



Next-Generation CAR T-Cell Therapy

Lyell Immunopharma — January 14, 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, 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: 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 in Lyell's Annual Report on Form 10-K for the year ended December 31, 2023, filed with the Securities and Exchange Commission (SEC) on February 28, 2024, and the Quarterly Report on Form 10-Q for the quarter ended September 30, 2024, filed with the SEC on November 7, 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 Next-Generation CAR T-Cell Therapy

Meaningfully improve outcomes in hematologic malignancies with innovative CAR T-cell therapy

Aggressively progress the next wave of cell therapy innovation for solid tumors

Advancing Next-Generation CAR T-Cell Therapy



Late-stage clinical company entering pivotal trials with a strong balance sheet

Lead program, IMPT-314, a dual-targeting CD19/CD20 CAR T-cell product candidate with potential to be a disruptive innovation for the treatment of 2nd and 3rd line+ aggressive large B-cell lymphoma

- Expected to enter pivotal development in mid-2025

Next-generation solid tumor preclinical CAR T-cell programs fully armed with a suite of proprietary technologies

- Proprietary clinically-validated anti-exhaustion and durable stemness technologies, as well as new enhancements designed to overcome the hostile tumor microenvironment

Scalable manufacturing strategy

- At full capacity, capable of commercial launch at Lyell's LyFE center (capacity of >1000 doses/year)

Strong balance sheet

- ~\$460 million of cash* with expected disciplined net cash use moving forward including of \$175-\$185 million for 2025, providing a cash runway further into 2027 through multiple clinical readouts, including new pivotal programs

Team of cell therapy pioneers and seasoned drug developers

- Experienced product developers in oncology and cell therapy

*Cash, cash equivalents and marketable securities as of 9/30/2024
CAR, chimeric antigen receptor

Lead Program, IMPT-314, a Dual-Targeting CD19/CD20 CAR T-Cell Product Candidate

Expected to enter 3rd line pivotal trial in aggressive large B-cell lymphoma in mid-2025

Phase 1- 2 multi-center trial ongoing; presented initial data at ASH 2024:

94% Overall Response Rate

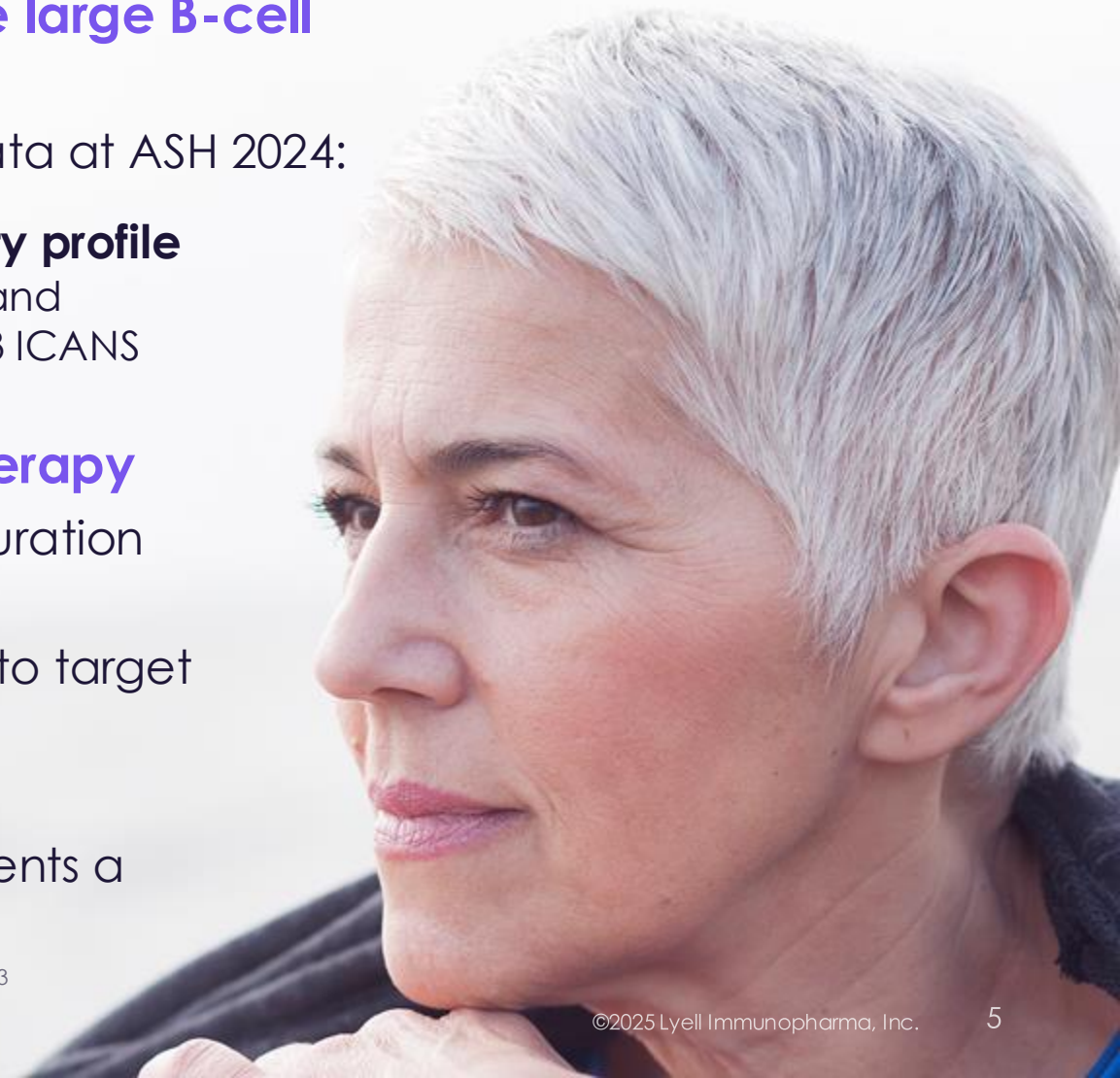
71% Complete Response Rate

Manageable safety profile

No high-grade CRS and
low rates of Grade 3 ICANS

Key Differentiators of Dual-Targeting CAR T-Cell Therapy

- Designed for more complete responses and longer duration of responses
 - True CD19/CD20 “OR” logic-gated CAR designed to target either CD19 or CD20 with full potency
 - Enriched for CD62L+ expressing cells
- One-time treatment has the potential to provide patients a longer disease-free, treatment-free period



Advancing Novel, Next Generation CAR T-Cell Therapy

Balance sheet of \$460M* provides cash runway into 2027, through multiple clinical milestones



