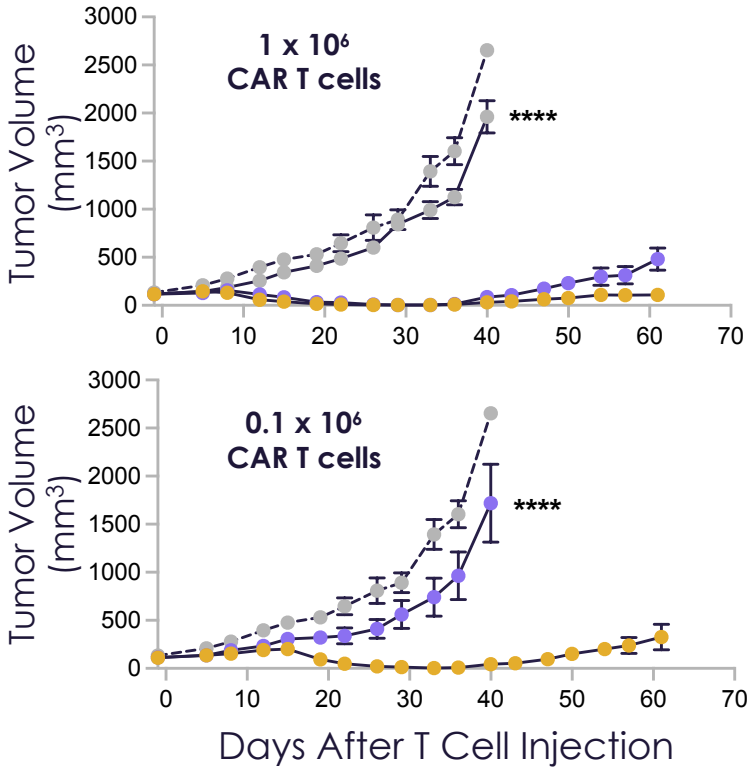
- Reducing NR4A expression enhances T-cell function associated with increased expression of AP-1–regulated genes
- NR4A family transcription factors contribute to T-cell exhaustion by restraining c-Jun/ AP-1 activity

Stim-R CAR T cells demonstrate prolonged persistence and enhanced cytotoxicity in response to serial antigen stimulation in preclinical models

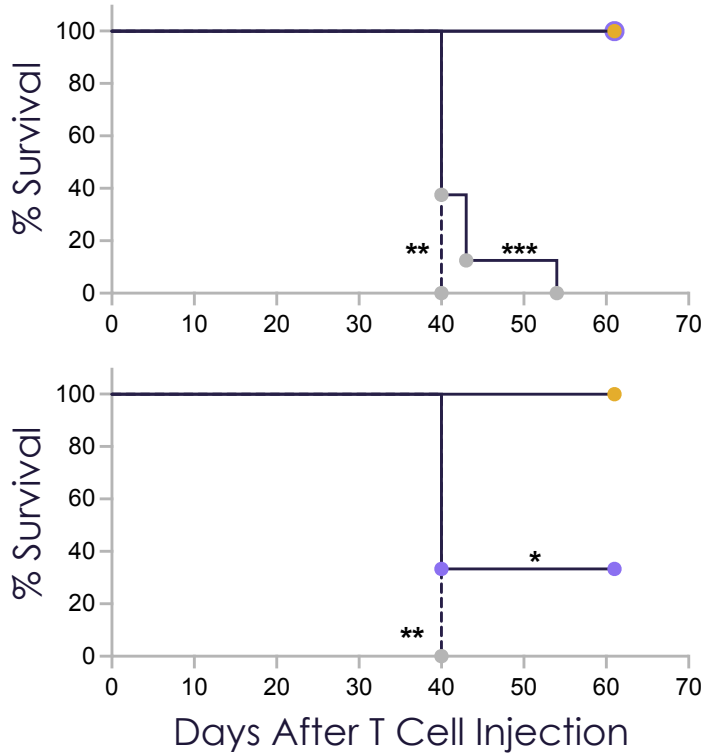
Lam et al., SITC, 2023. Chen J, et al. *Nature*. 2019; Tirosh I, et al. *Science*. 2016; Liu X, et al. *Nature*. 2019; Odagiu I, et al. *Proc Natl Acad Sci USA*.
Abbreviations: AP-1, activator protein 1; CAR, chimeric antigen receptor; KO, knockout; NR4A3, The nuclear receptor 4A3; NSCLC, non-small cell lung cancer; ROR1, receptor tyrosine kinase-like orphan receptor 1

LYL119, Next-generation ROR1-targeted CAR T, Demonstrated More Potent Anti-tumor Activity In Vivo

Significantly Improved Elimination of Xenograft Tumors at the Lower 0.1 x 10^6 CAR T-cell Dose



