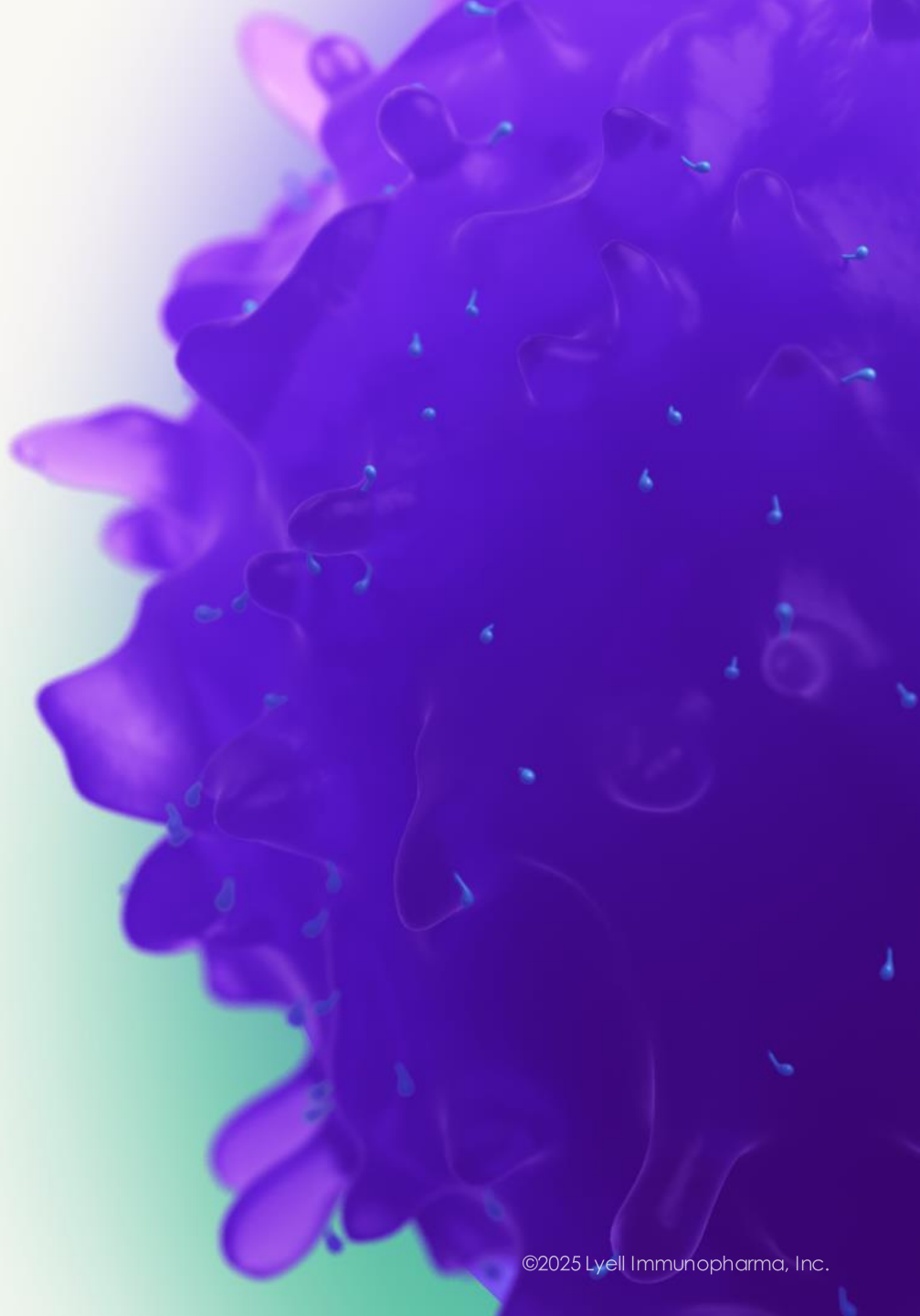
Lyell Presents New Ronde-Cel Clinical and Translational Data at ASH 2025

Lyell Immunopharma

December 8, 2025



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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"). Al such written or oral statements made in this presentation are forward-looking statements, including the potential attributes and benefits of our product candidates; cash runway; manufacturing capabilities; milestones; clinical trial initiation, enrollment, anticipated progress of clinical trials, timing of clinical data updates and other plans and expectations; market sizes and commercial opportunities; and other statements that are not statements of historical fact andare 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: interim results of a clinical trial as of the data cutoff are not necessarily indicative of final results and one or more of the clinical and safety outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, as follow-up on the outcome of any particular patient continues and as more patient or final data becomes available; our limited experience as a company in initiating and conducting clinical trials and lack of experience in completing clinical trials; the nonclinical profiles of our productcandidates or technology 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, including the risk that the ultimate safety profile ofronde-cel may not support outpatient administration; the translational data presented herein is not based on a head-to-head trial and differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials; 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; the complexity of manufacturing cellular therapies and our ability to manufacture and supply our product candidates for our clinical trials; implementation of our strategic plans for our business and product candidates; our realization of the expected benefits 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; potential changes to U.S. drug pricing; other risks, including general economic conditions and regulatory developments, not within our control; and those risks described under the heading "Risk Factors" inour Quarterly Report on Form 10-Q for the quarter ended September 30, 2025, filed with the SEC on November 12, 2025.

This presentation concerns product candidates and technologies that are under clinical investigation, and which have not yetbeen 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.

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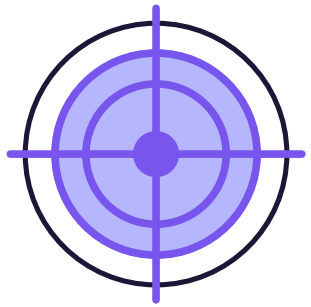
Advancing Next-Generation CAR T-Cell Therapies

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

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

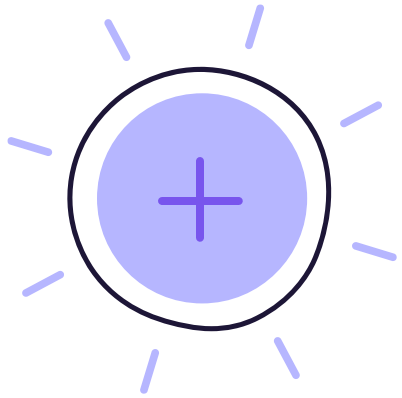
CAR, chimeric antigen receptor

Creating an Industry-Leading Pipeline of Next-Generation CAR T-Cell Therapies



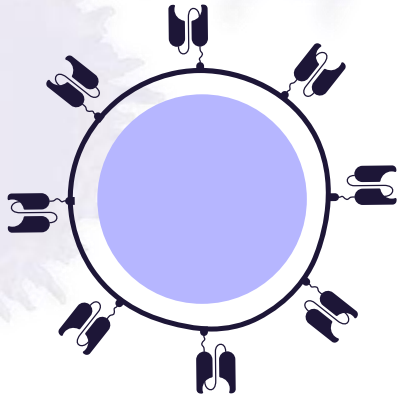
Identify promising targets

- High tumor expression to enhance benefit
- Low expression or inaccessible in normal tissue to avoid on-target, off-tumor toxicity



Arm with enhancements designed to improve the T cell's ability to fight cancer

- Expansion
- Stemness
- Anti-Exhaustion
- Infiltration
- Cytotoxicity



Develop one-time CAR T-cell therapies

- Designed to deliver lasting remission or even cure for patients with cancer

CAR, chimeric antigen receptor;

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Advancing Next-Generation CAR T-Cell Therapies

Lyell presents new CD19/CD20 clinical and translational data at ASH 2025

Rondecabtagene autoleucel (ronde-cel), a dual-targeting CD19/CD20 CAR T-cell candidate with potential to be a new standard of care for relapsed and/or refractory large B-cell lymphoma

- High rates of durable complete responses with a safety profile appropriate for outpatient administration
- CAR T cells manufactured with CD62L enrichment demonstrated sustained cytotoxicity two months after infusion following robust CAR T-cell expansion
- First pivotal trial (PiNACLE) underway, second to begin enrollment by early 2026 (PiNACLE – H2H)

LYL273, a novel GCC-targeted CAR T-cell candidate in clinical trial for metastatic colorectal cancer

- High response rates in refractory patients with a manageable safety profile in ongoing U.S. Phase 1 trial

Scalable wholly-owned LyFE manufacturing facility capable of commercial launch

- >1,200 doses/year at full capacity

Cash runway into 2027 through multiple expected clinical milestones

CAR, chimeric antigen receptor; CD62L+, CD62L or L-selectin positive T cells; GCC, guanylyl cyclase C

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Advancing Novel, Next Generation CAR T-Cell Therapies

Cash runway into 2027, through multiple expected clinical milestones

Product	Target	Target Indications	Enhancements	Phase 1/2	Pivotal	Next Expected Milestone
Ronde-cel	CD19/CD20	3L+ Aggressive LBCL • Regenerative Medicine Advanced Therapy Designation • Fast Track Designation	• CD62L+	PiNACLE		• Updated PiNACLE clinical data in 2H 2026 • Pivotal data in mid-2027 • BLA submission in 2027
Ronde-cel	CD19/CD20	2L Aggressive LBCL • Regenerative Medicine Advanced Therapy Designation	• CD62L+	PiNACLE-H2H		• Initiate pivotal trial by early-2026 • Progress update end 2026
LYL273	GCC	3L+ Metastatic CRC • Fast Track Designation	• CD19 CAR with controlled cytokine release	Phase 1/2		• Updated clinical data in 1H 2026 and 2H 2026 • EOP1 meeting 2H 2026 • 1H 2027 initiation of pivotal clinical trial

2L, second-line; 3L+, third- or later-line; BLA, Biologics License Application; CAR, chimeric antigen receptor; CD62L+, CD62L or L-selectin positive T cells; CRC, colorectal cancer; EOP1, end-of-Phase 1, GCC, guanylyl cyclase-C; LBCL, large B-cell lymphoma

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Ronde-Cel Delivered High Overall and Complete Responses, Even in High-Risk Patients

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

Data from the Phase 1/2 trial presented at ASH 2025

3L+ Setting:

93% ORR with 76% CRR

mPFS of 18 months

2L Setting (94% primary refractory):

83% ORR with 61% CRR

70% of patients with CR remained in CR at ≥ 6 months

Safety profile appropriate for outpatient administration

- No Grade 3 CRS and low rates (< 5%) of Grade ≥ 3 ICANS

Data presented at ASH, 2025
CAR, chimeric antigen receptor; CR, complete response; CRR, complete response rate; CRS, cytokine release syndrome, ICANS, immune effector cell-associated neurotoxicity syndrome; mPFS, median progression-free survival; ORR, overall response rate; LBCL, large B-cell lymphoma

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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]
Kite, A GILEAD Company — YESCARTA® (axicabtagene ciloleucel)	CD19	3+, R/R LBCL (ZUMA-1 N = 108)	72%	51%	5.8[2]	9%	31%
Bristol Myers Squibb™ — Breyanzi® (lisocabtagene maraleucel)	CD19	3+, R/R LBCL (TRANSCEND NHL 001, N = 268)	73%	54%	6.8[3]	3%	10%
NOVARTIS — KYMRIAH® (tisagenlecleucel)	CD19	3+, R/R DLBCL (JULIET N = 115)	50%	32%	2.9[4]	23%	19%

PHASE 1/2 TRIAL (Data from ASH 2025)	Target	Line of Therapy, Indication, Sample Size	Overall Response Rate	Complete Response Rate	Median PFS (months)	Grade ≥ 3 CRS	Grade ≥ 3 ICANS
Lyell — **Ronde-cel**	CD19/ CD20	3L+ R/R LBCL (N = 37*)	93%	76%	18	0%	4 -12%**

NOT FOR PROMOTIONAL USE; Ronde-cel has not been evaluated in head-to-head trials with any of these products. Differences exist between trial designs and patient characteristics and caution should be exercised when comparing data across trials

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; R/R, relapsed/refractory; PFS, progression-free survival
*29 3L+ LBCL patients evaluable for efficacy; 37 3L+ patients evaluable for safety; **Data from 69 patients in 2L and 3L+; Grade ≥ 3 ICANS rate with dexamethasone prophylaxis (N = 25) of 4% and total including patients with and without dexamethasone prophylaxis of 12%.

