The Future of Cell Therapy — Today

September 2026

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Forward-Looking Statements

Certain matters discussed in this presentation are “forward-looking statements” 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 progress, timing of data release and FDA submissions, enrollment and other plans and expectations; milestones; market size and commercial opportunity; cash runway; our manufacturing capabilities; the potential attributes and benefits of our product candidates; 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: our operating in a rapidly evolving industry and having a limited operating history; our ability to successfully develop, manufacture and commercialize product candidates or our experiencing significant delays in doing so; our dependence on the enrollment and retention of patients in our clinical trials for our product candidates; the potential for results of our research, nonclinical studies or earlier clinical trials to not be predictive of future results; clinical development involving a lengthy and expensive process with uncertain outcomes; our product candidates and technologies being based on novel technologies that are unproven and may not result in approvable or marketable products; our facing substantial competition in a rapidly changing industry; our ability to obtain and maintain sufficient intellectual property protection for our product candidates; the complexity of manufacturing cellular therapies and our ability to manufacture and supply our product candidates for our clinical trials; our reliance on third parties; implementation of our strategic plans for our business and product candidates and our realization of the expected benefits of such plans; the potential reduction of our cash resources and fluctuations in our operating results and financial condition as a result of our milestone, royalty and success payment obligations; the sufficiency of our capital resources and need for additional capital to achieve our goals; significant adverse events, toxicities or other undesirable side effects associated with our product candidates; our ability to make planned regulatory submissions or progress clinical trials on the anticipated timelines, if at all; RMAT and Fast Track designations may not actually lead to faster development, regulatory review or approval process, and do not assure ultimate FDA approval; the significant uncertainty associated with our product candidates ever receiving any regulatory approvals; other risks, including those risks described under the heading “Risk Factors” in our SEC filings, including in Lyell’s Quarterly Report on Form 10-Q for the quarter ended June 30, 2026, filed with the Securities and Exchange Commission (SEC) on August 6, 2026, 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.

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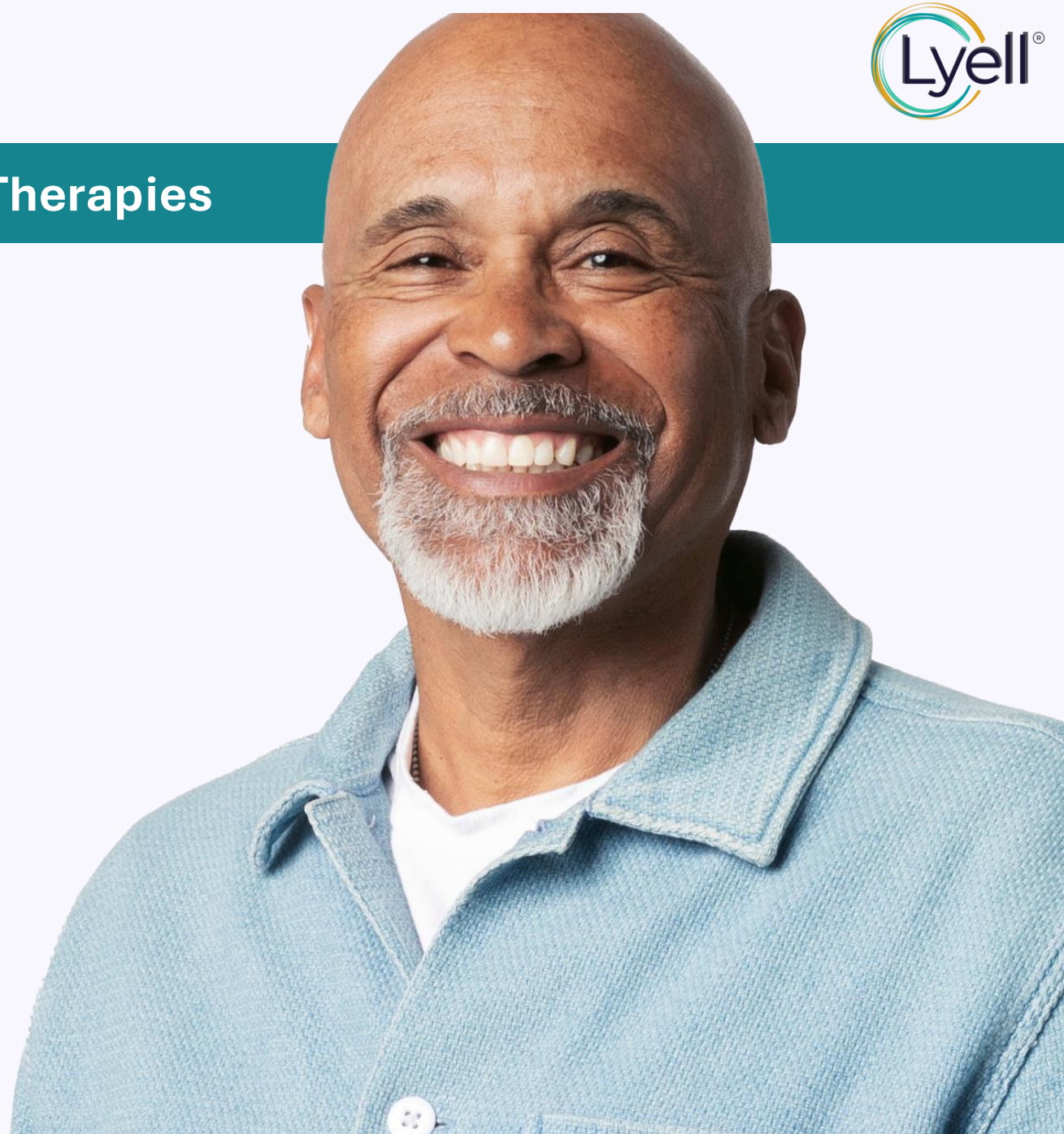
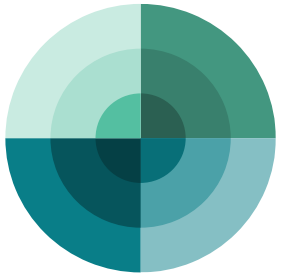
Advancing Next Generation CAR T-Cell Therapies

Improve outcomes for patients with first-in-class cell therapy innovation for hematologic malignancies and 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 accessibility in normal tissue to manage 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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Lyell Is Well Positioned for Significant Value Creation in the Next 12 to 18 Months

Multiple catalysts in multi-billion-dollar markets expected to unlock value

Lyell has two potentially first-in-class CAR T-cell programs targeting large markets with significant unmet need

- R/R LBCL is a growing $3 billion market for CD19 CAR T-cell therapies
- mCRC in the 3L+ setting is a large growing market with approved therapies offering limited benefit

Ronde-cel, a dual-targeting CD19/CD20 CAR T-cell product candidate, with the potential to become the standard of care in R/R LBCL based on high rates of durable complete responses and a safety profile for potential outpatient use

- Two pivotal trials underway: PiNACLE 3L+ pivotal data on track for mid-2027, with expected BLA submission in 2H 2027
- First-of-its-kind Phase 3 head-to-head CAR T-cell randomized controlled clinical trial dosing patients (PiNACLE-H2H)
- Updated data expected in 2H 2026

LYL273, an enhanced GCC-targeted CAR T-cell candidate for mCRC, with high response rates in R/R patients and a manageable safety profile in ongoing U.S. Phase 1/2 trial in 3L+ patients

- Tech transfer to LyFE Manufacturing Center™ complete
- Updated Phase 1/2 clinical trial data expected in 2027

Scalable wholly-owned LyFE capable of commercial launch

Datamonitor (2024); Gilead Sciences Q4/FY 2025 Earnings (Feb 2026); Bristol Myers Squibb Q4/FY 2025 Financial Results (Feb 2026); Novartis Q4/FY 2025 Condensed Financial Report (Feb 2026).
2L, second line; 3L+, third- or later-line; BLA, Biologics License Application; CAR, chimeric antigen receptor; GCC, guanylyl cyclase C; LBCL, large B-cell lymphoma; R/R, relapsed/refractory; mCRC, metastatic colorectal cancer.

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Advancing Next Generation CAR T-Cell Therapies

Multiple Near-Term Value-Creating Milestones

Product	Target	Target Indications	Enhancements	Phase 1/2	Pivotal	Next Expected Milestones
Ronde-cel	CD19/ CD20	3L+ Aggressive LBCL • Regenerative Medicine Advanced Therapy Designation • Fast Track Designation 2L Aggressive LBCL • Regenerative Medicine Advanced Therapy Designation	• CD62L+	PiNACLE PiNACLE-H2H		• Additional data from PiNACLE pivotal trial in 2H 2026 • Pivotal data in mid-2027 • BLA submission in 2H 2027 • Progress update 2H 2026
LYL273	GCC	3L+ Metastatic CRC • Fast Track Designation	• CD19 CAR with controlled cytokine release	CARAβiNER		• Updated clinical data in 2027 • End-of-Phase 1 Meeting in 2027 • Initiation of pivotal clinical trial in 2027

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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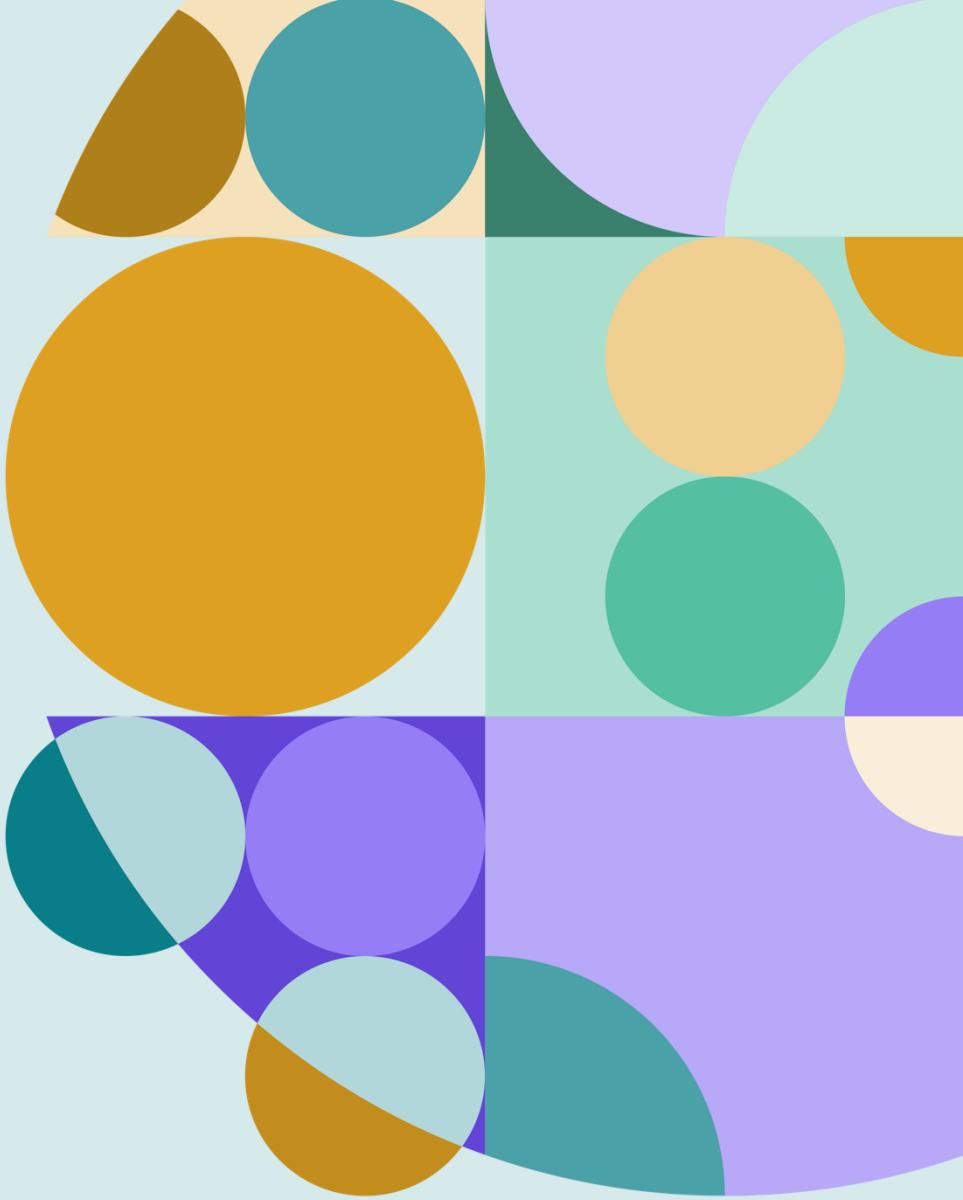
Ronde-Cel for Large B-Cell Lymphoma