Product	Target	Target Indications	Technology	Preclinical	Phase 1	Phase 2/ Pivotal	Next Expected Milestone
IMPT-314	CD19/CD20	3L+ Aggressive LBCL (Fast Track Designation)	<ul style="list-style-type: none"> CD62L+ 	3L+ CAR T Naïve			<ul style="list-style-type: none"> More mature data mid-2025 Initiate pivotal trial mid-2025
IMPT-314	CD19/CD20	2L Aggressive LBCL	<ul style="list-style-type: none"> CD62L+ 	2L CAR T Naïve			<ul style="list-style-type: none"> Initial data mid-2025 More mature data late-2025 Initiate pivotal trial by early-2026
Solid Tumor Programs	Undisclosed	Undisclosed	<ul style="list-style-type: none"> Anti-exhaustion Stemness TME functional enhancement 				<ul style="list-style-type: none"> First IND in 2026

*Cash, cash equivalents and marketable securities as of 9/30/2024

CAR, chimeric antigen receptor; CD62L+, CD62L or L-selectin positive T cells; IND, Investigational new drug; LBCL, large B-cell lymphoma; TME, tumor microenvironment; 2L, second-line; 3L+, third-line plus



IMPT-314 for Aggressive Large B-Cell Lymphoma



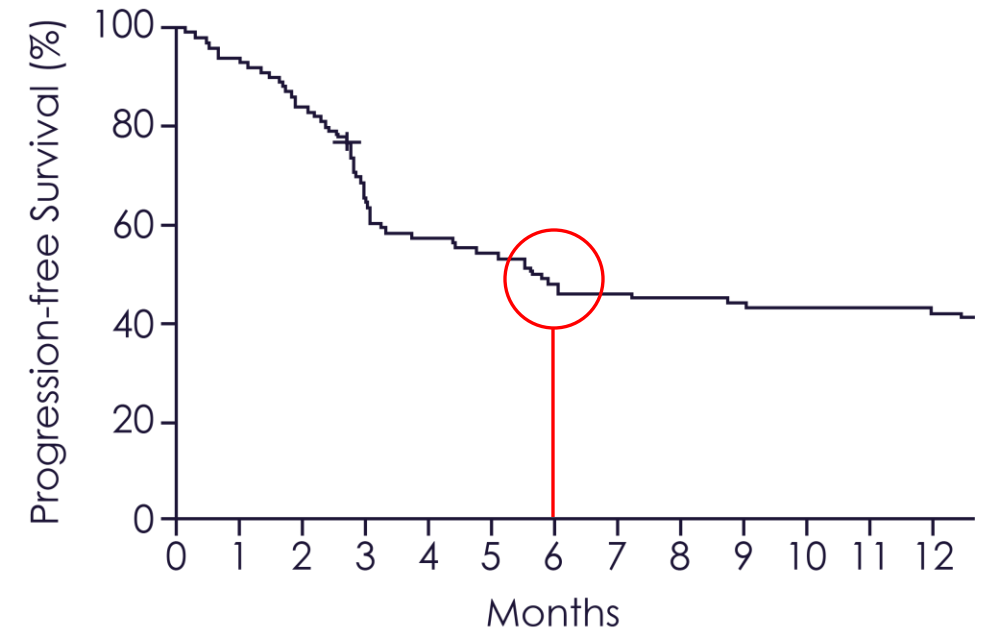
Higher Complete Response Rates and Longer Duration of Responses Are Needed for Patients with Large B-Cell Lymphoma in the 3rd Line+ Setting



CD19 CAR T-cell therapies represent a major clinical advance, but significant unmet medical need remains

- Approximately 50% of 3rd line patients treated with an approved CD19 CAR T-cell therapy do not achieve complete responses and 30% do not respond at all
- Approximately 50% of 3rd line patients treated with approved CD19 CAR T-cell therapy progress within six months
- The overall survival at one year after approved CAR T-cell therapy in the 3rd line is only 50-60%, and only 30% of patients remain in remission at 2 years

In a clinical trial for Yescarta[®], approximately 50% of patients treated with CD19-targeted CAR T-cells progressed or died by 6 months



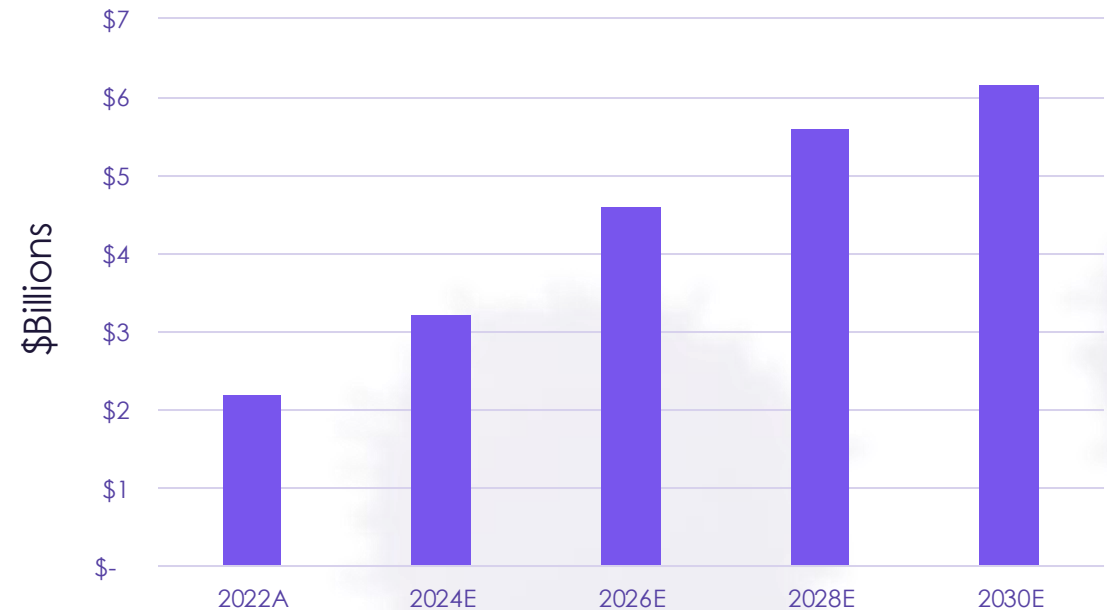
Zuma-1: YESCARTA[®]; n = 101 LBCL
3rd line+ setting

IMPT-314 Targets the \$3bn+ CD19 CAR T-Cell Therapy Market Expected to Nearly Double by 2030









- Growth will largely be driven by increased use in the 2nd line setting and greater availability as more community centers adopt cell therapy
- Approximately 30 to 40% of US patients with aggressive large B-cell lymphoma relapse or are unable to achieve remission within 12 months following first-line treatment
- Of the relapsed/refractory patients, up to 65% have a performance status eligible for CAR T cell therapy



WW Projected Sales of Currently Approved CD19 CAR T-Cell Products



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



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
		CD19	3+, R/R LBCL (ZUMA-1) (N = 108)	72%	51%	5.8 ²	9%	31%
		CD19	3+, R/R LBCL (TRANSCEND) (NHL 001, N = 268)	73%	54%	6.8 ³	3%	10%
		CD19	3+, R/R DLBCL (JULIET) (N = 115)	50%	32%	2.9 ⁴	23%	19%

PHASE 1 TRIALS (Interim Data)		Target	Line of Therapy, Indication, Sample Size	Overall Response Rate	Complete Response Rate	Median PFS (months)	Grade ≥3 CRS	Grade ≥3 ICANS
	UCLA-314	CD19/CD20	3L+ R/R NHL (N = 13)	92%	77%	--	0%	0%
	IMPT-314	CD19/CD20	3L+ R/R LBCL (N = 23*)	94%	71%	--	0%	13%

NOT FOR PROMOTIONAL USE; Differences exist between study or trial designs and subject characteristics and caution should be exercised when comparing data across studies.

