UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 11, 2023

Lyell Immunopharma, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-40502**	**83-1300510**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

201 Haskins Way **South San Francisco, California**		**94080**
(Address of Principal Executive Offices)		**(Zip Code)**

Registrant's Telephone Number, Including Area Code: 650 695-0677

(Former Name or Former Address, if Changed Since Last Report)
Not Applicable

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	LYEL	NASDAQ Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

Lyell Immunopharma, Inc. (the "Company") hereby furnishes the investor presentation the Company will present to analysts and investors on or after September 11, 2023 (the "Investor Presentation"). The slides of the Investor Presentation are attached hereto as Exhibit 99.1 and will be available on the Company's website at https://ir.lyell.com/news-events/presentations. The information contained in the Investor Presentation is summary information that is intended to be considered in the context of the Company's Securities and Exchange Commission ("SEC") filings and other public announcements that the Company may make, by press release or otherwise, from time to time. The Company undertakes no duty or obligation to publicly update or revise the information contained in this presentation, although it may do so from time to time. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases or through other public disclosure.

The information in this Current Report on Form 8-K, including Exhibit 99.1 attached hereto, is being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any filing made by the Company under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing. The furnishing of this information hereby shall not be deemed an admission as to the materiality of any such information.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Lyell Immunopharma, Inc.'s Investor Presentation dated September 11, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

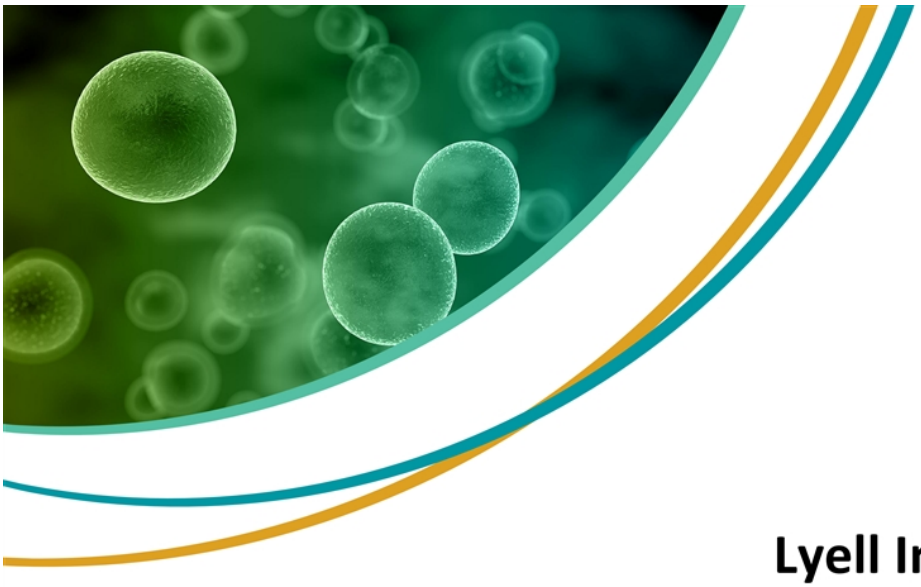
Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Lyell Immunopharma, Inc.

Date: September 11, 2023

By: /s/ Matthew Lang
Matthew Lang
Chief Business Officer

Exhibit 99.1



Lyell Immunopharma

September 11, 2023

Forward-looking statements

Certain matters discussed in this presentation are "forward-looking statements" of Lyell Immunopharma, Inc, 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, 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 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 and the lingering effects of the COVID-19 pandemic; our ability to submit planned INDs or initiate or progress clinical trials on the anticipated timelines, if at all; 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; the nonclinical profiles of our product candidates not translating in clinical trials; the potential for results from clinical trials to differ from nonclinical, early clinical, preliminary or expected results; 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 June 30, 2023 and subsequent filings with the SEC.

Advancing T cell therapies for solid tumors

Clinical data from two lead programs in 2024

Two clinical programs: wholly-owned, addressing large patient populations

LYL797: ROR1 targeted CAR T cell
- 1H2024: P1 clinical & translational data from 20+ patients
- TNBC, NSCLC

LYL845: Tumor Infiltrating Lymphocyte (TIL)
- 2024: P1 clinical & translational data
- Melanoma, NSCLC, CRC

Executing a scalable manufacturing strategy

Lyell's LyFE center producing current clinical supply
- 2024: Epi-R P2 process to shorten TIL manufacturing time without impacting cell number and phenotype

Planning for the future
- CAR T cell proof-of-concept collaboration with Cellares to build scale and reduce cost

Portfolio of novel reprogramming platform technologies

- 1H2024: IND filing for LYL119, ROR1 targeted CAR T cell designed for enhanced potency and durability; using four of our technologies

~$633 million in cash

- Runway into 2026

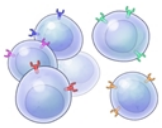
ROR1, receptor tyrosine kinase-like orphan receptor 1; TNBC, triple-negative breast cancer; NSCLC, non-small-cell lung cancer; CRC, colorectal cancer; P1, Phase 1

Lyell

Lyell is developing two types of personalized cell therapy:

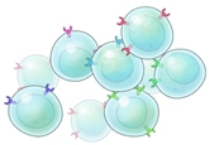
Focused on getting the T-cells right

OUR GOAL: Reprogram T cells to defeat solid tumors



CAR T cells

- Resist exhaustion
- Durable cytotoxicity
- Self-renewal
- Persistence



Tumor-infiltrating lymphocytes

- Durable cytotoxicity
- Maintain polyclonality
- Right phenotype
- Hot and cold tumors

CAR, chimeric antigen receptor

Lyell

Lyell's T-cell reprogramming technologies are designed to address primary barriers to success in solid tumors

TO ACHIEVE SUCCESS IN SOLID TUMORS, CELL THERAPY MUST:

