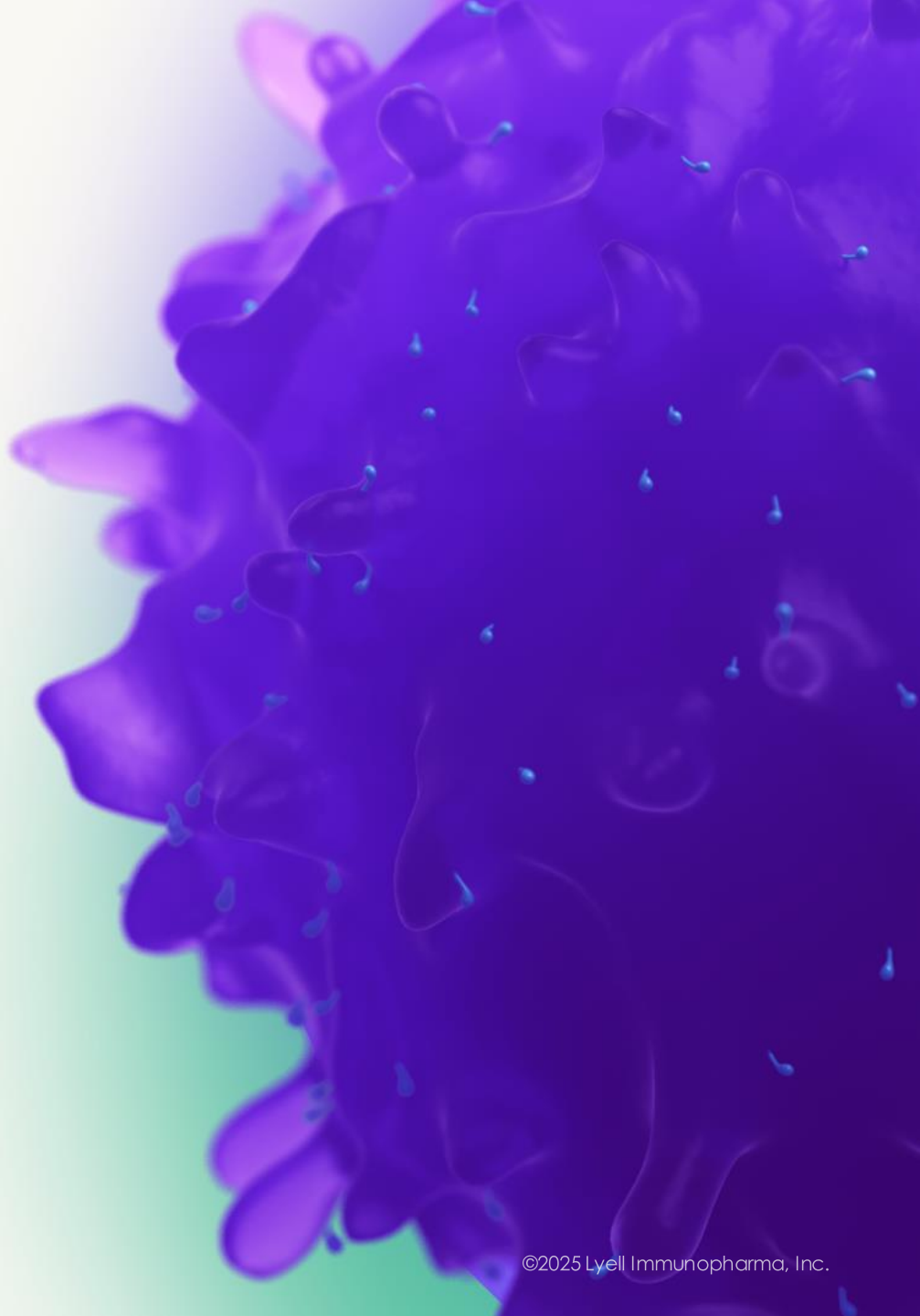
LYL314 Clinical Data Update from the International Conference on Malignant Lymphoma

Lugano, Switzerland

Lyell Immunopharma

June 17, 2025



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 clinical trial plans, the expected capacity and sufficiency of our LyFE Manufacturing Center™, milestones, commercial opportunity, expectations of financial position and cash runway 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 "potential," "continue," "anticipates," "expects," plans"," "intends," "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 include, but are not limited to, the following substantial known and unknown risks and uncertainties inherent in our business related to: the potential for results from clinical trials to differ from nonclinical, early clinical, preliminary or expected results; our ability to progress clinical trials on the anticipated timelines, if at all; our limited experience as a company in enrolling and conducting clinical trials and lack of experience in completing clinical trials; significant adverse events, toxicities or other undesirable side effects associated with our product candidates; RMAT and Fast Track designations may not actually lead to faster development, regulatory review or approval process, and does not assure ultimate FDA approval; the significant uncertainty associated with our product candidates ever receiving any regulatory approvals; the complexity of manufacturing cellular therapies and our ability to manufacture and supply our product candidates for our clinical trials; 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; the effects of macroeconomic conditions, including the effects of disruption between the U.S. and its trading partners due to tariffs or other policies, any geopolitical instability, actual or perceived changes in interest rates and economic inflation; potential changes to U.S. drug pricing, including the potential for "most-favored nations" pricing limitations; other risks, including general economic conditions and regulatory developments, not within our control; and those risks described under the heading "Risk Factors" in our Securities and Exchange Commission ("SEC") filings, including in Lyell's Quarterly Report on Form 10-Q for the quarter ended March 31, 2025, filed with the SEC on May 13, 2025, 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 Next-Generation CAR T-Cell Therapy

Pivotal-stage company targeting large established market

Lead program, LYL314, a dual-targeting CD19/CD20 CAR T-cell candidate with potential to be a disruptive innovation for aggressive large B-cell lymphoma

- 88% overall response rate and 72% complete response (CR) rate in the 3L+ setting (N = 25)
- 71% of patients with complete response remained in complete response at ≥ to 6 months
- Safety profile consistent with outpatient administration
  - No Grade 3 CRS and low rates of Grade ≥ 3 ICANS with rapid resolution

PiNACLE single-arm pivotal trial for patients treated in the 3L+ setting is underway

- Expected to enter pivotal development for 2nd line patients by early 2026

Scalable wholly-owned manufacturing strategy

- >1,200 doses/year at full capacity, capable of commercial launch from our LyFE Manufacturing Center

Cash runway into 2027 through multiple clinical readouts

- ~$330 million of cash* with expected disciplined net cash use moving forward of $175-$185 million for 2025, including multiple pivotal trials and preclinical solid tumor programs

*Cash, cash equivalents and marketable securities as of 3/31/2025
CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune cell-associated neurotoxicity syndrome