Significantly Improved Animal Survival at the Lower 0.1 x 10^6 CAR T-cell Dose



PBS | Mock non-transduced (Epi-R + Stim-R) 1.42 x 10^6 cells | LYL797 (non-edited + c-Jun + Epi-R) | LYL119 (NR4A3 KO + c-Jun + Epi-R + Stim-R)

*P<0.05, **P<0.01, ***P<0.001, ****P<0.0001
PBS, phosphate buffered saline; CAR, chimeric antigen receptor; ROR1, receptor tyrosine kinase-like orphan receptor 1

Harnessing Tumor Infiltrating Lymphocytes (TIL) to Fight Cancer

LYL845

A novel epigenetically reprogrammed TIL product candidate designed for differentiated potency and durability

LYL845 Targets Indications with Large Unmet Needs

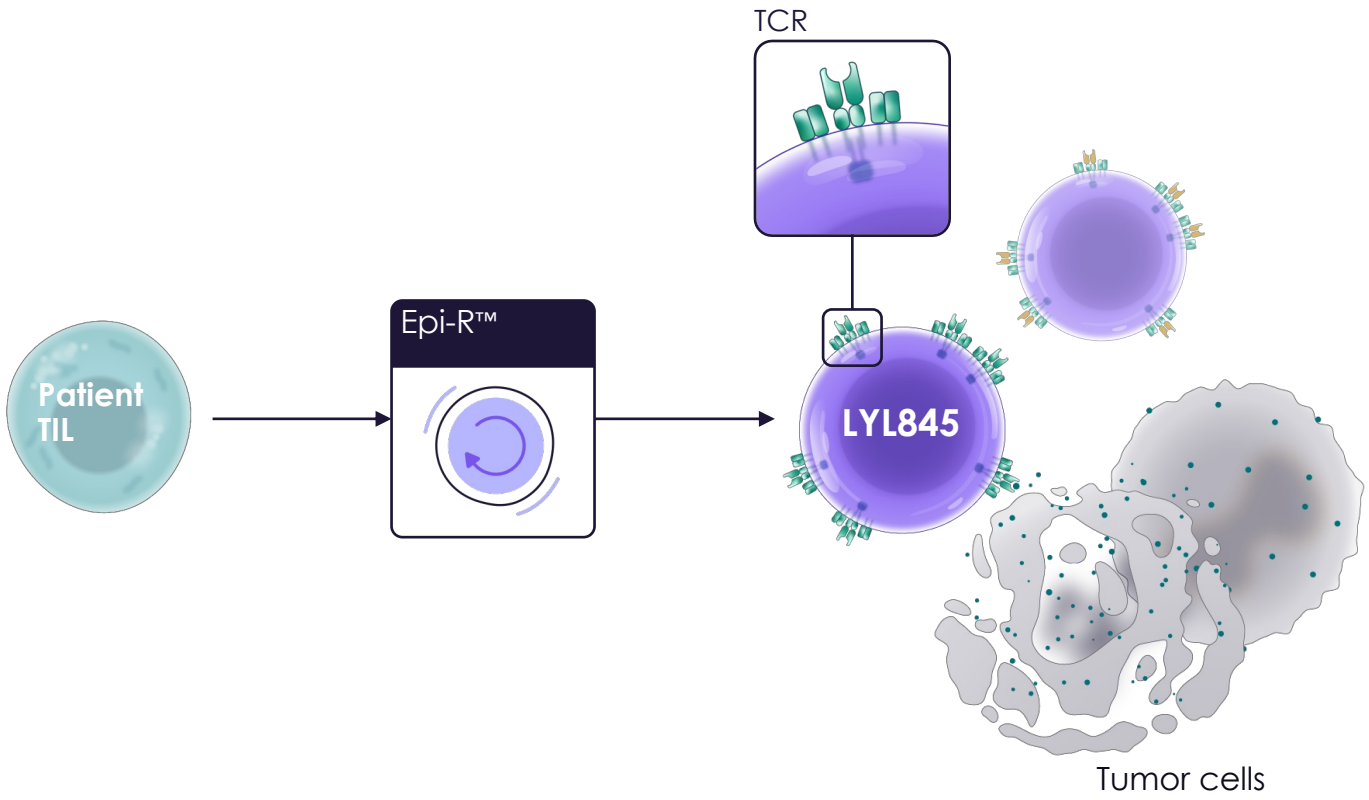
Advanced Melanoma
- 80% of all skin cancer-related deaths
- ~100K new cases, ~8K deaths

Non-small Cell Lung Cancer
- 84% of new lung cancer diagnoses each year
- ~200K new cases, ~110K deaths

Colorectal Cancer
- 3rd most common form of cancer
- ~150K new cases, ~53K deaths

[1]National Cancer Institute and the American Cancer Society and are based on US cases (2022).