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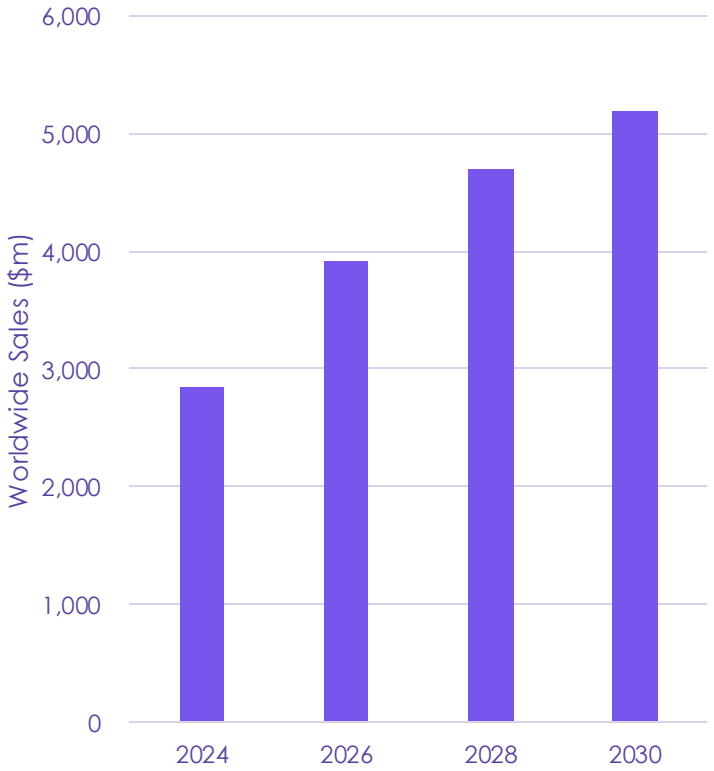
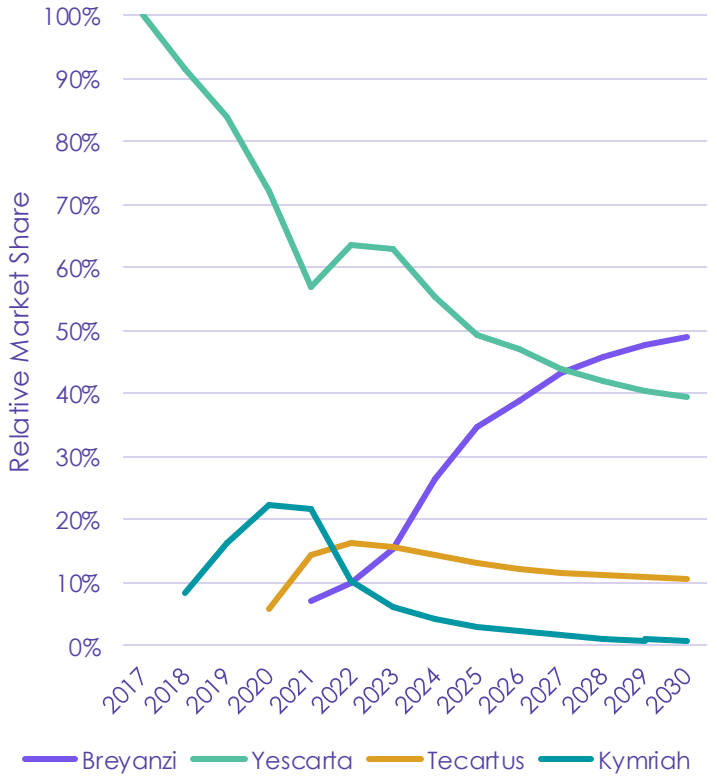
Ronde-Cel is Targeting a Multi-Billion Dollar Market Treated by Physicians with a Historical Willingness to "Switch" Based on Strength of Clinical Data

Differentiated Clinical Data Could Enable Ronde-cel to Disrupt the NHL Treatment Paradigm

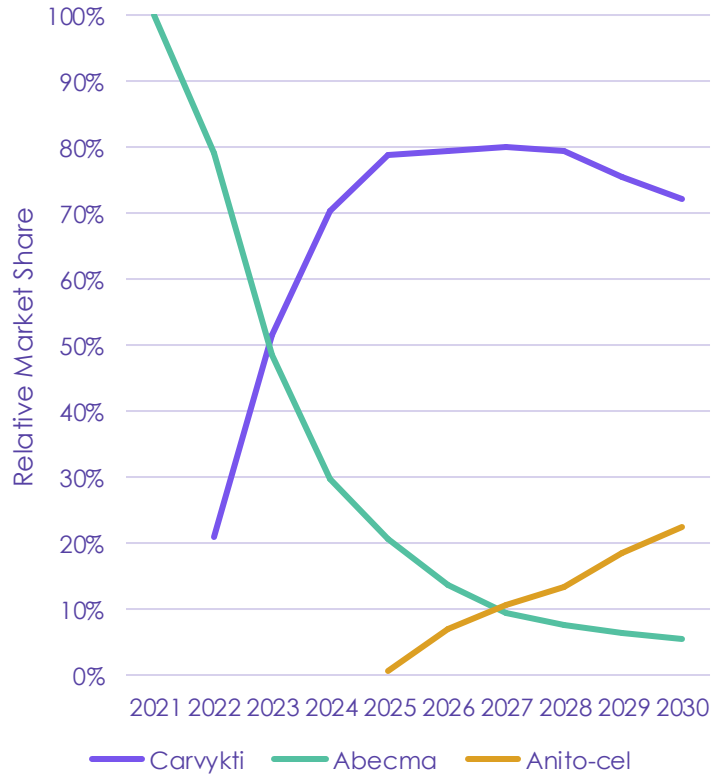
Projected Sales of Currently Approved CD19 CAR T-Cell Products[1]



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, BCMA, B-cell maturation antigen; NHL, non-Hodgkin lymphoma

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Ronde-Cel Clinical Data Presented at ASH 2025

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CD19 CAR T-Cell Products Transformed the Treatment of LBCL, But Have Limitations

A product with higher complete response rates, longer duration of response, and fewer toxicities is needed

- **Limited durability:**
  - ~40% of patients in 3L+ LBCL remain in complete response at 6 months
  - Median progression-free survival (mPFS) < 7 months in 3L+ LBCL
- **Exclusion of key populations:**
  - Axi-cel: Limited enrollment of age >75, no bridging therapy (ZUMA-1, 3L+) or steroids only (ZUMA-7, 2L)
  - Liso-cel: No patients > 75 (TRANSFORM, 2L)

- **Additional limitations:**
  - Complete response rate for liso-cel in older patients with primary refractory disease in the 2L setting (PILOT) was 42%
  - Limited data on duration of response have been published for patients in 2L with primary refractory disease (mPFS ~7 months in ZUMA-7)
  - Grade 3 and higher CRS and ICANS limit the use of the approved CD19 CAR T-cell products in the outpatient setting

Abramson JS et al. *Lancet* 2020, Kamdar M et al. *Lancet* 2022, Locke FL et al. *Lancet Oncol* 2019, Neelapu SS et al. *N Engl J Med* 2017, Sehgal A et al. *Blood Adv* 2022, Westin JR et al. *N Engl J Med* 2023.
CRS, cytokine release syndrome; ICANS, immune cell-associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; mPFS, median progression-free survival

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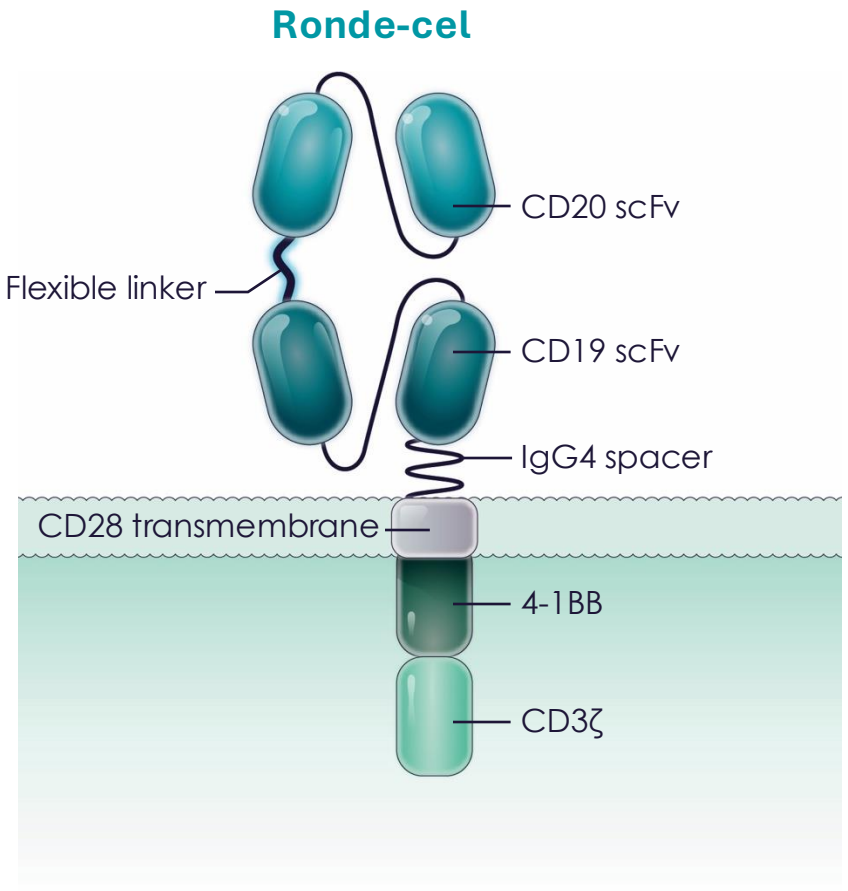
Ronde-Cel is a Dual-Targeting CD19/CD20 CAR T-Cell Product Enriched for Stem-Like Phenotype (CD62L+)

Ronde-cel designed to achieve high complete response rates and long duration of responses

- **Ronde-cel is a true CD19/CD20 "OR" logic-gated CAR designed to:**
  - Target either CD19 and CD20 with full potency
  - Overcome heterogeneous antigen density
  - Mitigate antigen loss following treatment



Aldoss et al., *Clin Cancer Res* 2023, Arcangeli et. al. *JCI* 2022, Chen GM et. al. *Cancer Discovery* 2021, Filosto et. al. *Blood Cancer Discov* 2024, Sommermeyer et. al. *Leukemia* 2016.