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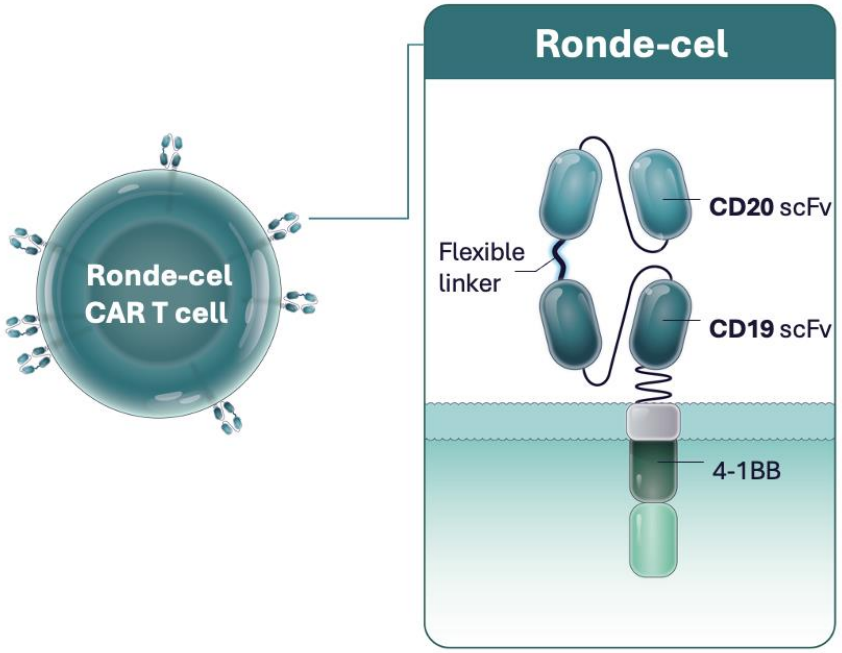
Ronde-Cel is a Dual-Targeting CD19/CD20 CAR T-Cell Product Enriched for Stemlike Phenotype (CD62L+ Cells)

Ronde-Cel Designed to Achieve High Complete Response Rates and Long Duration of Responses

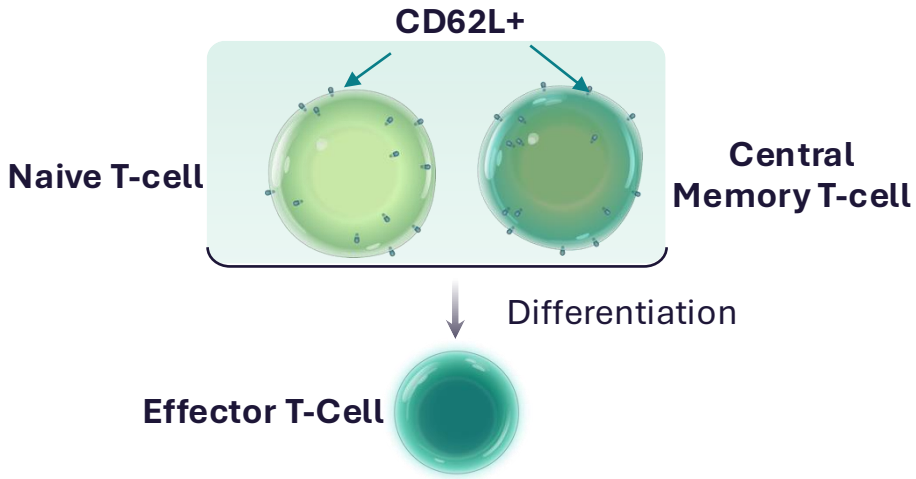
Ronde-cel is a true CD19/CD20 "OR" logic-gated CAR designed to:

- Target either CD19 or CD20 with full potency
- Overcome heterogeneous antigen density
- Mitigate antigen loss following treatment



Ronde-cel is manufactured with CD62L enrichment to achieve a high percentage of naïve and central memory T-cells in drug product

- Naïve T cells are associated with better CAR T-cell response
- CD62L+ cells include naïve and central memory T cells
- CD62L+ cells are associated with improved persistence, reduced exhaustion, and lower adverse cytokine production



Aldoss I, et al. *Clin Cancer Res* 2023; Arcangeli S, et al. *JCI* 2022; Chen GM, et al. *Cancer Discovery* 2021; Filosto S, et al. *Blood Cancer Discov* 2024; Sommermeyer D, et al. *Leukemia* 2016; Abramson J, et al. *Lancet* 2020; Arcangeli S, et al. *JCI* 2022; Bishop MR, et al. *N Engl J Med* 2021; Harris LJ, et al. *Int J Mol Sci*. 2020; Neelapu SS, et al. *N Engl J Med* 2017.
CAR, chimeric antigen receptor; CD62L+, CD62L or L-selectin positive T cells

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Ronde-Cel is Targeting a Growing Multi-Billion-Dollar Market

Ronde-Cel's Ongoing Clinical Trials Include Patients with Relapsed/Refractory Large B-Cell Lymphoma

Projected global sales of currently approved CD19 CAR T-cell products

30,000 patients with LBCL in U.S.

~12,000 patients progress to 2L
~40 to 50% of patients are refractory to or relapse following 1L treatment

PINACLE-H2H

~6,000 to 7,000 patients progress to 3L+

PINACLE

Leukemia and Lymphoma Society Facts and Statistics Overview; Datamonitor (2024); Flowers CR, et al. *Hematology Am Soc Hematol Educ Program* 2022; SEER (2023).
1L, first line; 2L, second line; 3L+, third- or later-line; CAR, chimeric antigen receptor; LBCL, large B-cell lymphoma.

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3L+ Setting Represents Significant, Underappreciated Opportunity

MSKCC and U.S. Medicare Claims Analyses Suggest Substantial Share of 2L Patients May Be 3L+

Memorial Sloan Kettering Retrospective Analysis[1]

Up to 50%

of patients who progress on 1L therapy received second regimen of chemo prior to apheresis for CAR T

Medicare Fee-for-Service Claims Analysis[2]

57%

of patients classified as 2L patients received a second regimen of chemo prior to apheresis for CAR T

Patients who have received two prior chemotherapy regimens are potential candidates for 3L+ CAR T-cell therapy

[1]Gomez-Llobell M, et al. *Blood* 2025. [2]Data on file based on analyses of Medicare Fee-for-Service claims conducted by BluePath Solutions.
1L, first line; 2L, second line; 3L+, third- or later-line; CAR, chimeric antigen receptor; MSKCC, Memorial Sloan Kettering Cancer Center.

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Relapsed/Refractory Large B-Cell Lymphoma Third- or Later-Line Setting (3L+)

CD19 CAR T-Cell Therapies Have Been Transformative for Patients With LBCL, But Better Therapies Are Needed

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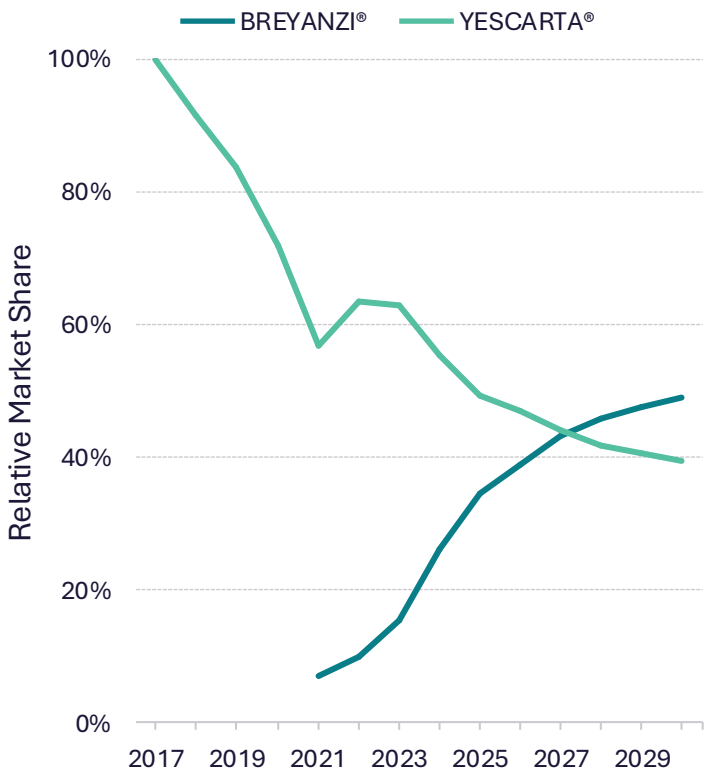
CAR T-Cell Therapy Treating Physicians Show Historical Willingness to "Switch" Based on Strength of Clinical Data

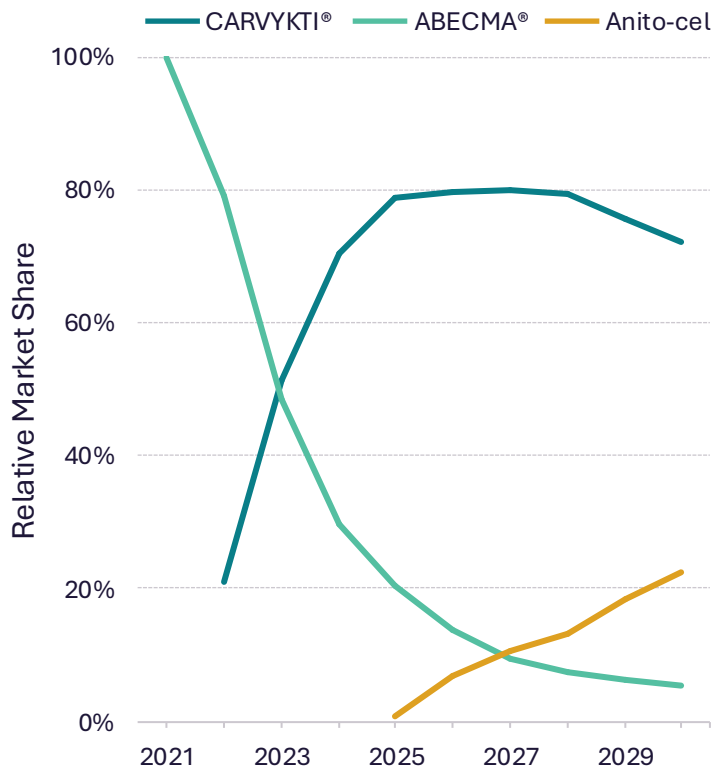
Differentiated efficacy and safety pivotal data could enable ronde-cel to disrupt LBCL treatment paradigm

- BREYANZI® sales are taking market share from YESCARTA® presumably due to **enhanced safety profile**
- CARVYKTI® rapidly took market share from ABECMA ® largely assumed to be based upon **enhanced efficacy**
- **Ronde-cel was designed to provide patients improved outcomes for both efficacy and safety over approved CD19 CAR T-cell therapies**

CD19 CAR T-Cell Therapy Market Share in Lymphoma



BCMA CAR T-Cell Therapy Market Share in Multiple Myeloma



EvaluatePharma
BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor.