RESIST EXHAUSTION, RETAIN FUNCTION

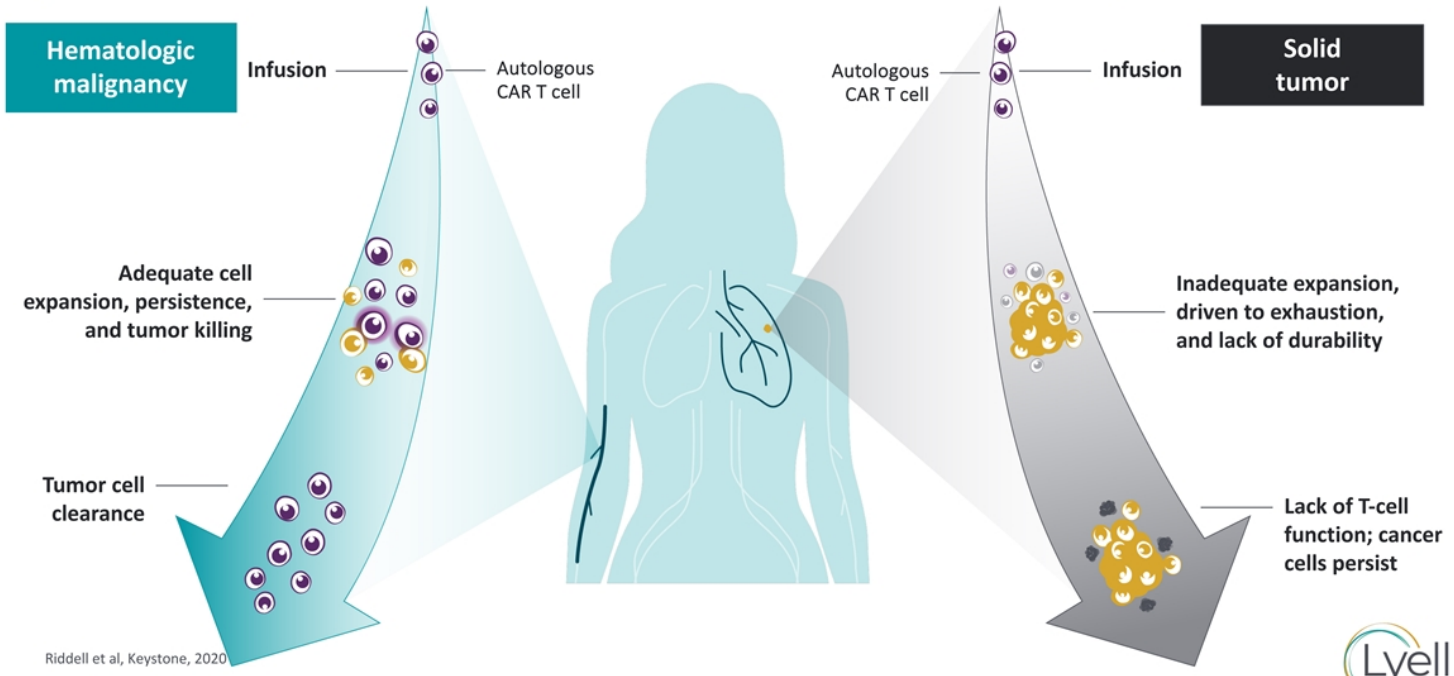
Maintain cancer cell killing in the immunosuppressive tumor microenvironment

ENHANCE DURABLE STEMNESS

Increase ability to self-renew and persist to drive durable tumor cytotoxicity

Lyell

Solid tumors drive T cells down a path to exhaustion



Riddell et al, Keystone, 2020

Stackable technologies designed to generate potent T cells with durable function

GENETIC REPROGRAMMING

c-Jun overexpression

NR4A3 knockout

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

EPIGENETIC REPROGRAMMING

Epi-R™

Stim-R™

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

Lyell

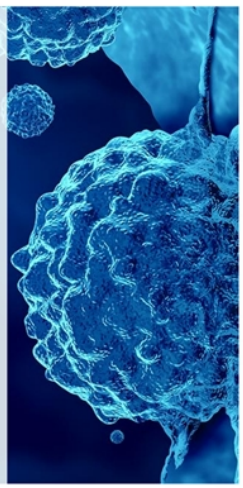
A clinical-stage company with a growing pipeline of novel therapies for solid tumors

Product Candidate/ Modality	Target	Genetic Reprogramming		Epigenetic Reprogramming		Target Indications	Preclinical	Phase 1	Phase 2 / Pivotal	Next Expected Milestone
		c-Jun	NR4A3	Epi-R™	Stim-R™					
LYL797 CAR T Cell	ROR1	√		√		TNBC NSCLC Other Solid Tumors				Initial data in 1H 2024
LYL119 CAR T Cell	ROR1	√	√	√	√	ROR1+ Solid Tumors				Submit IND in 1H 2024
LYL845 TIL	Multiple antigens			√		Melanoma CRC, NSCLC Other Solid Tumors				Initial data in 2024
2nd Generation TIL	Multiple antigens	**Genetic and Epigenetic Reprogramming**				Solid Tumors				

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

People with cancer need better therapies

90%
Cancer deaths caused by solid tumors



<2
Years before cancer progresses

<3
Years most metastatic cancer patients live after diagnosis

seer.cancer.gov; Deaths (Estimated 2021); Survival Rates by Time Since Diagnosis, 2000-2017
CDC Nat'l Ctr for Health Statistics, Mortality in the US, 2020

Lyell

Lyell product candidates target large unmet needs

~500K new cases and ~180K US deaths annually

TRIPLE-NEGATIVE BREAST CANCER

- 15% of breast cancer diagnoses in the US each year
- ~40,000 new cases
- ~10,000 deaths

LYL797

NON-SMALL CELL LUNG CANCER

- 84% of new lung cancer diagnoses each year
- ~200,000 new cases
- ~110,000 deaths

LYL797 & LYL845

MELANOMA

- 80% of all skin cancer-related deaths
- ~100,000 new cases
- ~8,000 deaths

LYL845

COLORECTAL CANCER

- 3rd most common form of cancer
- ~150,000 new cases
- ~53,000 deaths

LYL845

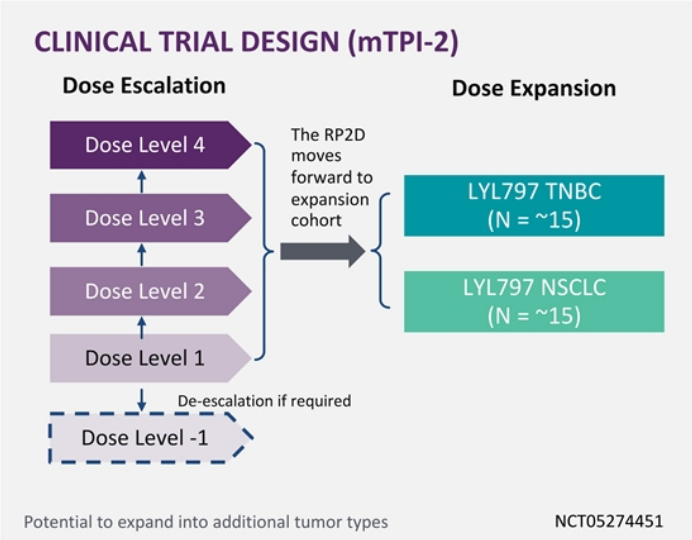
National Cancer Institute and the American Cancer Society and are based on US cases. (2022)

Reprogramming T cells to target aggressive cancers

LYL797: A genetically and epigenetically reprogrammed ROR1 CAR T cell product candidate designed for differentiated potency and durability