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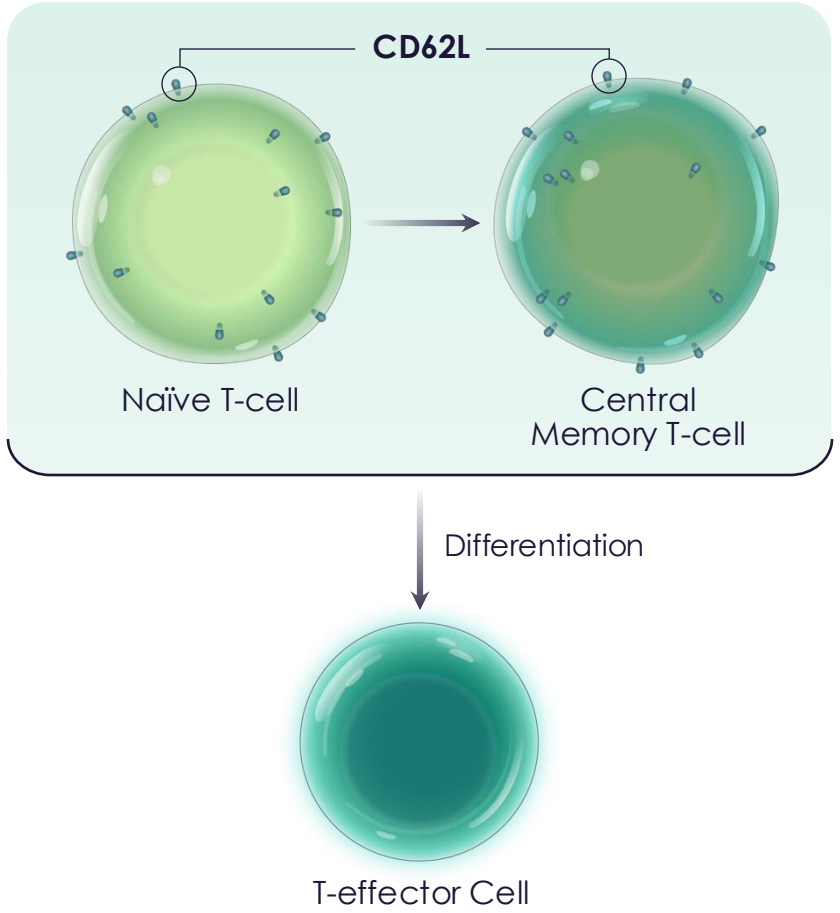
Ronde-Cel is a Dual-Targeting CD19/CD20 CAR T-Cell Product Enriched for Stem-Like Phenotype (CD62L+)

Enrichment for stem-like CAR T-cells has promise in improving outcomes for patients

- Naïve T cells are associated with better CAR T-cell response
- Higher CAR T-cell expansion is associated with better CAR T-cell response
- Ronde-cel is manufactured with CD62L+ enrichment to achieve a high percentage of naïve and central memory T-cells in drug product
  - CD62L is a surface protein that acts as a homing beacon, guiding white blood cells to sites of inflammation
  - CD62L+-enriched cells include more naïve and central memory T-cells
  - CD62L+ cells are associated with improved persistence, reduced exhaustion, and lower adverse cytokine production

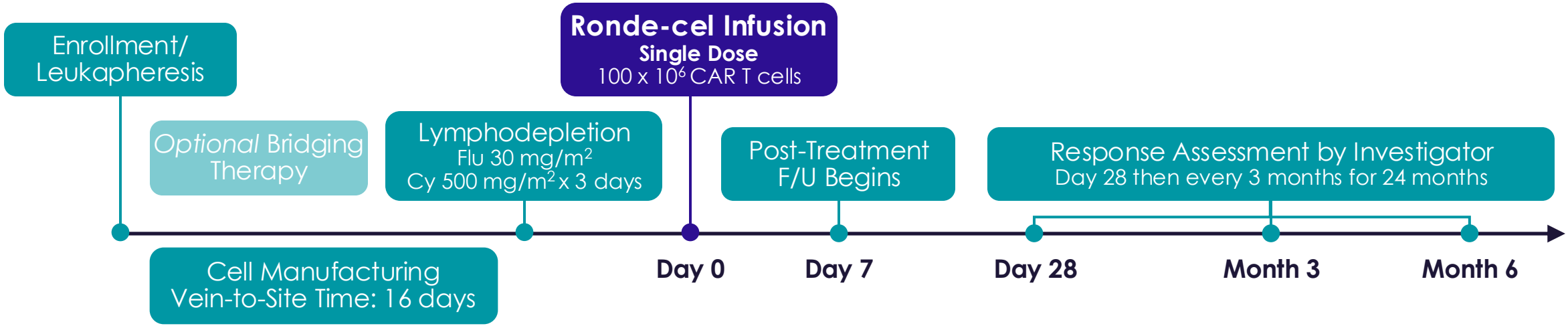


CAR, chimeric antigen receptor; CD62L+, CD62L or L-selectin positive T cells

Abramson et al. *Lancet* 2020, Arcangeli et. al. *JCI* 2022, Bishop et al. *N Engl J Med* 2021, Harris et al. *Int J Mol Sci*. 2020, Neelapu et al. *N Engl J Med* 2017.

Ronde-Cel Phase 1/2 Trial Schematic

Multi-cohort, multi-center trial in aggressive large B-cell lymphoma (3L+ and 2L CAR-naïve)



Patient Population

- Patients with relapsed/refractory DLBCL, PMBCL, HGBCL, 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

Trial 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

Trial 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; 3BFL, Grade 3B follicular lymphoma; HGBCL, high-grade B-cell lymphoma; PMBCL, primary mediastinal large B-cell lymphoma; tFL, transformed follicular lymphoma. NCT05826535

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

Baseline characteristics in 3L+ and 2L patients consistent with high risk compared to historical studies

Demographics and Disease Characteristics	3L+ Overall N = 45	2L Overall N = 24
Median (range) age, years	64 (21, 87)	65 (26, 85)
≥ 75 years, n (%)	9 (20%)	5 (21%)
ECOG 1, n (%)	29 (64%)	14 (58%)
IPI score 3 or 4, n (%)	12 (27%)	8 (33%)
LBCL histology n (%)		
DLBCL	23 (51%)	15 (63%)
tFL	8 (18%)	2 (8%)
HGBCL	8 (18%)	6 (25%)
Primary refractory, n (%)	22 (49%)	22 (92%)
Elevated (above normal) LDH, n (%)	20 (44%)	10 (42%)
Bulky disease (≥ 7 cm), n (%)	10 (22%)	5 (21%)
Double-/triple-hit status, n (%)	7 (16%)	7 (29%)
Received bridging therapy, n (%)	23 (51%)	14 (58%)

Data cutoff: September 5, 2025. 67 of 69 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
LBCL includes DLBCL, PMBCL, Grade 3B FL, and tFL. HGBCL defined by disease histology at study entry
Primary refractory defined as failure to achieve complete response to first-line therapy or complete response with relapse within 3 months
Bridging therapy consisted of approved lymphoma therapies including chemoimmunotherapy, corticosteroids, or corticosteroids plus radiation

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Higher-Risk Demographic and Disease Characteristics in 3L+ HGBCL Versus LBCL

Patients with HGBCL have bulkier disease, higher LDH, more extranodal disease, are older, and have more limited ECOG status

Demographics and Disease Characteristics	3L+ LBCL N = 37	3L+ HGBCL N = 8	3L+ Overall N = 45
Median (range) age, years	64 (21, 86)	68 (43, 87)	64 (21, 87)
≥ 75 years, n (%)	6 (16%)	3 (38%)	9 (20%)
ECOG 1, n (%)	22 (60%)	7 (88%)	29 (64%)
IPI score 3 or 4, n (%)	9 (24%)	3 (38%)	12 (27%)
LBCL histology n (%)			
DLBCL	23 (62%)	N/A	23 (51%)
tFL	8 (22%)	N/A	8 (18%)
Primary refractory, n (%)	16 (43%)	6 (75%)	22 (49%)
Elevated (above normal) LDH, n (%)	13 (35%)	7 (88%)	20 (44%)
Bulky disease (≥ 7 cm), n (%)	6 (16%)	4 (50%)	10 (22%)
Double-/triple-hit status, n (%)	3 (8%)	4 (50%)	7 (16%)
Received bridging therapy, n (%)	15 (41%)	8 (100%)	23 (51%)

Data cutoff: September 5, 2025
ECOG, Eastern Cooperative Oncology Group; LBCL; large B-cell lymphoma includes DLBCL, diffuse large B-cell lymphoma, primary mediastinal B-cell lymphoma, Grade 3B follicular lymphoma, and tFL, transformed follicular lymphoma. HGBCL defined by disease histology at trial entry; LDH, lactate dehydrogenase
Primary refractory defined as failure to achieve complete response to first-line therapy or complete response with relapse within 3 months
Bridging therapy consisted of approved lymphoma therapies including chemoimmunotherapy, corticosteroids or corticosteroids plus radiation

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Overall Response Rate of 93% and Complete Response Rate of 76% (3L+ LBCL)

High rate of durable complete responses in LBCL

Best Overall Response (3L+ LBCL)	**N = 29**
Overall Responses, n (%)	**27 (93%)**
Complete Responses, n (%)	**22 (76%)**
Partial Response, n (%)	5 (17%)

- **Median progression free survival (mPFS) is 18 months**
  - Median duration of follow-up 12 months
- 72% (13/18) of patients with complete response remained in complete response at ≥ 6 months

Best Overall Response (3L+ HGBCL)	**N = 8**
Overall Responses, n (%)	**7 (88%)**
Complete Responses, n (%)	**4 (50%)**
Partial Response, n (%)	3 (38%)

- 33% (1/3) of patients with complete response remained in complete response at ≥ 6 months
- PiNACLE will include only LBCL in order to enroll those patients most likely to receive durable benefit from ronde-cel in this single-arm trial

Data cutoff: September 5, 2025; all responses as determined by the Investigator.
LBCL, large B-cell lymphoma, HGBCL, high-grade B-cell lymphoma; HGBCL defined by disease histology at trial entry
Patients were evaluable for efficacy if they had a Day 84 or later response assessment, disease progression, or death from any cause.
8 patients were dosed without Day 84 follow up, disease progression, or death.

