Lyell Strengthens Next Generation CAR T Cell Pipeline

Lyell Immunopharma

October 24, 2024

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Next Generation CAR T-cell Therapy for Patients with Cancer

Acquiring ImmPACT Bio and its next-generation dual-targeting CD19/20 CAR T cell candidate with strong Phase 1 clinical data in B-cell lymphoma

- Potential for increased complete response rates with longer duration of response over approved CD19 CAR T cell therapies in aggressive relapsed/refractory B-cell non-Hodgkin's lymphoma with opportunity to take significant market share in 2nd and 3rd line
- Presenting initial data from multi-center Phase 1 clinical trial at major medical conference this year
- Expect to enter pivotal clinical trial in 2025 in 3rd line CAR-naïve patients

Prioritizing next generation CAR T cell candidates in hematologic malignancies and solid tumors

- Two wholly owned CAR T cell clinical programs addressing large patient populations: IMPT-314 in hematologic malignancies and LYL119 in solid tumors
- Discontinuing first-generation LYL797 CAR T cell and LYL845 TIL programs as they did not meet our criteria for differentiated patient benefit

Strong balance sheet to fund company through multiple clinical milestones

- Cash runway into 2027, through data milestones for each clinical program

CAR, chimeric antigen receptor; TIL, tumor infiltrating lymphocytes

Advancing Next Generation CAR T Cell Therapy

Innovative cell therapy for hematologic malignancies to improve outcomes

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

CAR, chimeric antigen receptor

Prioritizing Pipeline to Focus on Most Differentiated Product Candidates

ROR1-targeted CAR T-cell program update (LYL797 and LYL119)

- LYL797 demonstrated clinical activity and robust expansion and CAR T cell infiltration into solid tumors, however, we were constrained by a narrow therapeutic window; discontinuing the program to prioritize LYL119
- LYL119, with four anti-exhaustion and stemness technologies, moving forward
  - Enhanced serial cell killing over time demonstrated with LYL119 compared to LYL797
  - Greater tumor control with 10-fold lower cells administered in vivo
  - More gradual cell expansion at lower doses in in vivo models suggests greater tolerability
  - First patient with platinum-resistant ovarian cancer or R/R endometrial cancer expected to be treated by the end of 2024/early 2025
  - Step dosing to be explored (low priming dose followed by additional doses)

Discontinuing development of LYL845 and earlier-stage TIL programs

- Initial clinical data from LYL845 did not meet our rigorous criteria for advancement
- Research-stage TIL programs and rejuvenation will be discontinued

CAR, chimeric antigen receptor; R/R, relapsed/refractory; ROR1, receptor tyrosine kinase-like orphan receptor 1; TIL, tumor infiltrating lymphocytes

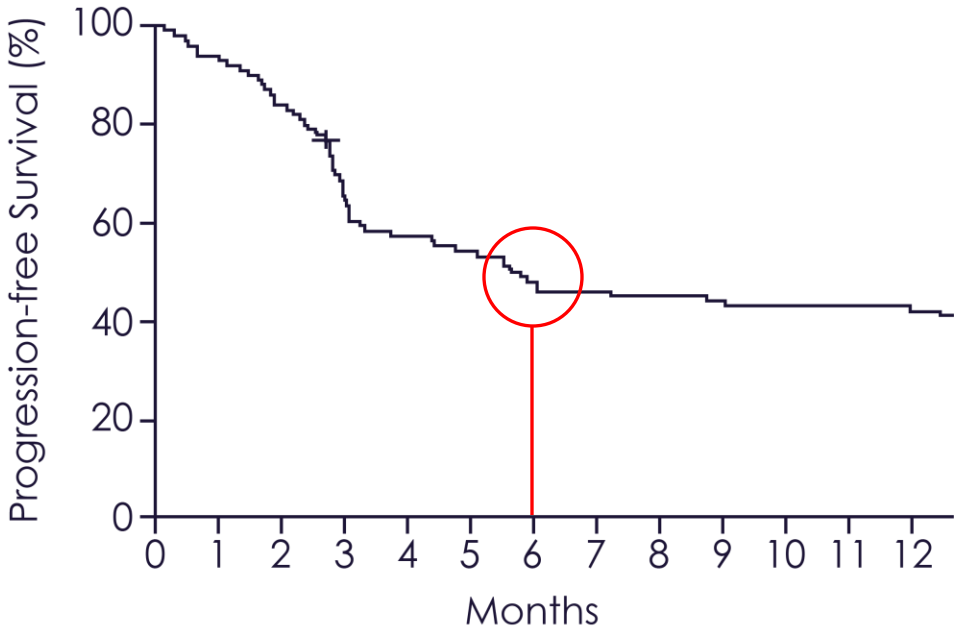
IMPT-314 for B-cell Malignancies

Higher Complete Response Rates and Longer Duration of Response Are Needed for Patients with R/R B-cell Lymphoma

CD19 CAR T-cell therapies represent a major clinical advance, but significant room to improve remains

- Over 40% of 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 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 is only 50-60%, and only 30% of patients remain in remission at 2 years

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



Zuma-1: YESCARTA®; n = 101 LBCL

Neelapu SS, et al., N Engl J Med. 2017; Harris LJ, et all, Int J Mol Sci. 2020
CAR, chimeric antigen receptor; R/R, relapsed/refractory