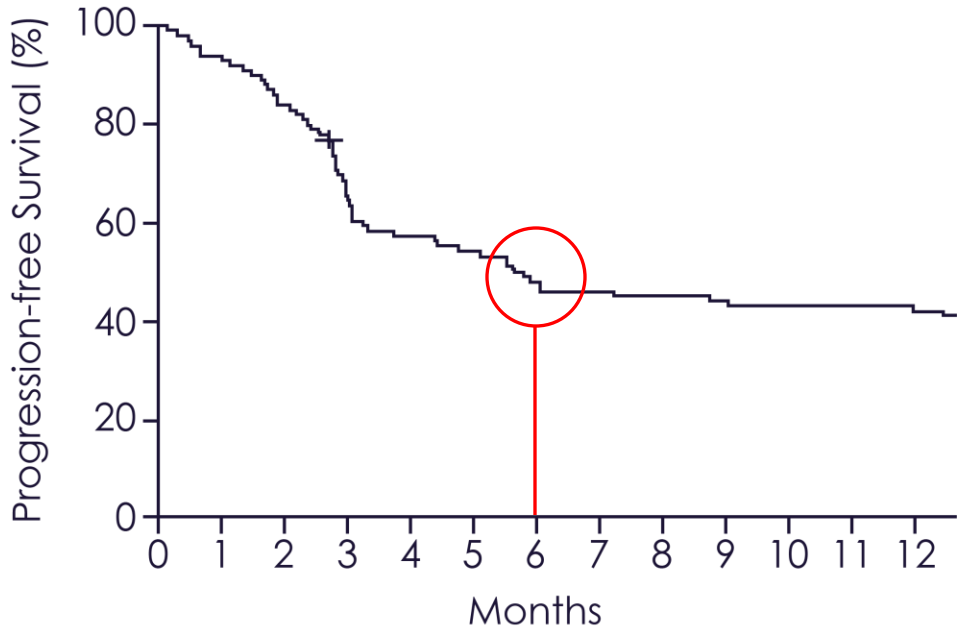
Higher Complete Response Rates and Longer Duration of Responses are Needed for Patients with LBCL in the 3L+ Setting

Only ~50% of 3L+ patients treated with currently approved CD19 CAR T-cell therapies achieved a CR

In addition, approximately:

- 40% of patients with CR remained in CR at 6 months
- 30% of patients did not respond at all
- 50% progressed or died within 6 months

In a clinical trial for Yescarta®, ~50% of patients progressed or died by 6 months



Zuma-1: YESCARTA®; N = 101 LBCL 3L+ setting

Abramson, J et al., The Lancet, 2020 (396: 839–52); Neelapu SS, et al., N Engl J Med 2017;377:2531-44; Harris LJ, et all, Int J Mol Sci. 2020
CAR, chimeric antigen receptor; CR, complete response; LBCL, large B-cell lymphoma.

Higher Response Rates and Longer Duration of Responses Could Result in Significant Penetration of the CD19 CAR T-Cell Therapy Market (3L+)

APPROVED THERAPIES	Target	Line of Therapy, Indication, Sample Size	Overall Response Rate	Complete Response Rate	Median PFS (months)	Grade ≥3 CRS[1]	Grade ≥3 Neurotoxicity[1]
Kite, A GILEAD Company — YESCARTA® (axicabtagene ciloleucel) Suspension for IV infusion	CD19	3+, R/R LBCL (ZUMA-1 N = 108)	72%	51%	5.8[2]	9%	31%
Bristol Myers Squibb™ — Breyanzi® (lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION	CD19	3+, R/R LBCL (TRANSCEND NHL 001 N = 268)	73%	54%	6.8[3]	3%	10%
NOVARTIS — KYMRIAH® (tisagenlecleucel) Dispersion for IV infusion	CD19	3+, R/R DLBCL (JULIET N = 115)	50%	32%	2.9[4]	23%	19%

Response rates of approved CD19 CAR T-cell therapies in the 2L are consistent with or higher than response rates in the 3L+ setting

Yescarta® prescribing information; Breyanzi® prescribing information; Kymriah® prescribing information
1. US PIs section 5.2; 2. N Engl J Med 377:26, 2017; 3. The Lancet, Volume 396, Issue 10254, 839 – 852, 2020; 4. N Engl J Med 380:45, 2019.
CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; NHL, non-Hodgkin lymphoma; R/R, relapsed/refractory; PFS, progression-free survival

Patient Demographics and Disease Characteristics Impact Outcomes

Patients with higher-risk disease achieve lower complete response rates

- **Two pivotal trials were conducted to support approval of Breyanzi® in 2L**
  - TRANSFORM: transplant-eligible patients
  - PILOT: transplant-ineligible patients (older with more co-morbid conditions)
- **High-risk features are generally associated with lower CR rates**
  - Primary refractory disease
  - Relapse before 12 months
  - Older age
  - Double-hit lymphoma (*MYC*, *BCL2* or 6)

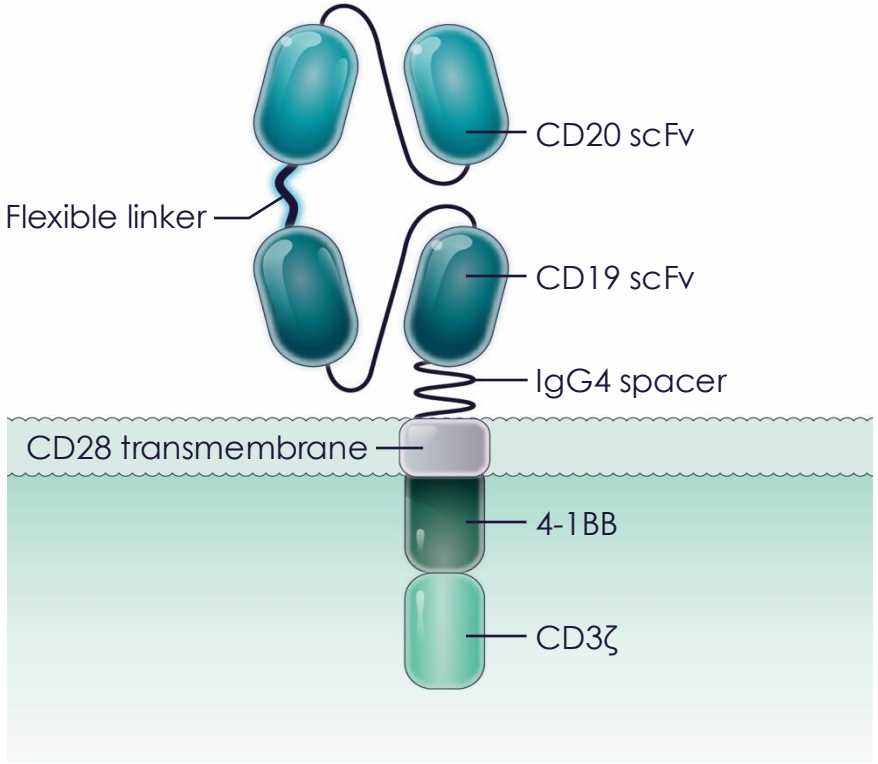
Characteristics	TRANSFORM Transplant-Eligible	PILOT Transplant-Ineligible
Age, median (years)	63	74
Primary refractory (%)	73%	53%
Relapse < 12 months	100%	23%
Relapse > 12 months	0%	25%
Median SPD, cm^2	11.4	-
Double-hit status, n (%)	10%	33%
Best Overall Response	**TRANSFORM Transplant-Eligible**	**PILOT Transplant-Ineligible**
Overall Response Rate	79%	80%
Complete Response Rate	61%	54%
CRR for primary refractory (n = 35)	N/A	46%
CRR for relapse ≤ 12 months (n =11)	61%	46%
CRR for relapse > 12 months (n = 15)	N/A	80%

Kamdar et al., Lancet 2022; 399: 2294 –308, Sehgal et al., Lancet Oncol 2022; 23: 1066–77
CRR, complete response rate; ECOG, Eastern Cooperative Oncology Group; LBCL, large B-cell lymphoma; SPD, sum of product diameters