Lyell

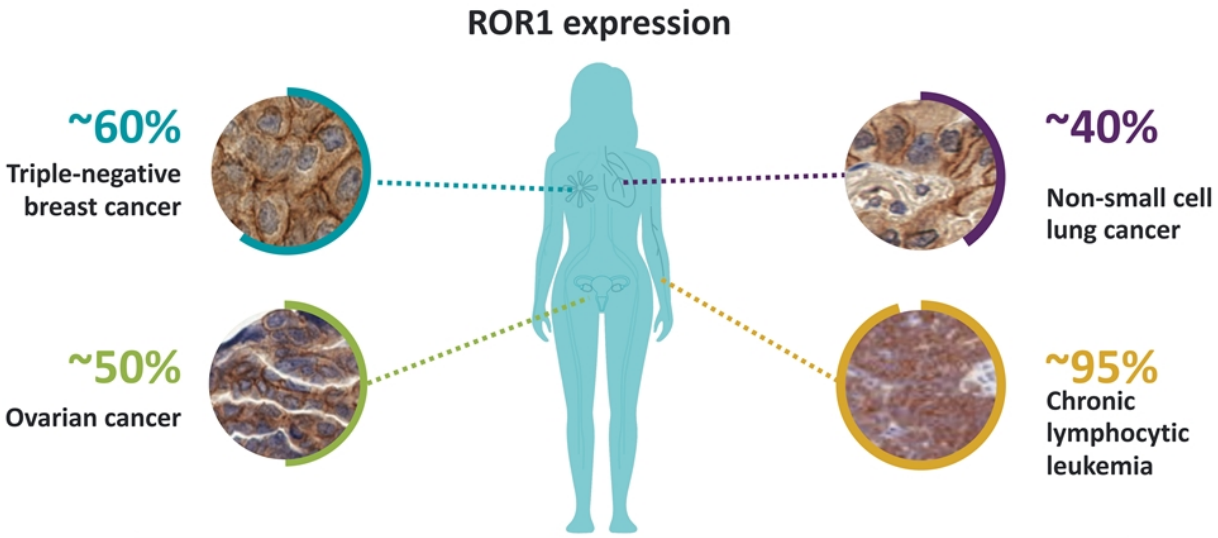
LYL797 CAR T cell Phase 1 trial design



- Patient population
  - Relapsed/Refractory TNBC patients who have failed two lines of therapy
  - Relapsed/Refractory NSCLC patients who have failed one line of therapy
  - ROR1 positive
- Study objectives
  - Patient safety and tolerability
  - Assessment of cytotoxicity and duration of T-cell function
  - Overall response rate and durability
  - Recommended phase 2 dose
  - CAR T cell pharmacokinetics

Spigel et al, ESMO 2022
mTPI-2, modified toxicity probability interval 2; NSCLC, non-small-cell lung cancer; ROR1, receptor tyrosine kinase–like orphan receptor 1; TNBC, triple-negative breast cancer; RP2D, recommended Phase 2 dose

ROR1 is highly expressed in many human cancers and correlates with a poor prognosis



In previous clinical trials and a non-human primate ROR1 CAR T cell toxicity study, no on-target off-tumor toxicity from ROR1-targeted therapies have been reported

ROR1, receptor tyrosine kinase-like orphan receptor 1

Jeong, *Medicina*, 2022; Chien, *Virchows Arch* 2016; Zhang, *PNAS*, 2014; Wang, *NEJM Evidence*, 2022; Berger, *Cancer Immunol Res*, 2015; Choi, *Cell Stem* Cell, 2018

Lyell's ROR1 assay and screening program support current and future clinical trials

Screening data with Lyell's assay consistent with ROR1 expression in the literature

TRIPLE-NEGATIVE BREAST CANCER

- 15% of breast cancer diagnoses/year
- ~40,000 new cases / ~10,000 deaths

53% ROR1+

N=77

NON-SMALL CELL LUNG CANCER

- 84% of new lung cancer diagnoses/year
- ~200,000 new cases / ~110,000 deaths

33% ROR1+

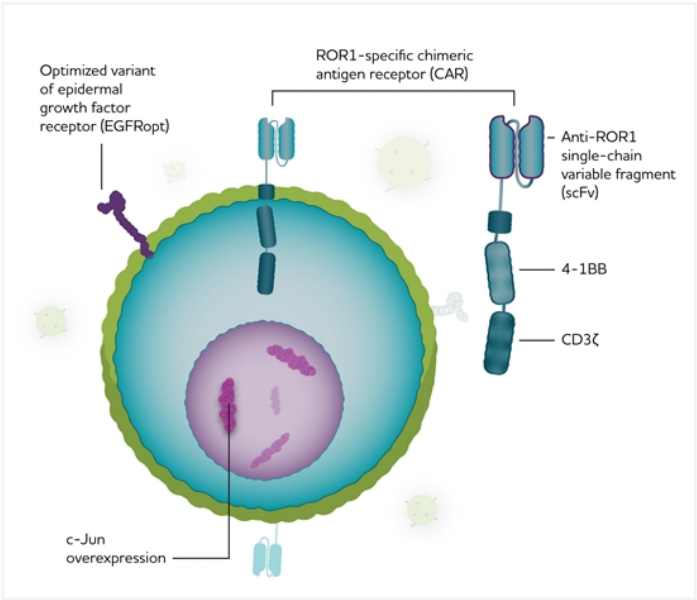
N=18

ROR1, receptor tyrosine kinase-like orphan receptor 1; National Cancer Institute and the American Cancer Society and are based on US cases (2022)

Published literature: Balakrishnan et al, Clin Cancer Res. 2017, TNBC ~60%, NSCLC ~40%

LYL797 clinical program supported by robust preclinical data

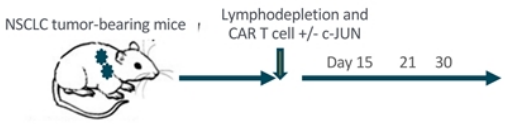
ROR1 CAR T cell + c-Jun + Epi-R



Key differentiators

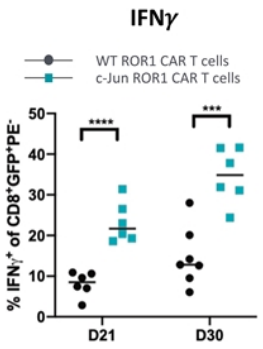
- **Tumor reduction, enhanced cytokine production and tumor infiltration** in aggressive NSCLC syngeneic animal model with c-Jun
- **Stem-like phenotype, durability and enhanced cytotoxicity** with Epi-R technology
- **Prolonged survival** by combining c-Jun and Epi-R technologies (LYL797) in xenograft NSCLC animal model

Superior preclinical efficacy demonstrated with c-Jun overexpressing ROR1 CAR T cells in aggressive NSCLC model

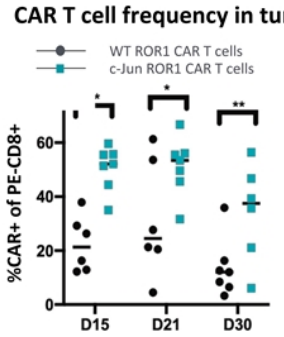


- Syngeneic Kras/p53 model that recapitulates human NSCLC
- Also recapitulates the barriers in treating human NSCLC with the ROR1 CAR T cells
- Extremely difficult model in which to achieve tumor regression