Higher Response Rates and Longer PFS Could Result in a Significant Increase in the Market Penetration of CAR T-cell Therapies

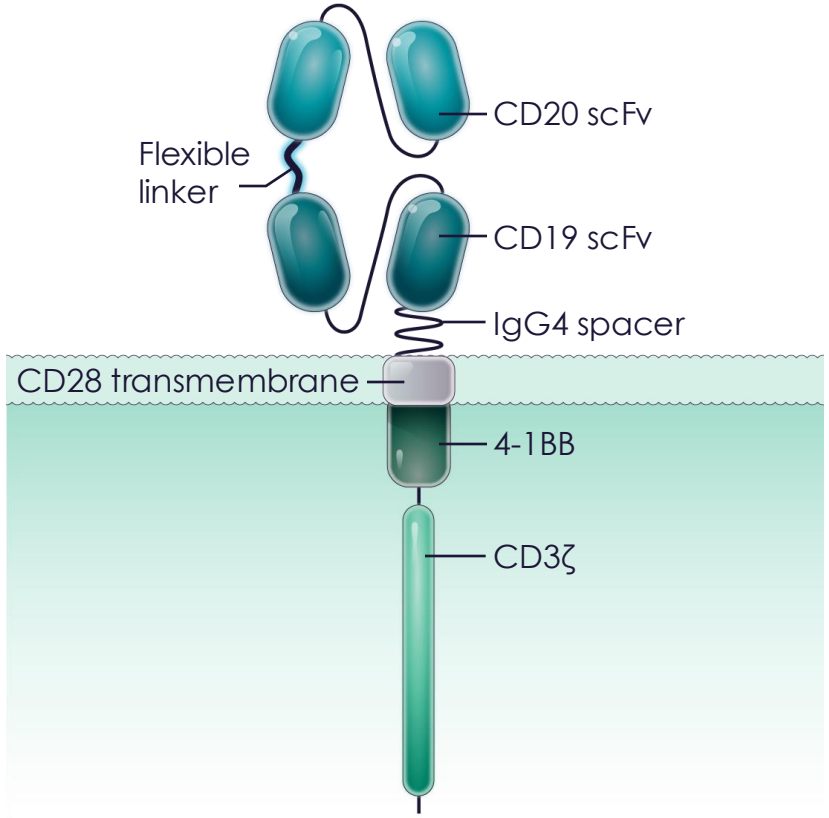
More than 40% of patients do not respond to currently approved CD19 CAR T-cell therapies and many responders progress

		Target	Line of Therapy, Indication	Objective 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)	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)	73%	54%	6.8[3]	3%	10%
NOVARTIS	KYMRIAH® (tisagenlecleucel) Dispersion for IV infusion	CD19	3+, R/R DLBCL (JULIET)	50%	32%	2.9[4]	23%	19%

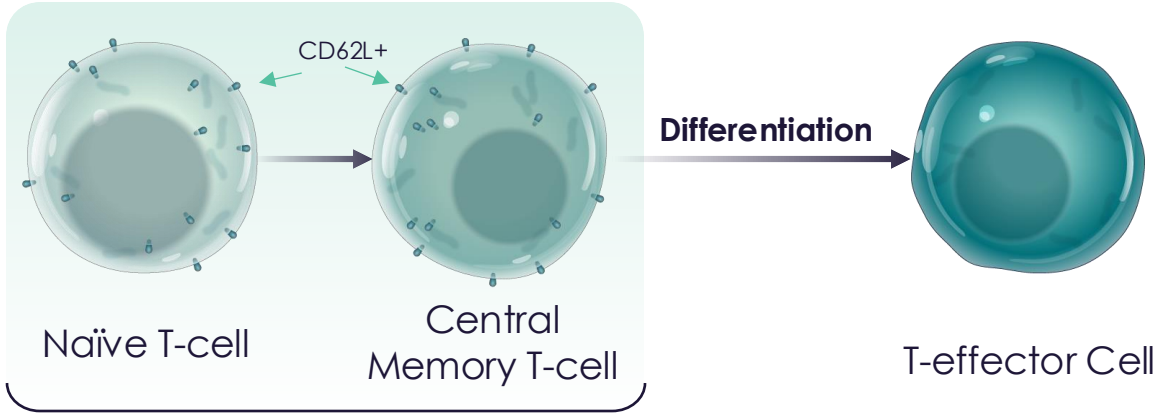
Yescarta® prescribing information; Breyanzi® prescribing information; Kymriah® prescribing information
1. US PIs section 5.2; 2. N Engl J Med 377:26, 2017. 3 The Lancet, Volume 396, Issue 10254, 839 – 852, 2020; 4. N Engl J Med 380:45, 2019
CR, complete response; CRS, cytokine release syndrome; NHL, non-Hodgkin lymphoma

IMPT-314: Dual-Targeting CD19/20 CAR T Cells Enriched for Stem-Like Phenotype (CD62L+)

IMPT-314 CAR Construct: True CD19/20 "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