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

PHASE 1/2 TRIAL (Data from ASH 2025)	Target	Line of Therapy, Indication, Sample Size	Overall Response Rate	Complete Response Rate	Median PFS (months)
Lyell Ronde-cel	CD19/CD20	3L+, R/R LBCL N = 29	93%	76%	18
APPROVED THERAPIES					
YESCARTA® (axicabtagene ciloleucel) Suspension for IV infusion	CD19	3L+, R/R LBCL (ZUMA-1) N = 108	72%	51%	6
Breyanzi® (lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION	CD19	3L+, R/R LBCL (TRANSCEND) N = 268	73%	54%	7
KYMRIAH® (tisagenlecleucel) Dispersion for IV infusion	CD19	3L+, R/R DLBCL (JULIET) N = 115	50%	32%	3

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

Ronde-cel data cutoff date: September 5, 2025; presented at the American Society of Hematology Annual Conference, 2025.
Abramson J, et al. *The Lancet* 2020; Neelapu SS, et al. *N Engl J Med* 2017; Schuster SJ, et al. *N Engl J Med* 2018.
3L+, third- or later-line; LBCL, large B-cell lymphoma; R/R, relapsed/refractory; PFS, progression-free survival

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Ronde-Cel Phase 1/2 Trial Multi-Cohort Trial (3L+ LBCL)

Patients with Higher-Risk Disease in General Achieve Lower Complete Response Rates

Patient Population

- Patients with relapsed/refractory DLBCL, PMBCL, 3BFL, and tFL who have had ≥ 2 lines of treatment (3L+ cohort) or > 1 line of therapy (2L cohort)
- 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

Demographics and Disease Characteristics	**3L+ LBCL** N = 37
Median (range) age, years	64 (21, 86)
≥ 75 years, n (%)	6 (16%)
ECOG 1, n (%)	22 (60%)
IPI score 3 or 4, n (%)	9 (24%)
LBCL histology n (%)	
DLBCL	23 (62%)
tFL	8 (22%)
Primary refractory, n (%)	16 (43%)
Elevated (above normal) LDH, n (%)	13 (35%)
Bulky disease (≥ 7 cm), n (%)	6 (16%)
Double-/triple-hit status, n (%)	3 (8%)
Received bridging therapy, n (%)	15 (41%)

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. NCT05826535
Data cutoff: September 5, 2025; presented at the American Society of Hematology Annual Conference, 2025. 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.
2L, second line; 3L+, third- or later-line; LBCL, large B-cell lymphoma; DLBCL, diffuse large B-cell lymphoma; 3BFL, Grade 3B follicular lymphoma; PMBCL, primary mediastinal large B-cell lymphoma; tFL, transformed follicular lymphoma; ECOG, Eastern Cooperative Oncology Group; IPI, International Prognostic Index; LDH, lactate dehydrogenase.

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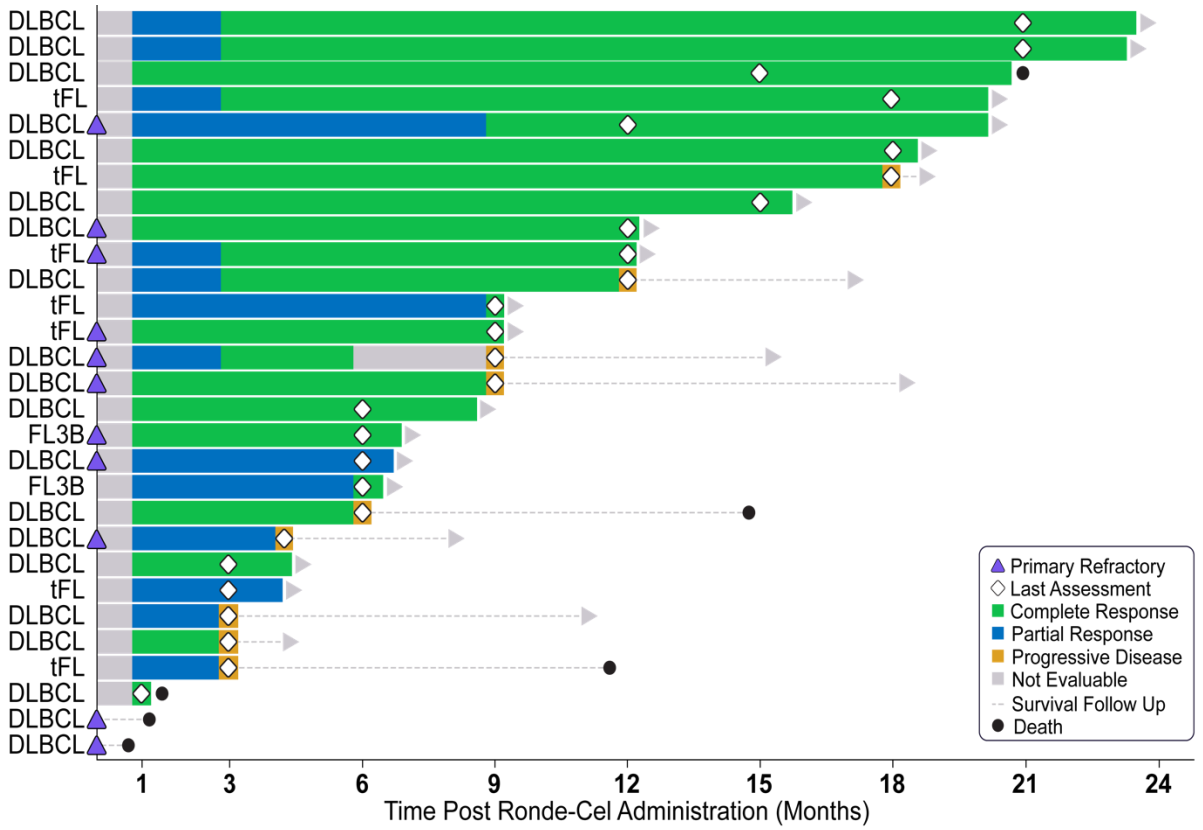
Overall Response Rate of 93% and Complete Response Rate of 76%

High Rate of Durable Complete Responses in 3L+ LBCL Cohort

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



Data cutoff date: September 5, 2025; presented at the American Society of Hematology Annual Conference, 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. 8 patients were dosed without Day 84 follow up, disease progression, or death.
3L+, third- or later-line; LBCL, large B-cell lymphoma.

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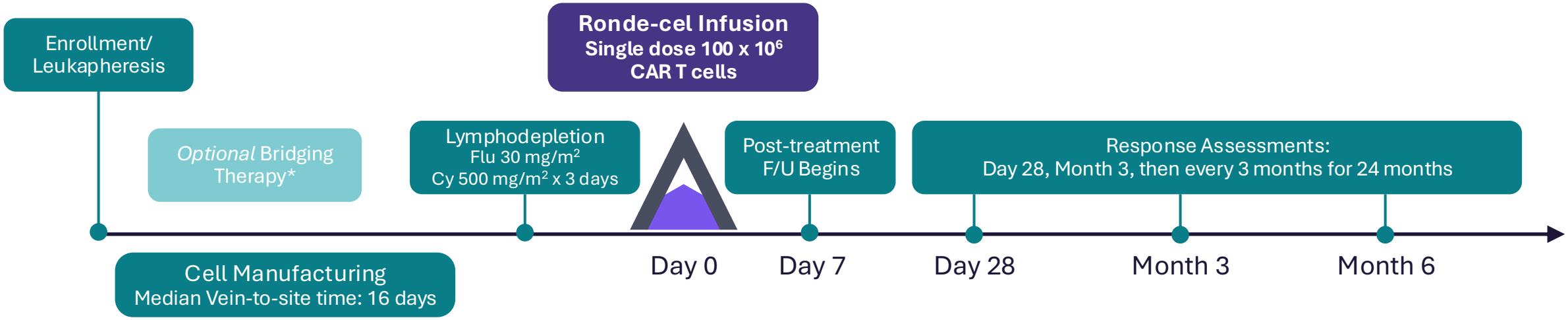
PiNACLE Clinical Trial Design

A Single-Arm Pivotal Trial in 3L+ CAR T-Cell Naïve Patients; Seamless Expansion of Phase 1/2 Cohort

Data readout on track for mid-2027, with BLA submission expected to follow in 2H 2027



Patient Population

- Patients with relapsed/refractory DLBCL, PMBCL, 3BFL, and tFL who have had ≥ 2 lines of treatment
- CD19/CD20 screening not required for enrollment
- CD19 CAR T-cell therapy naïve
- No upper age limit

Trial Objectives

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

*Bridging therapy allowed following leukapheresis.

3L+, third- or later-line; BLA, biologics license application; CAR, chimeric antigen receptor; F/U, follow-up; Cy, cyclophosphamide; DLBCL, diffuse large B-cell lymphoma; 3BFL, Grade 3B follicular lymphoma; Flu, fludarabine; PMBCL, primary mediastinal B-cell lymphoma; tFL, transformed follicular lymphoma. NCT05826535

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Relapse/Refractory Large B-Cell Lymphoma

Second-Line Setting (2L)

Patient Demographics and Disease Characteristics Impact Outcomes

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Patients with Higher-Risk Disease In General Achieve Lower Complete Response Rates With CD19 CAR T-Cell Therapies

Patient Demographics and Disease Characteristics are Critical to Understanding Dataset Outcomes

High-risk features in patients with relapsed/refractory LBCL

- Primary refractory disease
- Relapse before 12 months vs. late-relapsing patients
- Older age
- Use of bridging therapy (allows inclusion of sicker patients with more rapidly progressing disease)

Ronde-cel 2L patients include older patients (no upper age limit) and almost all have primary refractory disease

- YESCARTA® was studied in ZUMA-7, in which no bridging chemotherapy was allowed
- BREYANZI® was only studied in patients over the age of 75 in the single-arm PILOT study
- Limited data have been published for patients with primary refractory disease in the 2L-setting

Abramson J, et al. *The Lancet* 2020; Kamdar M, et al. *Lancet* 2022; Locke FL, et al. *N Engl J Med* 2021; Neelapu SS, et al. *N Engl J Med* 2017; Sehgal A, et al. *Lancet Oncol* 2022;
2L, second line; CAR, chimeric antigen receptor; CR, complete response; LBCL, large B-cell lymphoma.

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Higher Complete Response Rates and Longer Duration of Response Needed for Higher-Risk Patients with LBCL in 2L Setting

PHASE 1/2 TRIAL (Data from ASH 2025)	Target	Line of Therapy, Indication Sample Size	Overall Response Rate	Complete Response Rate	Median PFS (months)	
Lyell Ronde-cel	CD19/CD20	2L, R/R LBCL **Primary Refractory** (N=18, 94%)	83%	61%	--	
APPROVED THERAPIES						
Breyanzi (lisocabtagene maraleucel)	CD19	2L, R/R LBCL (PILOT, single-arm) Transplant Ineligible (N = 61)	80%	54%	9	
		Primary Refractory (N = 33; 54%)	Not reported	42%	Not reported	
Breyanzi (lisocabtagene maraleucel)	CD19	2L, R/R LBCL (TRANSFORM, RCT) All Patients (N = 184; 92 liso-cel)	86%	66%	15	No patients >75 years enrolled
		Primary Refractory (N = 67; 73%)	85%	69%	Not reported	
YESCARTA (axicabtagene ciloleucel)	CD19	2L, R/R LBCL (ZUMA-7, RCT) (N = 359; 180 axi-cel)	83%	65%	15	No bridging chemotherapy allowed
		Primary Refractory (N = 133, 74%)	Not reported	Not reported	7	

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Data cutoff date: September 5, 2025, presented at the American Society of Hematology Annual Conference, 2025.