Yescarta® prescribing information; Breyanzi® prescribing information; Kymriah® prescribing information

1. US Pls 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

*23 patients evaluable for safety, 17 patients evaluable for efficacy.

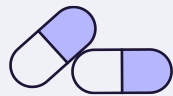
Significant Unmet Need and Opportunity in 2nd and 3rd Line+ DLBCL

Typical Patient Journey to CAR T-Cell Therapy



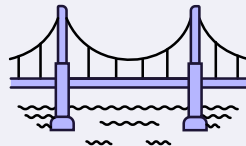
1st Line Therapy

Treatment with combination chemotherapy (eg, R-CHOP) with most patients treated in community centers



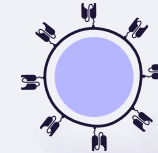
2nd Line Therapy

Bridging therapy/2L treatment for many patients initiated in community center while awaiting referral for CAR T



2nd or 3rd Line+ Therapy

Treatment in certified CAR T-cell treatment centers



US	~44,000	~24,000	~13,000
WW	~113,000	~62,000	~24,000

~200,000 globally-treated cases for DLBCL

IMPT-314 is Designed to Deliver Improved Complete Response Rates and Longer Duration of Responses



Feature

Function

Intended Outcome

True CD19/CD20 “OR” Logic-gated CAR

Designed to target either CD19 or CD20 with full potency

- Ability to target lower or heterogeneous CD19 antigen density potentially resulting in a higher percentage of CRs than a single targeting agent
- Increase in duration of response by preventing relapse due to CD19 antigen escape

Enriched for CD62L+ expressing cells

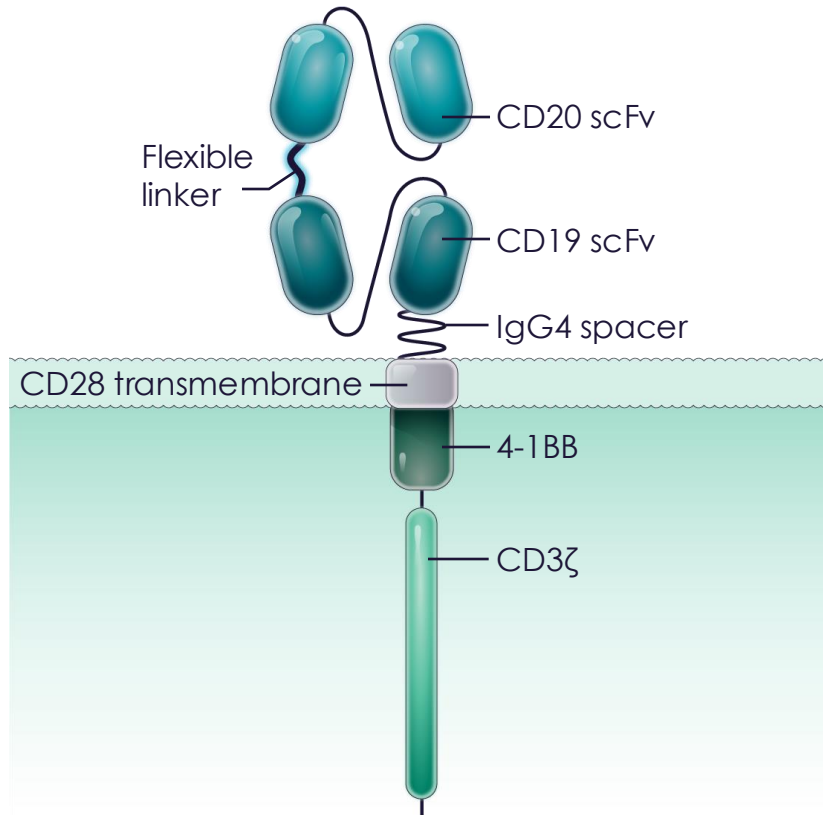
Designed to generate CAR T cells with enhanced antitumor activity and longer duration of activity without increasing manufacturing time

- Better engraftment
- Improved persistence
- Reduced exhaustion
- Lower cytokine production
- Manufacturing time of 8 days

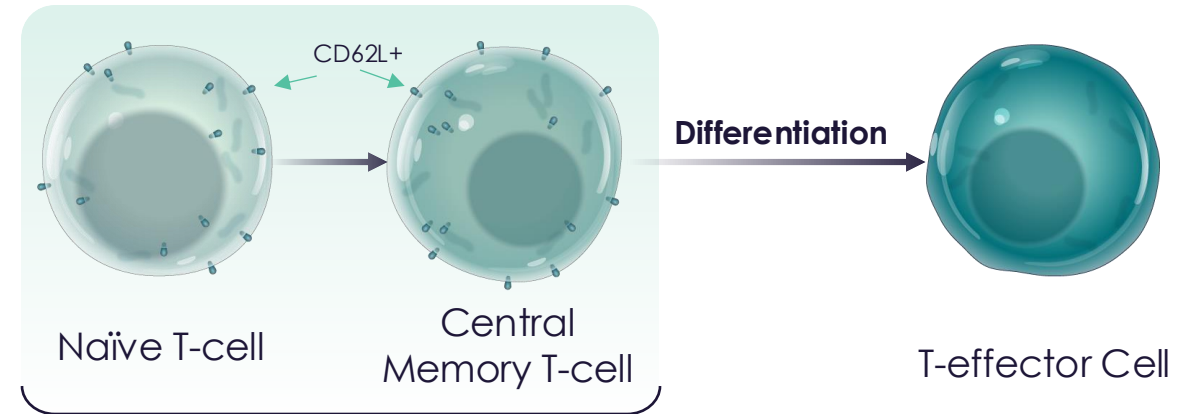
IMPT-314: Dual-Targeting CD19/CD20 CAR T-Cells Enriched for Stem-Like Phenotype (CD62L+)



IMPT-314 CAR Construct: True CD19/CD20 “OR” Logic-Gated CAR



CD62L⁺ Enrichment Selects for Naïve/Central Memory T-Cells



CD62L⁺ cells are associated with:

- Better engraftment
- Improved persistence
- Reduced exhaustion
- Lower cytokine production