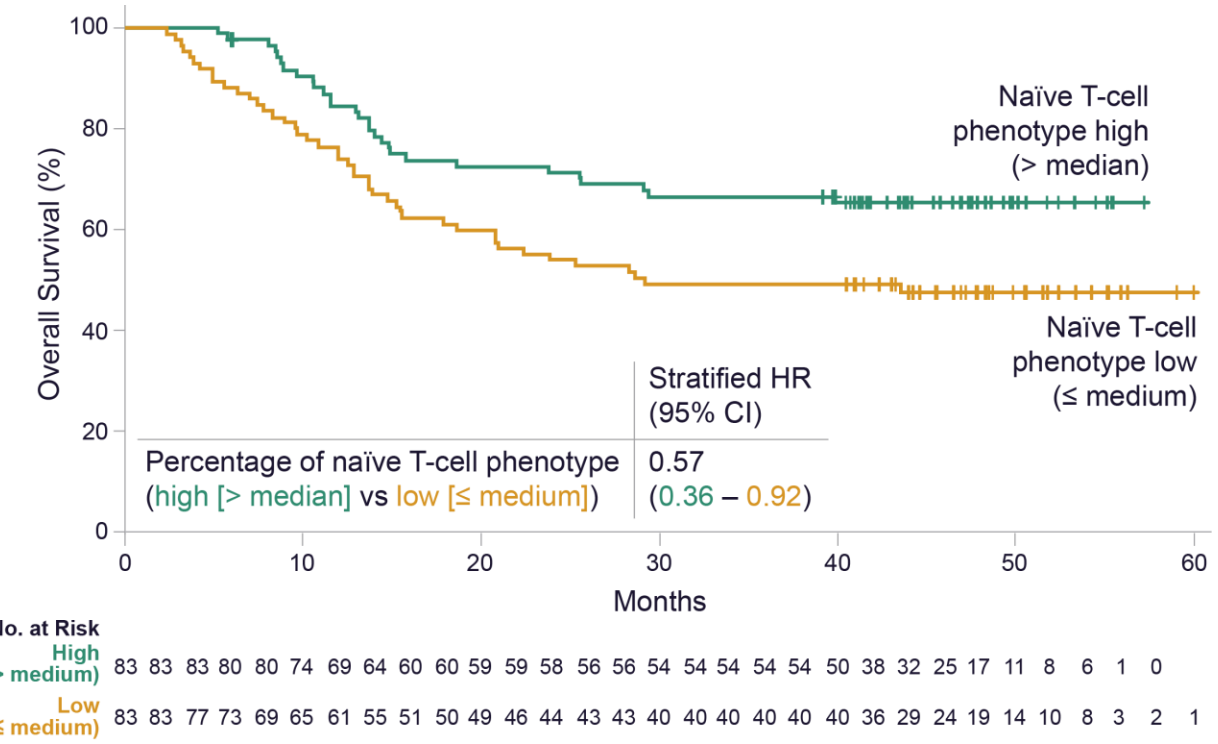
CAR, chimeric antigen receptor; scFv, single-chain variable fragments, IgG4, Immunoglobulin G4

Arcangeli et. al. JCI 2022, Sommermeyer et. al. Leukemia 2016, Chen et. al. Cancer Discovery 2021, Aldoss et al., Clin Cancer Res 2023

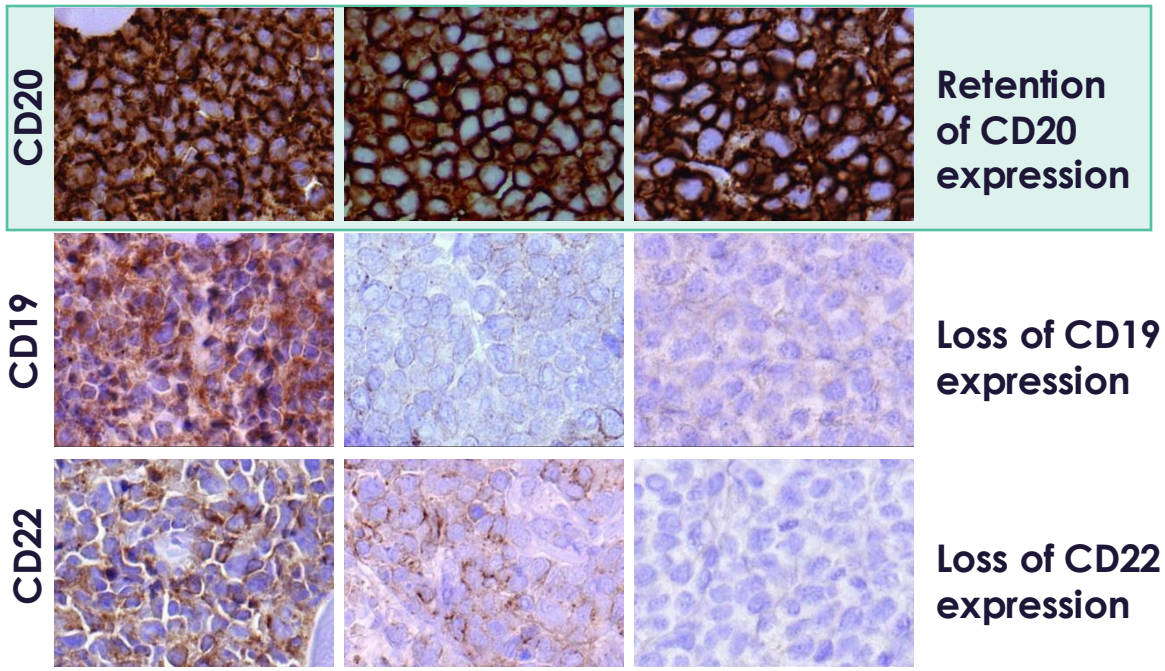
Low Naïve T Cells and CD19 Antigen Loss are Key Reasons for Progression Following CD19 CAR Therapy