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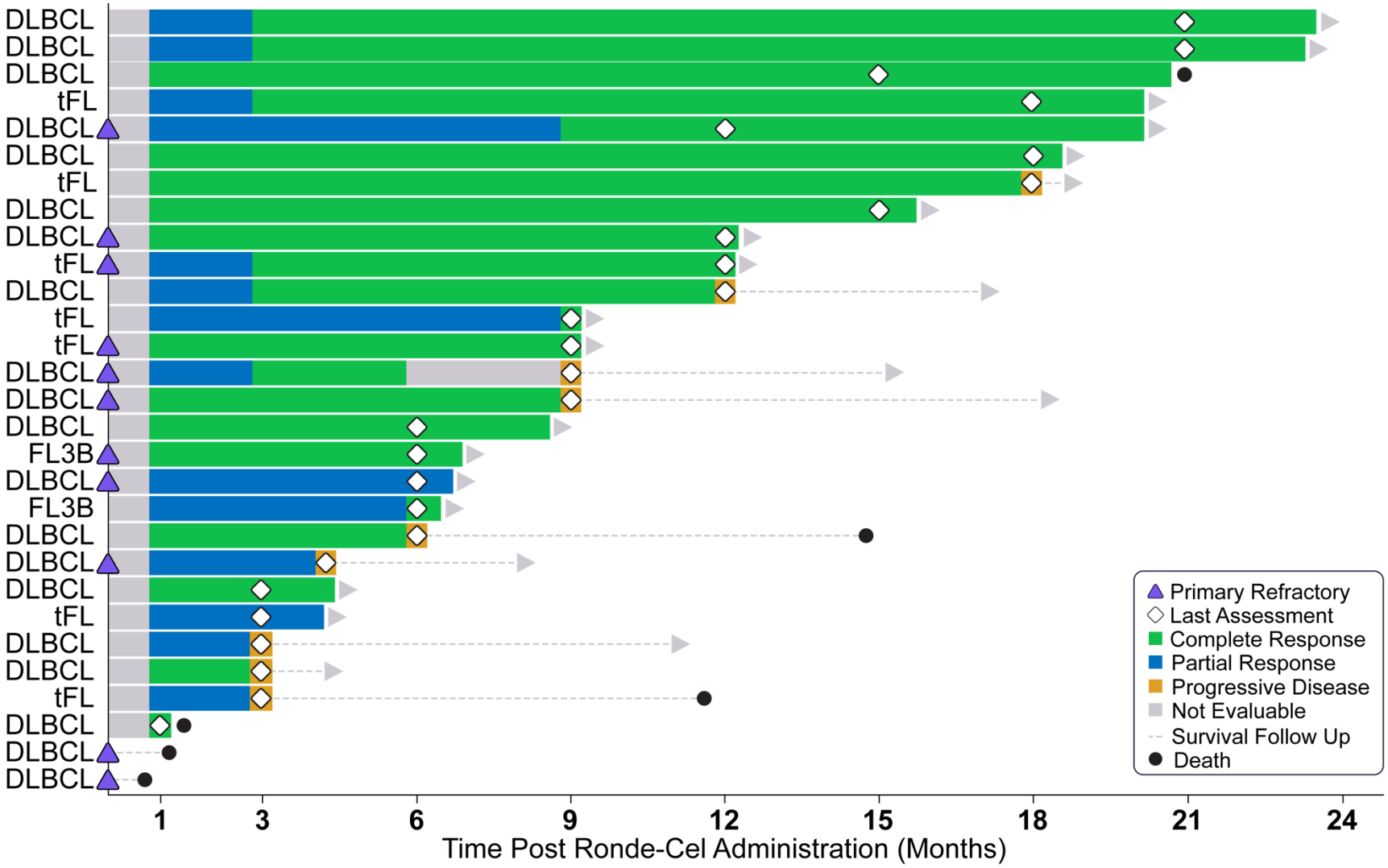
Durable Responses in Patients with 3L+ LBCL

Median progression-free survival of 18 months; 72% of patients with CR remained in CR at ≥ 6 months



Data cutoff: November 11, 2025

LBCL includes DLBCL, PMBCL, Grade 3B FL, and tFL. HGBCL not included. CR, complete response

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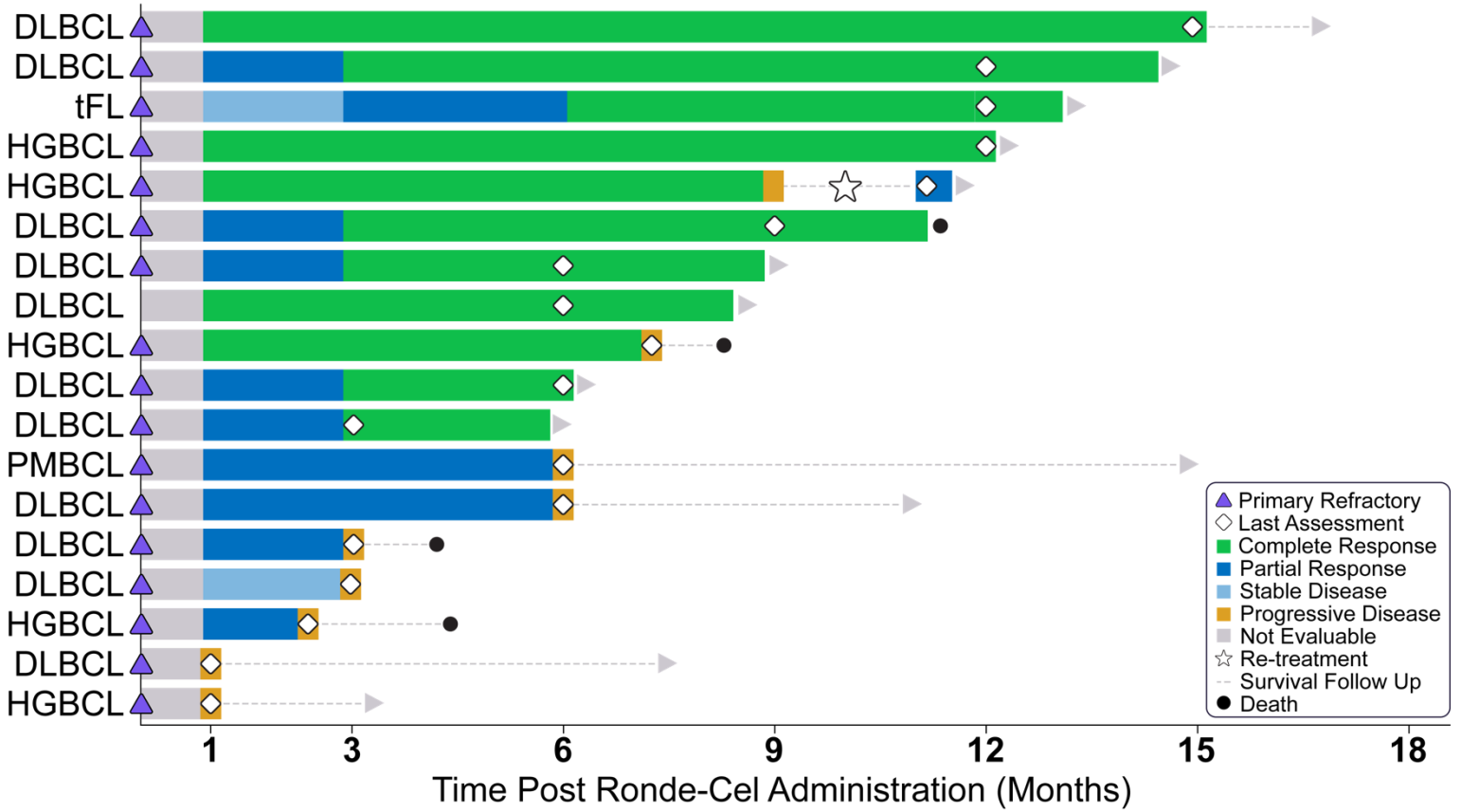
High Overall Response Rate in Patients with 2L Aggressive B-Cell Lymphoma

High-risk characteristics including HGBCL with 94% of patients with primary refractory disease

Best Overall Response (2L Overall)	**N = 18**
Overall Responses, n (%)	**15 (83%)**
Complete Responses, n (%)	**11 (61%)**
Partial Response, n (%)	4 (22%)

- 70% (7/10) of patients with complete response remained in complete response at ≥ 6 months
- Median duration of complete response not reached
- Median duration of follow up 9 months



Data cutoff: September 5, 2025 (response rates); November 11, 2025 (swimmer plot). 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.
6 patients were dosed without Day 84 follow up, disease progression, or death

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Dexamethasone Prophylaxis Reduced Grade ≥ 3 ICANS to < 5% of Patients

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

Adverse Event, n (%)	Prophylaxis N = 25	All N = 69
CRS	**13 (52%)**	**42 (61%)**
Grade 1	10 (40%)	22 (32%)
Grade 2	3 (12%)	20 (29%)
Grade ≥ 3	0 (0%)	0 (0%)
Median time to onset, days (range)	6 (3 - 18)	5 (1 - 18)
Median time to resolution, days (range)	2 (1 - 21)	3 (1 - 21)
ICANS	**3 (12%)**	**16 (23%)**
Grade 1	2 (8%)	6 (9%)
Grade 2	0 (0%)	2 (3%)
Grade ≥ 3	1 (4%)	8 (12%)
Median time to onset, days (range)	7 (4 - 14)	7 (2 - 14)
Median time to resolution, days (range)	4 (1 - 9)	4 (1 - 10)

Adverse Event, n (%)	Prophylaxis N = 25	All N = 69
IEC-HS		
Grade 1 or 2	1 (4%)	2 (3%)
Grade ≥ 3	0 (0%)	0 (0%)
Infections		
Grade 1 or 2	7 (28%)	19 (28%)
Grade ≥ 3	1 (4%)	8 (12%)
Prolonged cytopenias		
Grade ≥ 3	3 (12%)	15 (22%)

- Patients received 10 mg (IV/PO) of dexamethasone on Days 0, 1, and 2 after ronde-cel infusion
- Tocilizumab use in 37% of patients
- One case of Grade ≥3 ICANS was observed with dexamethasone prophylaxis in a patient with HGBCL, high tumor burden, and high LDH
- No deaths determined to be related to ronde-cel

- Data cutoff: September 5, 2025

Infections include all treatment emergent adverse events reported in the Infections and Infestations system organ class regardless of relationship to trial treatment
Prolonged cytopenias defined as Grade 3 or 4 values of hemoglobin, platelets, or neutrophils beyond Day 28 post ronde-cel administration
CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity; IV, intravenous; LBCL, large B-cell lymphoma; PO, orally