LYL845: Clinical Program Supported by Robust Preclinical Data



Key Differentiators

Robust TIL expansion across both immunologically hot and cold tumors

Phenotypes (stemness markers and cytotoxic cells) associated with clinical responses

Preserved polyclonal tumor reactive cells

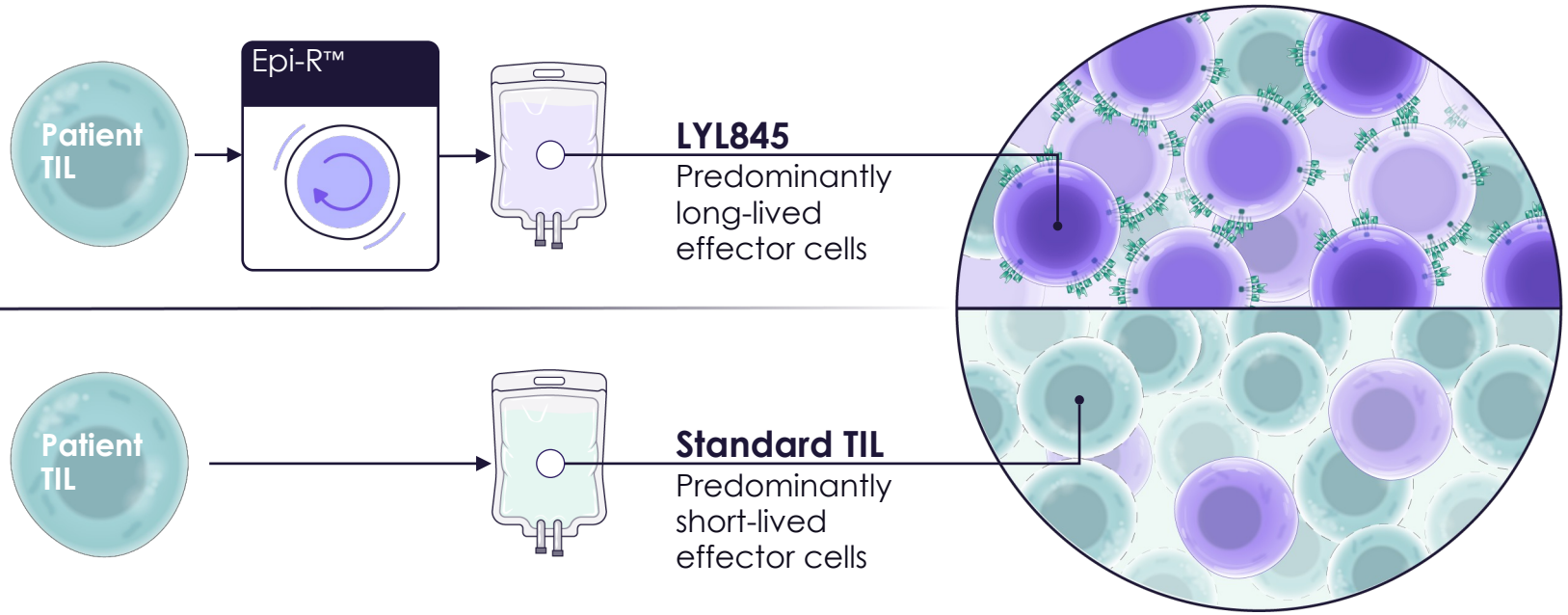
Improved tumor cell killing in vivo

Abbreviations: TCR, T-cell receptor; TIL, tumor-infiltrating lymphocytes.

LYL845: A Novel and Differentiated TIL Product Candidate

Lyell Epi-R Protocol Comprises

- ✓ Proprietary media
- ✓ Optimized cytokine compositions
- ✓ Well-defined cell activation and expansion protocols

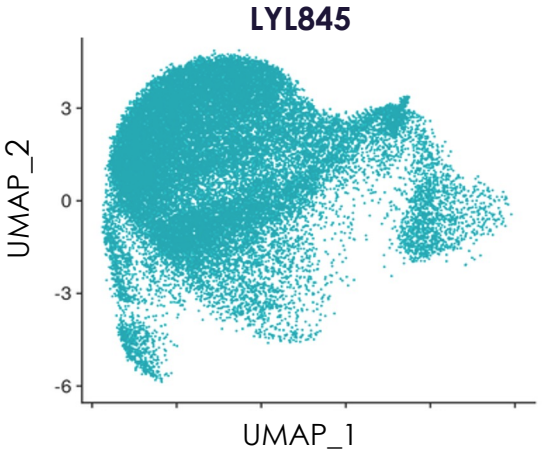


Abbreviations: TIL, tumor-infiltrating lymphocytes.