LYL314: Designed for More Complete and Durable Responses

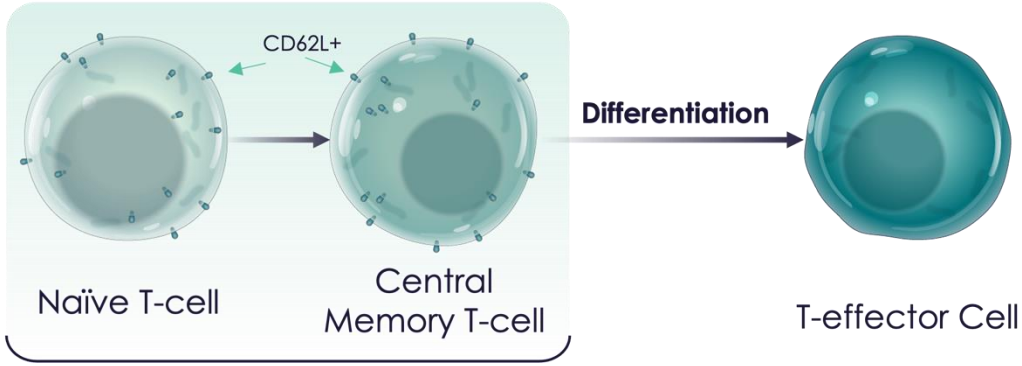
One-time treatment with potential to provide patients longer disease-free, treatment-free period

True CD19/CD20 "OR" Logic-Gated CAR targeting either CD19 or CD20 with full potency



CD19/CD20 CAR T-Cells Enriched for Naïve Phenotype (CD62L+)

- CD62L+ cells are associated with better engraftment, improved persistence, reduced exhaustion and lower cytokine production

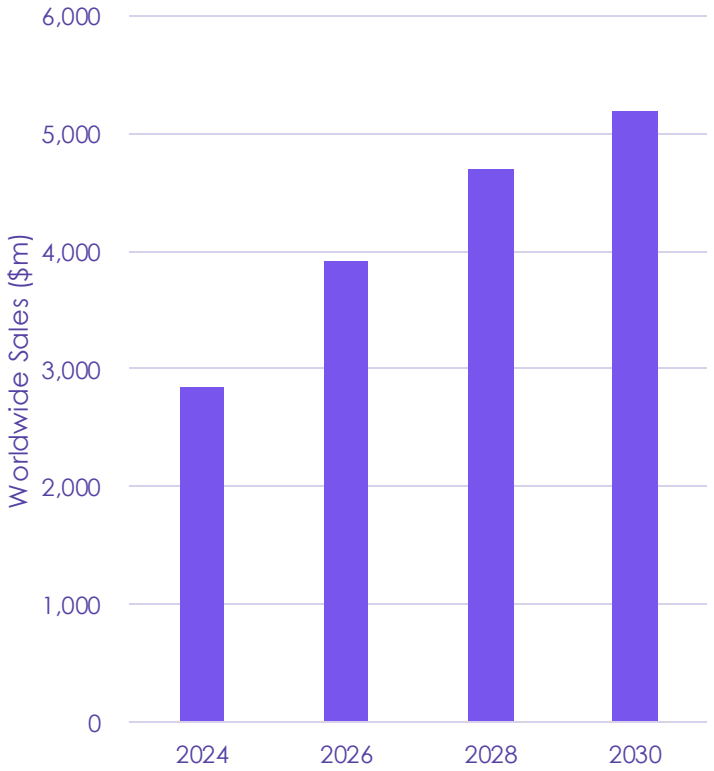


Arcangeli et. al. JCI 2022, Sommermeyer et. al. Leukemia 2016, Chen GM et. al. Cancer Discovery 2021, Aldoss et al., Clin Cancer Res 2023
CAR, chimeric antigen receptor; CD62L or L-selectin positive T cells; IgG4, Immunoglobulin G4; scFv, single-chain variable fragments,

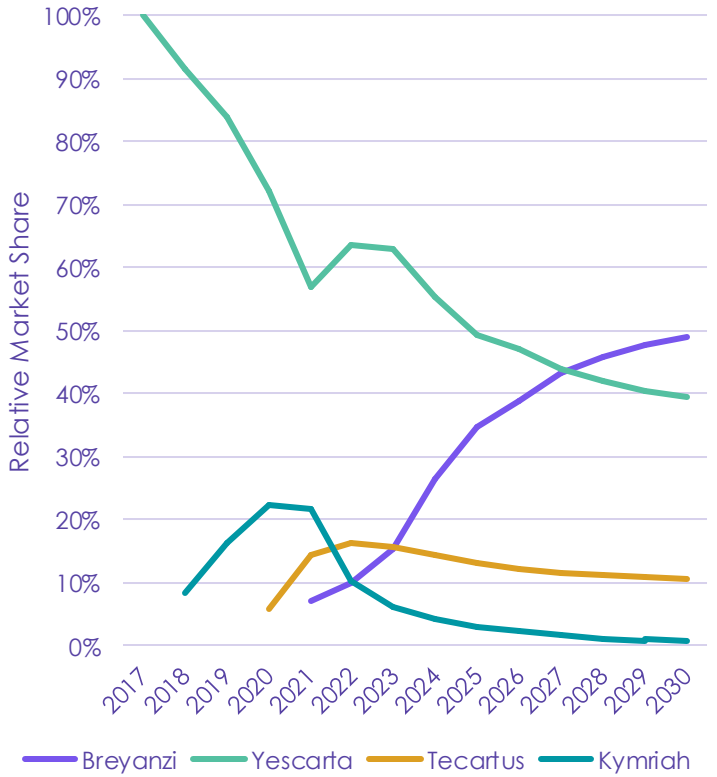
LYL314 is Targeting a Multi-billion Dollar Market Treated by Physicians with a Historical Willingness to "Switch" Based on Strength of Clinical Data

Differentiated Clinical Data Could Enable LYL314 to Disrupt the NHL Treatment Paradigm

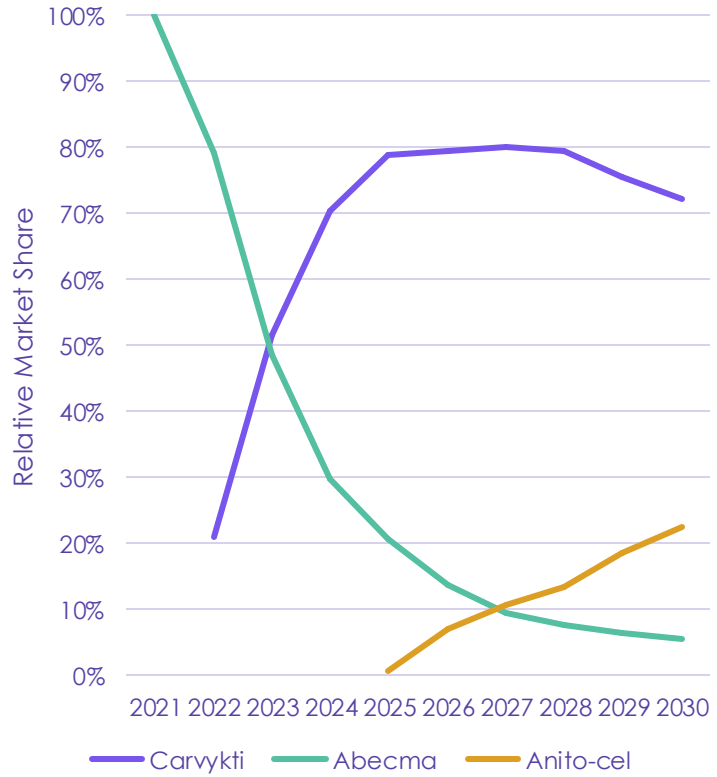
Projected Sales of Currently Approved CD19 CAR T-Cell Products[1]