Kamdar M, et al. *Lancet* 2022; Locke FL, et al. *N Engl J Med* 2021; Sehgal A, et al. *Lancet Oncol* 2022; Westin JR, et al. *TCT* 2025. Nastoupil LJ, poster presented at the 2023 American Society of Clinical Oncology Conference

2L, second line; LBCL, large B-cell lymphoma; PFS, progression-free survival; RCT, randomized controlled trial; R/R, relapsed/refractory.

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High Overall Response Rate in High-Risk Patients with LBCL in 2L Cohort

>90% of Patients with Primary Refractory Disease

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

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
- 94% of efficacy evaluable patients had primary refractory disease

Data cutoff date: September 5, 2025 (response rates); 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.
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
DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; tFL, transformed follicular lymphoma.

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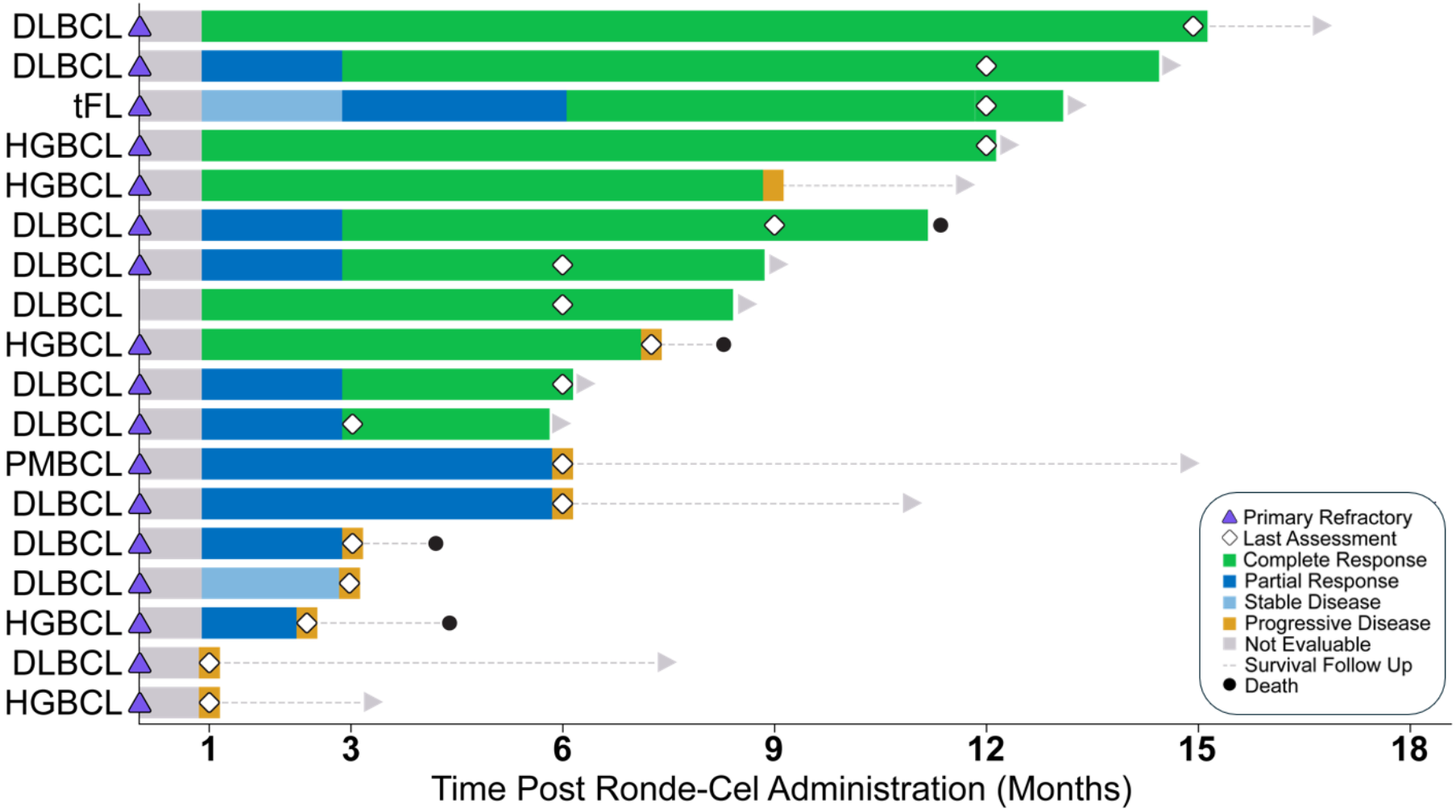
High Overall Response Rate in High-Risk Patients with 2L LBCL Cohort

High-Risk Characteristics with 94% of Patients with Primary Refractory Disease



Data cutoff date: September 5, 2025 (response rates); November 11, 2025 (swimmer plot). Presented at the American Society of Hematology Annual Conference, 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.
6 patients were dosed without Day 84 follow up, disease progression, or death.
DLBCL, diffuse large B-cell lymphoma; HGBCL, high grade B-cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma; tFL, transformed follicular lymphoma.

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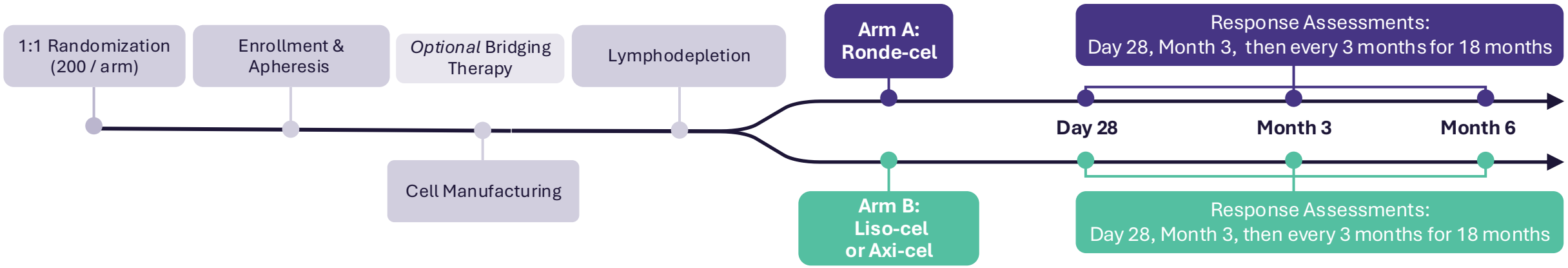
PiNACLE-H2H Clinical Trial Design

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



Patient Population

- Patients with relapsed/refractory DLBCL, PMBCL, HGBCL, 3BFL, and transformed indolent BCL who have received ≥ 1 lines of treatment
- Early and late relapse
- CD19/CD20 screening not required for enrollment
- No upper age limit

Trial Objectives

- Event-free survival (primary endpoint)
- Progression-free survival
- Overall survival
- Safety and tolerability
- Cell expansion pharmacokinetics

Bridging therapy allowed following leukapheresis; assessments are at Day 28, Month 3, then every 3 months through 18 months, then every 6 months through month 36.
Axi-cel, axicabtagene ciloleucel; BCL, B-cell lymphoma; 2L, second line; CAR, chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma; 3BFL, Grade 3B follicular lymphoma; HGBCL, high grade B-cell lymphoma; liso-cel, lisocabtagene maraleucel; LBCL, large B-cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma.

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Optimized Development Strategy Creates Multiple Catalysts for Potential Near-Term Value Creation

Ronde-cel clinical development plan

PiNACLE

Fast-to-Market

Pivotal trial supporting potential for full or accelerated approval in 3L+ LBCL

Data readout on track for mid-2027
BLA submission expected 2H 2027

RMAT Designation for 3L+ R/R LBCL

PiNACLE-H2H

Leave-No-Doubt Superiority Trial Design

First-of-its kind Phase 3 head-to-head CAR T clinical trial, supporting broad 2L label (confirmatory trial if accelerated approval for PiNACLE)

First patient dosed in Feb 2026

RMAT Designation for 2L R/R LBCL

2L, second line; 3L+, third- or later-line; CAR, chimeric antigen receptor.; BLA, biologics license application; LBCL, large B-cell lymphoma; R/R, relapsed/refractory; RMAT, Regenerative Medicine Advance Therapy.

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Ronde-Cel Safety Data

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Lower Rates of High Grade ICANS and CRS Needed to Enable Increased Use of CAR T-Cell Therapy in Outpatient Setting

PHASE 1/2 TRIAL (Data from EHA 2026)	Target	Line of Therapy, Indication, Sample Size	Grade ≥ 3 Cytokine Release Syndrome[1]	Grade ≥ 3 Neurotoxicity[1]
Lyell **Ronde-Cel**	CD19/CD20	3L+ and 2L LBCL (N = 64 with dex prophylaxis)	0%*	8%*
APPROVED THERAPIES				
YESCARTA® (axicabtagene ciloleucel)	CD19	All Lines Package Insert	9%	31%
Breyanzi® (lisocabtagene maraleucel)	CD19	All Lines Package Insert	3%	10%

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

Data cutoff date: May 5, 2026; presented at the European Hematology Association 2026 Congress. [1]YESCARTA® prescribing information; BREYANZI® prescribing information, section 5.2.
*Dexamethasone prophylaxis with 10 mg on days 0, 1 and 2 of CAR T-cell infusion. 2L, second line; 3L+, third- or late-line; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune mediated cell-associated neurotoxicity syndrome.

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Dexamethasone Prophylaxis Reduced Grade ≥ 3 ICANS

Adverse Events of Interest (3L+ and 2L Cohorts)

Adverse Event, n (%)	No Prophylaxis N = 44	Prophylaxis N = 64
CRS	**30 (68%)**	**44 (69%)**
Grade 1	13 (30%)	36 (56%)
Grade 2	17 (39%)	8 (13%)
Grade ≥ 3	0 (0%)	0 (0%)
Median time to onset, days (range)	3 (1 - 13)	6 (3 - 18)
Median time to resolution, days (range)	3 (1 - 13)	3 (1 - 21)
ICANS	**14 (32%)**	**10 (16%)**
Grade 1	5 (11%)	4 (6%)
Grade 2	2 (5%)	1 (2%)
Grade ≥ 3	7 (16%)	5 (8%)
Median time to onset, days (range)	6 (2 - 11)	7 (4 - 15)
Median time to resolution, days (range)	4 (1 - 10)	3 (1 - 9)

Adverse Event, n (%)	No Prophylaxis N = 44	Prophylaxis N = 64
IEC-HS / HLH		
Grade 1 or 2	1 (2%)	2 (3%)
Grade ≥ 3	0 (0%)	0 (0%)
Infections		
Grade 1 or 2	13 (30%)	14 (22%)
Grade ≥ 3	6 (14%)	3 (5%)
Prolonged cytopenias		
Grade ≥ 3	10 (23%)	9 (14%)

- Patients received 10 mg (IV/PO) of dexamethasone on Days 0, 1, and 2 after ronde-cel infusion
- No deaths determined to be related to ronde-cel

Data cutoff date: May 5, 2026; presented at the European Hematology Association 2026 Congress.
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; IEC-HS, immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; HLH, hemophagocytic lymphohistiocytosis; IV, intravenous; LBCL, large B-cell lymphoma; PO, orally.