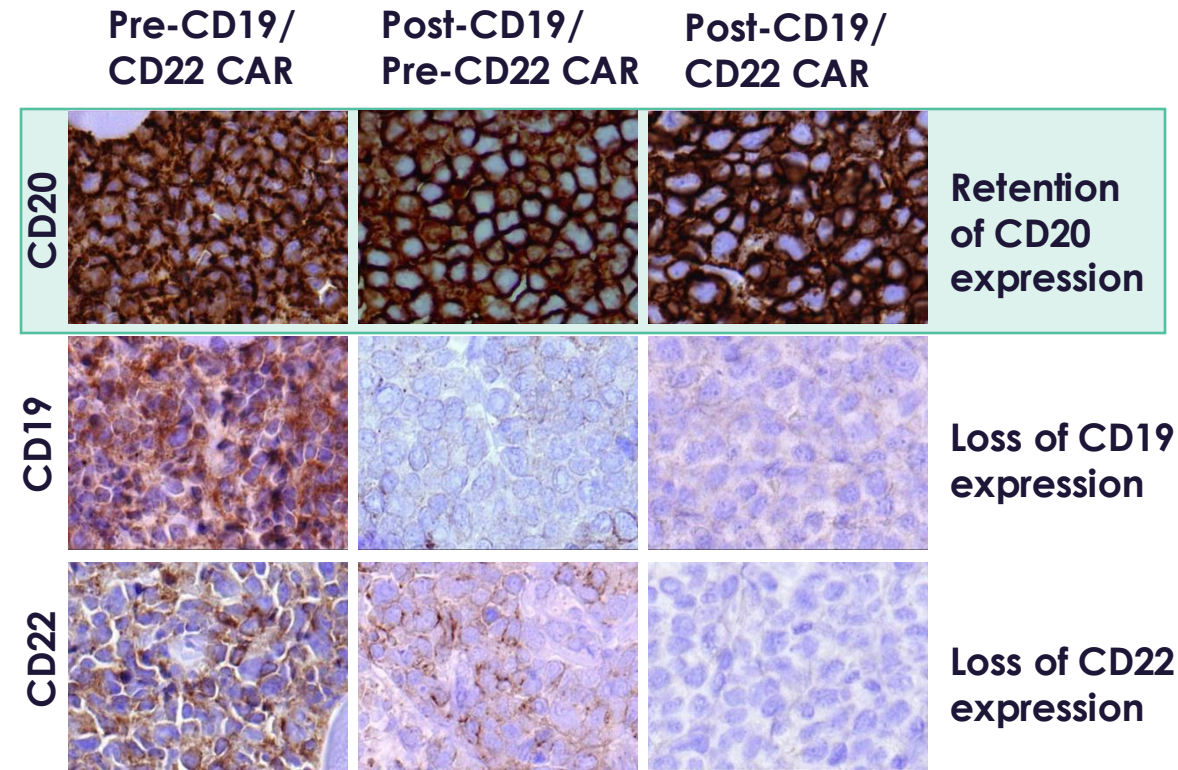
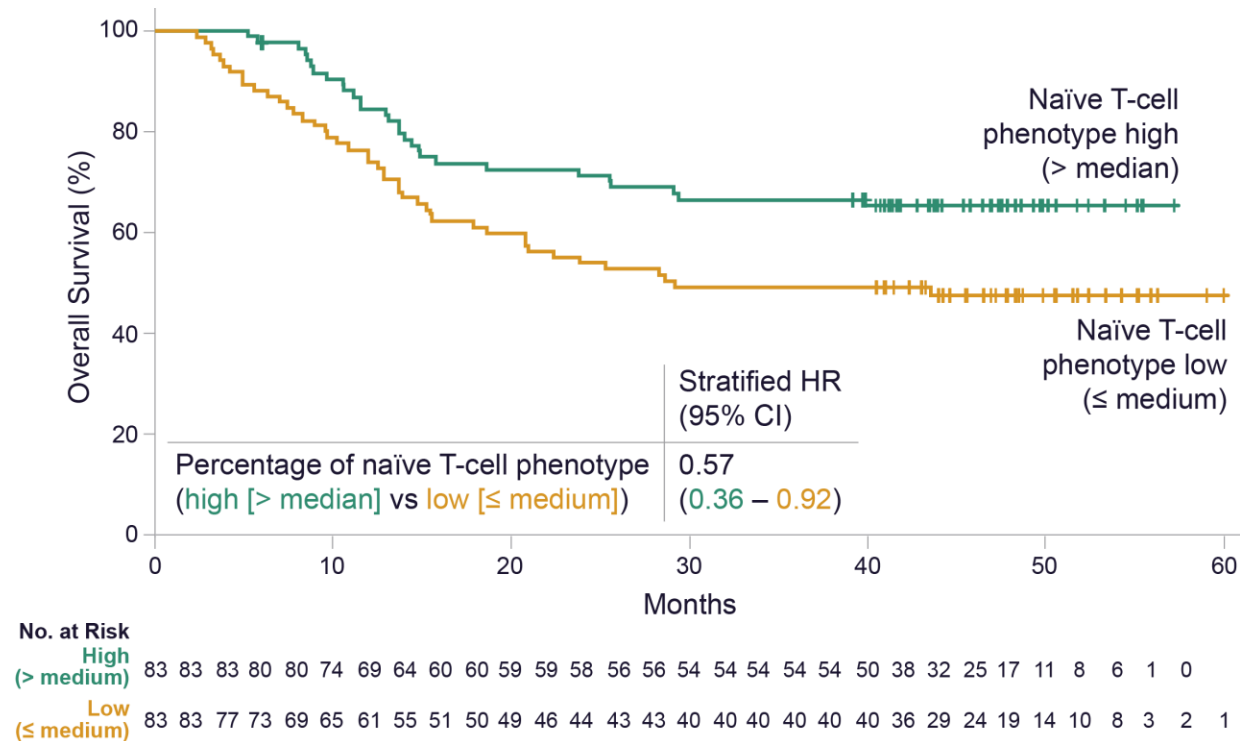
Low Naïve T Cells and CD19 Antigen Loss are Key Reasons for Progression Following CD19 CAR Therapy



Overall survival is increased in patients with a greater percentage of naïve T cells in the product

CD20 expression is retained and CD19 and CD22 are more likely to be lost following single targeted CAR T-cell therapy