Overall survival is increased in patients receiving a greater proportion of naïve T cells

ZUMA-7 Clinical Trial: Yescarta®



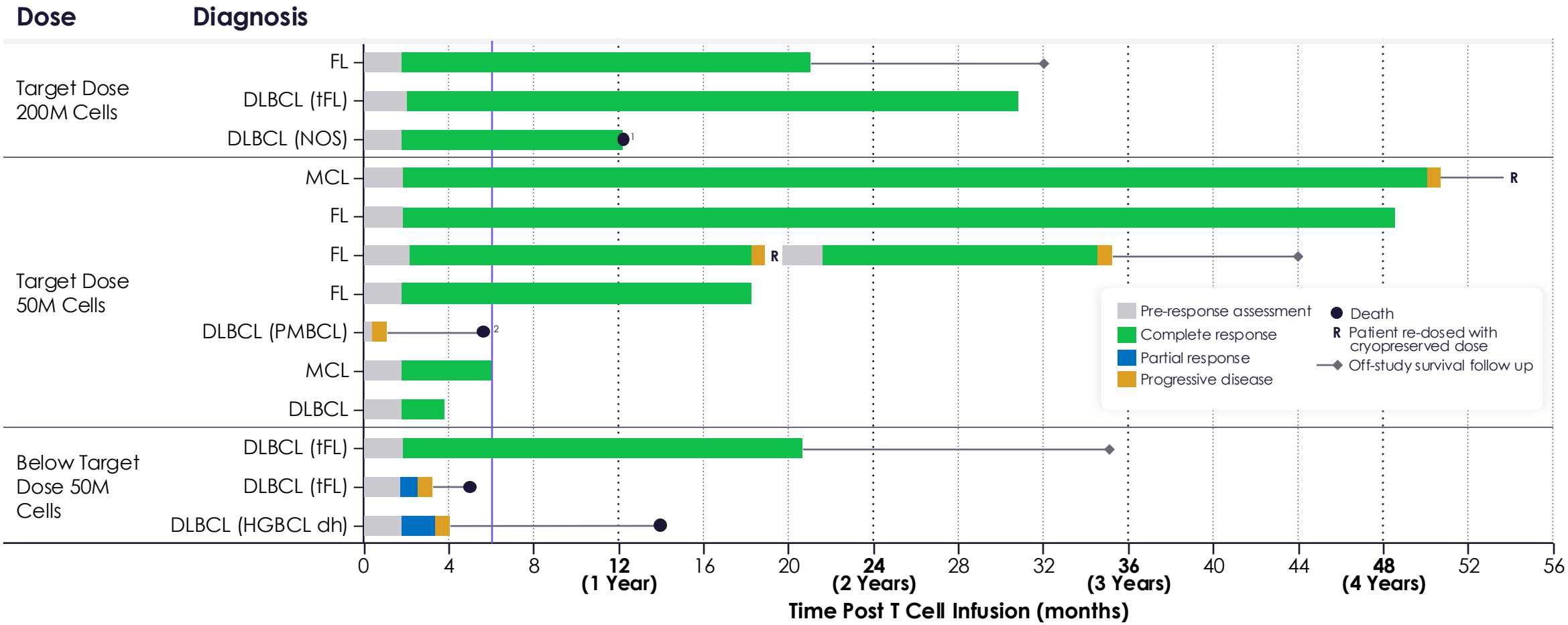
CD20 expression is retained and CD19 and CD22 are more likely to be lost following single targeted CAR T cell therapy



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

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

92% Objective Response Rate; 77% Complete Response Rate



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

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.

[1]Patient chose to enter hospice-level care at 12 months. [2]Day 14 BM involvement by a distinct $CD19^-$ $CD20^-$ $CD30^+$ lymphoma.