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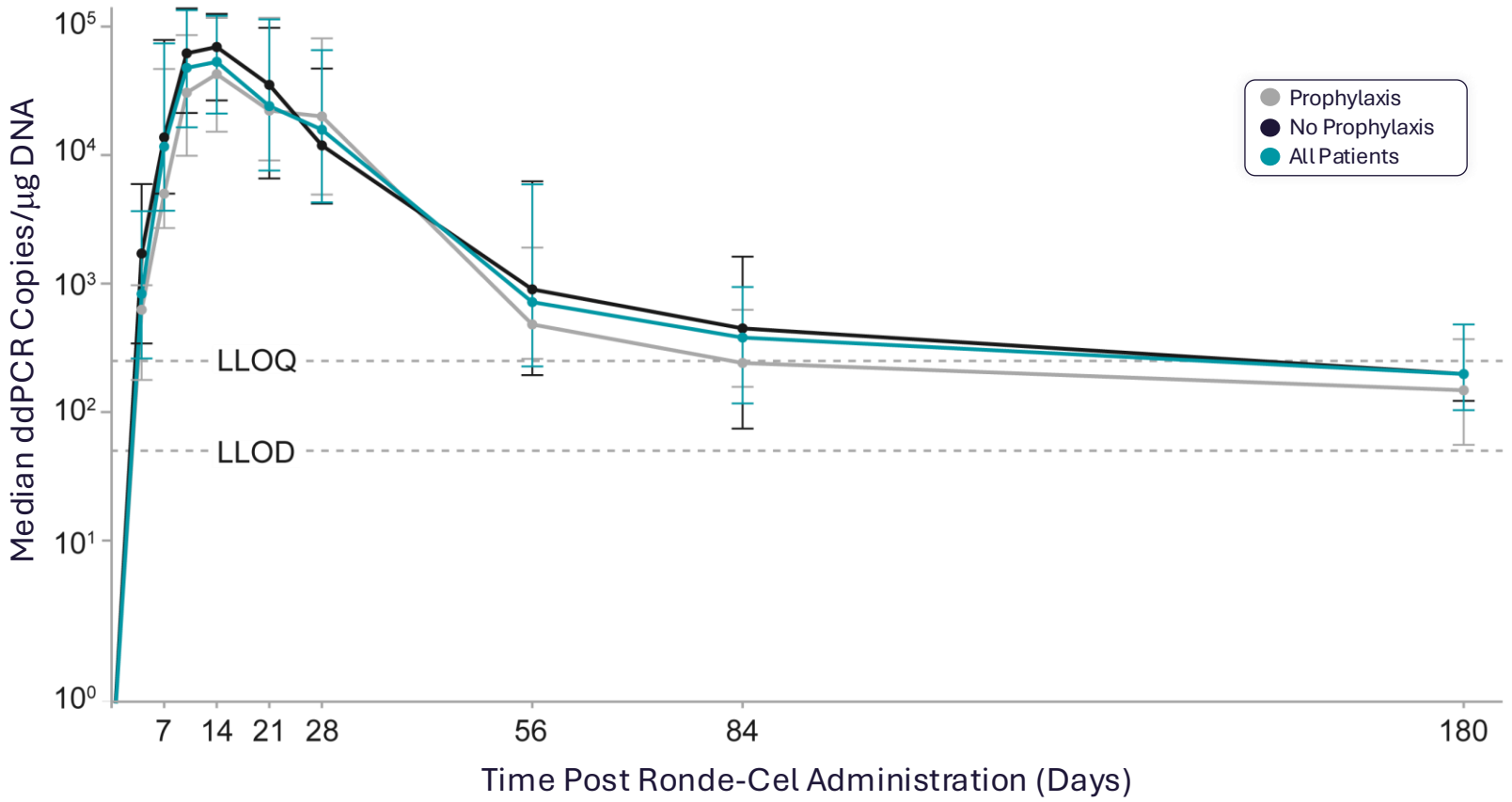
Ronde-Cel Expansion Was Robust in Patients With or Without Dexamethasone Prophylaxis

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 date: September 5, 2025; presented at the American Society of Hematology Annual Conference, 2025.
Neelapu SS, et al. *N Engl J Med* 2017. Assay used for measuring B cells/µl (Epiontis ID®) can detect as low as 2 cells/µl with high accuracy.
CAR, chimeric antigen receptor; IQR, interquartile range; ddPCR, droplet digital polymerase chain reaction.

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Robust and Scalable Manufacturing for Ronde-Cel

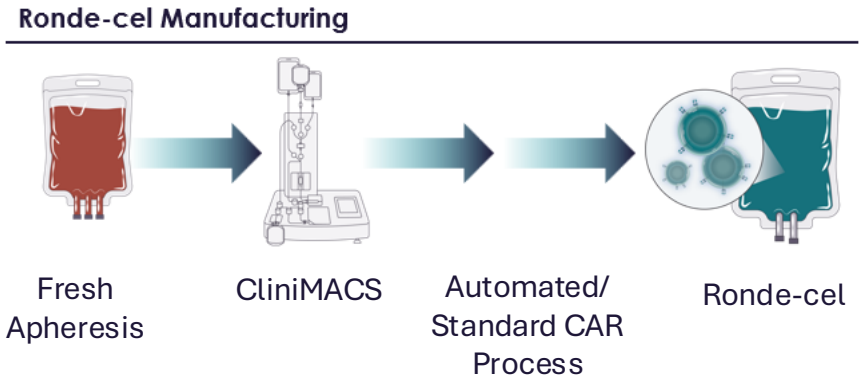
Competitive Median Vein-to-Site Time of 16 Days

LyFE Manufacturing Center™ Built for Scale

- State-of-the-art facility in Bothell, Washington designed specifically to enable commercial readiness
- > 1,200 CAR T-cell doses/year
- Fully electronic systems support secure chain of identity and low deviation rates

Robust, Reliable and Cost-Effective Process Underpins Ronde-Cel Manufacturing

- CD62L+ enrichment designed to improve durability, reduce exhaustion, and lower adverse cytokine production
- Does not extend manufacturing time
- Manufacturing success rate 97% with >100 patients treated with ronde-cel
- Delivers up to 3-fold higher in vivo expansion compared to market-leading CD19 CAR T-cell products



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

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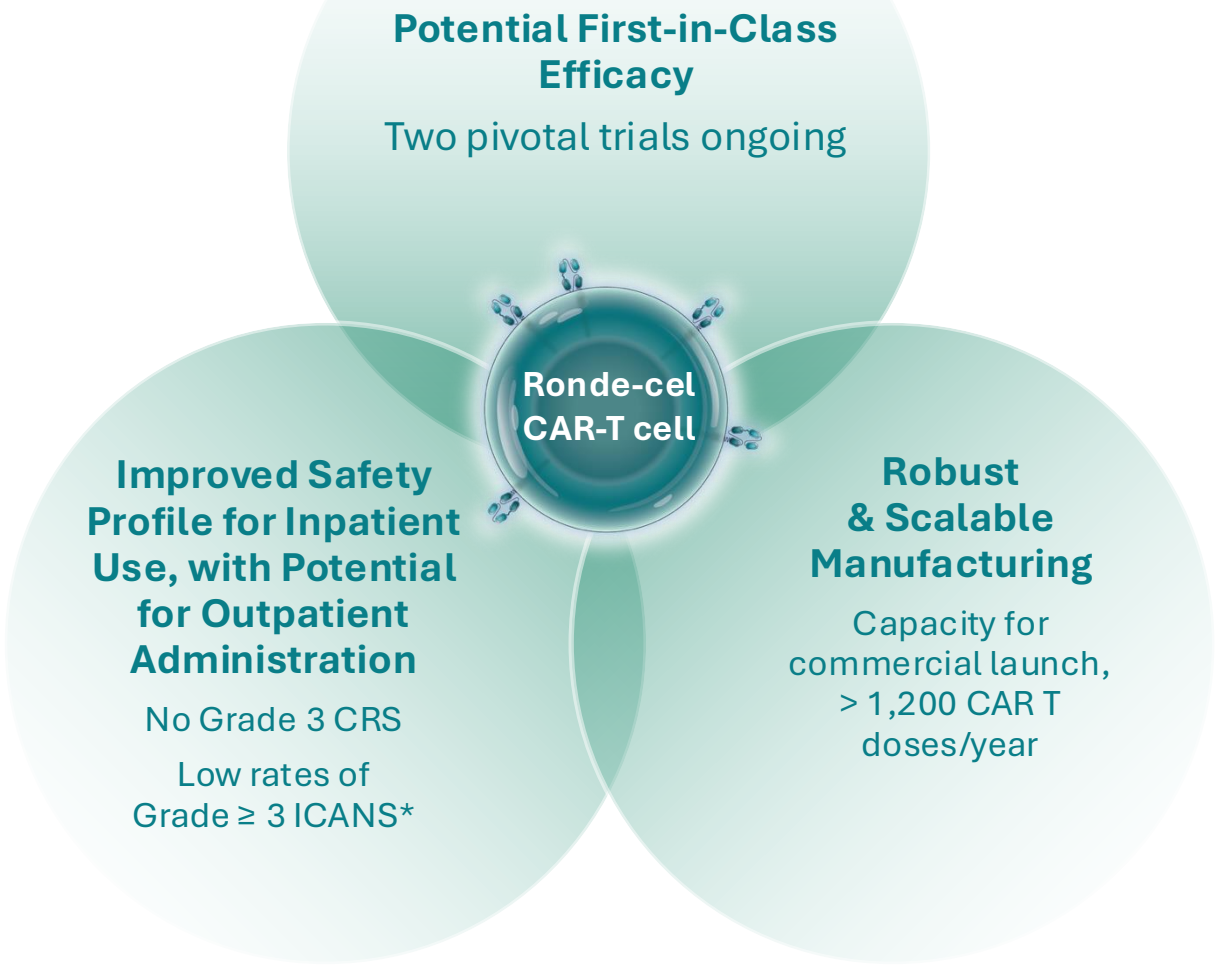
Ronde-Cel Well Positioned to Potentially Redefine the Standard of Care for Relapsed/Refractory Large B-Cell Lymphoma



CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune mediated cell-associated neurotoxicity syndrome: LBCL, large B-cell lymphoma; R/R, relapsed/refractory.
*Dexamethasone prophylaxis with 10 mg on days 0, 1 and 2 of CAR T-cell infusion

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LYL273 for Metastatic Colorectal Cancer

