LYL314, a CD19/CD20 CAR T-Cell Candidate Enriched for CD62L^{+} Stem-Like Cells, Achieves High Rates of Durable Complete Responses in R/R Large B-Cell Lymphoma

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Disclosures

Consulting or advisory roles

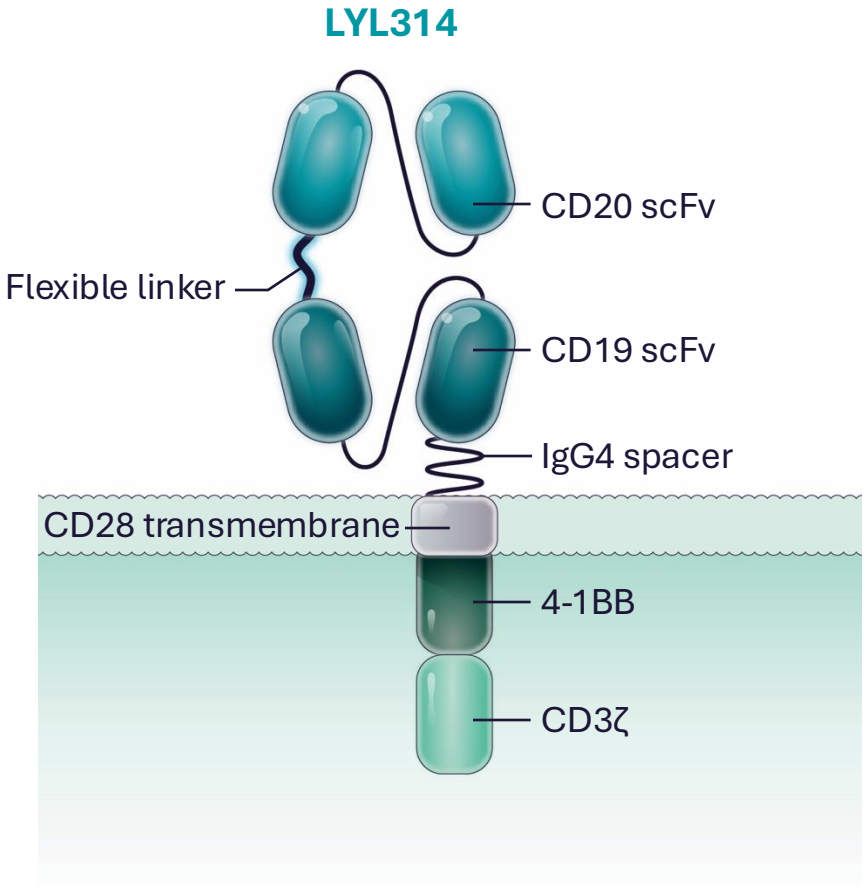
- AbbVie, Amgen, Bristol Myers Squibb, Genmab, Lyell Immunopharma

Dual-Targeting CD19/CD20 CAR T-Cells Enriched for Stem-Like Phenotype (CD62L$^+$)

LYL314 designed to achieve high complete response rates and long duration of responses

- **LYL314 is a true CD19/CD20 "OR" logic-gated CAR**
  - Designed to target either CD19 and CD20 with full potency, overcome heterogeneous antigen density, and mitigate antigen loss following treatment

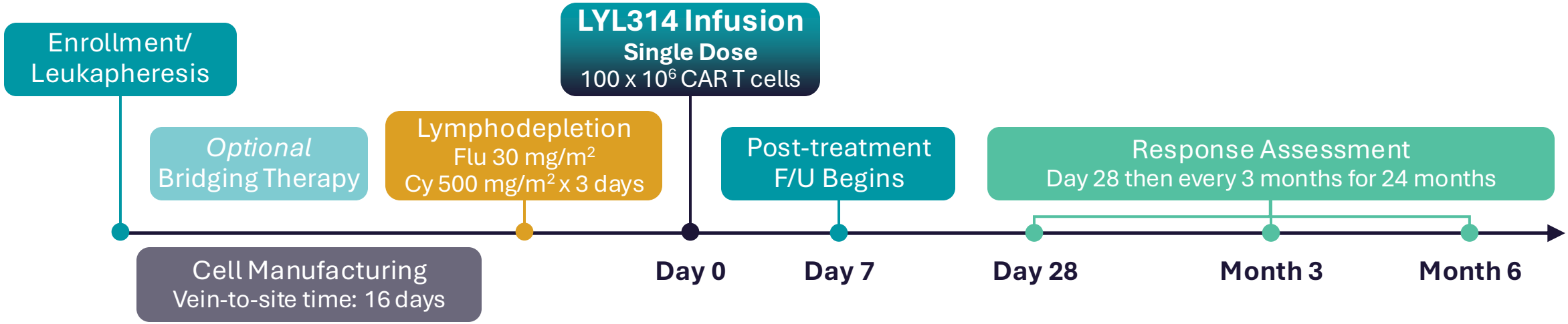
- **CD62L$^+$ enrichment selects for naïve an memory T-cells**
  - CD62L$^+$ cells are associated with better engraftment, improved persistence, reduced exhaustion, and lower cytokine production