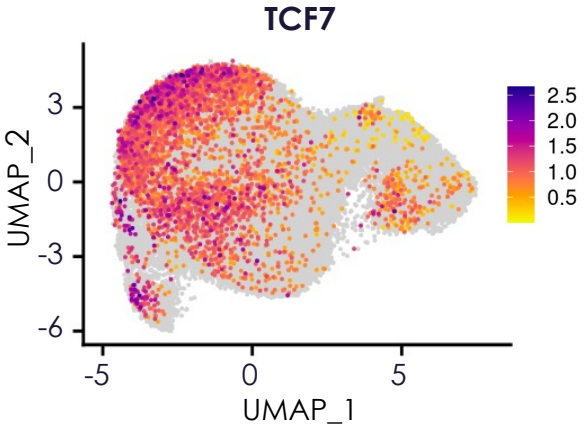
LYL845: Enriched for Stem-like TIL

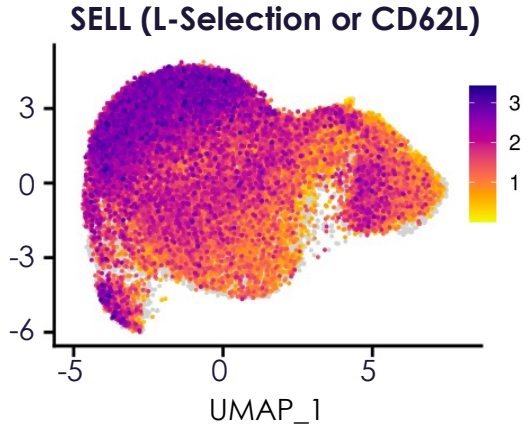
Transcriptomic data of TIL generated from 5 donor tissues using either standard or LYL845 Epi-R process (4 melanoma and 1 NSCLC)

LYL845

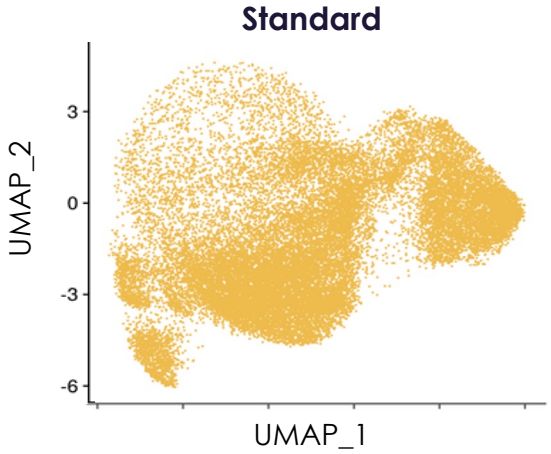


- LYL845 TIL express genes associated with stem-like phenotype (TCF7 and SELL)

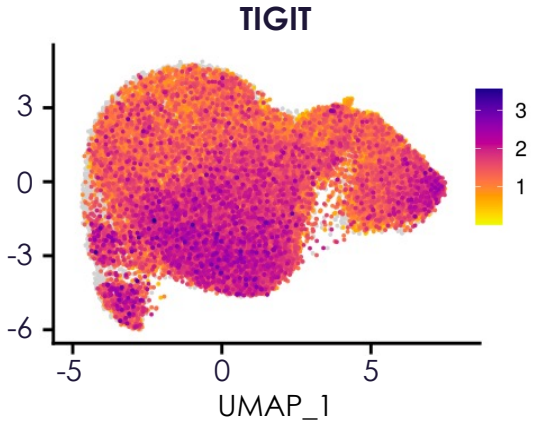


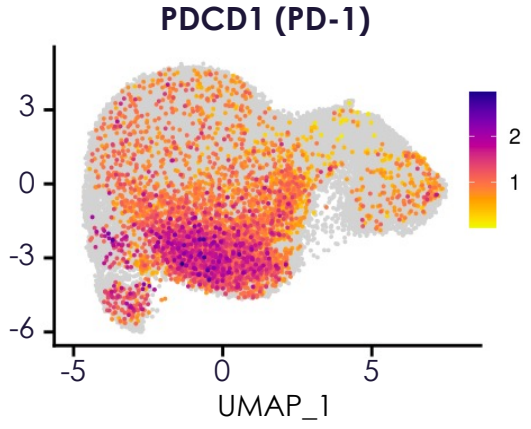


Standard TIL



- Standard TIL express genes associated with exhaustion (TIGIT and PD-1)