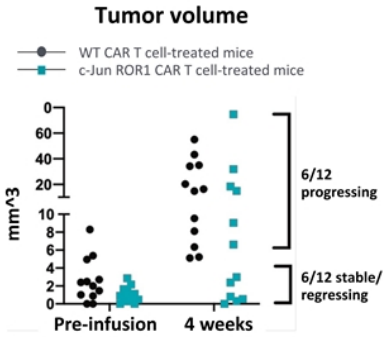
Enhanced intratumoral function



Enhanced infiltration



Tumor control in 50% of mice

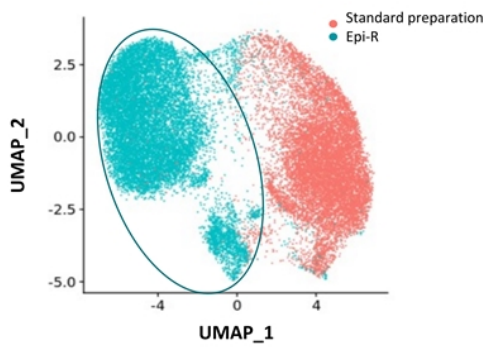


Riddell Lab, Fred Hutch, unpublished data

* is p<.05 ** is p<.01 *** is p<.001 **** is p<.0001

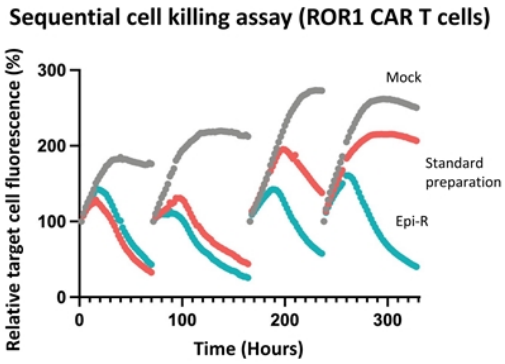
Epi-R™ technology produces transcriptionally distinct populations of T cells that resist exhaustion and maintain cytotoxicity

Distinct gene expression profile of Epi-R expanded cells vs. standard preparation



Park et al., AACR 2022

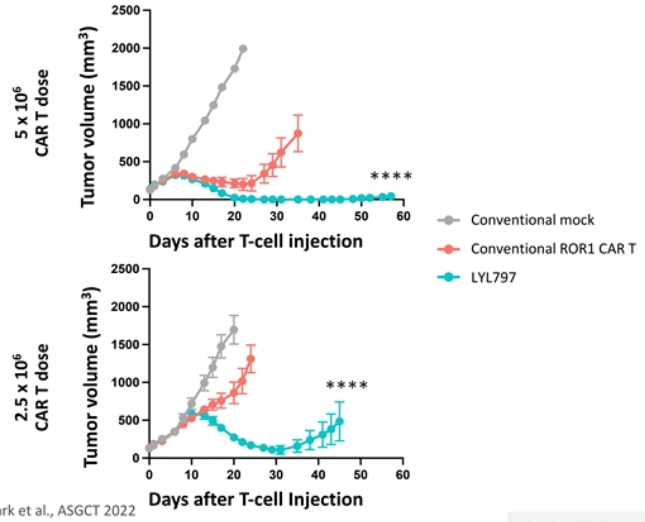
Epi-R expanded cells demonstrate prolonged cytotoxicity after removal from Epi-R conditions



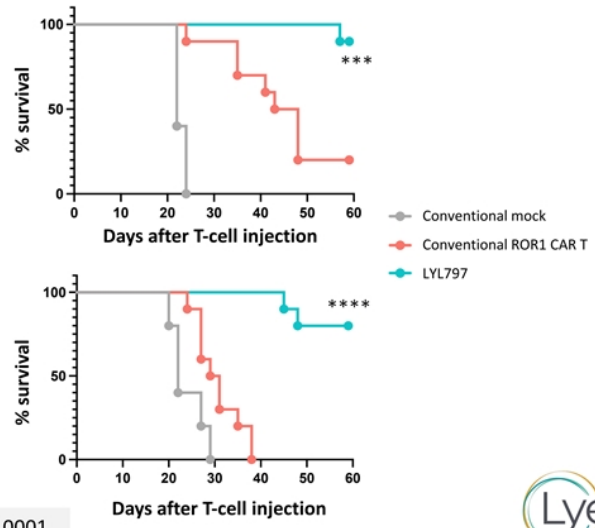
Tumor target: H1975

LYL797 combines c-Jun and Epi-R™ reprogramming technologies to prolong survival in NSCLC (H1975) xenograft model

LYL797 reduces tumor burden

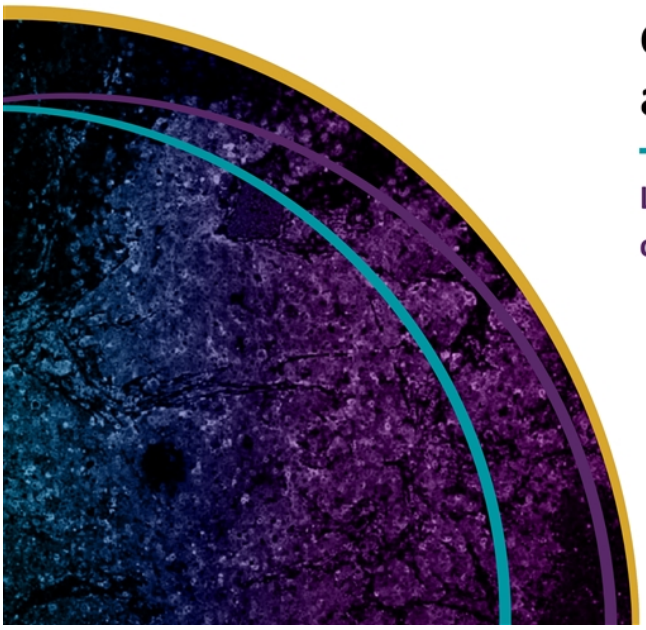


LYL797 prolongs survival



Park et al., ASGCT 2022

*** is p<.001 **** is p<.0001



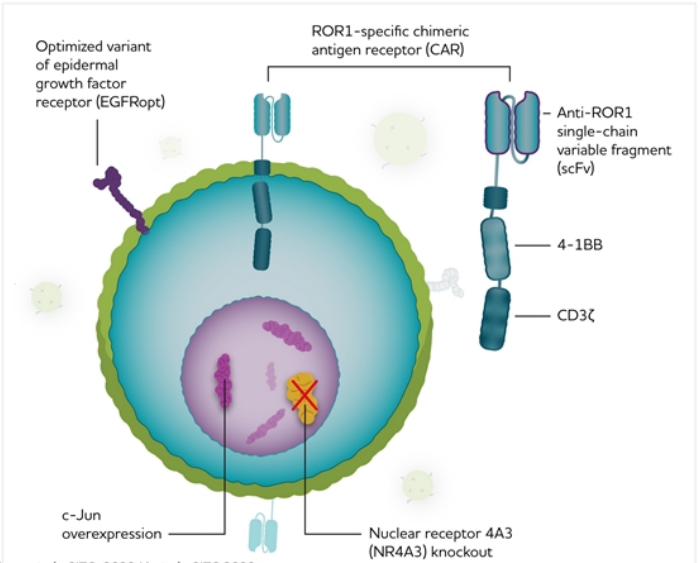
Novel stackable technologies designed to improve potency and durability