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

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 a pivotal study (PiNACLE) to enroll ~120 patients

NCT05826535. 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; DL, dose level; Flu, fludarabine.

High-Risk, Heavily Pre-Treated, Multi-Center US Patient Population

Key patient demographics and baseline disease characteristics

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. 2 patients (in 3L+) received 300 x 10^6 CAR T cells.

Data cutoff: April 15, 2025

SPD, sum of target lesion product diameters prior to lymphodepletion.

Bridging therapy consisted of approved lymphoma therapies most commonly including corticosteroids or corticosteroids plus radiation.

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

High rate of durable complete responses

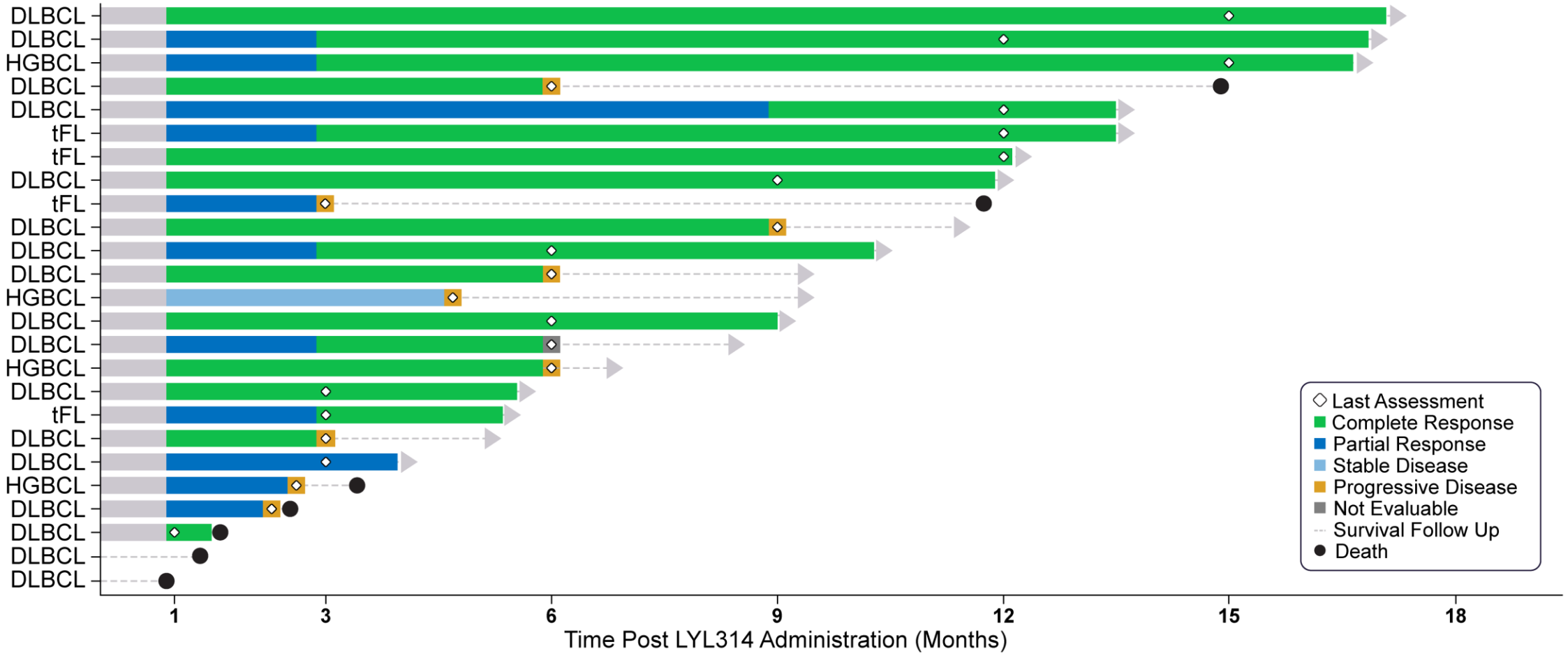
Best Overall Response (3L+)	N = 25
Overall Responses, n (%)	**22 (88%)**
Complete Responses, n (%)	**18 (72%)**
Partial Response, n (%)	4 (16%)
Stable Disease, n (%)	1 (4%)
Median follow up, months (maximum)	9 (17)
Median duration of response	Not reached