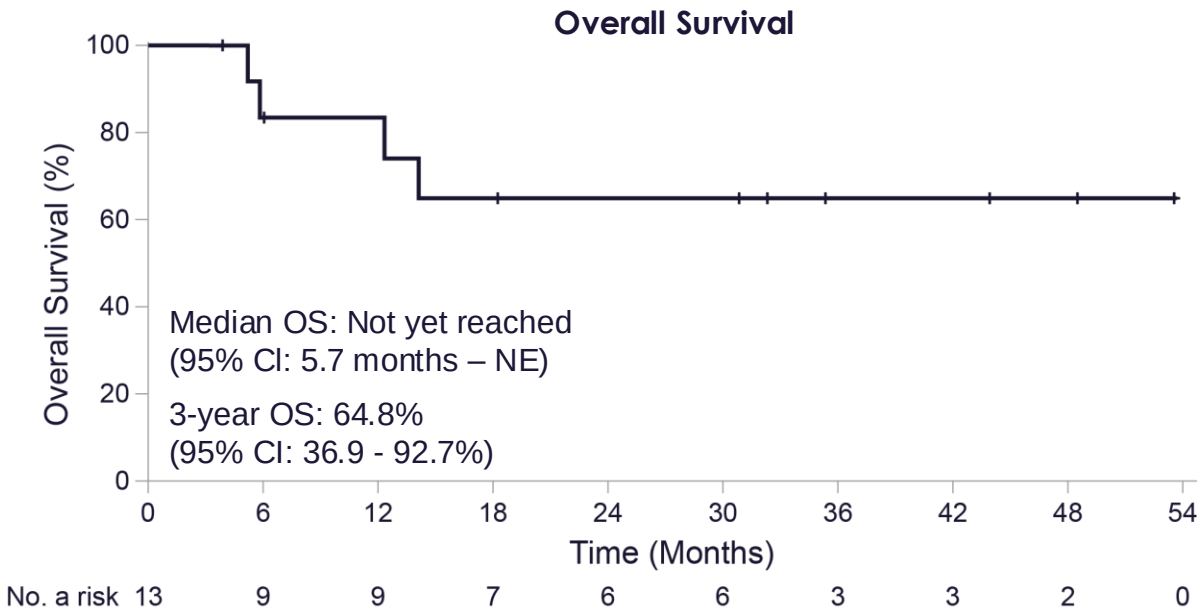
Dual-targeting CD19/20 CAR T Cell Therapy Results in Highly Differentiated Disease-free Duration Over Approved CD19 CARs

UCLA-314 Single Center Phase 1 Dose Escalation Clinical Trial

Durable responses with median progression-free survival of 50.1 months

Overall Survival: Median Not Reached

Median OS: Not yet reached (5.7 months – NE)



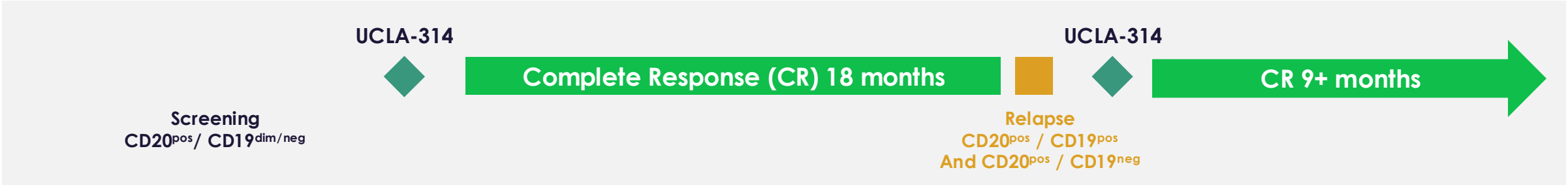
Favorable Safety Profile

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

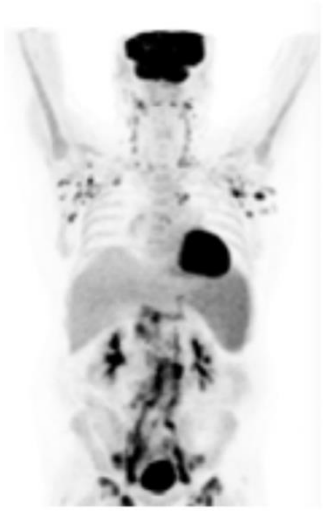
Data cutoff: May 6, 2024; Presented at AACR Special Conference in Cancer Research, Tumor Immunology and Immunotherapy, Oct. 2024
Abbreviations: CRS, cytokine release syndrome; Gr, grade; ICANS, immune effector cell-associated neurotoxicity syndrome; OS, overall survival; PFS, progression free survival; TEAE, treatment-emergent adverse event.

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

Patient 004 with follicular lymphoma grade 3A, stage IV

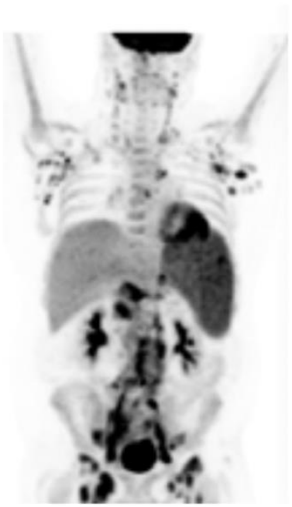


Screening



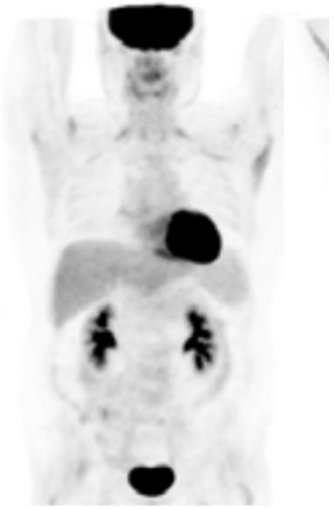
Extensive tumor burden at screening

After Bridging



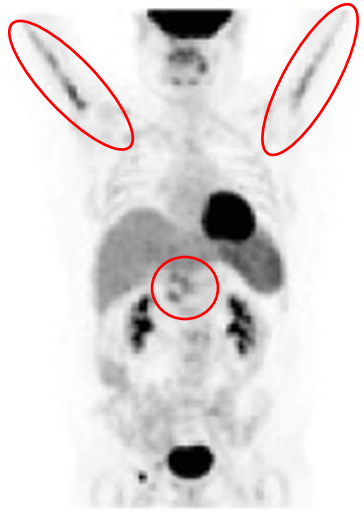
Comparable scans post-bridging vs screening