ZUMA-7 Clinical Trial: Yescarta®

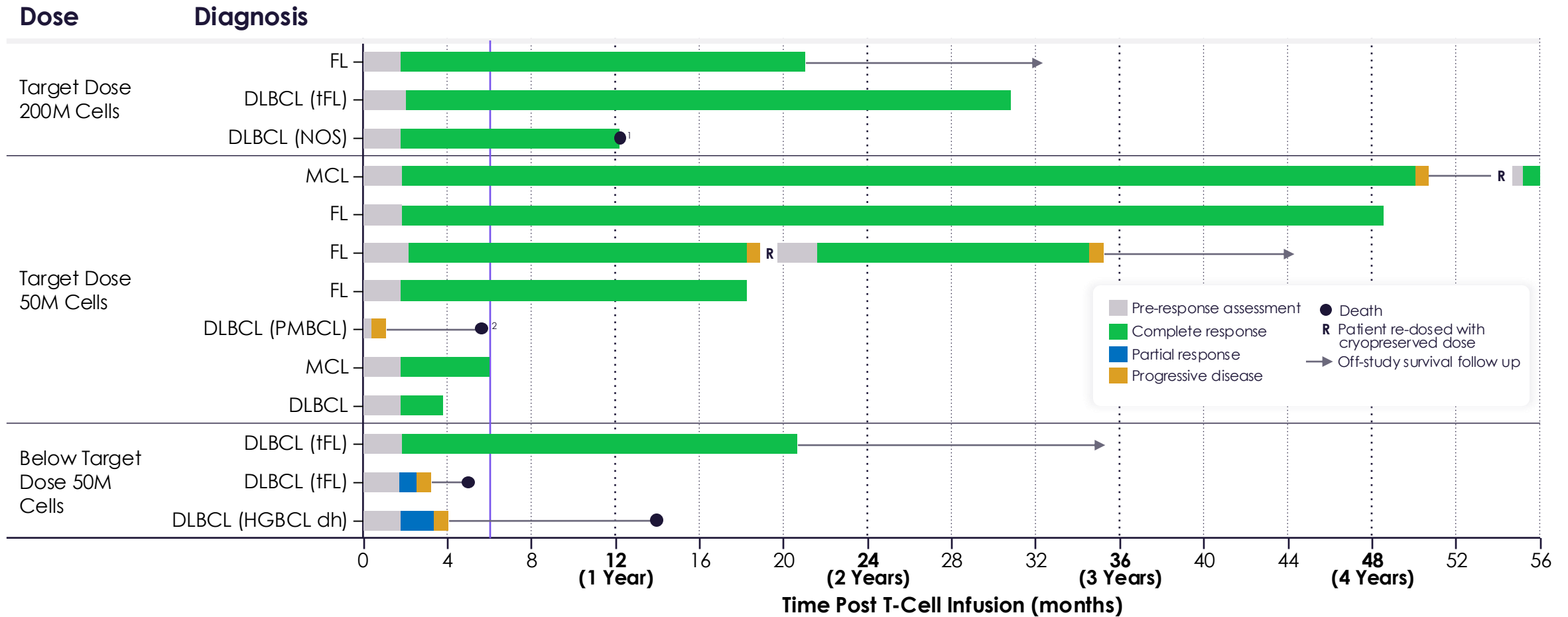


Westin JR et al., N Engl J Med. 2023; ; Shalabi H. et al., Haematologica. 2018 CAR, chimeric antigen receptor; ,



Data from CD19/CD20 CAR T (UCLA-314) Phase 1 Trial in R/R B-cell NHL

92% Overall Response Rate; 77% Complete Response Rate (N = 13)



Data cutoff: May 6, 2024; Presented at AACR Special Conference in Cancer Research, Tumor Immunology and Immunotherapy, Oct. 2024 and updated at 2024 ASH

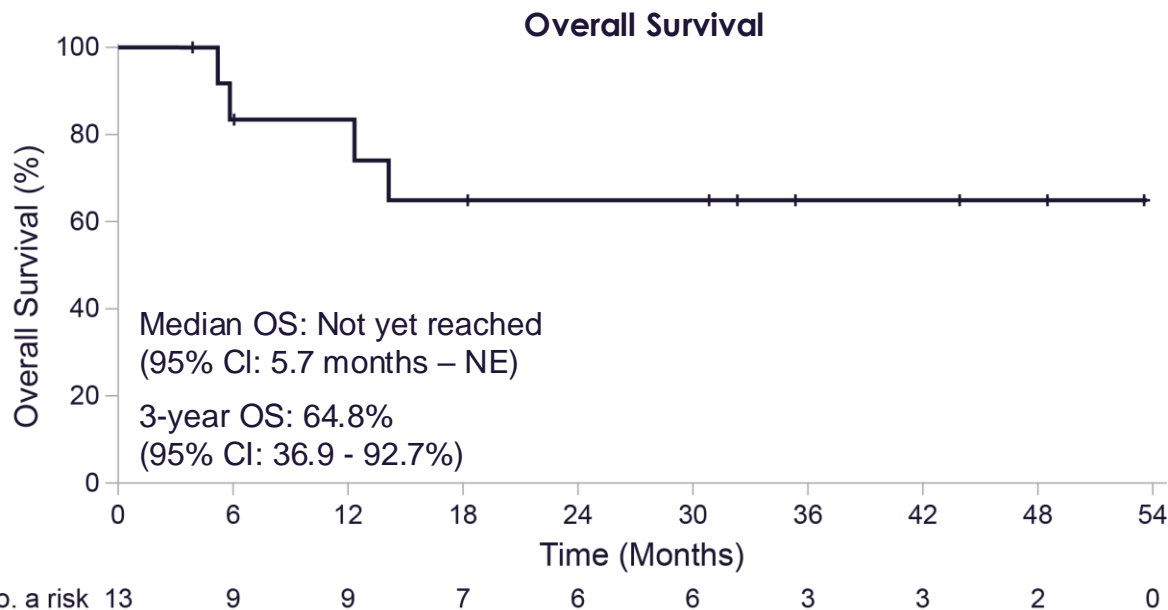
BM, bone marrow; CR, complete response; DLBCL, diffuse large B-cell lymphoma; FL, aggressive follicular lymphoma; HGBL dh, high grade B-cell lymphoma double hit; MCL, mantle cell lymphoma; NHL, non-Hodgkin lymphoma; NOS, not otherwise specified; PMBCL, primary mediastinal B-cell lymphoma; R/R, relapsed/refractory; tFL, transformed follicular lymphoma; UCLA-314: CART19/20.

Dual-targeting CD19/CD20 CAR T Cell Therapy Resulted in Highly Differentiated Disease-free Duration Over Approved CD19 CARs in UCLA-314 Single Center Phase 1 Dose-Escalation Clinical Trial



Durable responses with median progression-free survival of 50.1 months

Overall Survival: Median OS Not Reached (5.7 months – NE)



Favorable Safety Profile

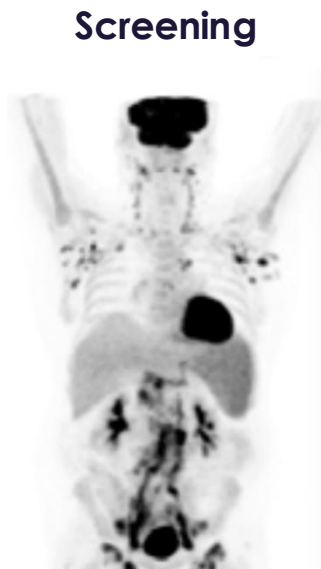
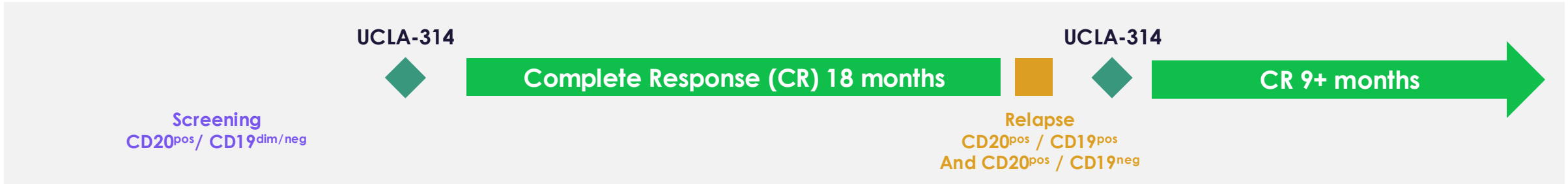
TEAEs, (N = 13)	Grade ≥2
CRS	0
ICANS	0

Data cutoff: May 6, 2024; Presented at AACR Special Conference in Cancer Research, Tumor Immunology and Immunotherapy, Oct. 2024
Abbreviations: CRS, cytokine release syndrome; Gr, grade; ICANS, immune effector cell-associated neurotoxicity syndrome; NE, not estimable, OS, overall survival; CI, confidence interval; TEAE, treatment-emergent adverse event.