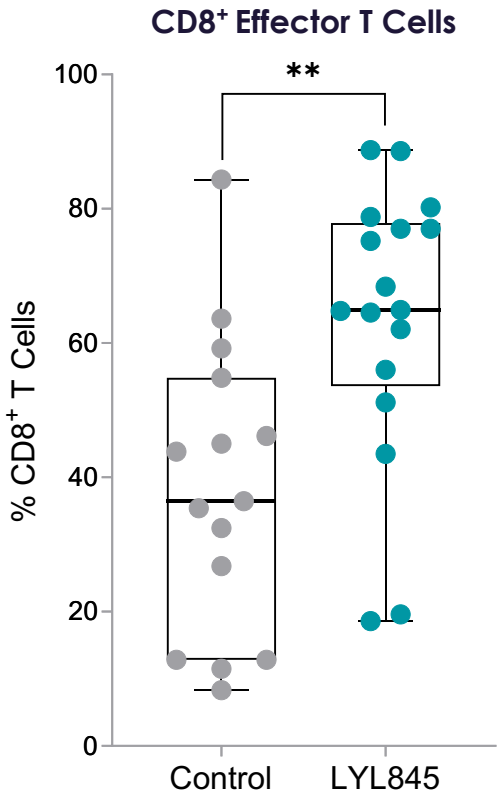




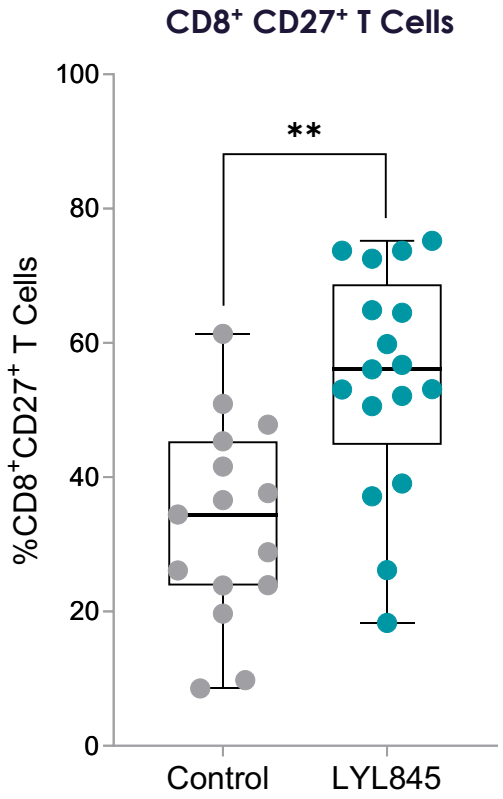
Lyell data on file
Abbreviation: UMAP: Uniform manifold approximation and projection.

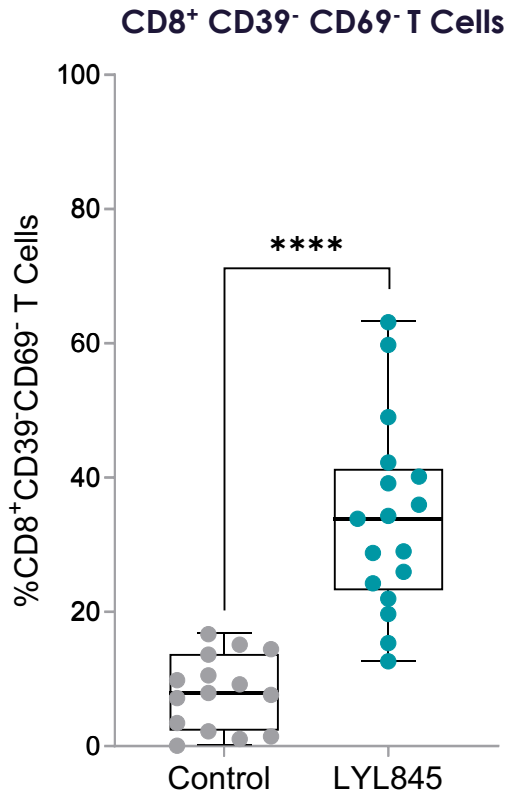
LYL845: Enriched for Cells With Characteristics Associated With Improved Clinical Outcomes from the Literature