Day 60

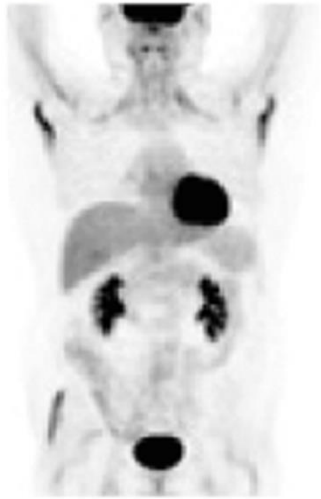


Tumor eradication 60 days post UCLA-314

18 months (relapse)



Day 60 (after relapse)



Repeat dosing of ULCA-314 with originally manufactured cells

Data cutoff March 6, 2023

Larson SM et al, Cancer Discovery, 2023; and data presented by presented by Puliafito, B at AACR conference, 2023

IMPT-314: Phase 1- 2 Trial Design

3 + 3 Dose Escalation Followed by Dose Expansion

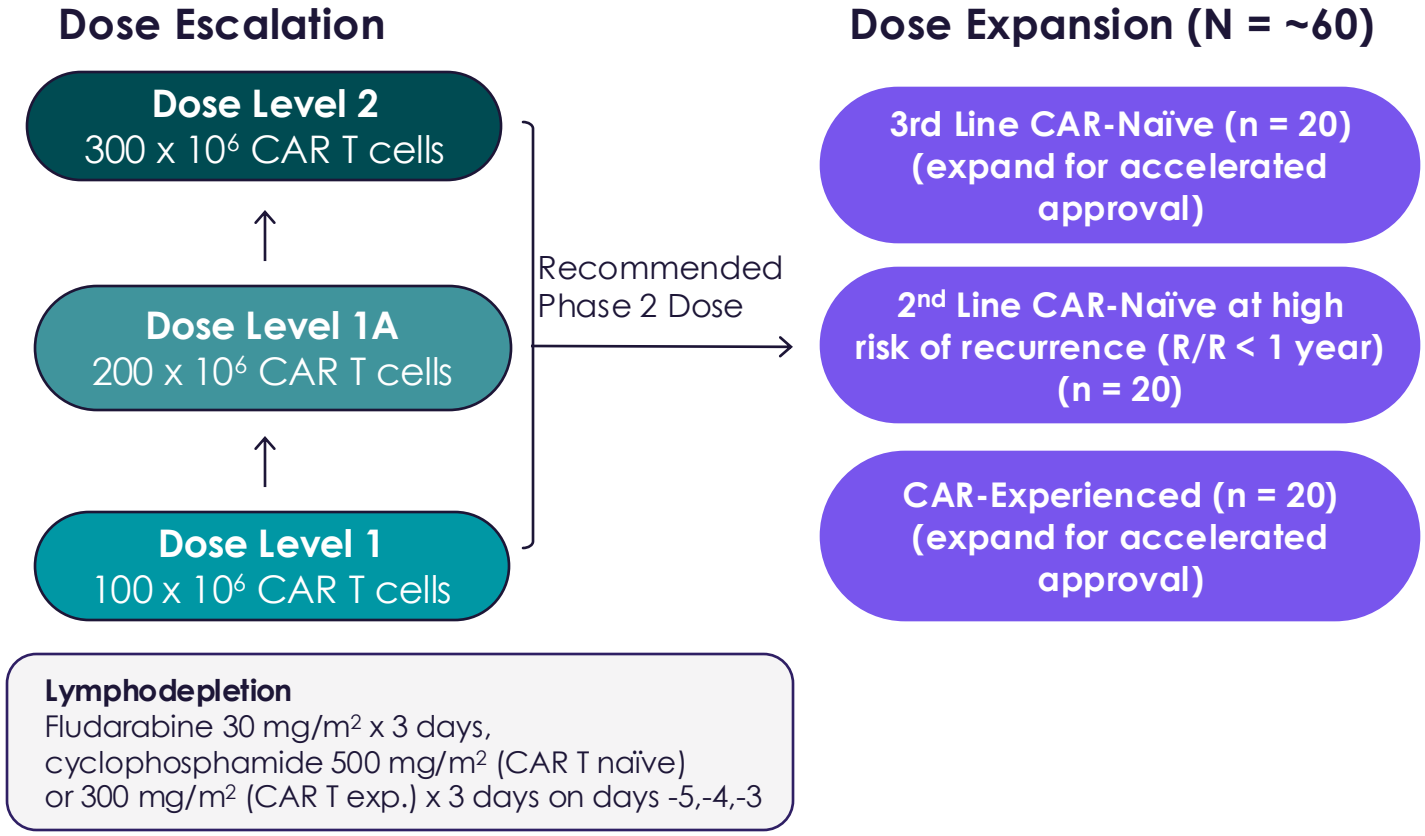
Initial results to be shared at a major medical conference in 2024