UCLA-314 Achieved Complete Response after Repeat Dosing in a Patient at Relapse



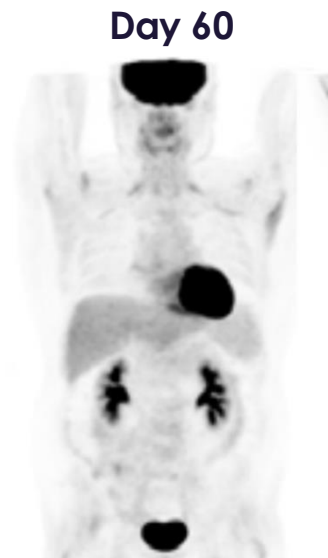
Patient 004 with follicular lymphoma grade 3A, stage IV



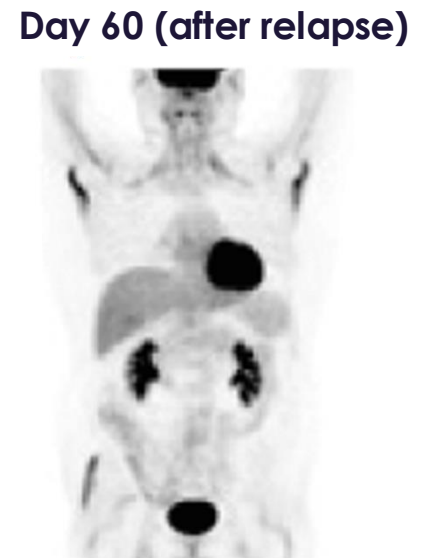
Extensive tumor burden at screening



Comparable scans post-bridging vs screening



Tumor eradication 60 days post UCLA-314



Repeat dosing of UCLA-314 with originally manufactured cells

IMPT-314: Phase 1- 2 Clinical Trial Design

3 + 3 Dose Escalation Followed by Dose Expansion



Initial results presented at the 2024 ASH Annual Meeting

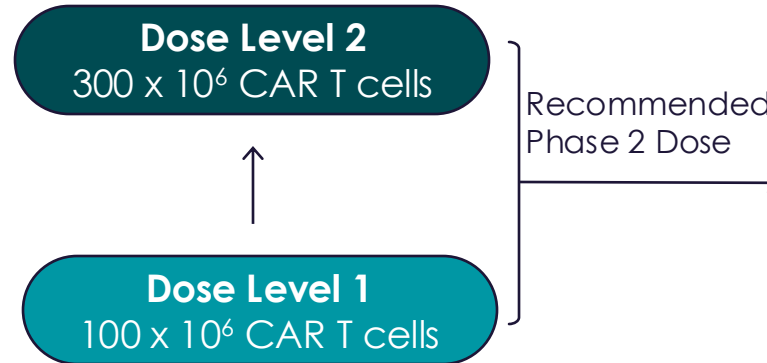
Patient Population

- Patients with relapsed/refractory DLBCL, PMBCL, HGBL, Grade 3bFL, and tFL who have had ≥ 1 line of tx
- CD19 CAR T-cell therapy naïve or experienced
- Eligible for CAR T-cell therapy

Study Objectives

- Safety and tolerability
- Overall response rate, complete response rate
- Duration of response
- Cell expansion pharmacokinetics

Dose Escalation



Lymphodepletion

Fludarabine 30 mg/m² x 3 days,
cyclophosphamide 500 mg/m² (CAR T naïve)
or 300 mg/m² (CAR T exp.) x 3 days on days -5,-4,-3

Dose Expansion (N = ~60)

3rd Line+ CAR-Naïve (n = 20)
(expand for potential accelerated approval)

2nd Line CAR-Naïve at high risk of recurrence (R/R < 1 year) (n = 20)

CAR-Experienced (n = 20)
(expand for potential accelerated approval)



**Initial Clinical Data from the
Phase 1-2 Trial of IMPT-314
Presented at the
2024 ASH Annual Meeting**

Demographics and Baseline Characteristics

CAR T-Naïve Cohort in the 3rd Line+ Setting

Characteristics	N = 23
Median (range) age, years	65 (21–87)
LBCL histology n (%)	
DLBCL	14 (61%)
HGBCL	4 (17%)
tFL	3 (13%)
Other	2 (9%)
Male n (%)	16 (70%)
Hispanic or Latino n (%)	4 (17%)
Race n (%)	
Asian	1 (4%)
Black or African American	1 (4%)
Caucasian	18 (78%)
Not Reported	1 (4%)
Other	2 (9%)

Characteristics	N = 23
ECOG Performance Status: n (%)	
0	7 (30%)
1	16 (70%)
IPI score ³ 3 at study entry	9 (39%)
Stage ≥ 3 at diagnosis	13 (57%)
Median lines of prior therapy (range)	3 (2–6)
Elevated (above normal) LDH %	11 (48%)
Received bridging therapy n (%)	12 (53%)

Data cutoff: October 22, 2024

DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; HGBCL, high-grade B-cell lymphoma; IPI, international prognostic index for DLBCL; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; tFL, transformed follicular lymphoma to DLBCL.

Manageable Safety Profile: No High-Grade CRS and Low Rates of Grade 3 ICANS

Adverse Event, n (%)	N = 23
CRS	
Grade 1 or 2	16 (70%)
Grade 3+	0
Median time to onset, days (range)	1.5 (0–13)
Median time to resolution days (range)	4 (2–8)
ICANS	
Grade 1 or 2	3 (13%)
Grade 3	3 (13%)
Median time to onset, days (range)	6 (3–10)
Median time to resolution, days (range)	5 (3–12)
Prolonged Cytopenias	
Neutropenia	3 (13%)
Thrombocytopenia	1 (4%)
Infections	
Grade 3*	4 (17%)

- No cases of Grade 3 CRS were reported. Grade 1 and 2 CRS were reported in 70% (16/23) of patients and 50% (8/16) of those with CRS received tocilizumab.
- Grade 3 ICANS was reported in 13% (3/23) of patients with a median time to complete ICANS resolution of 5 days, and rapid improvement to Grade 2 or lower with standard therapy
- Four patients had Grade 3 infection (bacteremia NOS, tooth, UTI, zoster), all of which responded to treatment and resolved

Data cutoff: October 22, 2024.