Increased % of Cytotoxic Cells



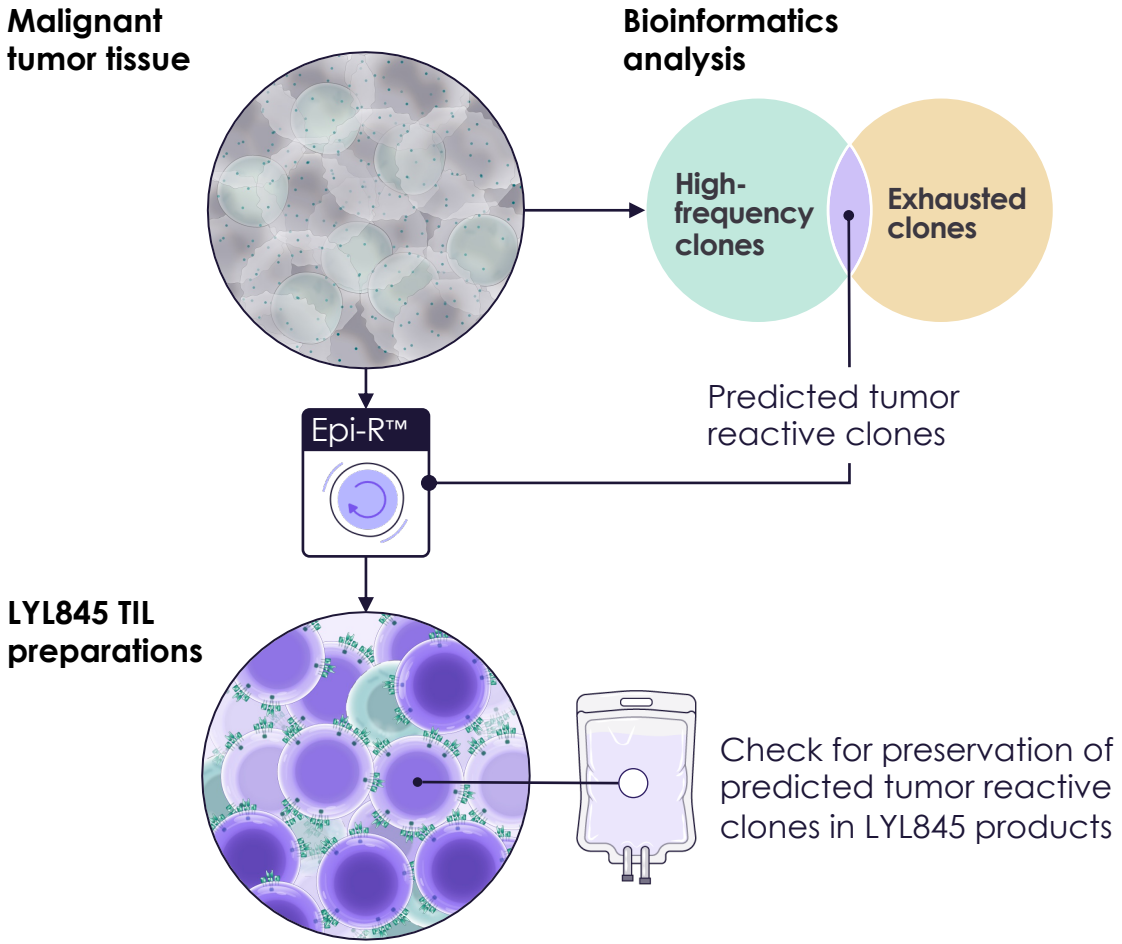
Increased % of Stem-like T Cells





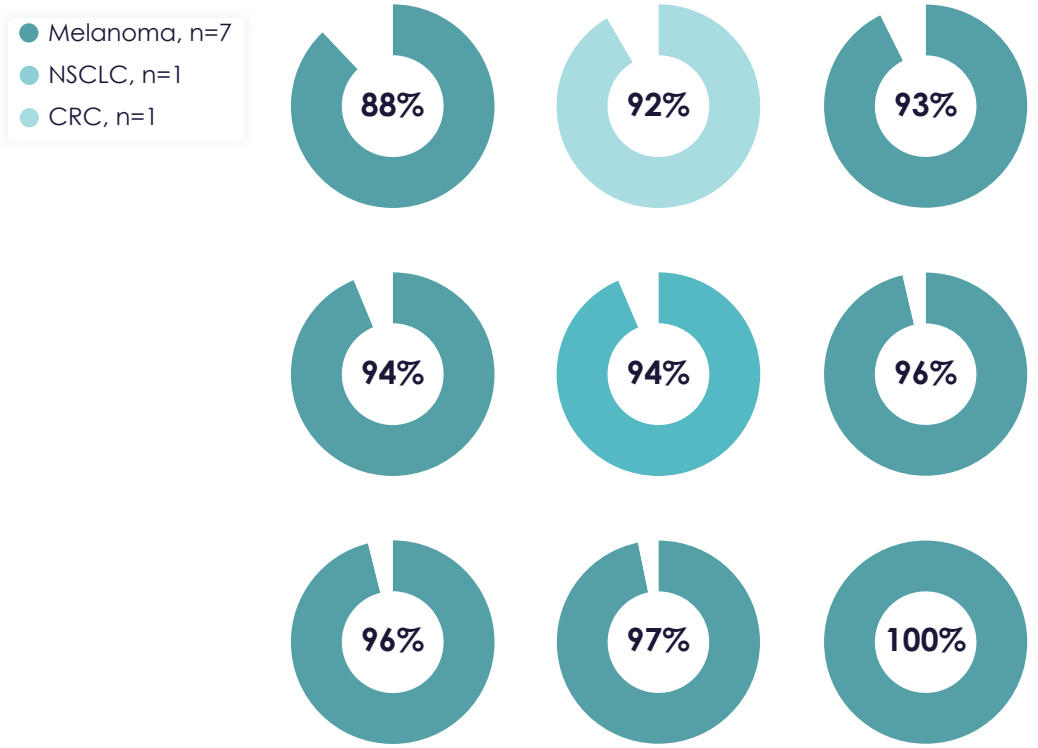
Krishna et al., *Science* Dec. 2020. Patel et al., SITC 2022.
*P<0.05, **P<0.01, ***P<0.001, ****P<0.0001

LYL845 TIL Preserve ~94% of Predicted Tumor-reactive Clones to Enable Targeting of Heterogeneous Solid Tumors