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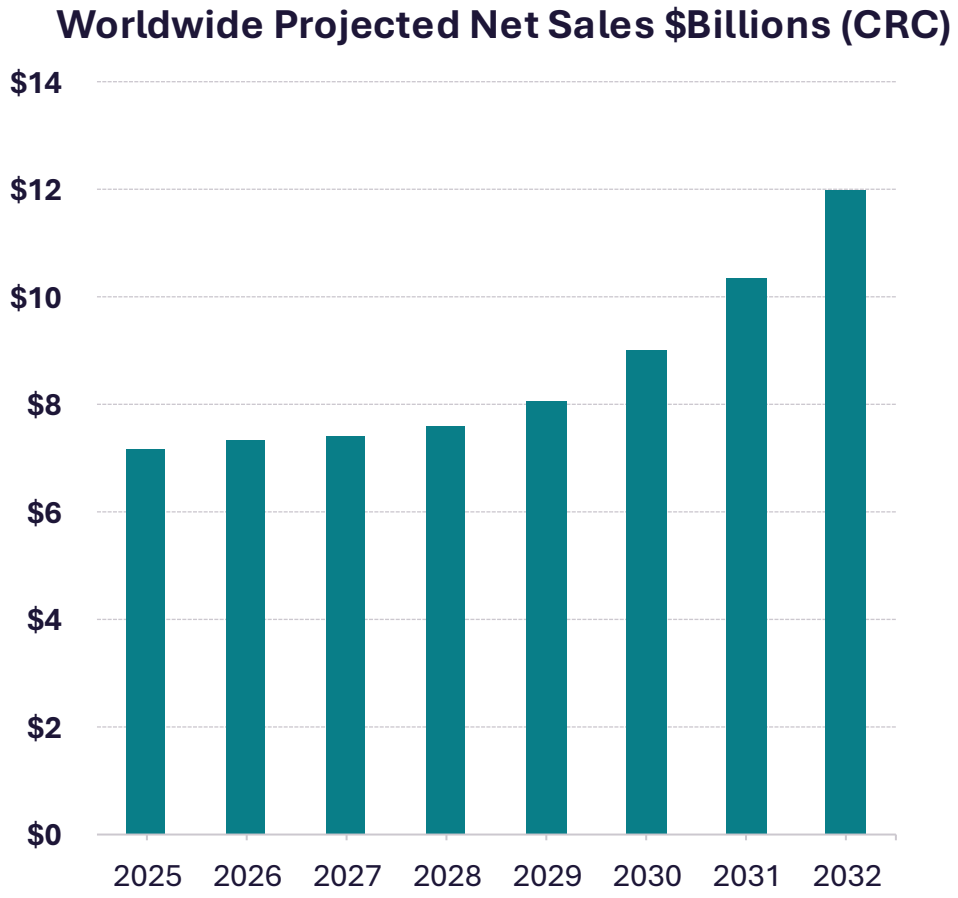
Colorectal Cancer Is the Second Leading Cause of Cancer Deaths Worldwide and is a Large and Growing $6+ Billion Market

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
- Incidence rising rapidly in patients 50 years of age and younger
- ~25% of patients have metastatic disease at diagnosis
- Up to 60% of patients diagnosed with colorectal cancer will develop distant metastases at some point



American Cancer Society and are based on US cases. (2024 and 2025); EvaluatePharma; SEER; Roberson J, et al. *Seminars in Colon and Rectal Surgery* 2023.

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Standard of Care Therapies in 3L+ mCRC Do Not Achieve Meaningful Response Rates or Survival Benefit

A Response Rate of > 20% Would Represent a Meaningful Improvement to Current Standard of Care

Treatment	Overall Response Rate (CR + PR)	Disease Control Rate (CR + PR + SD)	mPFS (months)	mOS (months)
LONSURF® (trifluridine/tipiracil) + AVASTIN® (bevacizumab) SUNLIGHT Trial (N = 246/group)	**6%**	77%	6	11
LONSURF® (trifluridine/tipiracil) RECOURSE Trial (N = 534 TAS-102)	**2%**	44%	2	7
FRUZAQLA® (fruquintinib) FRESCO-2 Trial (N = 461 fruquintinib)	**2%**	56%	4	7
STIVARGA® (regorafenib) CORRECT Trial (N = 505 regorafenib)	**1%**	45%	2	6

Grothey A, et al. *Lancet*, 2013; Mayer RJ, et al. *N Engl J Med* 2015; Prager GW, et al. *N Engl J Med* 2023; Dasari A,et al. *Lancet* 2023.
3L, third- or later-line; mCRC, metastatic colorectal cancer; mPFS, median progression-free survival; mOS, median overall survival.

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

High response rates and manageable safety profile in relapsed/refractory (R/R) metastatic colorectal cancer (mCRC)

LYL273 exhibits significant anti-tumor activity in patients with R/R mCRC with a manageable safety profile

- 50% overall response rate across Dose Levels 1 and 2 in U.S. Phase 1 trial*
- Enrolling patients with R/R mCRC with or without liver metastases in the 3L+ setting

Proof of Concept 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 Dose Level 2 of 25 months with mPFS of 6.0 months, including patients with 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

Scalable, automated closed system manufacturing

*Data cutoff date: October 28, 2025.; LYL273 was licensed in November 2025; Danaee et al, *PLOS One* 2017 and internal data; Chen N, et al. *JAMA Oncol* 2024.
CAR, chimeric antigen receptor; GCC, guanylyl cyclase C; mCRC, metastatic colorectal cancer; mPFS, median progression-free survival.

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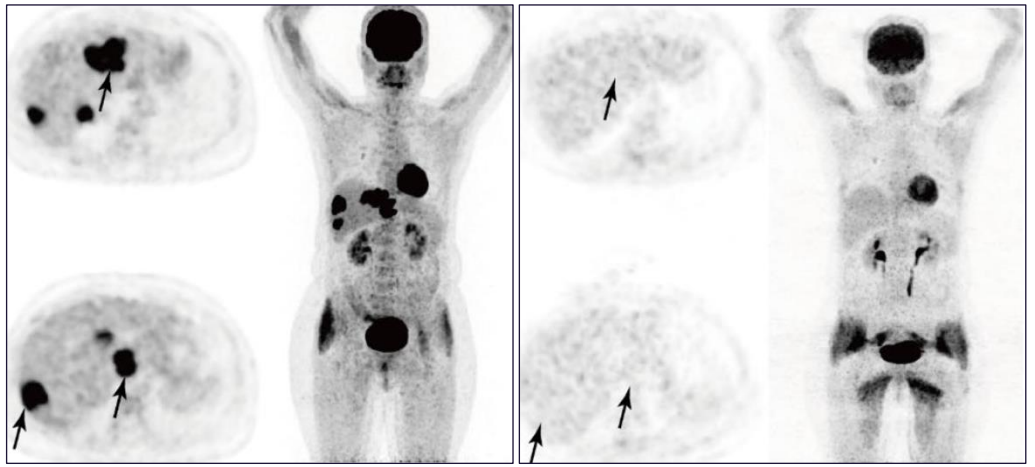
Proof-of-Concept Case Study

Compelling Clinical Responses in Chinese Patients Published in *JAMA Oncology* 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 chemotx
  - 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 on imaging as early as Month 1
- 50% tumor reduction on CT imaging and 96% reduction 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%**

Chen, N, et al, *JAMA Oncol* 2024.

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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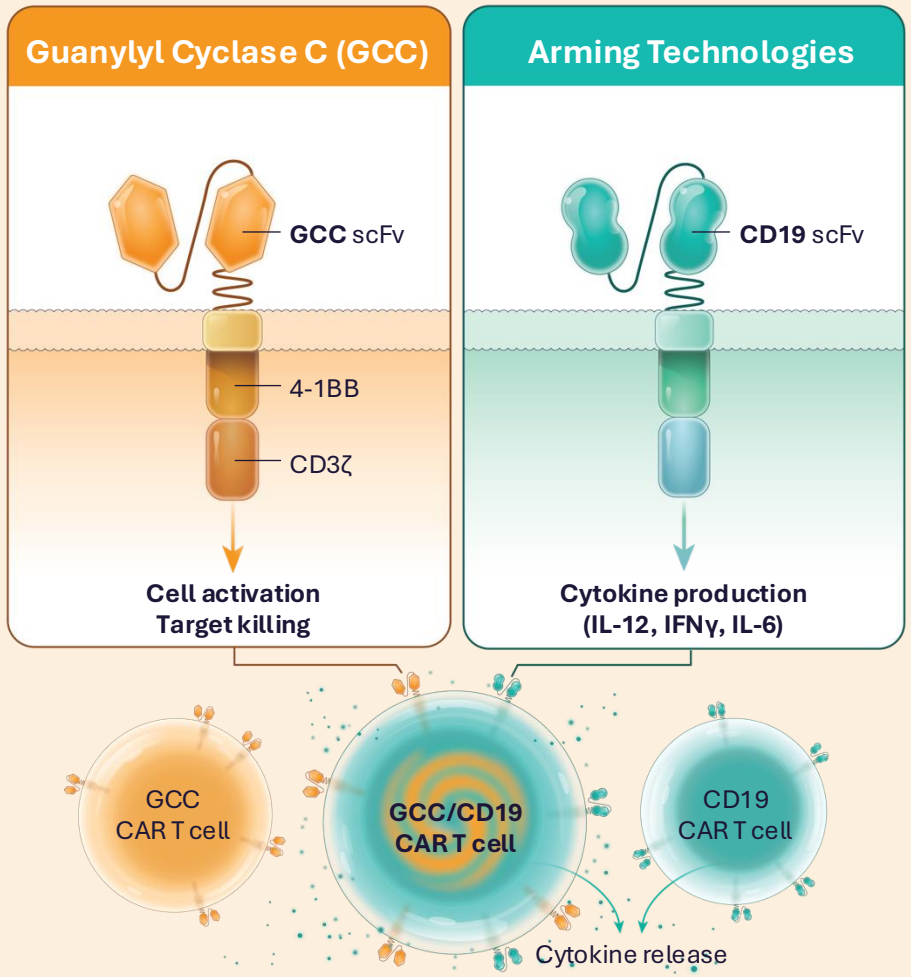
LYL273 is a GCC-Targeted CAR T-Cell Product Candidate Armed with Enhancements to Improve CAR T-Cell Expansion and Cancer Cell Killing



CD19 CAR engineered to release cytokines after engaging B cells, resulting in expansion of CAR T cells that express GCC, CD19, or both

CD19 CAR Arming

- Jump starts CAR T-cell activation and expansion upon infusion by engaging B cells

Controlled Release of Multiple Cytokines Upon T-Cell Activation

- Level of cytokines regulated by specific vector design and usage during manufacturing
- Cytokines enhance CAR T-cell expansion, remodel the suppressive tumor microenvironment and enhance immune cell infiltration and cancer cell killing

CAR, chimeric antigen receptor; GCC, guanylyl cyclase C.

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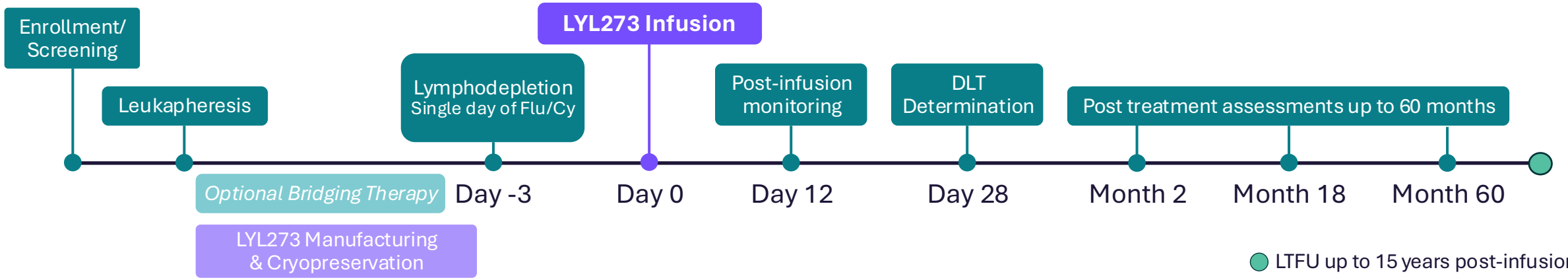
Phase 1 Clinical Trial Design

A Phase 1 Multicenter Trial Evaluating the Safety and Efficacy of LYL273 in Patients with Relapsed/Refractory (R/R) Metastatic Colorectal Cancer (mCRC)



Patient Population

- Adults with relapsed/refractory mCRC
- Prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy
- Anti-VEGF therapy and anti-EGFR therapy (RAS wild-type tumors) required
- ECOG performance status 0 or 1
- Liver mets allowed if no more than 7 and largest lesion < 3 cm
- GCC screening not required for enrollment

Trial Objectives

- Safety and tolerability / maximum tolerated dose
- Overall response rate, complete and partial response rate
- Duration of response
- Progression-free survival and overall survival
- Cell expansion pharmacokinetics

Abbreviations: Cy, cyclophosphamide; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; F/U, follow-up; Flu, fludarabine; GCC, guanylyl cyclase C; LTFU, long-term follow-up; mets, metastases; RAS, rat sarcoma virus; SOC, standard of care; VEGF, vascular endothelial growth factor.