*Prolonged cytopenias were defined as Grade 3 or higher reported adverse events of neutropenia, anemia, thrombocytopenia or pancytopenia initiating or persisting on or after study day +28. CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome, NOS, not otherwise specified, UTI, urinary tract infection.

Overall Response Rate of 94% and Complete Response Rate of 71% Were Achieved By 3 Months After IMPT-314 Treatment

CAR T-Naïve Cohort in the 3rd Line+ Setting

Best Overall Response	N = 17
Overall Responses, n (%)	16 (94%)
Complete Responses, n (%)	12 (71%)
Partial Responses, n (%)	4 (24%)
Stable Disease, n (%)	1 (6%)
Median Follow Up, months (range)	6.3 (1.2–12.5)
Median Duration of Response	Not reached

- 71% of patients were in response at last follow-up, with a median follow-up of 6.3 months (range, 1.2 – 12.5)
- No deaths occurred during the study treatment period (prior to disease progression or subsequent anti-cancer therapy)

The efficacy evaluable population included 17 patients with LBCL, including DLBCL (n = 10), HGBCL (n = 4), and tFL (n = 3)

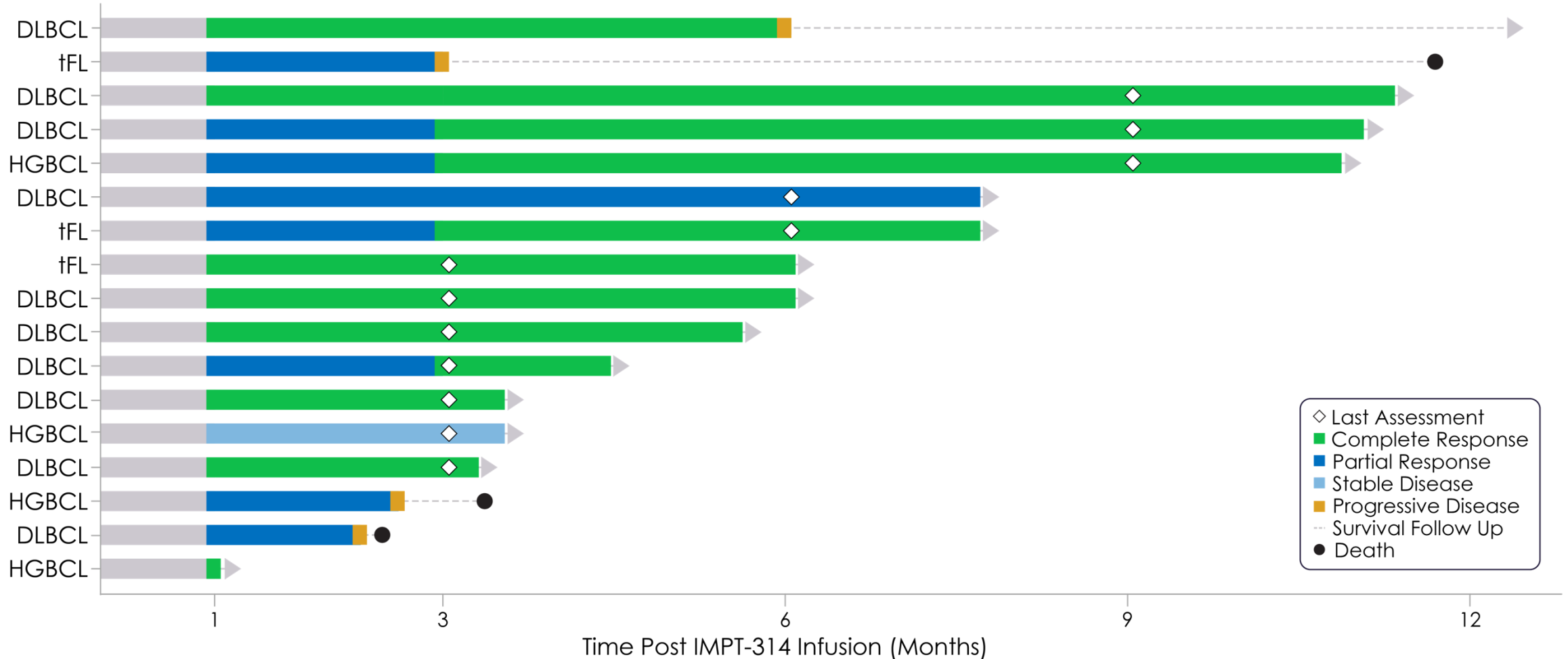
Two patients with T-cell histiocyte-rich LBCL were not included in the analysis (1 PR, 1 PD) and this histology will not be enrolled moving forward

Patients were evaluable for a response assessment at Day 84 or later, or if they had a prior CR or PD

Overall Response Rate of 94% and Complete Response Rate of 71% Were Achieved By 3 Months after IMPT-314 Treatment



Swimmer Plot of Individual Patient Trajectories over Time; CAR T-Naïve Cohort in the 3rd Line+ Setting

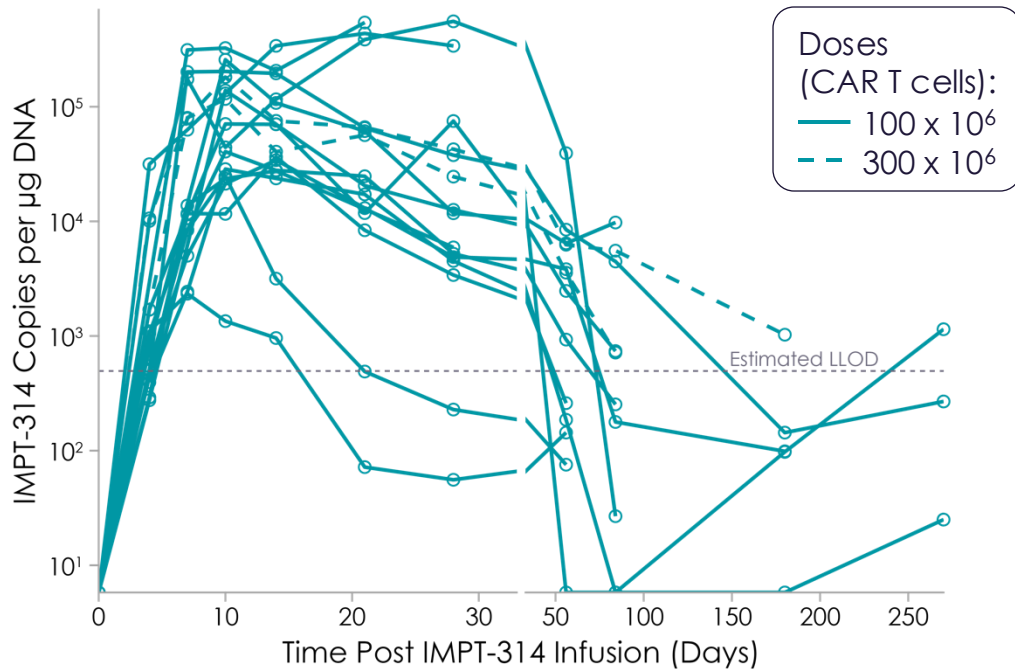


Individual patient trajectories demonstrated a 94% ORR and a 71% CR rate with 71% of patients in response at last follow-up with median follow up of 6.3 months (range, 1.2 – 12.5 months)