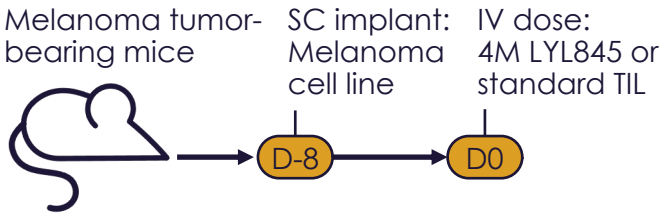
% of Tumor-reactive Clones Preserved in Clinical Scale TIL Products

Donor, N=9



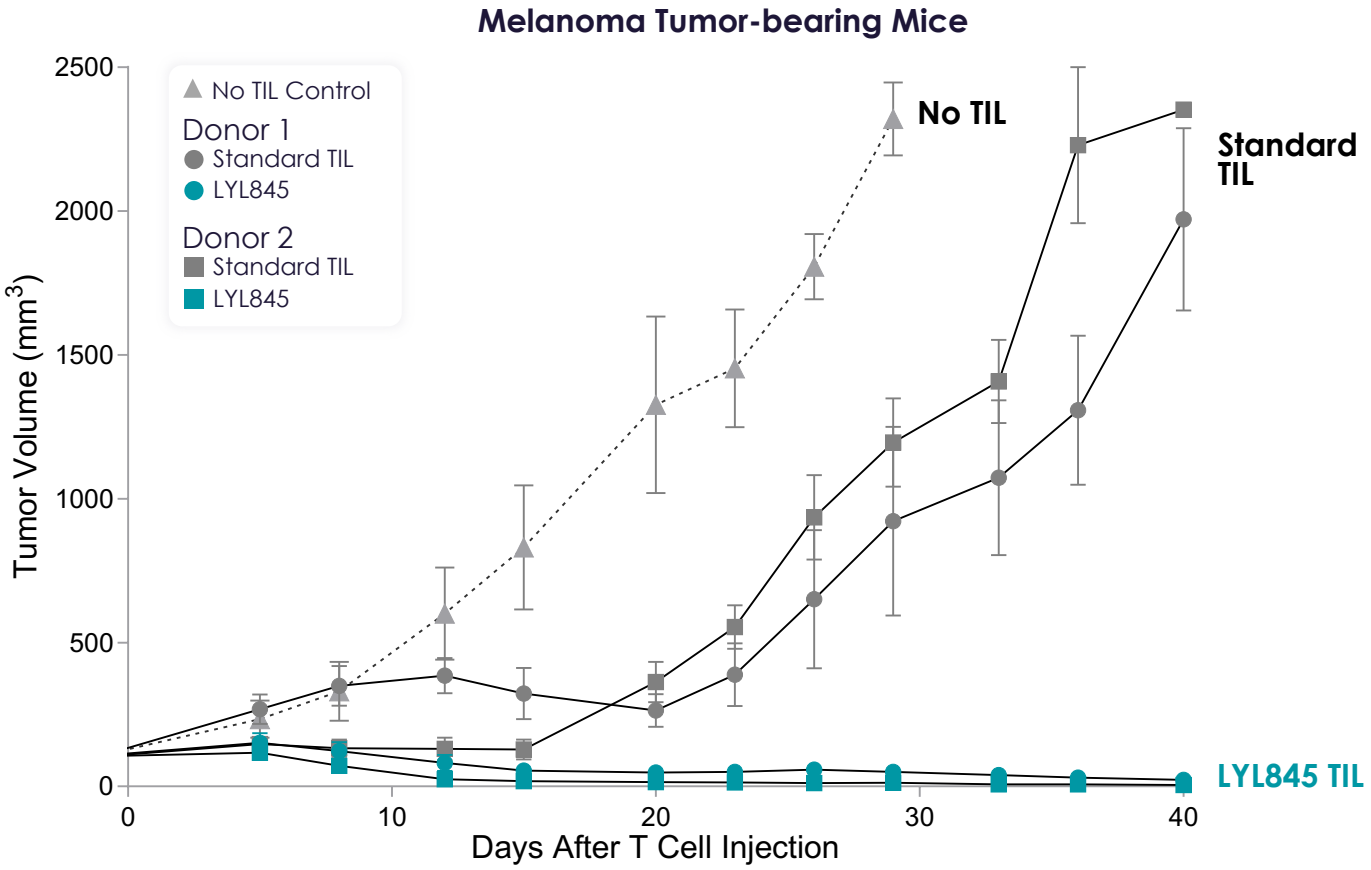
Harris et al., SITC 2022. Pasetto et al., *CIR* 2016. Lowrey et al., *Science* 2022, Oliveira et al., *Nature* 2021.
Abbreviations: CRC, colorectal cancer; NSCLC, non-small cell lung cancer; TIL, tumor-infiltrating lymphocytes.