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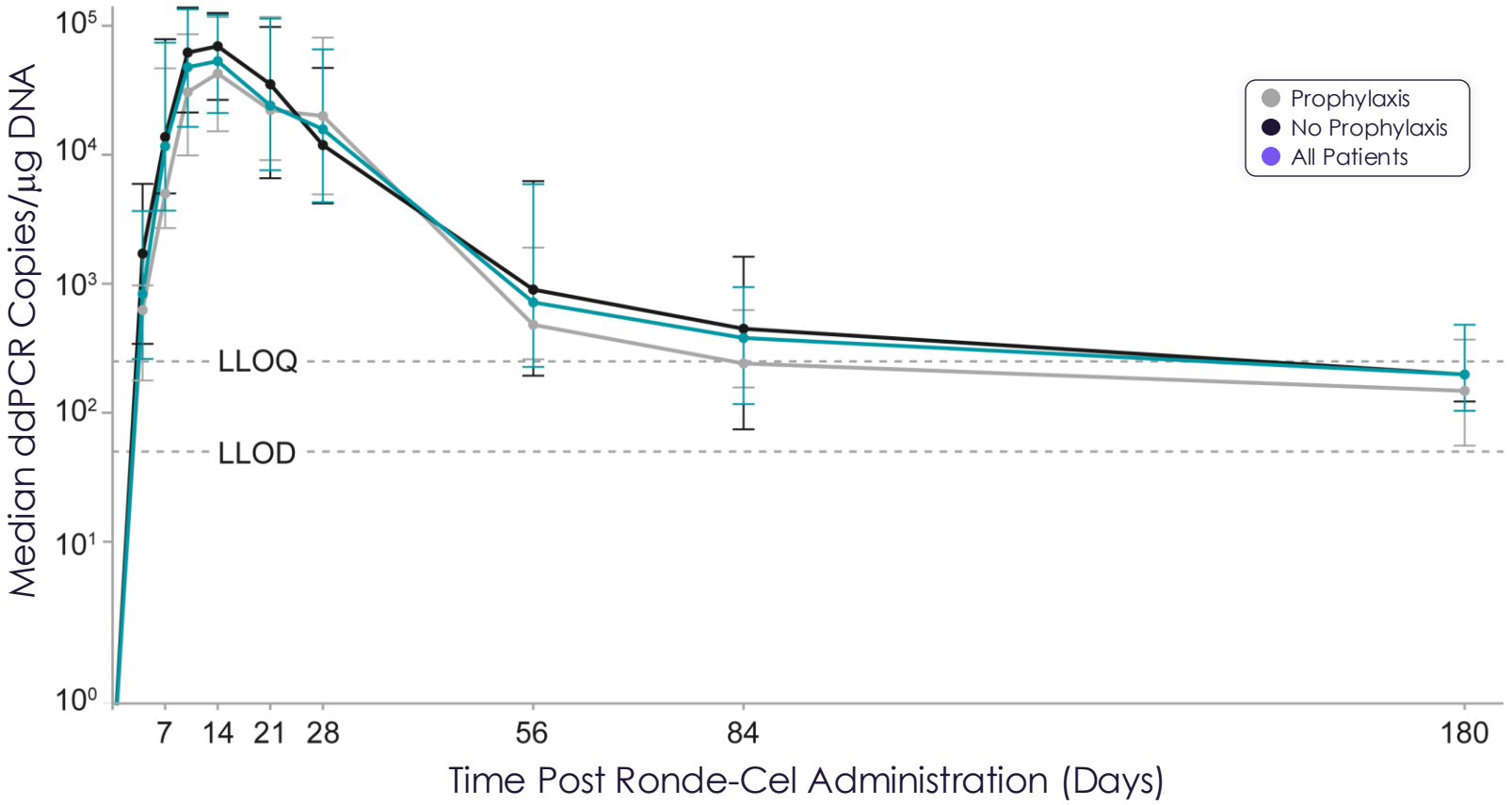
Ronde-Cel Expansion Was Robust in Patients With or Without Dexamethasone Prophylaxis

Higher CAR T-cell expansion is associated with better CAR T-cell response

CAR T-Cell Expansion With or Without Dexamethasone Prophylaxis



- No significant differences were observed in peak CAR T-cell expansion (C_{max}) or overall exposure (AUC) between patients who received dexamethasone (N = 25) and those who did not (N = 42)

Data cutoff: September 5, 2025.
CAR, chimeric antigen receptor
Assay used for measuring B cells/µl (Epiontis ID®) can detect as low as 2 cells/µl with high accuracy. IQR, interquartile range.
Neelapu et al. *N Engl J Med* 2017

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Conclusions

Phase 1/2 multi-cohort multi-center trial evaluating ronde-cel in 3L+ and 2L patients

High rate of durable complete responses in high-risk patients in 3L+ LBCL:

- Overall response rate of 93% and a complete response rate of 76%
- Median progression-free survival of 18 months

High rate of durable complete responses in primary refractory patients in the 2L setting:

- Overall response rate of 83% and a complete response rate of 61%
- 70% of patients with complete response remained in complete response at ≥ 6 months

Manageable safety profile appropriate for outpatient administration:

- No Grade ≥ 3 CRS
- Single case of Grade ≥ 3 ICANS with dexamethasone prophylaxis (≤ 5%)

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

- Additional translational data on CD62L enrichment presented in separate oral presentation demonstrated sustained cytotoxicity of CAR T-cells obtained from patients 2 months after infusion

Data presented at ASH, 2025

CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome, ICANS, immune effector cell-associated neurotoxicity syndrome; LBCL, large B-cell lymphoma

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Ronde-Cel Pivotal Clinical Development Strategy

PiNACLE-H2H

Phase 3 Head-to-Head CAR-T Cell Randomized Controlled Trial in 2L LBCL

Enrollment target: ~200/arm
Enrollment to begin by early 2026

- Phase 3 head-to-head CAR T-cell therapy randomized controlled trial of ronde-cel vs. Investigator's choice of axi-cel or liso-cel
- No upper age-limit; early or late-relapsing/refractory patients; includes HGBCL
- Primary endpoint: event-free survival
- Key secondary endpoints: progression-free survival and overall survival

PiNACLE

Single-Arm Trial for Approval in 3L+ LBCL

Enrollment target: ~120 patients

- Seamless expansion of the 3L+ cohort from the Phase 1/2 trial
- No upper age-limit; early relapse or refractory patients; will not include HGBCL
- Primary endpoint: overall response rate (and duration of response)

Axi-cel, axicabtagene autoleucel; CAR, chimeric antigen receptor; LBCL, large B-cell lymphoma; liso-cel, lisocabtagene maraleucel

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Ronde-Cel Translational Data Presented at ASH 2025

Gary Lee, PhD
Chief Scientific Officer

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CD62L+ Enrichment of T Cells Achieved Robust Expansion, Memory Phenotype and Sustained Function After Infusion in Patients with LBCL

Summary of Key Translational Findings

1. Ronde-cel drug products have shown a high proportion of CD62L+ cells with a **stronger memory-cell phenotype** compared to approved CD19 CAR T-cell products (axi-cel, tisa-cel) prior to infusion.

2. Ronde-cel has shown up to 3-fold **higher expansion** after infusion in patients compared to approved CD19 CAR T-cell products (tisa-cel and liso-cel). A higher product memory-cell phenotype is positively correlated with expansion.

3. Ronde-cel has shown a **higher memory phenotype** at one month after infusion compared to axi-cel.

4. Ronde-cel CAR+ T cells collected from patients two months after infusion **sustained the capacity to proliferate, kill tumor cells**, **and secrete cytokines**.

Axi-cel, axicabtagene autoleucel; CAR, chimeric antigen receptor; LBCL, large B-cell lymphoma; liso-cel, lisocabtagene maraleucel; tisa-cel, tisagenlecleucel.

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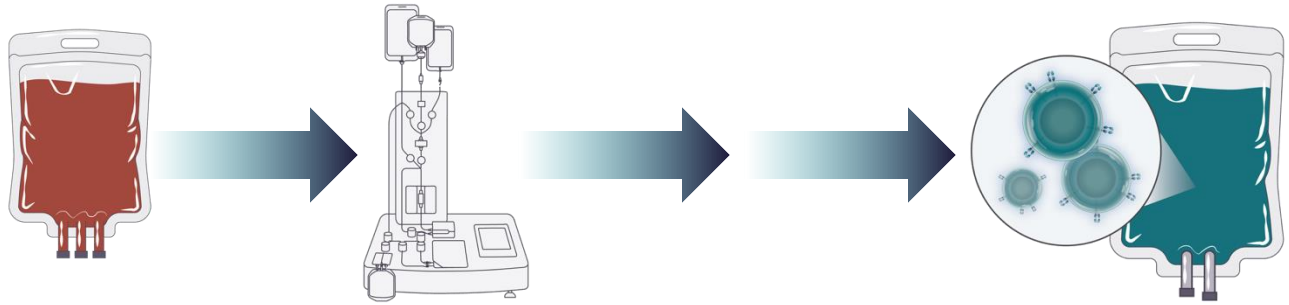
Ronde-Cel Has a High Percentage of CD62L+ Cells in the Final Drug Product

CD62L+ enrichment is a simple process that does not increase overall manufacturing time

Ronde-cel Manufacturing



Fresh Apheresis → CliniMACS → Standard CAR Process → **Ronde-cel**

Product Characteristics

- Ronde-cel drug products profiled with flow cytometry (N = 84)

	Median (Range)
% CD3+ of Viable Cells	**99 (90 - 99)**
% CD62L+ of CD3+ Cells	**96 (84 - 99)**

CD62L+ selection uses CliniMACS as part of an overall process with a vein-to-site median time of 16 days.

CAR, chimeric antigen receptor; CD62L or L-selectin positive T cells.
Aldoss et al., *Clin Cancer Res* 2023, Arcangeli et. al. *JCI* 2022, Chen GM et. al. *Cancer Discovery* 2021, Sommermeyer et. al. *Leukemia* 2016.

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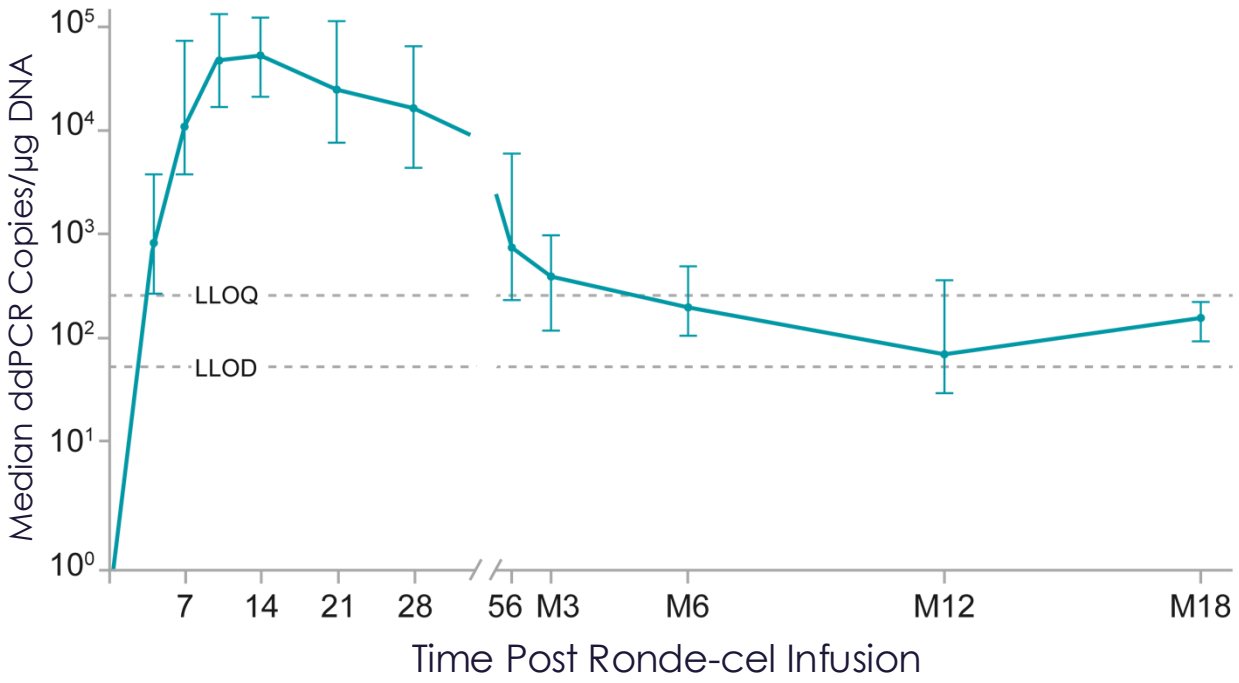
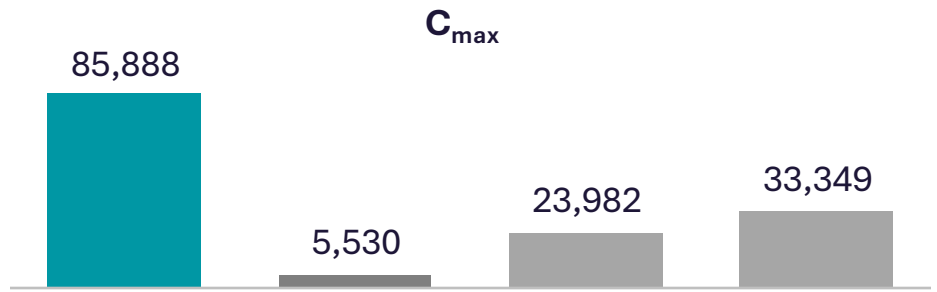
Up to 3-Fold Higher Cell Expansion Shown with Ronde-Cel Compared to CD19 CAR T-Cell Products After Infusion