New CD19 CAR T Market Entrants Have Successfully Captured Market Share Based on Perceived Improved Product Profiles[1]



The Same Dynamic Occurred with BCMA CAR Ts as Physicians Rapidly Shifted Prescribing Preferences Based on Clinical Data[1]



(1) EvaluatePharma
CAR, chimeric antigen receptor, NHL, non-Hodgkin lymphoma

LYL314 Clinical Data to be Presented at the International Conference on Malignant Lymphoma

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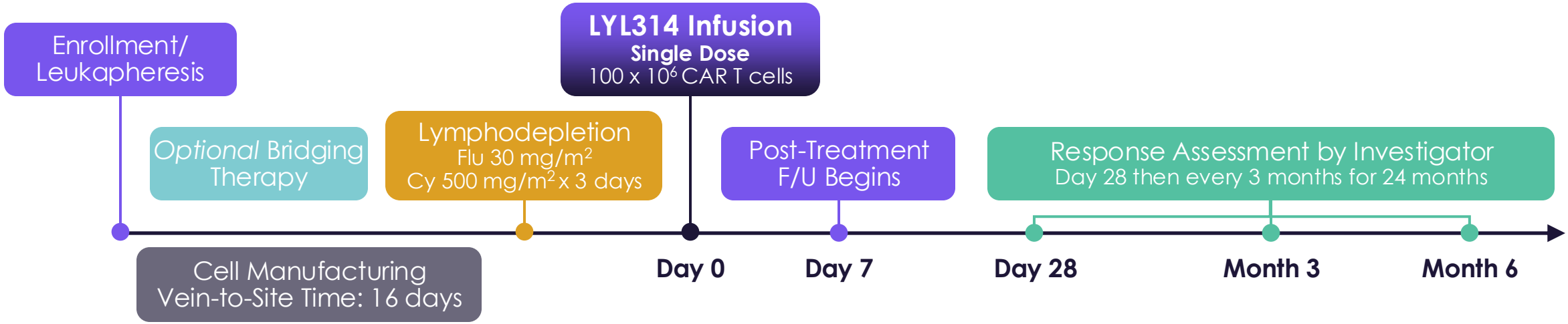
Cedars-Sinai Medical Center, Los Angeles, CA

LYL314 Study Schematic

Phase 1/2 multi-cohort, multi-center study in aggressive large B-cell lymphoma (3L+ and 2L CAR-naïve cohorts)



Patient Population

- Patients with relapsed/refractory DLBCL, PMBCL, HGBCL, Grade 3BFL, and tFL who have had ≥1 line of treatment
- CD19/CD20 screening not required for enrollment
- CD19 CAR T-cell therapy naïve
- No upper age limit

Study Objectives

- Safety and tolerability
- Overall response rate, complete response rate
- Duration of response
- Selection of Phase 2 dose
- Cell expansion pharmacokinetics

The 3L+ cohort has expanded into the pivotal trial (PiNACLE) to enroll ~120 patients

Study included two dose levels (DL1 = 100 x 10^6 CAR T cells; DL2 = 300 x 10^6 CAR T cells). 100 x 10^6 CAR T cells is the recommended Phase 2 dose.
Cy, cyclophosphamide; DLBCL, diffuse large B-cell lymphoma; Flu, fludarabine; Grade 3BFL, Grade 3B follicular lymphoma; HGBCL, high-grade B-cell lymphoma; PMBCL, primary mediastinal large B-cell lymphoma; tFL, transformed follicular lymphoma. NCT05826535.

High-Risk Disease Typical of a Multi-Center US Patient Population

Key patient demographics and baseline disease characteristics (N = 51)

Characteristics	3L+ N = 34	2L N = 17
Median (range) age, years	**65 (21, 87)**	**69 (44, 85)**
≥ 65 years, n (%)	18 (53%)	12 (71%)
≥ 75 years, n (%)	7 (21%)	6 (35%)
Male, n (%)	23 (68%)	10 (59%)
White, n (%)	24 (71%)	10 (59%)
ECOG 1, n (%)	24 (71%)	12 (71%)
IPI score 3 or 4, n (%)	13 (38%)	8 (47%)
Stage IV disease at study entry, n (%)	14 (41%)	11 (65%)
LBCL histology n (%)		
DLBCL	21 (62%)	10 (59%)
HGBCL	4 (12%)	2 (12%)
tFL	5 (15%)	3 (18%)

Characteristics	3L+ N = 34	2L N = 17
Primary refractory, n (%)	16 (47%)	14 (82%)
Elevated (above normal) LDH, n (%)	16 (47%)	5 (29%)
Median lines of prior therapy (range)	2 (2-6)	1
Bulky disease (≥ 5 cm), n (%)	8 (24%)	6 (35%)
Median SPD (range) cm^2	13 (1.5-180.1)	17 (4.5-92.8)
Double-/triple-hit status, n (%)	5 (15%)	5 (29%)
Received bridging therapy, n (%)	18 (53%)	9 (53%)

49 of 51 patients received the recommended Phase 2 dose of 100 x 10^6 CAR T cells. Two patients (in 3L+) received 300 x 10^6 CAR T cells.

Data cutoff: April 15, 2025

DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; HGBCL, high-grade B-cell lymphoma; IPI, International Prognostic Index; tFL, transformed follicular lymphoma. SPD, sum of target lesion product diameters prior to lymphodepletion

Overall Response Rate of 88% and Complete Response Rate of 72% (3L+ LBCL)

High rate of durable complete responses

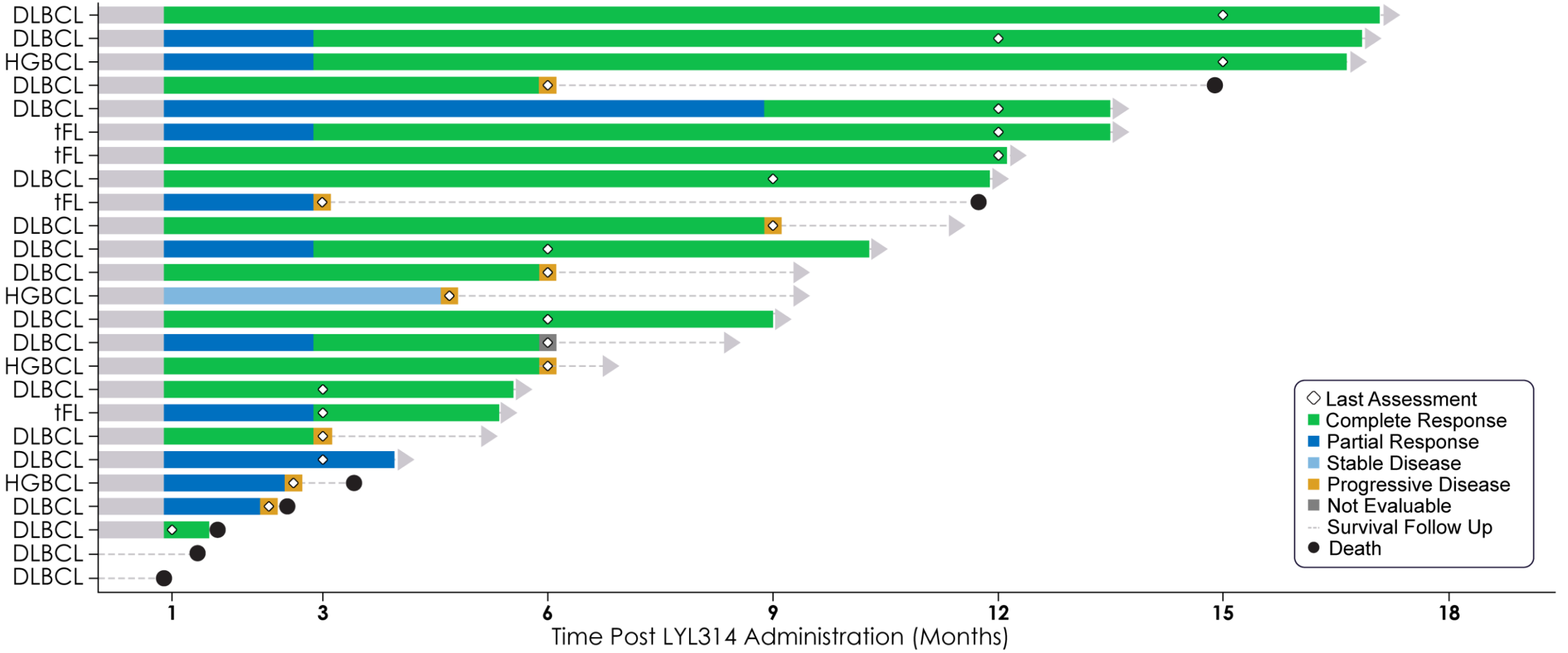
Best Overall Response (3L+)	N = 25
Overall Responses, n (%)	**22 (88%)**
Complete Responses, n (%)	**18 (72%)**
Partial Response, n (%)	4 (16%)
Stable Disease, n (%)	1 (4%)
Median follow up, months (maximum)	9 (17)
Median duration of response	Not reached