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Baseline Patient Demographics and Disease Characteristics

Characteristics	Dose Level 1 (N = 6)	Dose Level 2 (N = 6)	Overall (N = 12)
Age, year			
Median (range)	46 (39-52)	53 (46-57)	49 (39-57)
Sex, n, %			
Male	3 (50%)	3 (50%)	6 (50%)
Female	3 (50%)	3 (50%)	6 (50%)
Prior Therapies			
Median prior lines, n (range)	3 (2-6)	3 (2-5)	3 (2-6)
Median 5-FU combo regimens e.g., FOLFOX/FOLFIRI, n (range)	2 (1-3)	2 (1-4)	2 (1-4)
LONSURF® (trifluridine/tipiracil), n (%)	1 (17%)	2 (33%)	3 (25%)
AVASTIN® (bevacizumab), n (%)	6 (100%)	6 (100%)	12 (100%)
Disease Sites			
Median (range)	2.5 (1-3)	2 (1-3)	2 (1-3)
Mutations			
MSS/pMMR	6 (100%)	6 (100%)	12 (100%)
RAS mutated	1 (17%)	3 (50%)	4 (33%)

Data cutoff date: October 28, 2025.
FOLFOX, folinic acid (leucovorin), fluorouracil (5-FU), and oxaliplatin; FOLFIRI, folinic acid (leucovorin), 5-fluorouracil (5-FU), and irinotecan.
MSS, microsatellite stable; pMMR, proficient mismatch repair.
LONSURF is a registered trademark of Taiho Pharmaceutical Co., Ltd., AVASTIN is a registered trademark of Genentech, Inc.

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Best Overall Response Rates

Best Overall Response	Dose Level 1 (1×10^6 CAR T cells/kg) N = 6	Dose Level 2 (2×10^6 CAR T cells/kg) N = 6	Total N = 12
Overall Response Rate n (%)	**2 (33%)**	**4 (67%)**	**6 (50%)**
Complete Response	0	1 (17%)*	1 (8%)*
Partial Response	2 (33%)	3 (50%)	5 (42%)
Stable Disease	3 (50%)	1 (17%)	4 (33%)
Progressive Disease	1 (17%)	1 (17%)	2 (22%)
Disease Control Rate (CR + PR + SD)	**5 (83%)**	**5 (83%)**	**10 (83%)**
Median Follow Up (months)	17.0	10.2	11.2
Median PFS (months)	4.0	7.8	4.0
Median Overall Survival (months)	17.0	NR	NR

*This patient was a pathological complete response at autopsy

Data cutoff date: October 28, 2025.
CR, complete response; NR, not reached; PR, partial response; PFS, progression-free survival; SD, stable disease.

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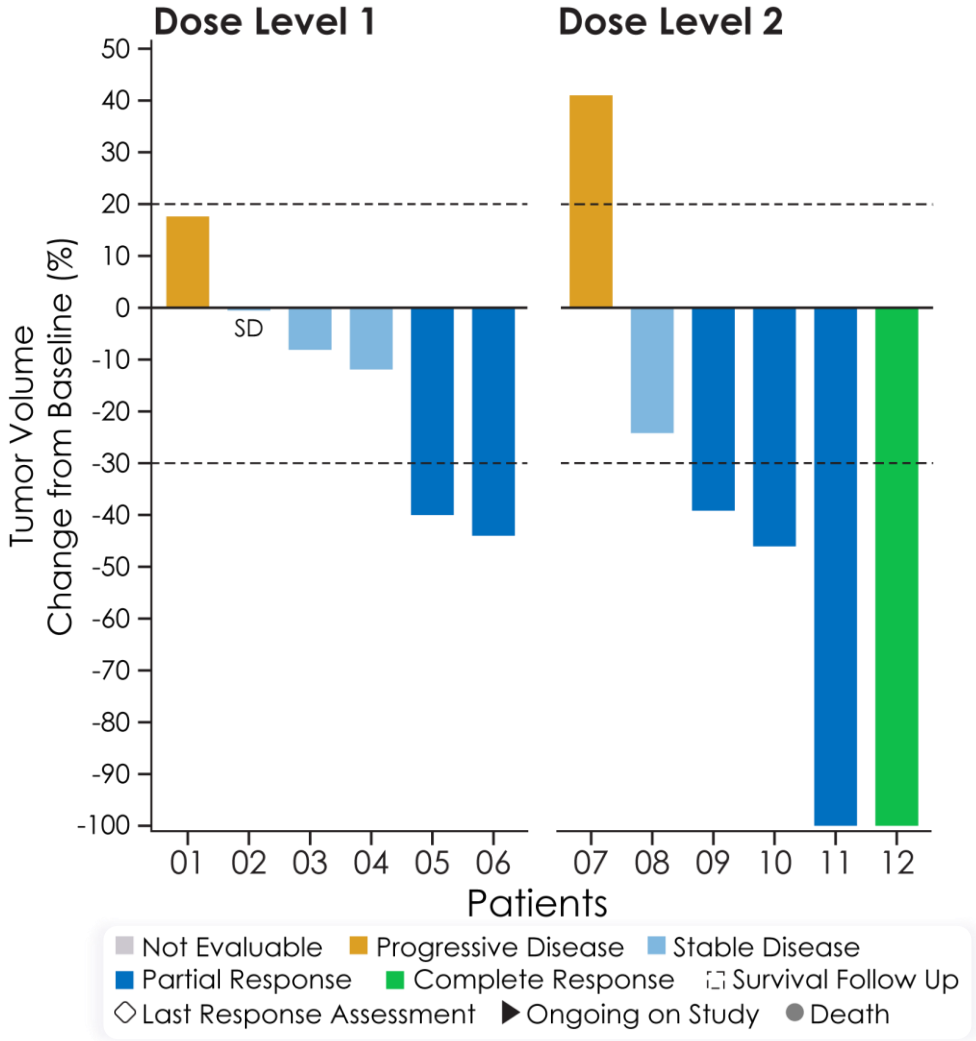
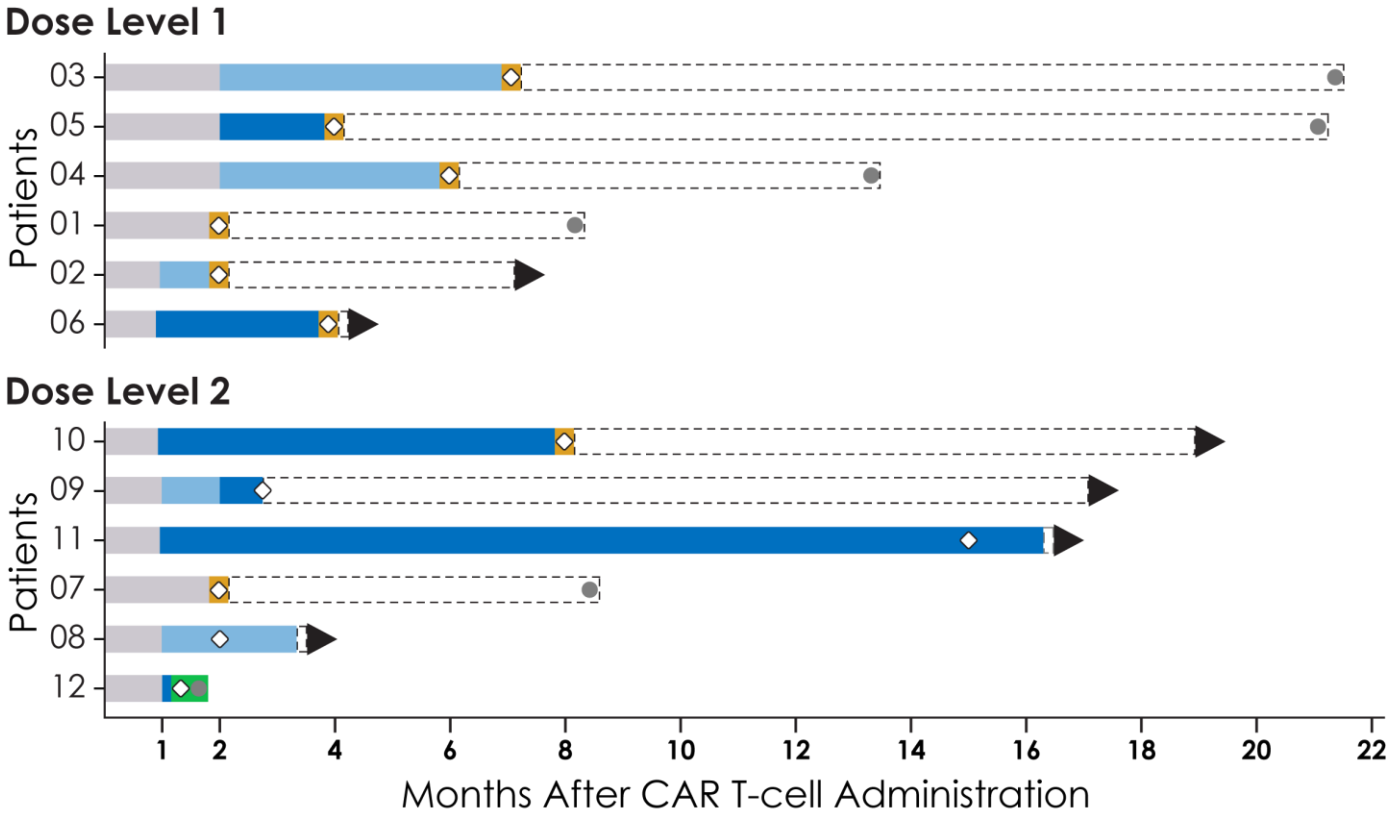
LYL273: High Overall Response Rates in Patients with Relapsed/Refractory Metastatic Colorectal Cancer

Tumor Reduction: Best Overall Response



Swimmer Plot of Each Patient's Response



Pt 09:	Censored after receiving radiation to slightly enlarging lesions (non PD)
Pt 11:	Resolution of target lesions and complete metabolic response by PERCIST, but non-target pulmonary lesion received radiation therapy for micro-foci of adenocarcinoma on biopsy so PR rather than CR by RECIST
Pt 12:	Pathological complete response on autopsy; patient had more than 600 pulmonary lesions at baseline

Data cutoff date: October 28, 2025; all responses as determined by the Investigator; CR, complete response; PD, progressive disease; PERCIST, Positron Emission tomography Response Criteria in Solid Tumors; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors.

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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/Colitis	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/colitis, including GI prophylaxis with infliximab, vedolizumab, and budesonide

Data cutoff date: October 28, 2025.
CRS, cytokine release syndrome; GI, gastrointestinal; ICANS, immune effector cell-associated neurotoxicity syndrome.