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

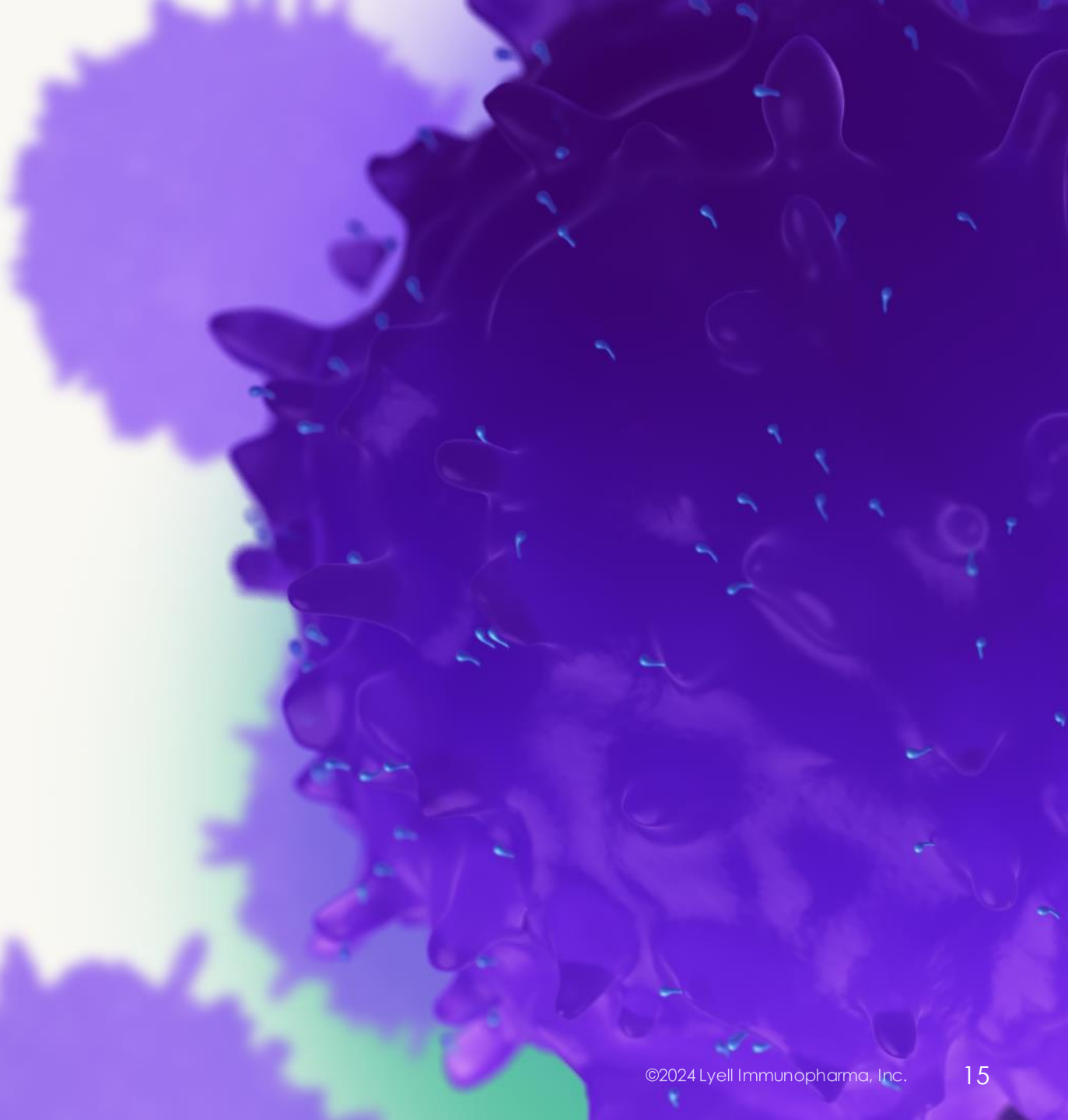
- Safety and tolerability
- Objective response rate, complete response rate
- Duration of response
- Cell expansion pharmacokinetics



NCT05826535

CAR, chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma grade; HGBL, high grade B-cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma; tx, therapy

Transaction Overview, Market Opportunity and Upcoming Milestones



Lyell to Acquire ImmPACT Bio
History, Strategic Rationale and Deal Terms

History

2019	2021	2023	2024	2025
UCLA opens Ph 1 clinical trial of CD19/20 CAR T	ImmPACT Bio formed and licenses CD19/20 CAR T (IMPT-314)	Initiation of IMPT-314 Ph 1 clinical trial; Publication of UCLA Phase 1 data	Q4: Presentation of IMPT-314/LYL314 data at a major medical conference	IMPT-314/LYL314 expected to enter pivotal trial