LYL119: Innovative ROR1 CAR T cell product candidate designed for enhanced cytotoxicity

Lyell

LYL119 incorporates novel stackable technologies designed to improve potency and durability

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



Lam et al., SITC, 2022 Li et al., SITC 2022

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*

Key Differentiators

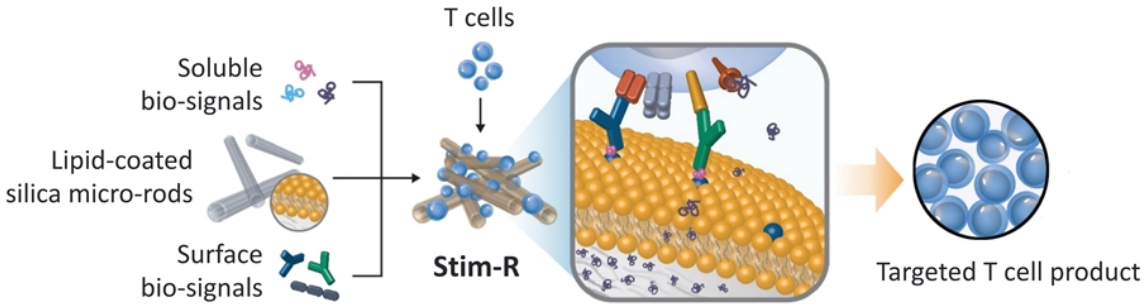
- Combining NR4A3 knockout and c-Jun overexpression further **reduces T cell exhaustion and enhances cytotoxicity**
  - Reducing NR4A expression enhances T-cell function associated with increased expression of AP-1–regulated genes
  - NR4A family transcription factors may contribute to T-cell exhaustion by restraining c-Jun activity

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

Stim-R technology mediates precise signal-molecule presentation during T-cell activation

- **Stim-R technology mimics physiologic presentation:**
  - Multiple signals presented in precise densities and stoichiometries
  - Controlled presentation of both soluble and surface signals

Stim-R technology is a programmable cell-signaling platform



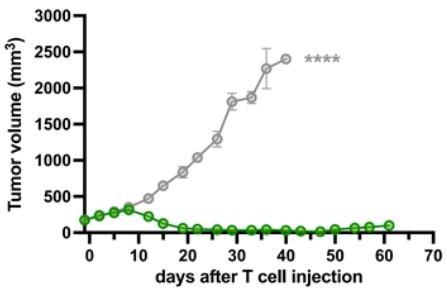
Li et al., SITC 2022

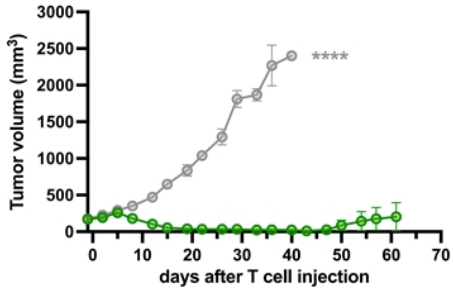
LYL119 is potent and eliminated H1975 (NSCLC) xenograft tumors even at low doses of CAR T cells

Low Dose
4x10^5 CAR T cells

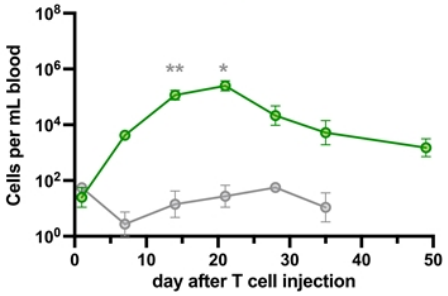
High Dose
2x10^6 CAR T cells

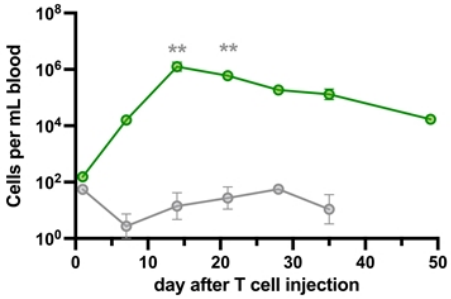
Elimination of xenograft tumors at both low and high CAR T cell doses





Robust CAR T cells expansion *in vivo*





LYL119
Mock

Lam et al., ASGCT, 2023

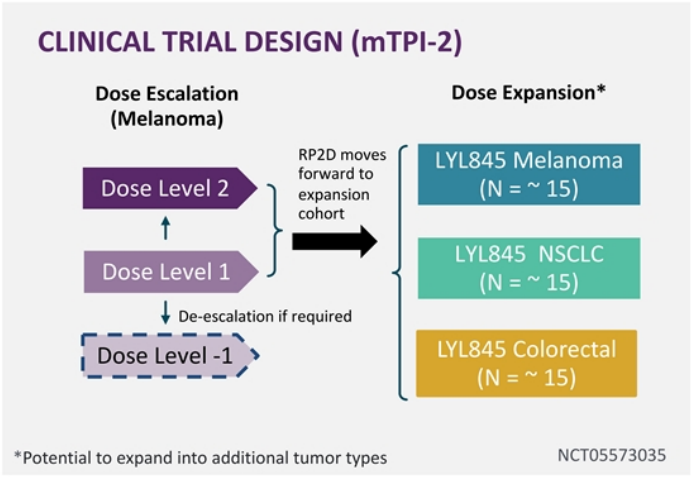
Lyell

Harnessing tumor-infiltrating lymphocytes to fight cancer

LYL845: A novel epigenetically reprogrammed TIL product candidate designed for differentiated potency and durability