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Safety Update for LYL273

June 8, 2026

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Safety Update for Patients With and Without GI Prophylaxis

GI prophylaxis and standardized safety management plan were added to mitigate LYL273 adverse events

GI prophylaxis was added to the protocol to mitigate diarrhea and colitis

- Infliximab, vedolizumab and budesonide after infusion and prior to symptoms

10 patients have been treated with GI prophylaxis and 9 patients without GI prophylaxis at Dose Levels 1 and 2

No difference in patient demographics and disease characteristics were observed between the two groups

- Median age 52 years (range, 39 to 74)
- Median of 4 prior lines of therapy for mCRC (range, 2 to 7)
- Microsatellite stable disease in all patients

Adverse events for Dose Levels 1 and 2 with and without prophylaxis and cell expansion kinetics are presented

The maximum tolerated dose has not been reached

- Escalation to Dose Level 3 recently initiated (data to be presented in 2H 2026)
- Current protocol allows for dose escalation to Dose Level 4 (4 million CAR+ cells/kg)

Data cutoff date: May 5, 2026
GI, gastrointestinal; mCRC, metastatic colorectal cancer

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Updated Safety Data for LYL273 With and Without GI Prophylaxis

LYL273 has a Manageable Safety Profile

Grade ≥ 2 diarrhea/colitis decreased from 55% to 10% with GI prophylaxis

Adverse Events of Interest

	No GI Prophylaxis N = 9	GI Prophylaxis N = 10
CRS, %		
Grade 2	33	0
Grade ≥ 3	0	0
ICANS, %		
Grade 2	11	10
Grade ≥ 3	11	0
Diarrhea/Colitis, %		
Grade 2	33	10
Grade ≥ 3	22	0

Data cutoff date: May 5, 2026.

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

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LYL273 has a Manageable Safety Profile at Dose Level 2

No Grade ≥ 3 CRS, ICANS, or Diarrhea/Colitis Reported for Patients Receiving GI Prophylaxis

Optimization of GI prophylaxis and safety management plan ongoing as recommended Phase 2 dose determined

Adverse Events of Interest	Dose Level 1 (1×10^6 CAR T cells/kg) N = 6		Dose Level 2 (2×10^6 CAR T cells/kg) N = 13	
	No GI Prophylaxis N = 4	GI Prophylaxis N = 2	No GI Prophylaxis N = 5	GI Prophylaxis N = 8
CRS, %				
Grade 2	50	0	20	0
Grade ≥ 3	0	0	0	0
ICANS, %				
Grade 2	0	0	20	13
Grade ≥ 3	0	0	20	0
Diarrhea/Colitis, %				
Grade 2	25	0	40	13
Grade ≥ 3	25	0	20	0

Data cutoff date: May 5, 2026.

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

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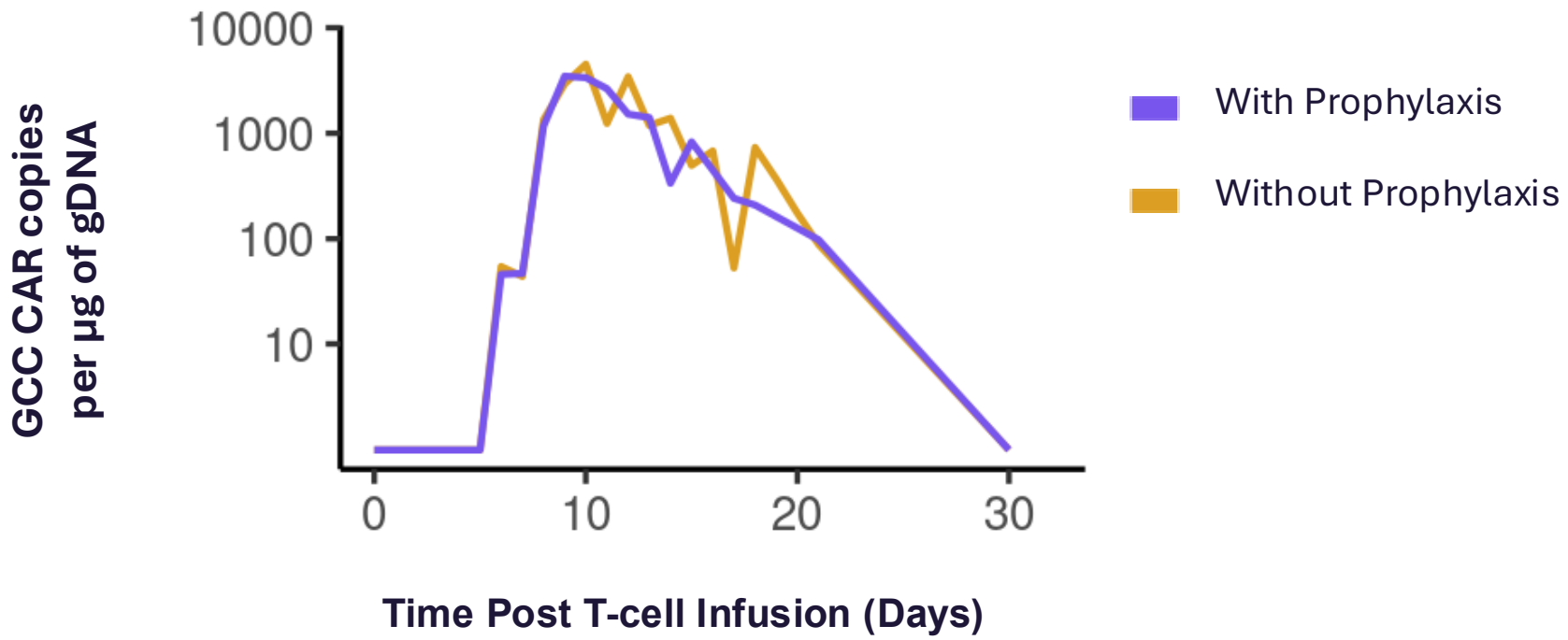
No Difference Observed in GCC-CAR Cell Expansion Kinetics Between Patients With or Without GI Prophylaxis

Both peak and overall exposure for GCC CAR T-cell expansion are similar with and without GI prophylaxis at Dose Levels 1 and 2



Data cutoff date: May 5, 2026.
CAR, chimeric antigen receptor; GI, gastrointestinal; GCC, guanylyl cyclase C.

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LYL273 Has a Manageable Safety Profile With GI Prophylaxis

Grade ≥2 diarrhea/colitis decreased from 55% to 10% with GI prophylaxis

- Based on new safety data and cell expansion kinetics, Lyell has amended the Phase 1 trial to enable seamless expansion into a pivotal single-arm Phase 1/2 trial, pending FDA agreement
- New cohorts to explore LYL273 in patients with 2L mCRC and in combination with radiotherapy are added
- New centers are being activated to support trial expansion
- Dose exploration and optimization of the GI prophylaxis and safety management plan continue to determine the recommended Phase 2 dose

Data cutoff date: May 5, 2026.
FDA, Food and Drug Administration; GI, gastrointestinal; mCRC, metastatic colorectal cancer.

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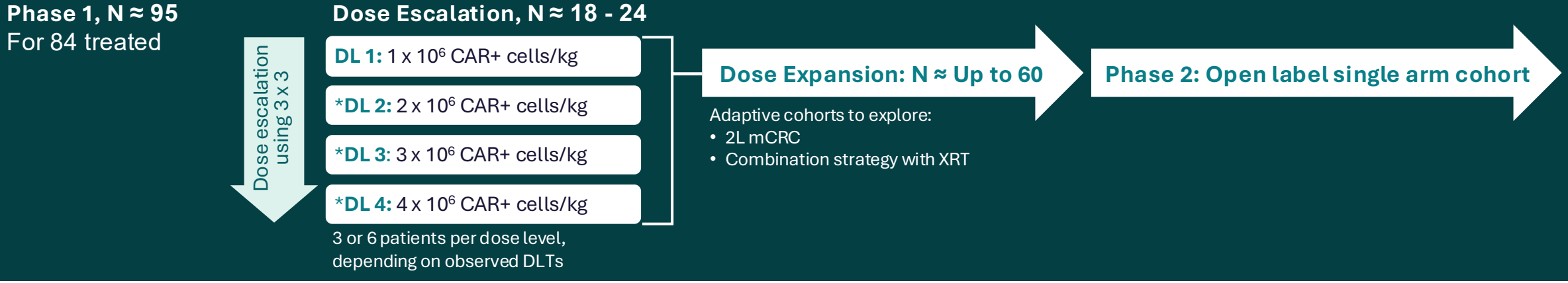
CARAβiNER Trial Overview

A Phase 1/2 Multicenter Trial Evaluating the Safety and Efficacy of LYL273 in Patients with Relapsed/Refractory (R/R) Metastatic Colorectal Cancer (mCRC)

Patient Population: Adult patients with R/R mCRC



Phase 1 Trial Objectives and Endpoints

Primary

- Safety and tolerability
- Determine Maximum Tolerated Dose and/or the RP2D

Secondary

- Best overall response rate per RECIST v1.1 by investigator
- Duration of response, median PFS, overall survival
- Cell expansion pharmacokinetics

Phase 2 Trial Objectives and Endpoints

Primary

- Best overall response rate per RECIST v1.1 by blinded independent central review

Secondary

- Duration of response and median PFS by BICR
- Best overall response rate and mPFS by investigator
- Overall survival
- Adverse event incidence and severity
- Cell expansion pharmacokinetics

*All dose levels above Dose Level 1 are capped at 100 kg of body weight. Abbreviations: AE, adverse event; DL, dose level; DLT, dose-limiting toxicity; BICR, blinded independent central review; MTD, maximum tolerated dose; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, recommended Phase 2 dose; XRT, radiotherapy

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LYL273 Automated Manufacturing Process Fits Seamlessly into the LyFE Manufacturing Center™ Footprint

LyFE capable of commercial launch, can supply > 1,200 CAR T-cell doses/year

- Miltenyi CliniMACS Prodigy® closed, automated manufacturing system for LYL273
- Standardized 7-day manufacturing process
- Easily transferable and scalable
- Clinical product for LYL273 now manufactured at LyFE

Photo: CliniMACS Cell Prodigy System – Cell Factory.

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Cash Runway into Q3 2027 Through Multiple Expected Clinical Milestones

~$228 million* at the end of Q2 2026

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
Early 2026	✓ First patient dosed in Phase 3 randomized controlled trial (PiNACLE-H2H) in 2L
2H 2026	❑ Report updated PiNACLE clinical data ❑ Progress update on PiNACLE-H2H (by end of 2026)
2027	❑ Report pivotal PiNACLE data (mid-2027) ❑ BLA submission for R/R LBCL 3L+ 2H 2027

LYL273	GCC-Targeted CAR T-Cell Therapy for Metastatic Colorectal Cancer
1H 2026	✓ Report updated clinical data from Phase 1 trial
2027	❑ Report updated clinical data from Phase 1/2 trial ❑ End-of-Phase 1 meeting ❑ Initiation of pivotal clinical trial

*Cash, cash equivalents and marketable securities as of June 30, 2026

2L, second line; 3L+, third- or later-line; ASH, American Society of Hematology; BLA, Biologics License Application; CAR, chimeric antigen receptor; GCC, guanylyl cyclase C; ICML, International Conference on Malignant Lymphoma; LBCL, large B-cell lymphoma; R/R, relapsed/refractory.

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Lyell Immunopharma is Well Positioned for Success

- Two clinical-stage programs, one in pivotal trials
- First pivotal trial read-out mid-2027
- Multi-billion-dollar commercial opportunities
- Manufacturing facility with commercial launch capability
- Multiple clinical milestones over the next 12 to 18 months
- Cash runway into Q3 2027

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The Future of Cell Therapy – Today

For more information, please contact
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