- 71% (10/14) of patients with 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.

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

71% of patients with complete response remained in complete response at ≥ 6 months

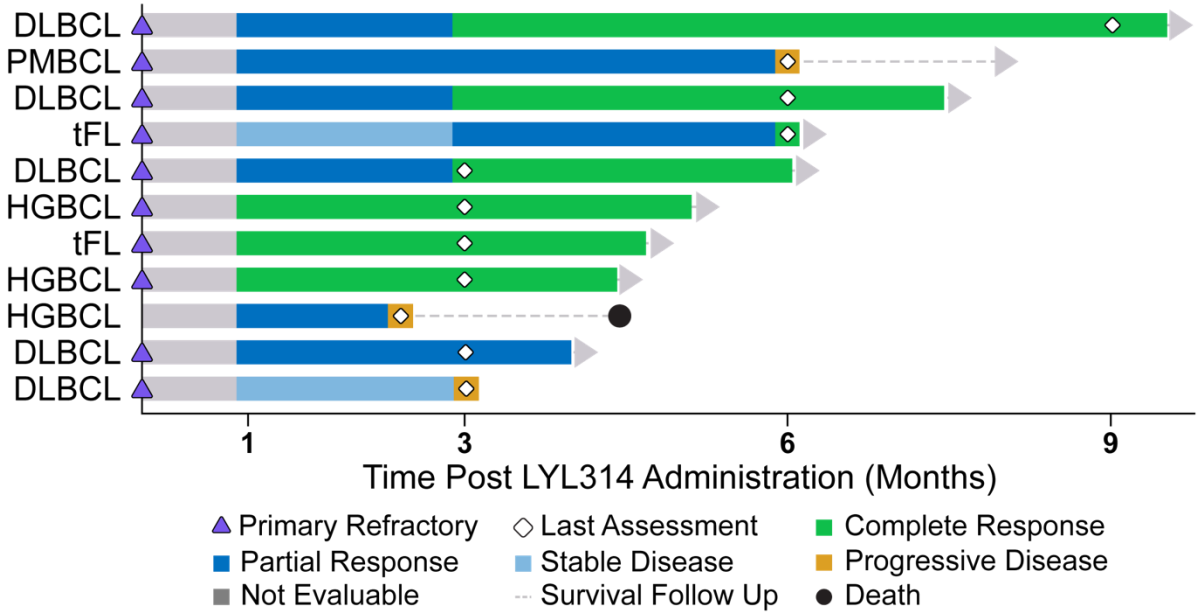


Data cutoff: April 15, 2025

High Overall Response Rate in Patients with 2L LCBL

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 (maximum)	5 (10)
Median duration of response	Not reached



- 100% (7/7) of patients with CR remained in CR at last assessment, including 3/3 at ≥ 6 months
- 70% (7/10) of patients with primary refractory disease reached a complete response

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.

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 resolution 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