Lyell

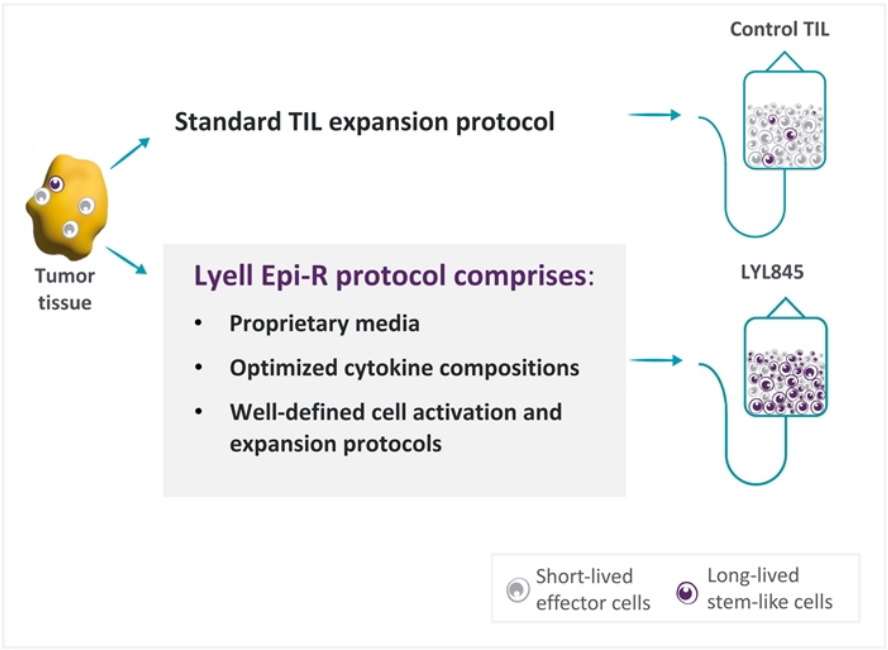
LYL845 TIL Phase 1 trial design



- Patient population
  - Relapsed and/or refractory metastatic or locally advanced solid tumors:
    - Melanoma
    - Non-small cell lung cancer
    - Colorectal cancer
- Study objectives
  - Patient safety and tolerability
  - Overall response rate and durability
  - Recommended Phase 2 dose
  - Evaluation of expansion, phenotype, clonal diversity and persistence

mTPI-2, modified toxicity probability interval 2; NSCLC, non-small-cell lung cancer; RP2D, recommended Phase 2 dose

LYL845: A novel and differentiated TIL product candidate

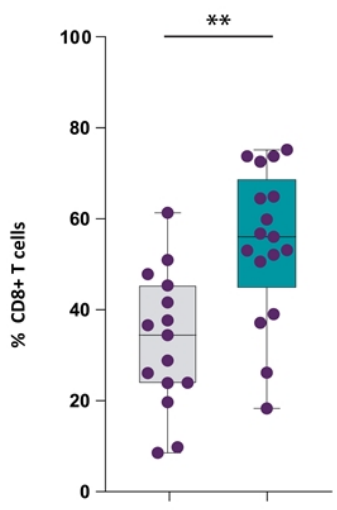


Key differentiators

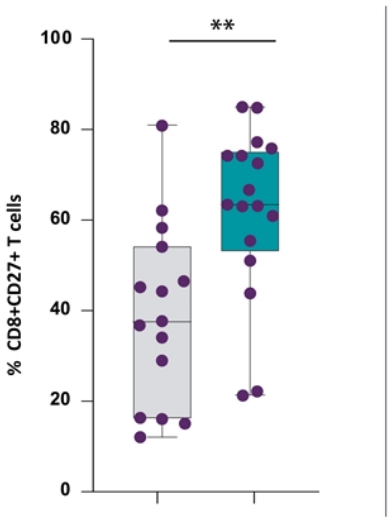
- **Phenotypes** (stemness markers and cytotoxic cells) **associated with clinical responses**
- **Preserved polyclonal** tumor reactive cells
- Robust TIL expansion across **both hot and cold tumors**

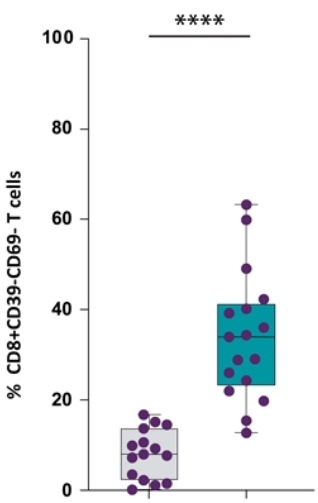
LYL845 is enriched for cells with characteristics associated with improved clinical outcomes