- **71% (10/14) of patients achieving a complete response remained in complete response at ≥ 6 months**

Data cutoff: April 15, 2025; all responses as determined by the Investigator.
Patients were evaluable for efficacy if they had a Day 84 or later response assessment, disease progression, or death from any cause.
Two patients with T-cell histiocyte-rich lymphoma not included (1PR, 1 PD); histology no longer enrolled. Seven patients were dosed without Day 84 follow up, disease progression, or death.
CAR, chimeric antigen receptor; CR, complete response

Durable Responses in Patients with 3L+ R/R LBCL

71% of patients with CR remained in CR at ≥ 6 months



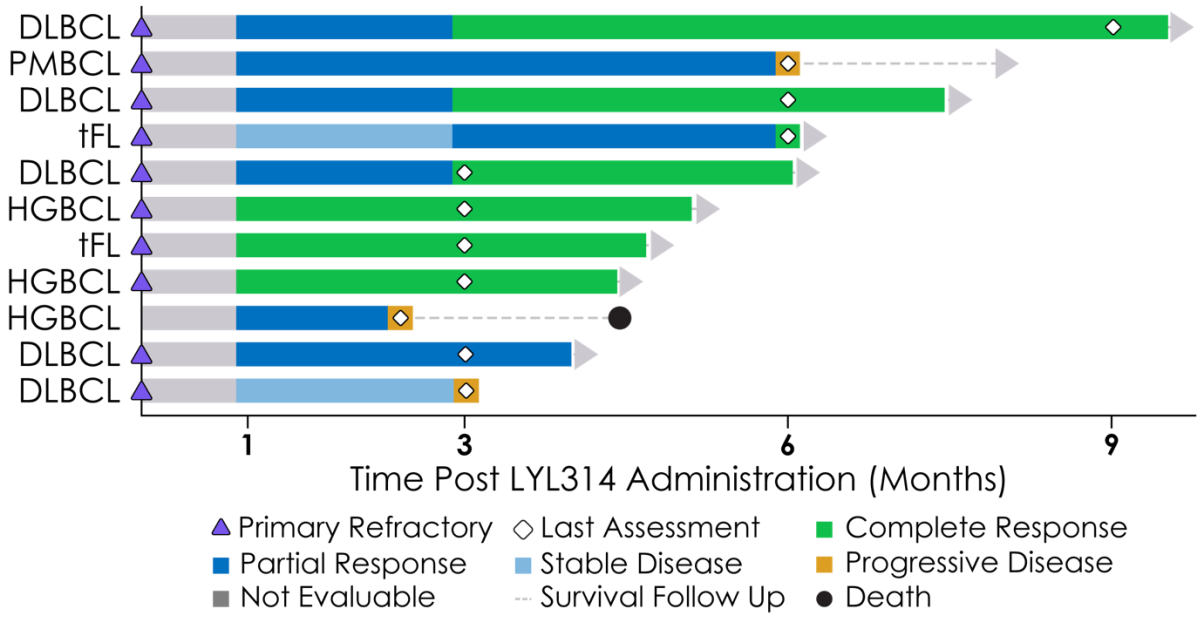
Data cutoff: April 15, 2025

CAR, chimeric antigen receptor, CR, complete response; LBCL, large B-cell lymphoma; R/R, relapsed and/or refractory

High Overall Response Rate in Patients with 2L LBCL

High-risk characteristics with 91% of patients with primary refractory disease

Best Overall Response (2L)	N=11
Overall Responses, n (%)	**10 (91%)**
Complete Responses, n (%)	**7 (64%)**
Partial Response, n (%)	3 (27%)
Stable Disease, n (%)	1 (9%)
Median follow up, months (max)	5 (10)
Median duration of response	Not reached



- **100% (7/7) of patients with CR remain in CR at last assessment, including 3/3 at ≥ 6 months**
- **70% (7/10) of patients with primary refractory disease achieved a CR**

Data cutoff: April 15, 2025; all responses as determined by the Investigator.
Patients were evaluable for efficacy if they had a Day 84 or later response assessment, disease progression, or death from any cause
SIx patients were dosed without Day 84 follow up, disease progression, or death.
CAR, chimeric antigen receptor; CR, complete response

Manageable Safety Profile Allowing for Outpatient Administration

Adverse events of interest (3L+ and 2L LBCL)

Adverse Event, n (%)	N = 51
CRS	
Grade 1	11 (22%)
Grade 2	18 (35%)
Grade ≥ 3	0 (0%)
Median time to onset, days (range)	4 (1-13)
Median time to resolution, days (range)	3 (1-8)
ICANS	
Grade 1	3 (6%)
Grade 2	1 (2%)
Grade ≥ 3	7 (14%)
Median time to onset, days (range)	7 (4-11)
Median time to resolution, days (range)	5 (2-10)
Median time to Grade < 3, days (range)	2 (1-4)

Adverse Event, n (%)	N = 51
IEC-HS	
Grade 1or 2	1 (2%)
Grade ≥ 3	0 (0%)
Infections	
Grade 1 or 2	13 (25%)
Grade ≥ 3	7 (14%)
Prolonged cytopenias	
Grade ≥ 3	14 (27%)

- 41% of patients received tocilizumab
- ICANS rate has decreased since the introduction of prophylactic dexamethasone
- No deaths related to LYL314

Data cutoff: April 15, 2025

Infections include all treatment emergent adverse events reported in the Infections and Infestations system organ class regardless of relationship to study treatment.