LYL845: In Vivo Efficacy is Superior With LYL845 TIL Using Epi-R Process Compared to TIL Using Standard Process in Novel Model



- Two refractory melanoma donor samples were collected
- TIL products were generated from each sample using the standard or Lyell Epi-R (LYL845) process

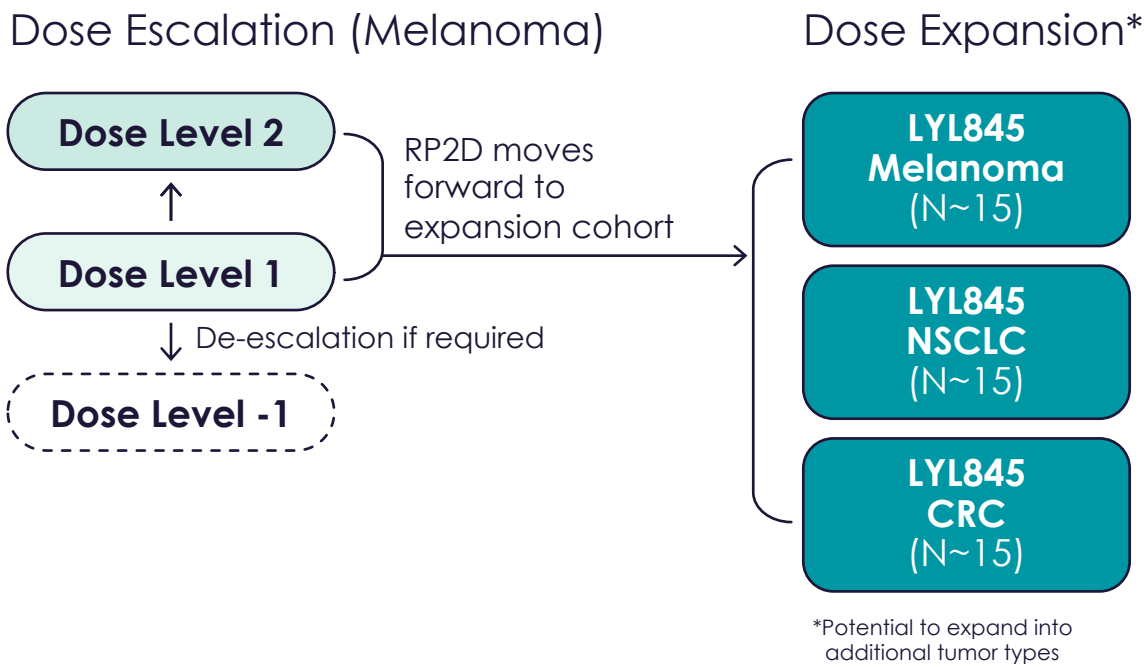
LYL845 Eliminated Tumor Growth



Lyell data on file.
Abbreviations: IV, intravenous; M, million; SC, subcutaneous; TIL, tumor-infiltrating lymphocytes.

LYL845: TIL Phase 1 Trial Design

Clinical Trial Design (mTPI-2)



Patient Population

- Relapsed/refractory metastatic or locally advanced solid tumors:
  - Melanoma
  - NSCLC
  - CRC

Study Objectives

- Patient safety and tolerability
- Overall response rate and durability
- Recommended Phase 2 dose
- Evaluation of expansion, phenotype, clonal diversity, and persistence

NCT05573035; Samhouri et al, SITC 2023.
Abbreviations: CRC, colorectal cancer; m-TPI-2, Modified Toxicity Probability Interval; NSCLC, non-small cell lung cancer; RP2D, Recommended phase 2 dose; TIL, tumor-infiltrating lymphocytes.

Upcoming Potential Milestones

Balance sheet of $526M* provides cash runway into 2027, through multiple clinical milestones

LYL797	**ROR1 CAR T cell + c-Jun + Epi-R**
2H24	❑ Begin enrolling patients with ovarian or endometrial cancers
	❑ Submit IND for trial in patients with multiple myeloma or CLL
	❑ Clinical data update including initiation of dose expansion (late-2024/early-2025)
1H25	❑ Present updated Phase 1 data at a major medical conference
LYL119	**ROR1 CAR T cell + c-Jun + NR4A3 CRISPR Knockout + Epi-R + Stim-R**
2H24	❑ IND clearance
1H25	❑ Progress update on Phase 1 trial
2H25	❑ Initial clinical data
LYL845	**TIL + Epi-R**
2H24	❑ Initial clinical data in patients with advanced melanoma

*Cash, cash equivalents and marketable securities as of 3/31/2024

CAR, chimeric antigen receptor; CLL, chronic lymphocytic leukemia; IND, investigational new drug application; NR4A3, nuclear receptor 4A; ROR1, receptor tyrosine kinase-like orphan receptor 1; TIL, tumor-infiltrating lymphocytes

It’s all about the cells.

For more information, please contact
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