Strategic Rationale

- Strengthens pipeline with the addition of a development stage program generating compelling Phase 1 data
- Accelerates path to commercialization with lead program expected to enter pivotal trial in 2025
- Targets large markets in 2nd and 3rd line aggressive B-cell lymphoma by improving upon the efficacy of approved CD19 CAR T and bispecific T-cell engagers
- Provides further upside potential in autoimmune indications and earlier-stage preclinical assets
- Robust intellectual property with significant patent term

Deal Terms

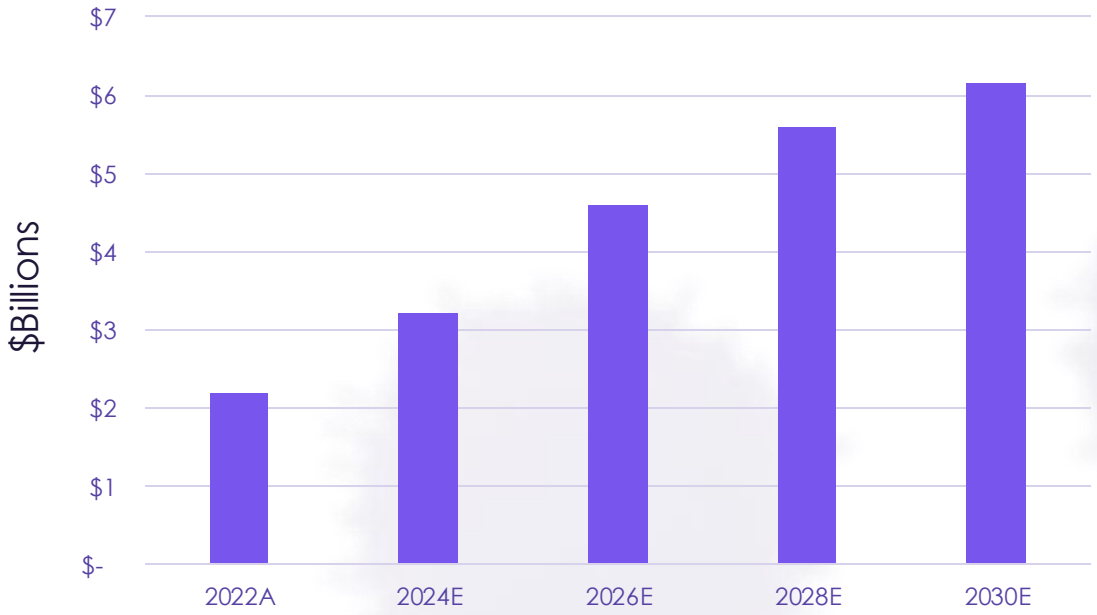
- Upfront consideration:
  - $30mm of cash
  - 37.5mm LYEL common shares
- Contingent consideration:
  - 12.5mm LYEL common shares upon achievement of a derisking clinical milestone
  - Low single-digit royalty on US sales
- Transaction expected to close in 4Q2024 following Hart-Scott-Rodino clearance

CAR, chimeric antigen receptor

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

- The CAR T-cell therapy market for hematologic malignancies is a $3bn+ market growing to $6bn+ by 2030
- Growth will largely be driven by increased use in the 2nd line setting and greater availability as more community centers are opened
- Approximately 30 to 40% of patients with aggressive B-cell non-Hodgkin's lymphoma relapse within 12 months following first-line treatment and of those, up to 65% have performance status eligible for CAR T cell therapy

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



EvaluatePharma; Harris LJ, et all, Int J Mol Sci. 2020; Puckrin, et al, Transplantation and Cellular Therapy, 2022
bn, billion; CAR, chimeric antigen receptor, WW, worldwide

Advancing Novel, Next Generation CAR T-cell Therapies

$491mm** in cash provides runway into 2027, through multiple clinical milestones

Product	Target	Technology	Target Indications	Preclinical	Phase 1	Phase 2/ Pivotal	Next Expected Milestone
ONCOLOGY							
IMPT-314	CD19/20	• CD62L+	Aggressive B-cell Non-Hodgkin's Lymphoma (Fast Track Designation)				• Initial Ph1 data at major medical meeting in 2024 • Initiate pivotal trial 2025
LYL119	ROR1	• c-Jun • NR4A3 • Epi-R • Stim-R	ROR1+ Ovarian, Endometrial, TNBC, and NSCLC				• First patient enrolled late 2024 or early 2025 • Progress update in 1H25 • Initial data in 2H25
Undisclosed CAR T-cell Programs in Solid Tumors							• New IND in 2026
AUTOIMMUNE							
IMPT-314*	CD19/20	• CD62L+	• SLE / LN[1] • SLE, AAV, & IIM[2]				• Under evaluation

*IMPT-514 ** As of June 30, 2024 10-Q filing

[1]Development in lupus is partially supported by a grant from the California Institute of Regenerative Medicine (CIRM) [2]Investigator-initiated trial in China

AAV: ANCA-associated vasculitis; CAR, chimeric antigen receptor; IIM: Idiopathic inflammatory myopathy; IND: Investigational new drug; LBCL, large B-cell lymphoma; LN: Lupus nephritis; NR4A3, nuclear receptor 4A; NSCLC, non-small cell lung cancer; ROR1, receptor tyrosine kinase-like orphan receptor 1; SLE: Systemic lupus erythematosus; TNBC, triple-negative breast cancer

Q&A