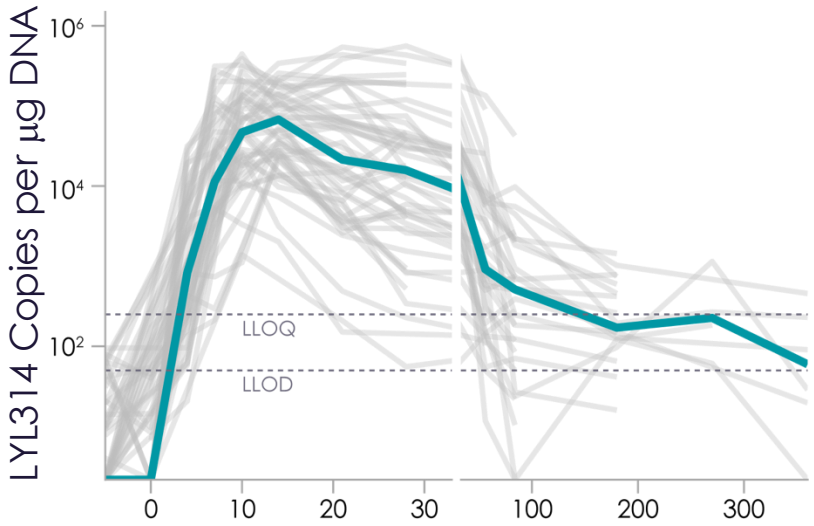
Prolonged cytopenias defined as Grade 3 or 4 values of hemoglobin, platelets, or neutrophils beyond Day 28 post LYL314 administration.

CRS, cytokine release syndrome; ICANS, immune cell-associated neurotoxicity syndrome; IEC-HS, immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome.

Robust CAR T-Cell Expansion Resulting in Rapid and Durable B-Cell Depletion

95% of final drug product is CD62L+ (naïve T cells)

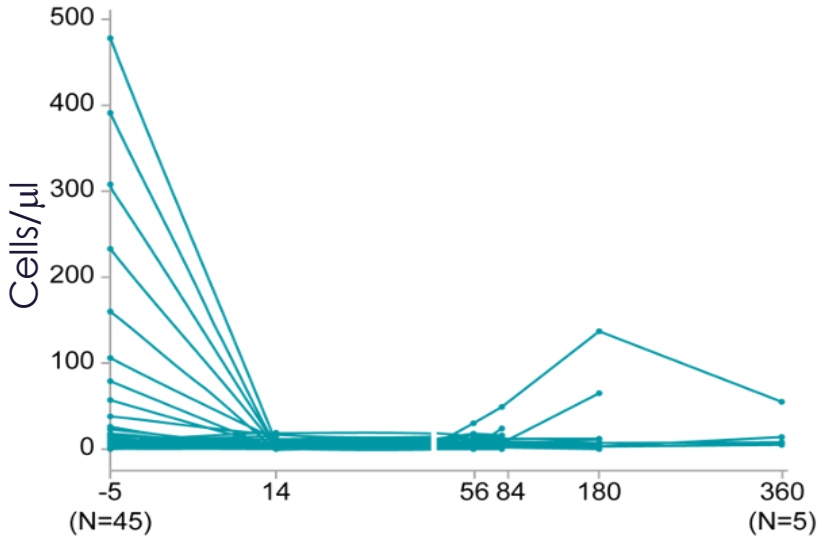
CAR T-Cell Expansion



Time Post LYL314 Administration (Days)

LYL314 showed robust expansion (N=51) with peak CAR T cells of 70,685 copies/μg (1,387 – 569,039), AUC CAR T cells of 819,198 days x copies/μg (14,596 – 9,109,115), and time to peak of 10 days (7 – 28)

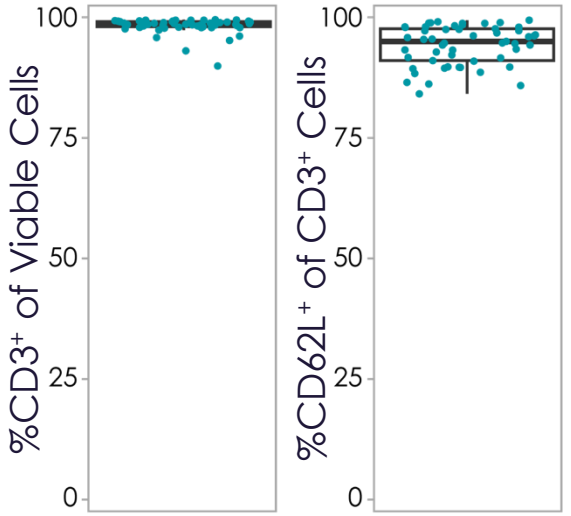
B-Cell Depletion



Time Post LYL314 Administration (Days)

Rapid and durable B-cell depletion through Month 6 and up to the Month 12 assessment for patients with available data using a highly-sensitive and robust method

Final Drug Product



Final drug product with a median of 95% CD62L$^+$ cells (median, 95%; range, 84.1% – 99.4%)

Data cutoff: April 15, 2025

Assay used for measuring B cells/µl (Epiontis ID®) can detect as low as 2 cells/µl with high accuracy.

LYL314 is a Promising CAR T-Cell Candidate for Patients with Large B-Cell Lymphoma

Results from a Phase 1/2 multi-center study evaluating LYL314 in 3L+ and 2L CAR-naïve patients

High response rates in high-risk patients

- Overall response rate of 88% and a CR rate of 72% in the 3L+ setting

High rate of durable complete responses

- 71% of patients with complete response remained in complete response at ≥ 6 months in the 3L+ setting

Safety profile appropriate for outpatient administration

- No Grade 3 CRS and low rates of Grade ≥ 3 ICANS with rapid resolution

Robust CAR T-cell expansion with final drug product enriched for naïve T cells (CD62L+)

- Rapid and durable depletion of B cells

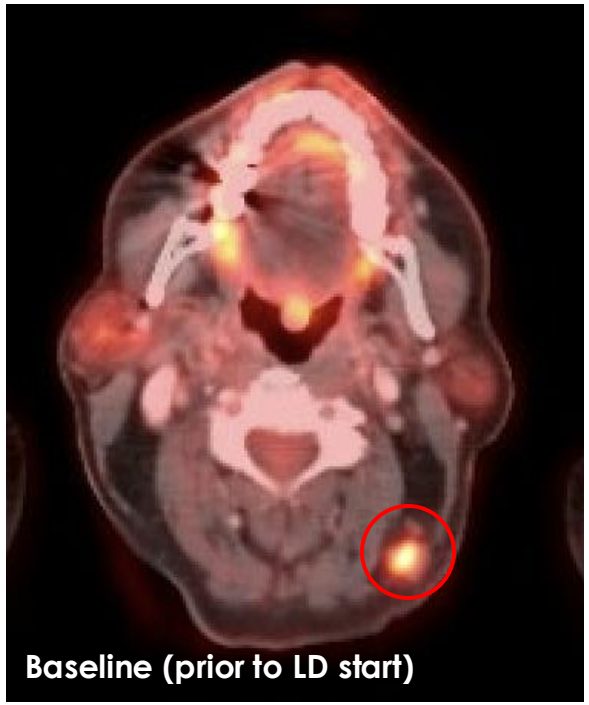
The 3L+ cohort has expanded into a pivotal study (PiNACLE) to enroll ~120 patients