Better clinical response in CAR T-cell therapies has been shown to be associated with higher expansion

Ronde-cel Expansion



Ronde-cel vs CD19 CAR T-Cell Products



	Ronde-cel	Tisa-cel	Liso-cel	Liso-cel
	3L+, 2L N = 67	**3L+** N = 86	**3L+** N = 245	**2L** N = 83
$AUC_{[0-28]}$	819,198	64,600	213,730	270,345
T_{max}	14	9	12	12

Note: Axi-cel not included since cell expansion is assessed with a different method.

All metrics in table are median except tisa-cel is mean; C_{max} = peak concentration of CAR transgene in peripheral blood mononuclear cellss post infusion (copies per µg DNA); AUC = days x copies/ µg g; T_{max} = days; Error bars = Interquartile range (IQR); M, month. CAR, chimeric antigen receptor

Abramson et al. *The Lancet* 2020, Abramson et al. *Blood* 2022, Schuster et al. *NEJM* 2018.

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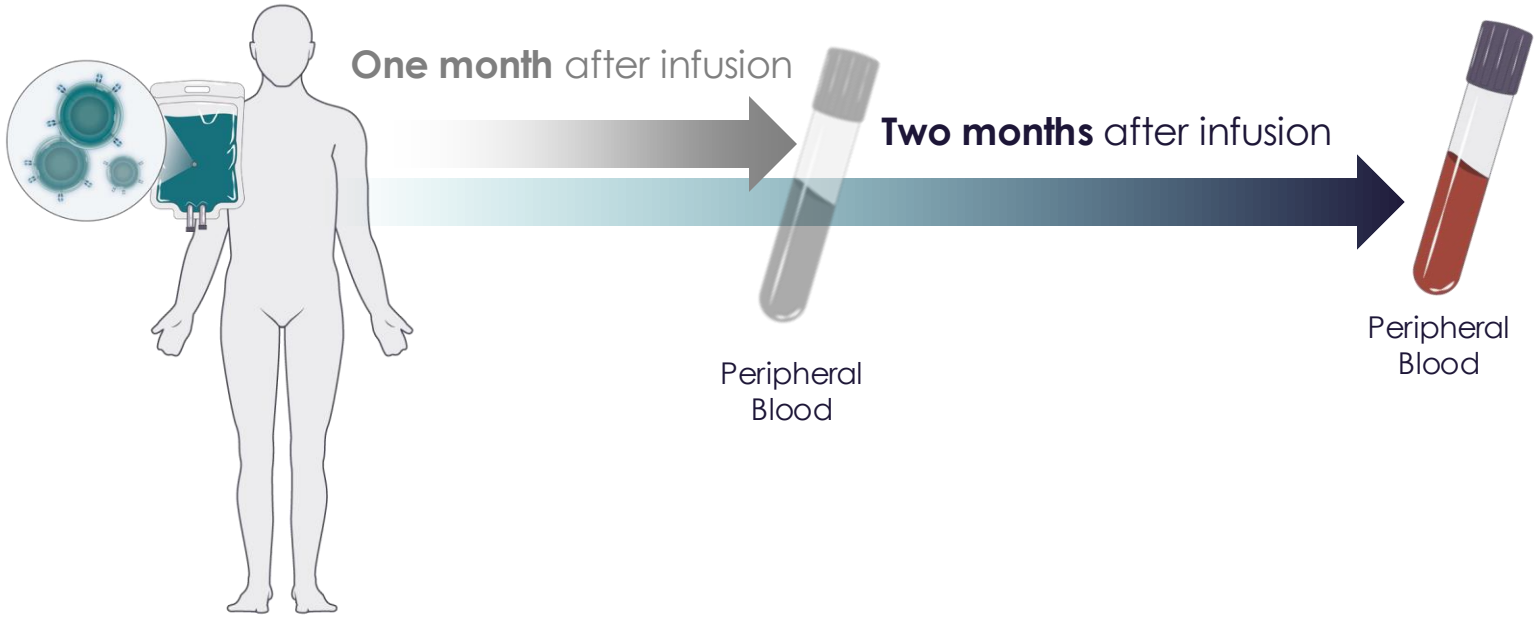
Sustained Anti-Tumor Activity of Ronde-Cel's CD62L+ Enriched Cells Was Assessed After Infusion

Experimental method enabled by high numbers of CAR T-cells in circulation two months after infusion

CAR T-Cell Infusion



Study Description

- Co-culture peripheral blood cells with tumor cell line
- Assess **functional activity** of CAR+ cells for proliferation, cytotoxicity, and cytokine secretion (N = 3)

Post-infusion functional analyses not reported in CD19 CAR T-cell trials, yet provide key insight into function

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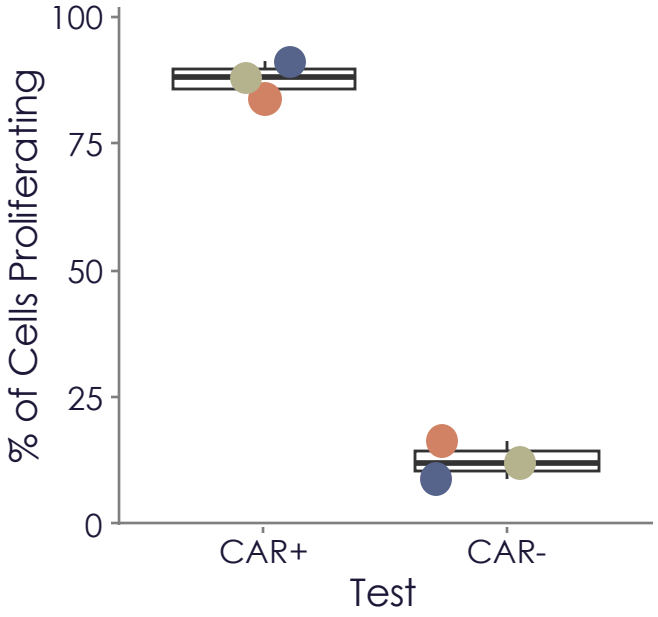
Ronde-Cel Two Months After Infusion Proliferated, Killed and Secreted Cytokines In Vitro

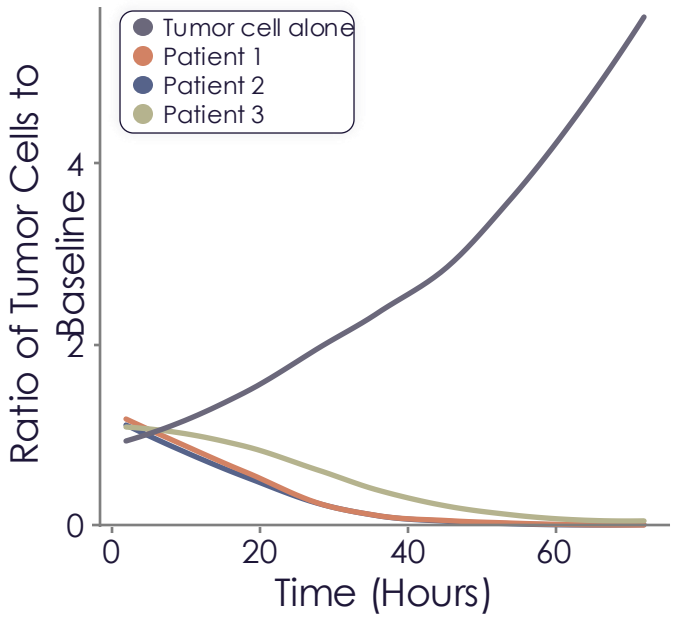
High memory phenotype and enhanced expansion of ronde-cel enable sustained functional capacity

Proliferation



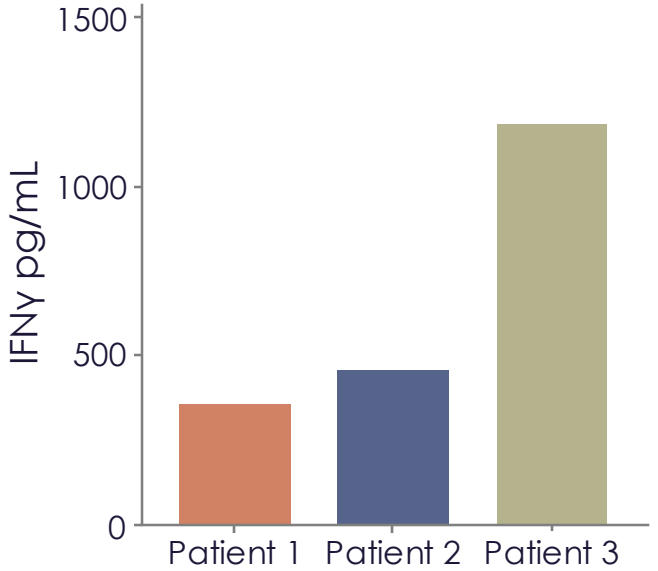
Proliferation assessed by flow cytometry with Cell Trace Violet (CTV) dye at Day 5

Cytotoxicity



Cytotoxicity assessed by measuring live tumor cells with Incucyte

Cytokine Secretion



Cytokine assessed with Meso Scale Diagnostics (MSD) assay

Similar functional data also obtained on seven patient samples collected at one month after infusion

Tumor cell line used is Nalm6. The PBMC alone and the tumor cell alone controls are below the limit of detection in the cytokine secretion assay.
CAR, chimeric antigen receptor; PBMC, peripheral blood mononuclear cells.

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4. Ronde-cel CAR+ T cells collected from patients two months after infusion **sustained the capacity to proliferate, kill tumor cells**, **and secrete cytokines**.