Increased % of cytotoxic cells



Increased % of stem-like T cells



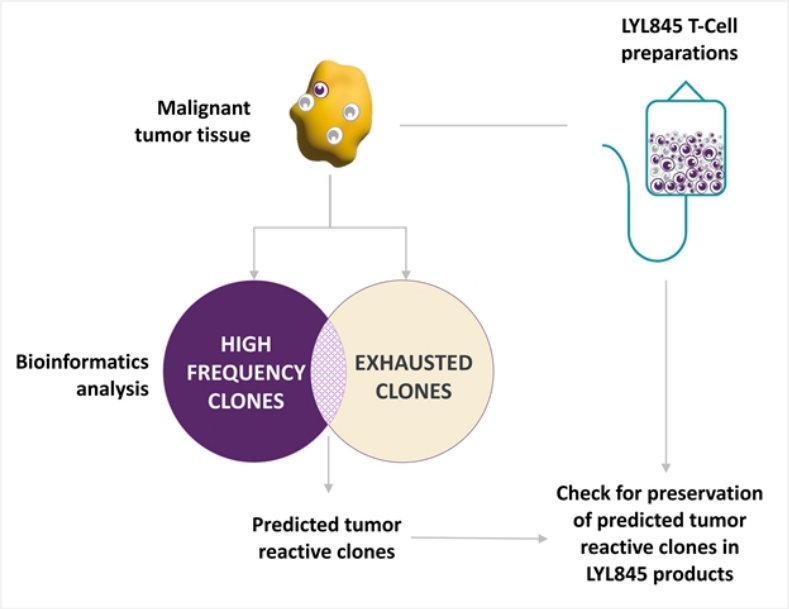


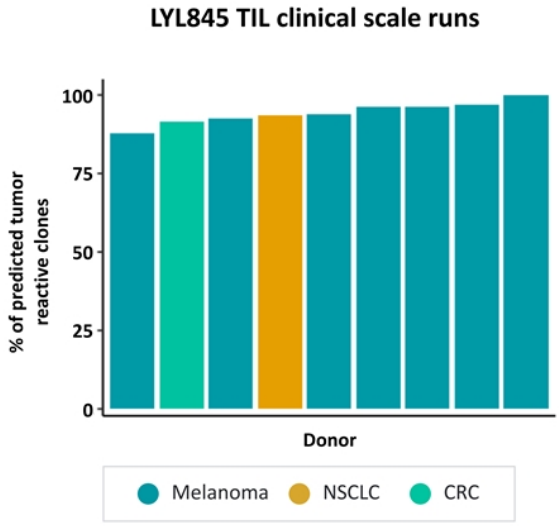
Control LYL845

* is p<.05 ** is p<.01 *** is p<.001 **** is p<.0001

Krishna et al., *Science* Dec. 2020
Patel et al., SITC 2022

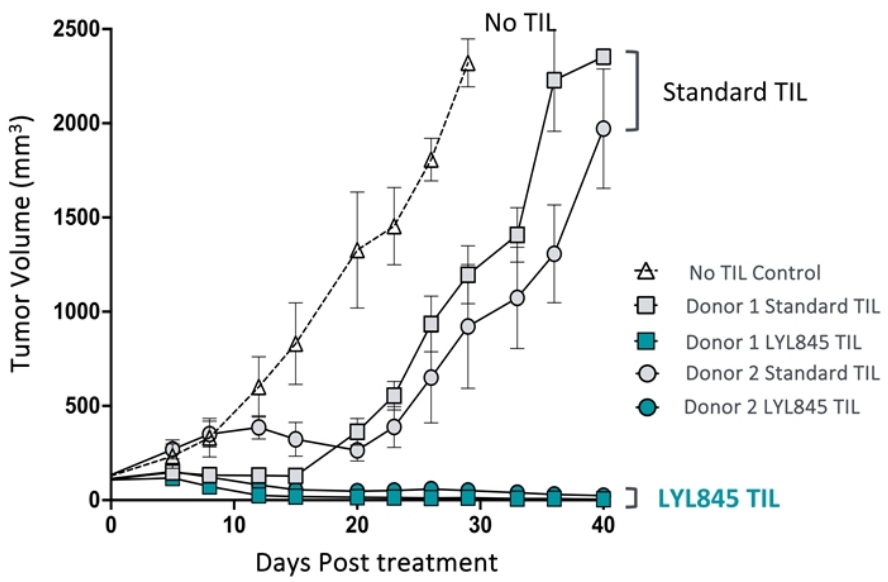
LYL845 TIL preserve ~94% of predicted tumor reactive clones to enable targeting of heterogeneous solid tumors





Harris et al., SITC 2022
Pasetto et al., *CIR* 2016, Lowrey et al., *Science* 2022, Oliveira et al., *Nature* 2021

In vivo efficacy is superior with LYL845 TIL using our Epi-R process compared to TIL using standard conditions in novel model



In this study:

- Two refractory melanoma donor samples were collected.
- Samples were split processed to generate TIL products using either the Epi-R (LYL845) or the standard process.
- Mice were implanted with subcutaneous melanoma cell line on day -8.
- 4 million LYL845 or standard TIL were dosed intravenously on day 0.

Epi-R P2 is a new manufacturing process designed to shorten product delivery time to patients

- **Compared to Epi-R, Epi-R P2:**
  - Does not compromise yield, stemness phenotype or tumor reactive clones
  - Reliably produces 10+ billion cells in substantially shorter manufacturing time
- **Expect to implement Epi-R P2 into our TIL manufacturing in 2024**

	Epi-R™	Epi-R™ P2
10+ billion cells	✓	✓
Maintains stem-like qualities and tumor killing functionality	✓	✓
Preserves tumor reactive clones	✓	✓
Manufacture time	**~24 days**	**~16 days**

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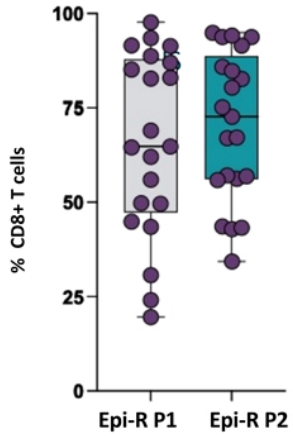
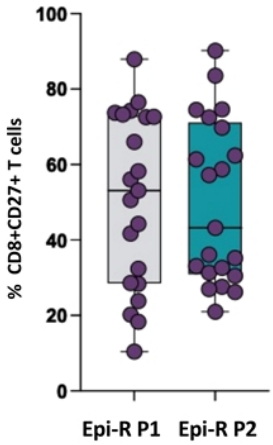
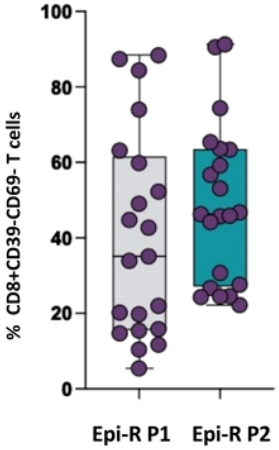
Epi-R and Epi-R P2 processes demonstrate comparable product profiles across CD8 cells

Comparable % of cytotoxic cells



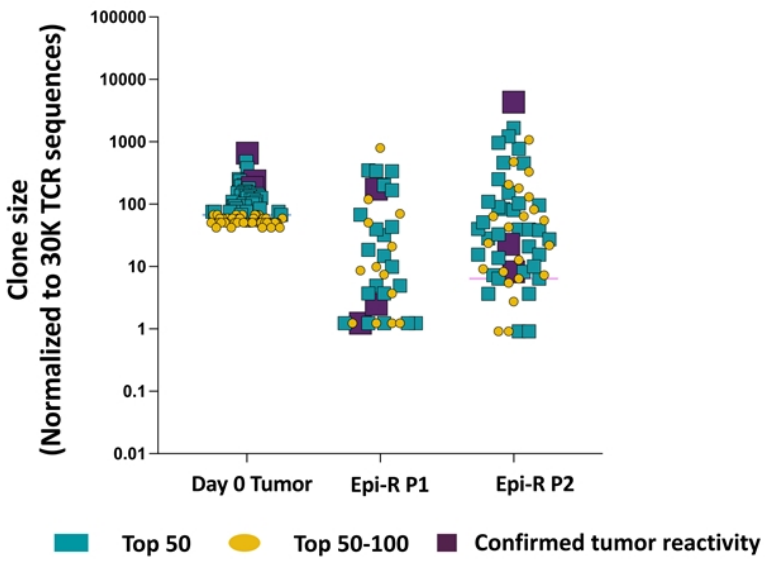
Comparable % of stem-like T cells





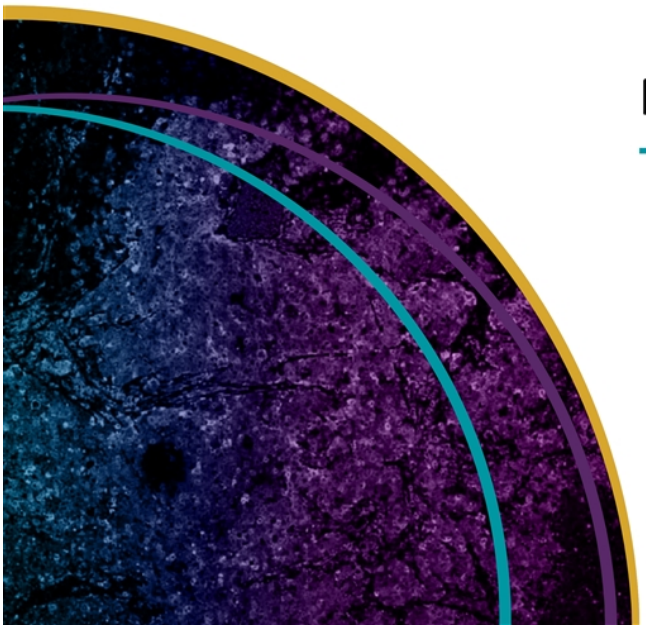
N=21 include metastatic melanoma, lung cancer and colorectal cancers