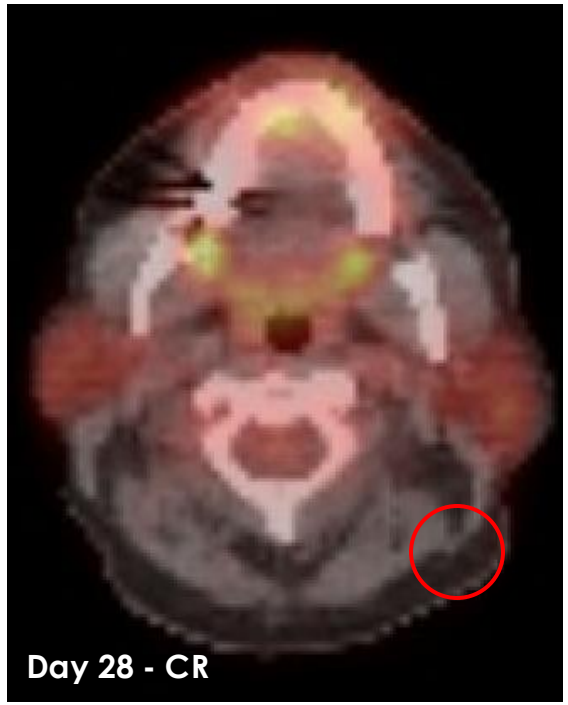
Data cutoff: April 15, 2025
CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome, ICANS, immune effector cell-associated neurotoxicity syndrome

Patient Cases

High-Risk Patient with Rapid and Durable Complete Response

64-year-old male with DLBCL transformed from follicular lymphoma with palpable neck mass which demonstrated rapid reduction by Day 5





CR ongoing at 12+ months

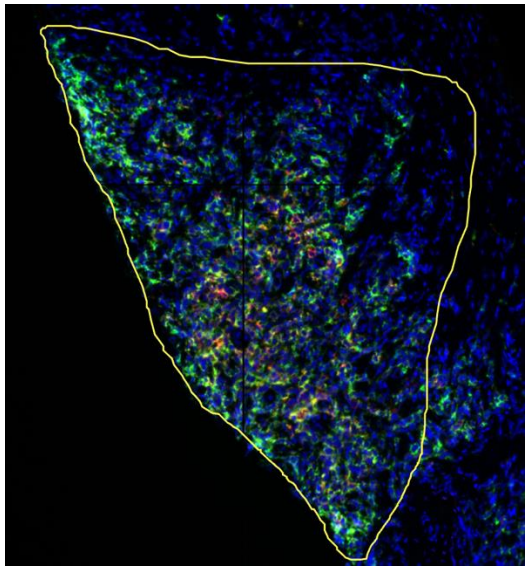
Patient History
Prior Therapy
Relapsed after second-line salvage chemotherapy and autologous stem cell transplant
Medical History
Prior myocardial infarction with stent
Baseline Labs
LDH > ULN
Adverse Events
CRS Grade 1 (resolved without tocilizumab or dexamethasone); COVID-19 infection resolved as outpatient

Investigator assessed response reported
CR, complete response; CRS, cytokine release syndrome; LDH, lactate dehydrogenase; DLBCL, diffuse large B-cell lymphoma; ULN, upper limit of normal

Low CD19-Antigen DLBCL With Complete Response

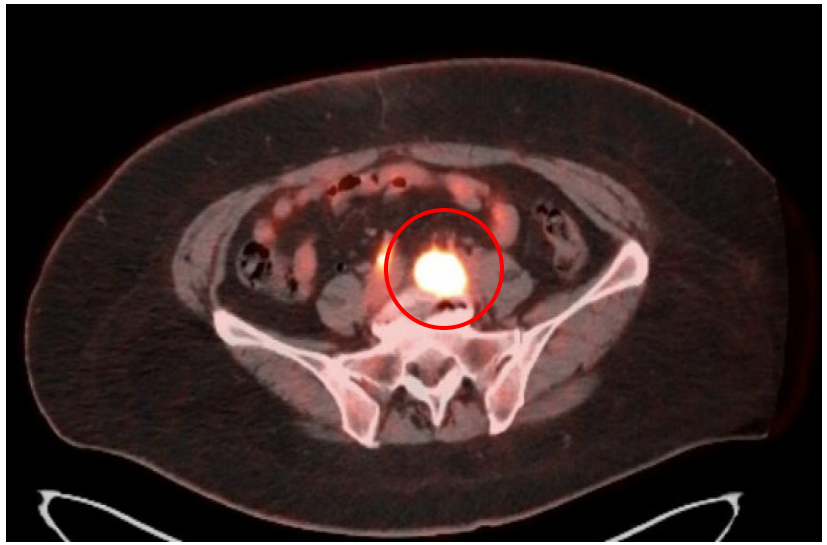
Highlights benefit of LYL314's CD19/CD20 dual targeting

52-year-old female with DLBCL that relapsed 3 months after first-line therapy

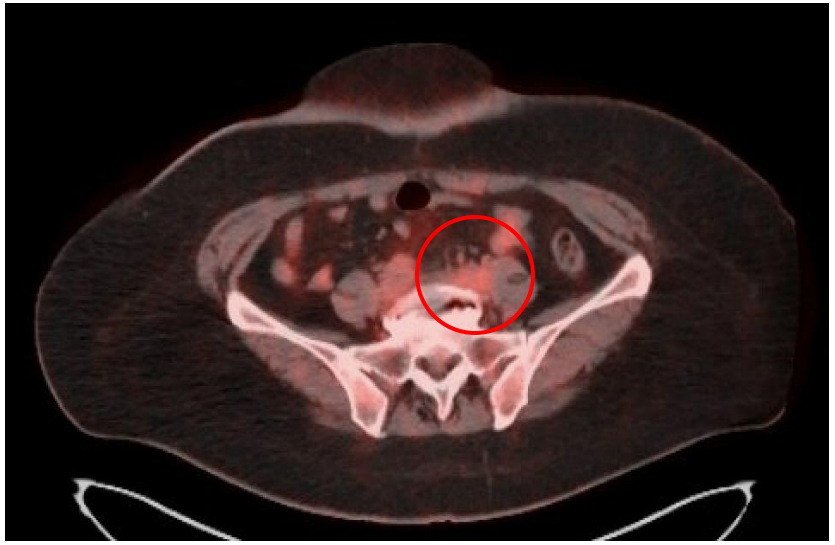


Lymphoma Characteristics

CD19 (red) low, and CD20 (green) positive DLBCL by immunofluorescence



Baseline (prior to LD start)



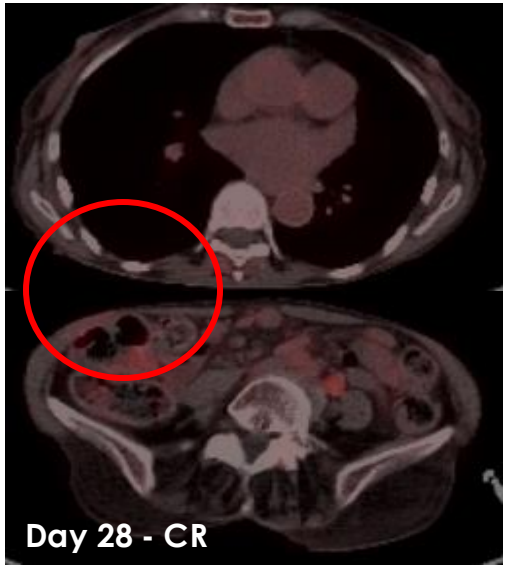
Day 28 complete response

CR ongoing at 3+ months

CD19/CD20 testing not required prior to enrollment
CR, complete response; DLBCL, diffuse large B-cell lymphoma; LD, lymphodepletion;

LYL314 Shows Durable Complete Response in High-Risk Patient

85-year-old female, primary refractory disease, double-hit HGBCL



CR ongoing at 6+ months

Patient and Lymphoma Characteristics

Prior Therapy

R-CHOP x 6 cycles
Primary refractory disease (Deauville 5) confirmed on PET/CT

Lymphoma Characteristics

Double hit (translocations of *MYC* and *BCL2*) lymphoma with multiple sites of extranodal disease (pleura and soft tissue)