Robust CAR T-cell Expansion and Final Drug Product Comprised of Naïve and Central Memory T-Cell Populations

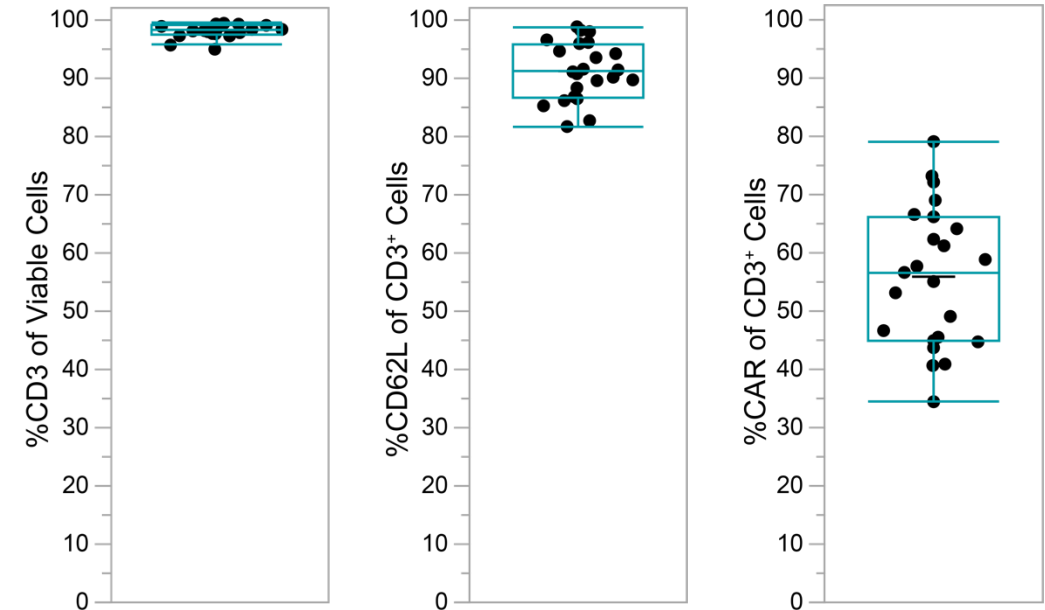


Robust CAR T-Cell Expansion in IMPT-314-Treated CAR-T-Naïve Patients



- IMPT-314 showed robust expansion in 16 efficacy evaluable patients. Peak cell expansion occurred between Days 7-28 post IMPT-314 infusion (median T_{max} = 10 days)
- Median peak of expansion (C_{max}) was 93,723 copies/ μ g gDNA (range 2,338–555,284). IMPT-314 cells persisted multiple weeks post infusion across multiple patients with median expansion at Day 28 of 11,766 copies/ μ g gDNA (range 56–555,284)

IMPT-314 Final Drug Product Characteristics



- The CD3 component of the final drug product is a CD62L-rich product comprising naïve and central memory populations (median, 91%; range, 82–99%)

16 patients in the efficacy evaluable set were evaluable for pharmacokinetics
 CAR, chimeric antigen receptor; CD, cluster of differentiation; DNA, deoxyribonucleic acid; LLOD, lower limit of detection; PCR, polymerase chain reaction; PK, pharmacokinetics.








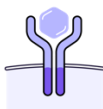
Next Generation CAR T-Cell Therapy for Solid Tumors



Multiple Approaches Designed to Create Next-Generation CAR T Cells with Potent Anti-Tumor Functionality

Technology/ Manufacturing Approach

Potential Benefits

	Anti-Exhaustion	Enhanced Stemness	Increased Proliferation/ Persistence	Improved Cytotoxicity	
 c-Jun	✓		✓	✓	c-Jun and NR4A3 regulate the AP-1 transcription factor pathway, which plays a key role in T-cell effector function
 NR4A3	✓		✓	✓	
 Epi-R		✓	✓		Manufacturing protocols designed to generate more stem-like cells that self renew and persist despite repeat antigen stimulation
 Naïve/Central Memory T-cell Enrichment		✓	✓		
 Stim-R			✓	✓	Customizable synthetic T-cell activation reagent designed to closely emulate natural antigen presentation to generate more potent T cells
 Undisclosed new technologies			✓	✓	Expression of novel chimeric proteins to optimize CAR T-cell killing in the hostile TME (eg, TGFβ blockade and local cytokine signals)



Advancing Next-Generation CAR T-Cell Therapy

Lead program, IMPT-314, expected to enter pivotal trial in aggressive large B-cell lymphoma in 2025



IMPT-314 is a dual-targeting CD19/CD20 CAR T cell product candidate designed to increase complete responses and prolong the duration of responses as compared to the approved CD19-targeted CAR T cell therapies

Phase 1 -2 multi-center trial ongoing in patients with R/R large B-cell lymphoma; presented initial data at ASH 2024:

94% Overall Response Rate
71% Complete Response Rate

Manageable safety profile
No high-grade CRS and low rates of Grade 3 ICANS

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

Multiple proprietary technologies designed to improve T-cell function in solid tumors

Scalable in-house manufacturing strategy of >1000 doses/year

Strong balance sheet with \$460 million of cash* provides runway into 2027

*Cash, cash equivalents & marketable securities as of 9/30/2024. ASH, American Society of Hematology Annual Meeting; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, Immune effector cell-associated neurotoxicity syndrome; R/R, relapsed/refractory

Upcoming Potential Milestones

Balance sheet of \$460M* provides cash runway into 2027, through multiple clinical milestones



IMPT-314	Dual-Targeting CD19/CD20 CAR T-Cell Therapy for Aggressive Large B-Cell Lymphoma
Q4 2024	✓ Presented initial Phase 1 -2 data at ASH 2024 Annual Meeting in December
Mid-2025	<input type="checkbox"/> More mature data in 3 rd line+ setting <input type="checkbox"/> Initial clinical data in 2 nd line setting <input type="checkbox"/> Initiate pivotal trial in 3 rd line+ setting
Late 2025	<input type="checkbox"/> More mature data in 2 nd line setting
By Early 2026	<input type="checkbox"/> Initiate pivotal trial in 2 nd line setting
Undisclosed	CAR T-Cell Product Candidates – Solid Tumors
2026	<input type="checkbox"/> IND for new product candidate

*Cash, cash equivalents and marketable securities as of 9/30/2024
CAR, chimeric antigen receptor; IND, investigational new drug application



It's all about the cells.

For more information, please contact
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