Epi-R P2 preserves and allows expansion of tumor reactive TIL



In this study:

- T-cell receptor (TCR) sequencing was performed across Day 0 tumor, and TIL samples to assess retention of tumor reactive clones in products
- T cell clones that are more highly represented in the Day 0 tumor sample (e.g., top 50 or top 100 in frequency) are more likely to be tumor reactive
- We also experimentally confirmed several top frequency TCR clones to be tumor reactive (shown in purple)



Manufacturing

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Advancing manufacturing strategy to deliver for the future

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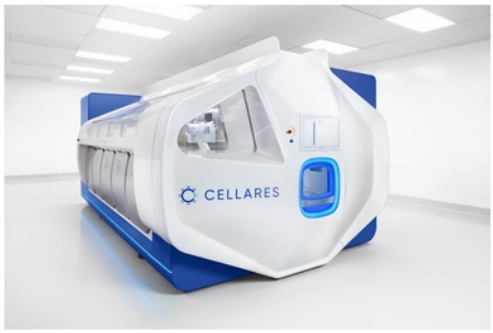
- Currently producing Phase 1 clinical supply
- Capabilities include CAR T cell, TIL and GMP vector
- Capacity for up to ~500 doses/year depending on product mix

CELLARES



- Automated manufacturing processes to rapidly and cost-effectively scale to meet anticipated patient demand for our CAR T-cell product candidates
- Proof-of-concept technology transfer for the manufacture of LYL797 CAR T-cell therapy
- Single Cell Shuttle capacity of up to ~800 LYL797 cell doses/year

CAR T, chimeric antigen receptor T cell; TIL, tumor infiltrating lymphocytes; GMP, good manufacturing practice

Lyell

Advancing T cell therapies for solid tumors

Clinical data from two lead programs in 2024

Two clinical programs: wholly-owned, addressing large patient populations

LYL797: ROR1 targeted CAR T cell
- 1H2024: P1 clinical & translational data from 20+ patients
- TNBC, NSCLC

LYL845: Tumor Infiltrating Lymphocyte (TIL)
- 2024: P1 clinical & translational data
- Melanoma, NSCLC, CRC

Executing a scalable manufacturing strategy

Lyell's LyFE center producing current clinical supply
- 2024: Epi-R P2 process to shorten TIL manufacturing time without impacting cell number and phenotype

Planning for the future
- CAR T cell proof-of-concept collaboration with Cellares to build scale and reduce cost

Portfolio of novel reprogramming platform technologies

- 1H2024: IND filing for LYL119, ROR1 targeted CAR T cell designed for enhanced potency and durability; using four of our technologies

~$633 million in cash

- Runway into 2026

ROR1, receptor tyrosine kinase-like orphan receptor 1; TNBC, triple-negative breast cancer; NSCLC, non-small-cell lung cancer; CRC, colorectal cancer; P1, Phase 1

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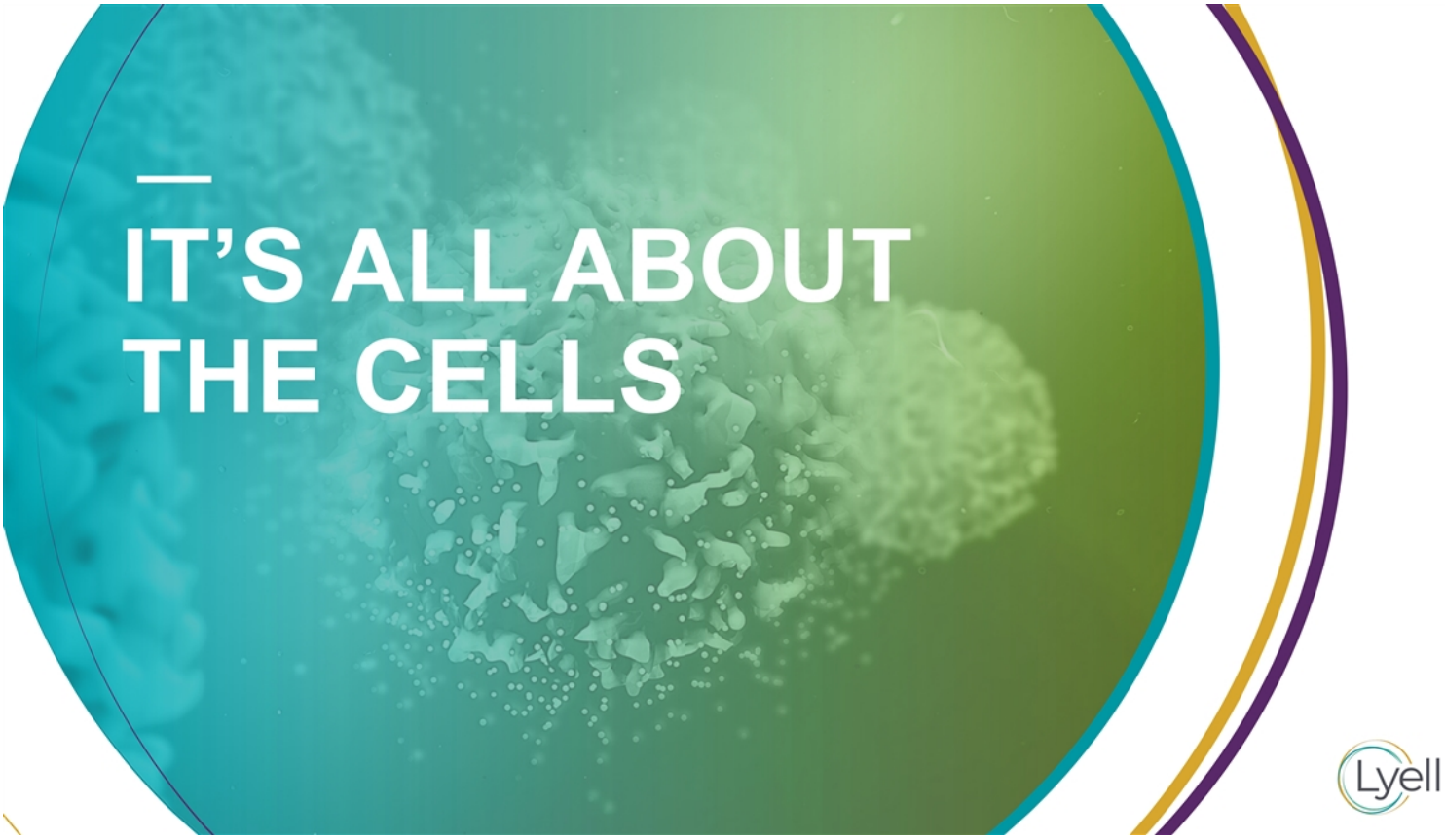
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