Baseline Labs

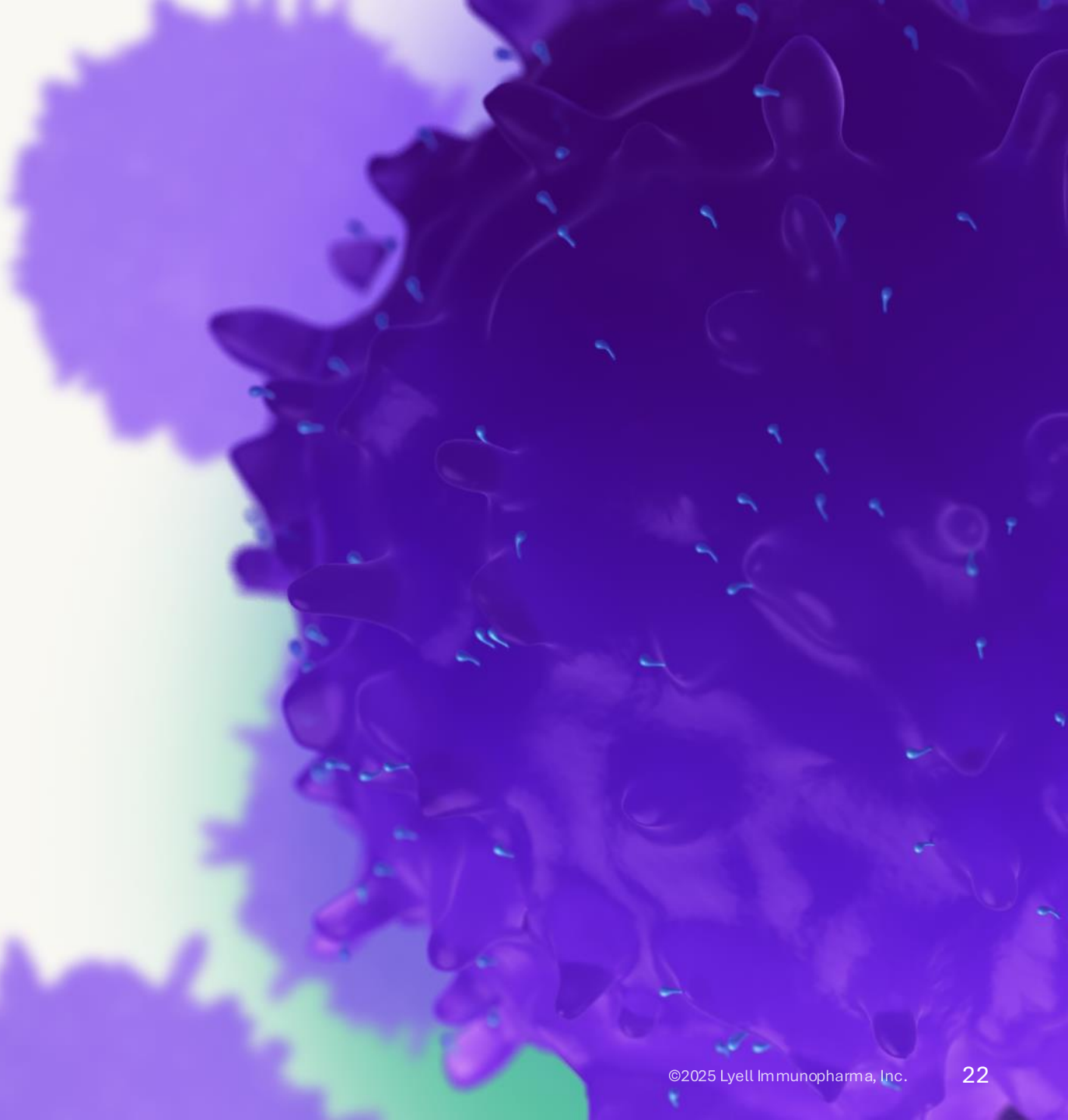
LDH > ULN

Adverse Events

Grade 1-2 CRS treated with tocilizumab, Grade 1 ICANS with full recovery in less than 24 hours

Investigator assessed response reported
CR, complete response; CRS, cytokine release syndrome; HGBCL, high-grade B-cell lymphoma; ICANS, immune effector cell-associated neurotoxicity syndrome; LDH, lactate dehydrogenase; PET/CT, positron emission tomography/computed tomography; R-CHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin), vincristine sulfate (Oncovin), and prednisone; ULN, upper limit of normal

LYL314 Development Strategy and Next Steps



LYL314 Pivotal Clinical Development Strategy

PiNACLE

Single-Arm Trial for Approval in 3L+ Setting

- Single-arm trial for approval is underway
- Seamless expansion of the ongoing Phase 1/2 trial
- Opening additional sites to further accelerate enrollment

Randomized Controlled Trial for Approval in 2L Setting

- On track to begin by early 2026

- Granted Regenerative Medicine Advanced Therapy (RMAT) designation from FDA for the treatment of adult patients with R/R LBCL in the 3L+ setting
- Clinical supply manufactured in Lyell's state-of-the-art LyFE Manufacturing Center
  - > 1,200 doses/year at full capacity, capable of meeting demand through early commercial launch

CAR, chimeric antigen receptor; LBCL, large B-cell lymphoma; R/R, relapsed and/or refractory

LYL314 Demonstrates Potential To Deliver More Complete and Durable Responses

Designed to give patients longer disease-free, treatment-free periods

- **High response rates in high-risk patients**
  - Overall response rate of 88% and a complete response rate of 72% in 3L+ setting
- **High rate of durable complete responses**
  - 71% of patients with complete response remained in complete response at ≥ 6 months in 3L+ setting

PiNACLE

Pivotal trial in patients with R/R LBCL in 3L+ setting is underway

Single-arm, multi-center trial of ~120 patients	Seamless expansion of Phase 1/2 3L+ cohort	Dose: 100 x 10^6 CAR T cells	Inpatient and outpatient administration	Primary Endpoint - Overall Response Rate (Duration of Response)

CAR, chimeric antigen receptor, CR, complete response, LBCL, large B-cell lymphoma, R/R, relapsed and/or refractory

Upcoming Potential Milestones

Balance sheet of ~$330M* provides cash runway into 2027, through multiple clinical milestones

LYL314	**Dual-Targeting CD19/CD20 CAR T-Cell Therapy for Aggressive LBCL**
Q4 2024	✓ Presented initial Phase 1/2 data at ASH 2024 Annual Meeting in December
	✓ Reported more mature data in 3L+ setting in June (ICML)
Mid-2025	✓ Reported initial clinical data in 2L setting in June (ICML)
	✓ Initiated pivotal trial in 3L+ setting
Late 2025	❑ Report more mature data in 2L setting
By Early 2026	❑ Initiate pivotal trial in 2L setting
Undisclosed	**CAR T-Cell Product Candidates – Solid Tumors**
2026	❑ Submit IND for new product candidate

*Cash, cash equivalents and marketable securities as of 3/31/2025

CAR, chimeric antigen receptor; ICML, International Conference on Malignant Lymphoma; IND, investigational new drug application.

Lyell Immunopharma is Well Positioned for Success

- Key clinical milestones in mid *and* late 2025
- First of two planned pivotal trials underway
- Multi-billion dollar commercial opportunity
- Manufacturing facility with commercial launch capability
- Cash runway into 2027

It’s all about the cells.

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