Correlative analysis of translational data to clinical response from PiNACLE (single-arm, pivotal trial in 3L+ patients) is ongoing

Axi-cel, axicabtagene autoleucel; CAR, chimeric antigen receptor; LBCL, large B-cell lymphoma; liso-cel, lisocabtagene maraleucel; tisa-cel, tisagenlecleucel.

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LYL273: GCC-Targeted CAR T-Cell Therapy Candidate for Metastatic Colorectal Cancer

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LYL273, a Potentially Transformative Clinical-Stage Program in Colorectal Cancer (CRC)

High response rates and manageable safety profile in refractory metastatic CRC

- **LYL273 (formerly GCC19CAR T) exhibited meaningful anti-tumor activity in patients with refractory mCRC with a manageable safety profile consistent with CAR T-cell therapy and GCC-target**
  - **67% overall response rate and 83% disease control rate at highest dose studied in US Phase 1 trial**
- **Phase 1 data from China published in *JAMA Oncology* (2024) support U.S. clinical data**
  - 40% overall response rate in 15 patients across two dose levels; median overall survival at high dose of 25 months with mPFS of 6.0 months including patients with and without liver metastases; manageable safety profile
- **Novel GCC-targeted CAR T-cell product candidate enhanced with CD19 CAR expression and controlled cytokine release**
  - GCC expression present on > 95% of mCRC and a majority of pancreatic cancers
  - Designed to enhance CAR T-cell expansion, immune cell infiltration and cancer cell killing
- **Automated closed system scalable manufacturing**

LYL273 was licensed in November 20025; Danaee et al, 2017, PLOS One and internal data
CAR, chimeric antigen receptor; GCC, guanylyl cyclase C; mCRC, metastatic colorectal cancer; mPFS, median progression-free survival

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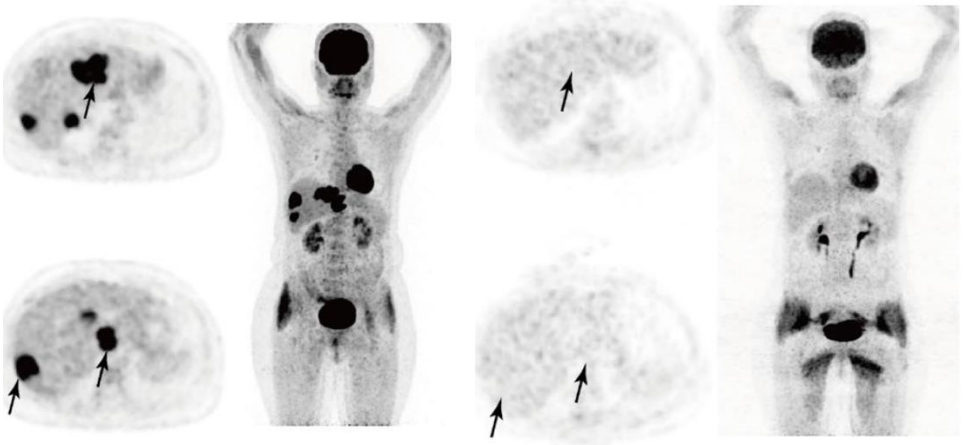
Proof-of-Concept Case Study

The compelling clinical responses in Chinese patients published in *JAMA Oncology*, such as that described below, led to the initiation of an FDA-cleared clinical trial in the U.S.

- 48-year-old woman diagnosed with mCRC
- Surgical resection and four prior lines of chemotherapy
- Multiple courses of radiation to liver and lungs
- Received 2 x 10^6 CAR+ T cells/kg
- Grade 1 CRS, no ICANS reported, Grade 3 diarrhea
- Dramatic reduction in liver metastases as early as Month 1
- 50% tumor reduction on CT imaging and 96% reduction on on FDG-PET scan at Month 3
- Duration of partial response was 8 months and the patient lived for 46 months after CAR therapy

Baseline	Month 3



Baseline CT imaging liver mets highlighted by arrows	RECIST Tumor Reduction **-50%**
Baseline FDG-PET	PERCIST Decrease **-96%**

CAR, chimeric antigen receptor; CT, computerized tomography; FDA, U.S. Food and Drug Administration; FDG-PET, flurodeoxyglucose positron emission tomography; mCRC, metastatic colorectal cancer. PERCIST, Positron Emission tomography Response Criteria in Solid Tumors; RECIST, Response Evaluation Criteria in Solid Tumors

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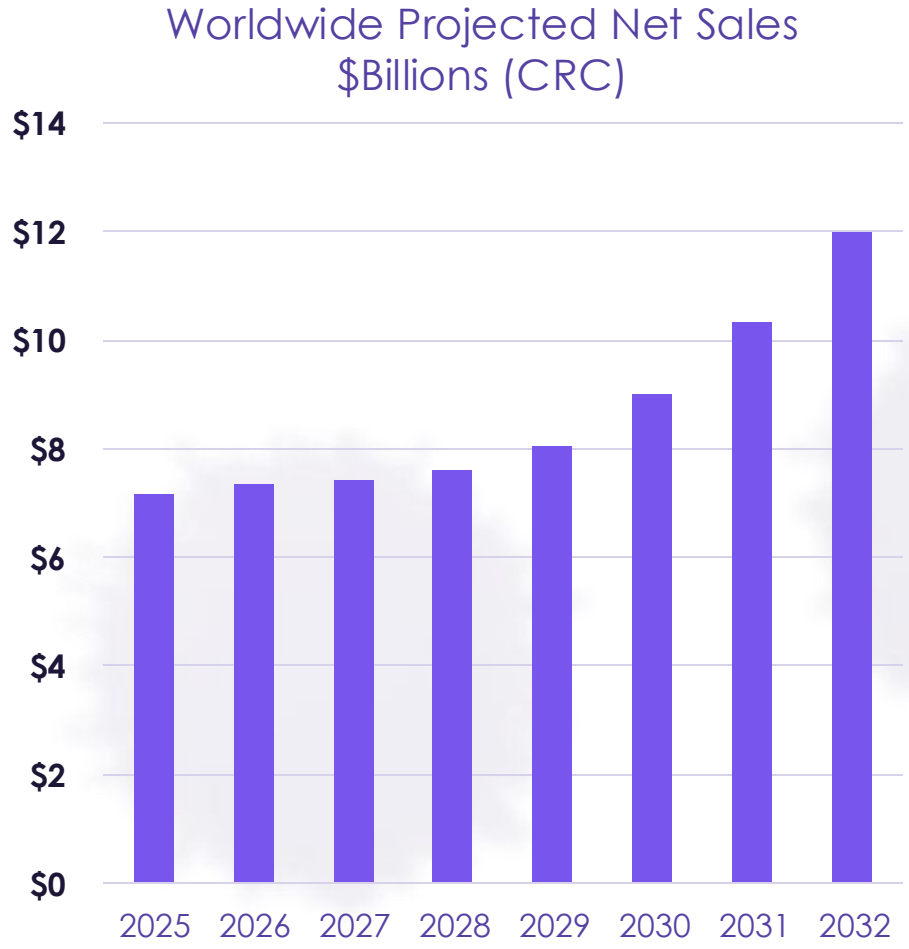
Colorectal Cancer Is the Second Leading Cause of Cancer Deaths Worldwide and is a Large and Growing $6+ Billion Market

A common cancer that is often diagnosed late:

- Over 150,000 new cases and more than 50,000 deaths expected in the U.S. in 2025
- Approximately 25% of patients have metastatic disease at diagnosis
- Up to 60% of patients diagnosed with colorectal cancer will develop distant metastases at some point

More effective and safer therapies are needed:

- Median survival is < 12 months for patients treated with approved agents in the third- or later-line setting
- **Overall response rates are < 6%**



American Cancer Society and are based on US cases. (2024 and 2025); SEER; Roberson et al., 2023, Seminars in Colon and Rectal Surgery
EvaluatePharma; package inserts for regorafenib, trufluridine tipiracil, and fruquintinib

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U.S. Phase 1 Clinical Trial of LYL273 with High Overall Response Rates and Manageable Safety Profile

Dose-Escalation, Dose-Expansion Clinical Trial

- Four enrolling centers
- Patients with mCRC with disease progression on at least two prior lines of therapy

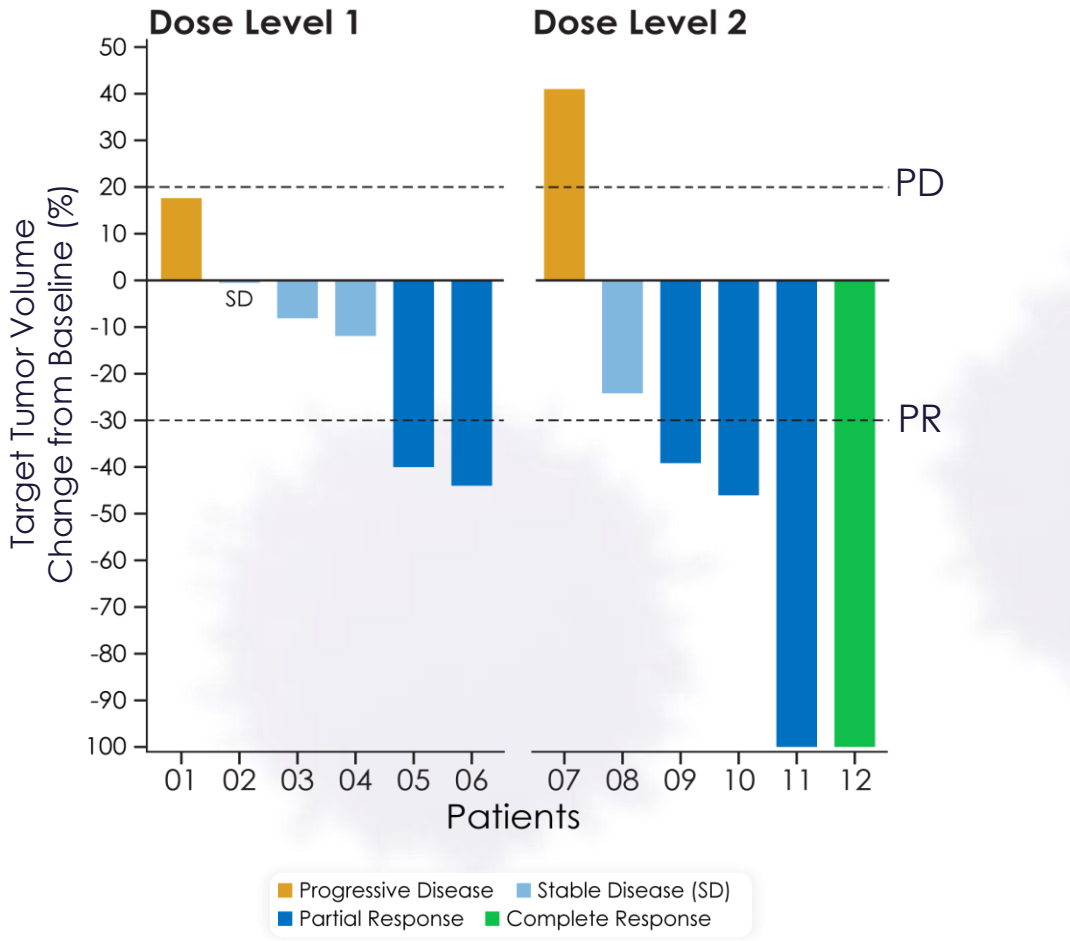
Dose-dependent increase in overall response rate