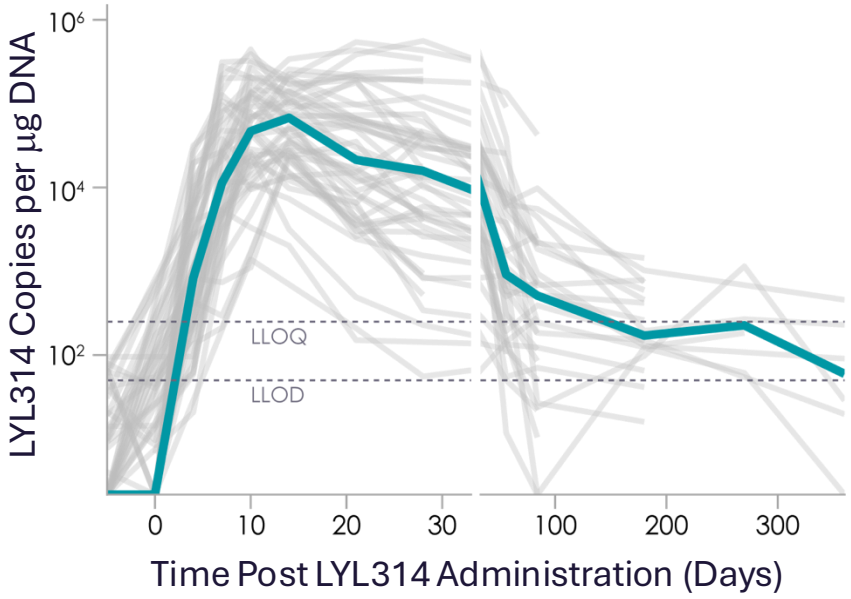
Infections include all treatment emergent adverse events reported in the Infections and Infestations system organ class regardless of relationship to study treatment.

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

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

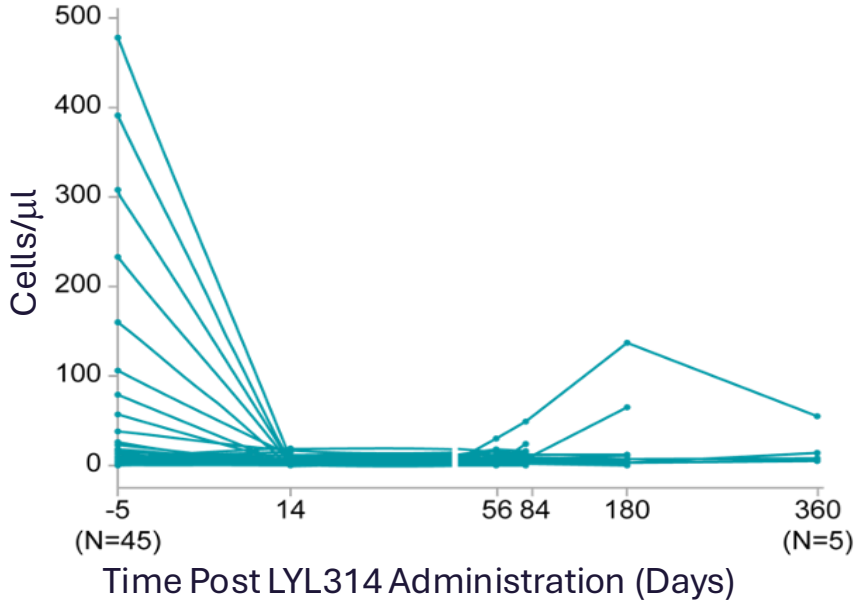
95% of final drug product is CD62L+ (naïve T cells)

CAR T-Cell Expansion



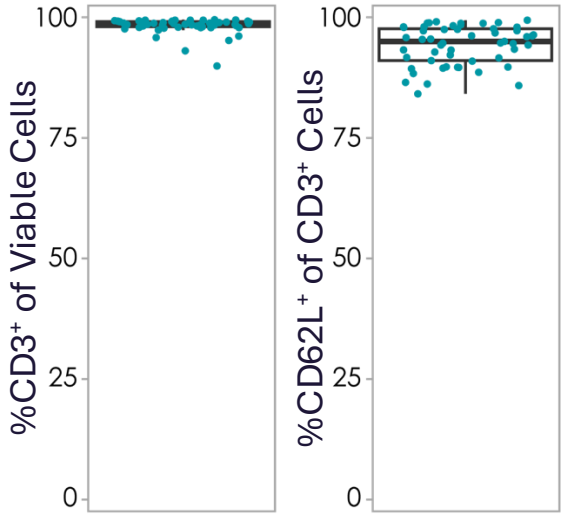
LYL314 showed robust expansion (N = 51) with peak CAR T cells of 70,685 copies/μg (1,387 – 569,039), AUC CAR T cells of 819,198 days x copies/μg (14,596 – 9,109,115), and time to peak of 10 days (7 – 28)

B-Cell Depletion



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 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 complete response rate of 72% in the 3L+ setting
- **High rate of durable complete responses**
  - 71% (10/14) of patients with CR remained in CR at ≥ 6 months in the 3L+ setting
- **Manageable 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 stem-like 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