- 50% overall response rate in 12 evaluable patients
- **67% (4/6) overall response rate at Dose Level 2**
  - One pathological complete response
  - One confirmed partial response with 100% target lesion tumor reduction
  - Two additional confirmed partial responses

Manageable Safety Profile

- Optimized management protocol for diarrhea, including prophylaxis

Tumor Reduction / Best Overall Response



NCT05319314
mCRC, metastatic colorectal cancer; PD, progressive disease; PR, partial response

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Manageable Safety Profile
Treatment-Related Adverse Events

Adverse Events of Interest, N (%)

CRS	Dose Level 1 (N = 6)	Dose Level 2 (N = 6)
Grade 1	4 (67%)	4 (67%)
Grade 2	2 (33%)	1(17%)
Grade 3	0	0
ICANS		
Grade 1	0	0
Grade 2	0	1 (17%)
Grade 3	0	1 (17%)

Diarrhea	Dose Level 1 (N = 6)	Dose Level 2 (N = 6)
Grade 1	2 (33%)	2 (33%)
Grade 2	1 (17%)	2 (33%)
Grade ≥ 3	1 (17%)	1 (17%)
Other Common Adverse Events		
Fatigue	2 (33%)	4 (67%)
Nausea	2 (33%)	3 (50%)

- One patient treated at Dose Level 2 experienced a dose-limiting toxicity of Grade 3 diarrhea, Grade 4 colitis, and died from fungal sepsis 48 days after infusion.
- No Grade 3 or higher diarrhea occurred in the three patients enrolled since establishing an optimized management protocol for diarrhea, including prophylaxis.

CRS, cytokine release syndrome; GI, gastrointestinal; ICANS, immune effector cell-associated neurotoxicity syndrome

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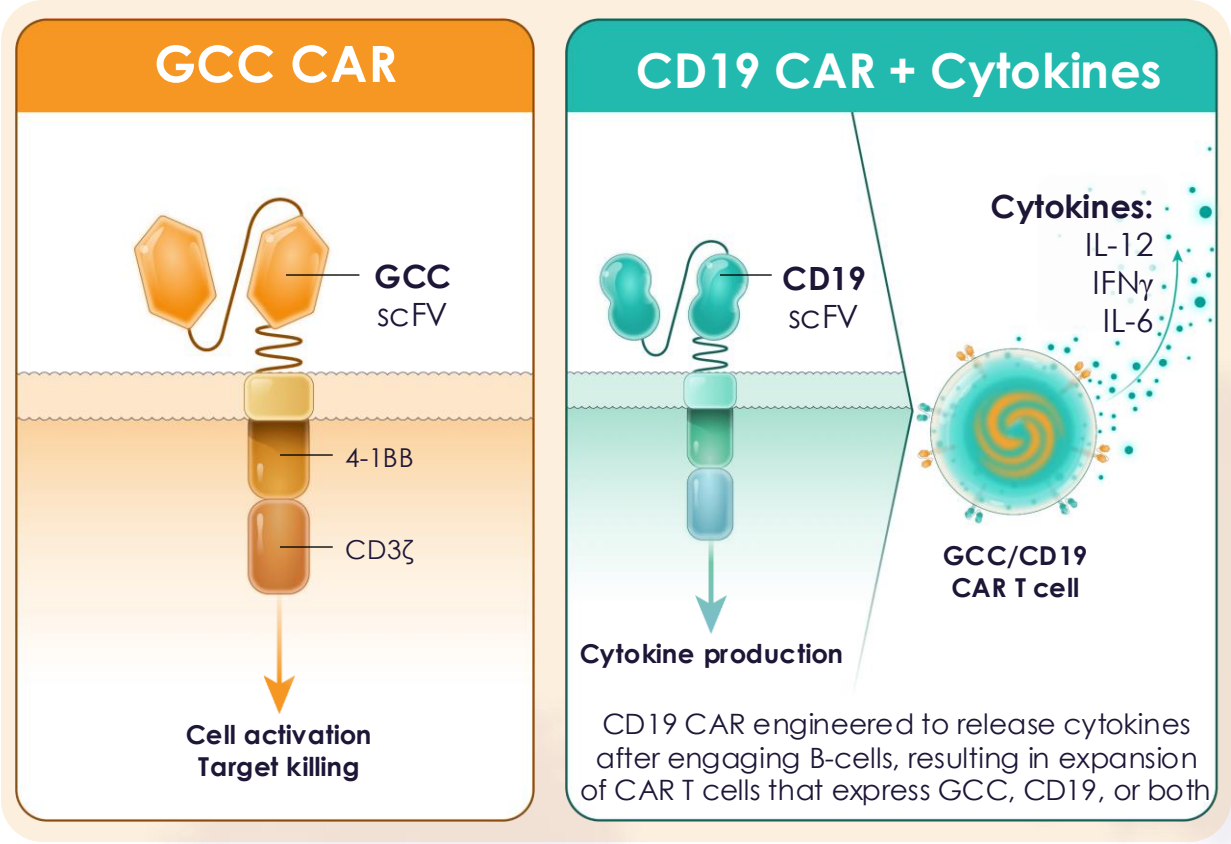
LYL273: GCC-Targeted CAR T-Cell Therapy with Novel Enhancements and Potential to be Transformational for Patients with Refractory mCRC

What is the Breakthrough?

Identify the Target:
Guanylyl cyclase-C (GCC)

- Expressed on over 95% of metastatic colorectal cancers
- Regulates electrolyte balance in healthy intestinal tissue



Arm with Enhancements:
CD19 CAR/Cytokines

- Patient T cells are engineered to express GCC and/or CD19 CARs
- GCC/CD19 CAR T cells expand, infiltrate and kill colorectal cancer cells

Danaee et al, 2017, PLOS One and internal data
GCC, guanylyl cyclase-C; mCRC, metastatic colorectal cancer

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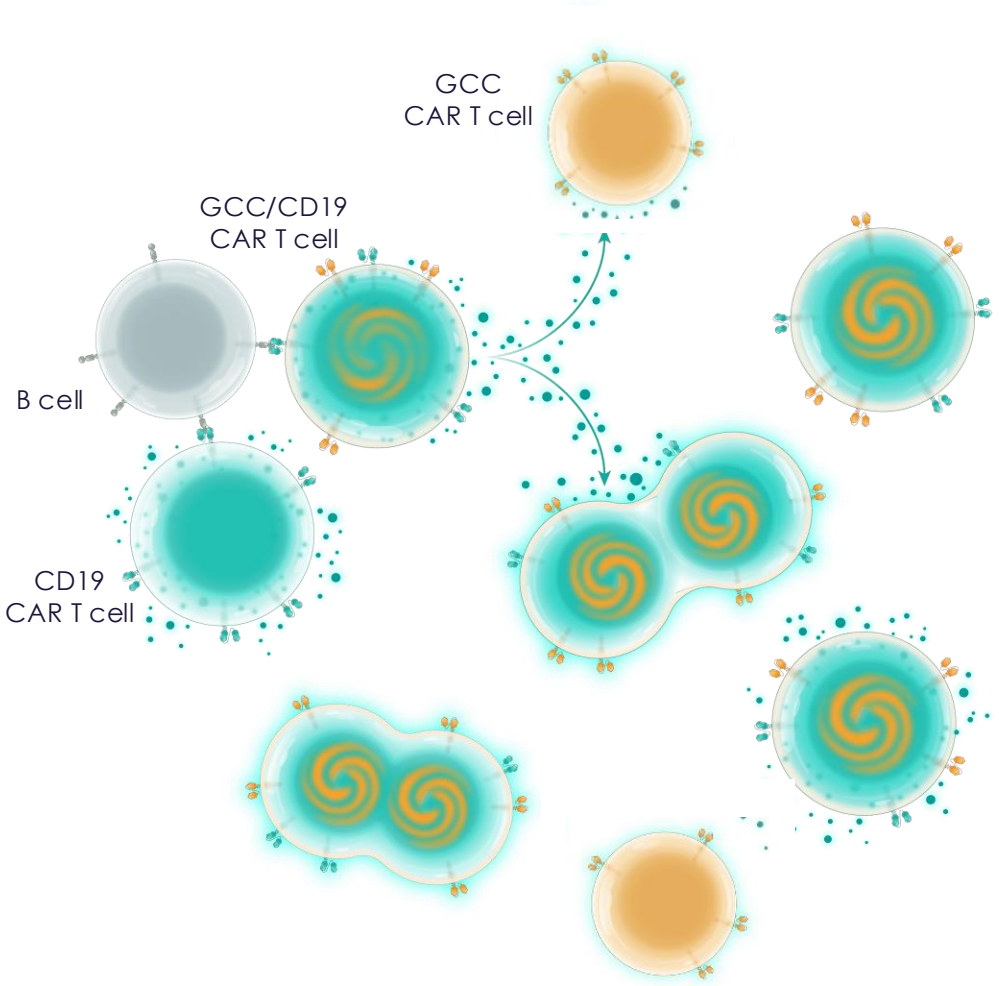
LYL273: A Single Product with 3 Key CAR T-Cell Types



- **GCC CAR T cells:** kill GCC-positive tumor cells
- **CD19 CAR T cells:** activate and expand upon engagement of B cells; release cytokines to support CAR T-cell expansion
- **GCC/CD19 (doublet) CAR T cells:** activate and expand upon engagement of B cells, release cytokines, kill GCC-positive tumor cells; doublets represent the majority of anti-GCC CAR T cells at peak expansion
- **Three cytokines** released based on proportional control
  - Multi-vector co-transduction at a defined ratio
  - Cytokines include IL-12, IFN**γ**, and IL-6

CAR, chimeric antigen receptor; GCC, guanylyl cyclase C

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Upcoming Potential Clinical Milestones

Ronde-cel	Dual-Targeting CD19/CD20 CAR T-Cell Therapy for Aggressive LBCL
Mid-2025	✓ Reported more mature data in 3L+ and initial data in 2L in June (ICML) ✓ Initiated pivotal trial in 3L+
Late 2025	✓ Reported updated PiNACLE data and 2L data from Phase 1/2 trial ASH
By Early 2026	❑ Initiate Phase 3 randomized controlled trial (PiNACLE – H2H) in 2L
2H 2026	❑ Updated PiNACLE clinical data ❑ Progress update on PiNACLE – H2H (by end of 2026)
2027	❑ Pivotal PiNACLE data (mid-2027) ❑ BLA submission for R/R LBCL 3L+
LYL273	**GCC-Targeted CAR T-Cell Therapy for Metastatic Colorectal Cancer**
1H 2026	❑ Updated clinical data from Phase 1 trial
2H 2026	❑ Updated clinical data from Phase 1 trial ❑ End-of-Phase 1 meeting
1H 2027	❑ Initiation of pivotal clinical trial

ASH, American Society of Hematology; BLA, Biologics License Application; CAR, chimeric antigen receptor; ICML, International Conference on Malignant Lymphoma; IND, investigational new drug application; LBCL, large B-cell lymphoma; R/R, relapsed and/or refractory

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Q&A

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