CARIBOU BIOSCIENCES®

December 2024

Corporate presentation

Transformative genome-edited therapies for patients

Forward-looking statements

All statements in this presentation, other than statements of historical facts, are forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements speak only as of the date of this presentation and are subject to a number of known and unknown risks, assumptions, uncertainties, and other factors that may cause the actual results, levels of activity, performance, or achievements of Caribou Biosciences, Inc. (the "Company," "Caribou," "we," or "our") to be materially different from those expressed or implied by any forward-looking statements. The words "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential," or "continue" or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. All statements, other than statements of historical facts contained in this presentation, are forward-looking statements, including but not limited to any statements regarding the initiation, timing, progress, strategy, plans, objectives, expectations (including as to the results) with respect to our product candidate preclinical studies, clinical trials, and research programs, including our expectations and timing regarding plans to present ANTLER phase 1 clinical trial data from both the additional second line and prior CD19 relapsed large B cell lymphoma patient cohorts in H1 2025 and the timing of an ANTLER pivotal phase 3 clinical trial; plans to present dose escalation data from the ongoing CaMMouflage phase 1 clinical trial for CB-011 in related or refractory multiple myeloma in H1 2025; plans to provide updates on dose escalation from the AMpLify phase 1 clinical trial for CB-012; the timing of and updates from the GALLOP phase 1 clinical trial for CB-010 in patients with lupus nephritis and extrarenal lupus; our ability to successfully develop our product candidates and to obtain and maintain regulatory approval for our product candidates; the number and type of diseases, indications, or applications we intend to pursue for our product candidates; the beneficial characteristics, safety, efficacy, therapeutic effects, and potential advantages of our product candidates; the expected timing or likelihood of regulatory filings and approval for our product candidates; our expected cash runway; and the sufficiency and anticipated use of our existing capital resources to fund our future operating expenses and capital expenditure requirements and needs for additional financing. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this presentation is given. This presentation discusses product candidates that are or will be under clinical investigation and that have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these product candidates for the therapeutic uses for which such product candidates are being or will be studied.

As a result of many factors, including risks related to our limited operating history, history of net operating losses, financial position and our ability to raise additional capital as needed to fund our operations and product candidate development; uncertainties related to the initiation, cost, timing, and progress, and results of our current and future research and development programs, preclinical studies, and clinical trials; risks that initial or interim clinical trial data will not ultimately be predictive of the safety and efficacy of our product candidates or that clinical outcomes may differ as more clinical data becomes available; the risk that preclinical study results we observed will not be borne out in human patients; our ability to obtain and maintain regulatory approval for our product candidates; risks that our product candidates, if approved, may not gain market acceptance due to negative public opinion and increased regulatory scrutiny of cell therapies involving genome editing; our ability to meet future regulatory standards with respect to our products; our ability to obtain key regulatory input and approvals, our ability to establish and/or maintain intellectual property rights covering our product candidates and genome-editing technology; risks of third parties asserting that our product candidates infringe their patents; developments related to our competitors and our industry; our reliance on third parties to conduct our clinical trials and manufacture our product candidates; the impact of public health crises and geopolitical events on our business and operations; and other risks described in greater detail in our filings with the Securities and Exchange Commission (the "SEC"), including the section titled "Risk Factors" of our Annual Report on Form 10-K for the year ended December 31, 2023, and other filings we make with the SEC; the events and circumstances reflected in our forward-looking statements may not be achieved or may not occur, and actual results could differ materially from those described in or implied by the forward-looking statements contained in this presentation.

Caution should be exercised when interpreting results from separate trials involving other CAR-T cell therapies. The results of other CAR-T cell therapies presented or referenced in these slides have been derived from publicly available reports of clinical trials not conducted by us, and we have not performed any head-to-head trials comparing any of these other CAR-T cell therapies with CB-010. As such, the results of these other clinical trials may not be comparable to clinical results for CB-010. The design of these other trials vary in material ways from the design of the clinical trials for CB-010, including with respect to patient populations, follow-up times, the clinical trial phase, and subject characteristics. As a result, cross-trial comparisons may have no interpretive value on our existing or future results. For further information and to understand these material differences, you should read the reports for the other CAR-T cell therapies' clinical trials and the sources included in this presentation.

In light of the foregoing, you are urged not to rely on any forward-looking statement in reaching any conclusion or making any investment decision about our securities. The forward-looking statements in this presentation are made only as of the date hereof. Except to the extent required by law, the Company assumes no obligation and does not intend to update any of these forward-looking statements after the date of this presentation or to conform these statements to actual results or revised expectations. From time to time, we may release additional clinical data from our ongoing ANTLER phase 1 clinical trial, our CaMMouflage phase 1 clinical trial, our AMpLify phase 1 clinical trial, and our GALLOP phase 1 clinical trial. We make no representations regarding such additional clinical data or the timing of its release, or whether any such data will support or contradict the findings of the clinical data reported earlier.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities.

Precision genome editing with industry-leading expertise

chRDNA precision genome-editing technology

- Novel, next-generation CRISPR technology engineered for **superior specificity and precision**
- **Multiplex editing** designed to maintain genomic integrity

Armored off-the-shelf cell therapies

- Allogeneic CAR-T **enhanced activity**
  - Checkpoint disruption
  - Immune cloaking
- **4 clinical-stage programs** targeting hematologic malignancies and autoimmune diseases

Resourced for successful execution

- Experienced, mission-driven leadership
- Strong in-house process development capabilities
- Robust IP portfolio
- $281M[1] in cash, runway into H2 2026

chRDNA: CRISPR hybrid RNA-DNA

[1] $281.0M in cash, cash equivalents, and marketable securities as of September 30, 2024.

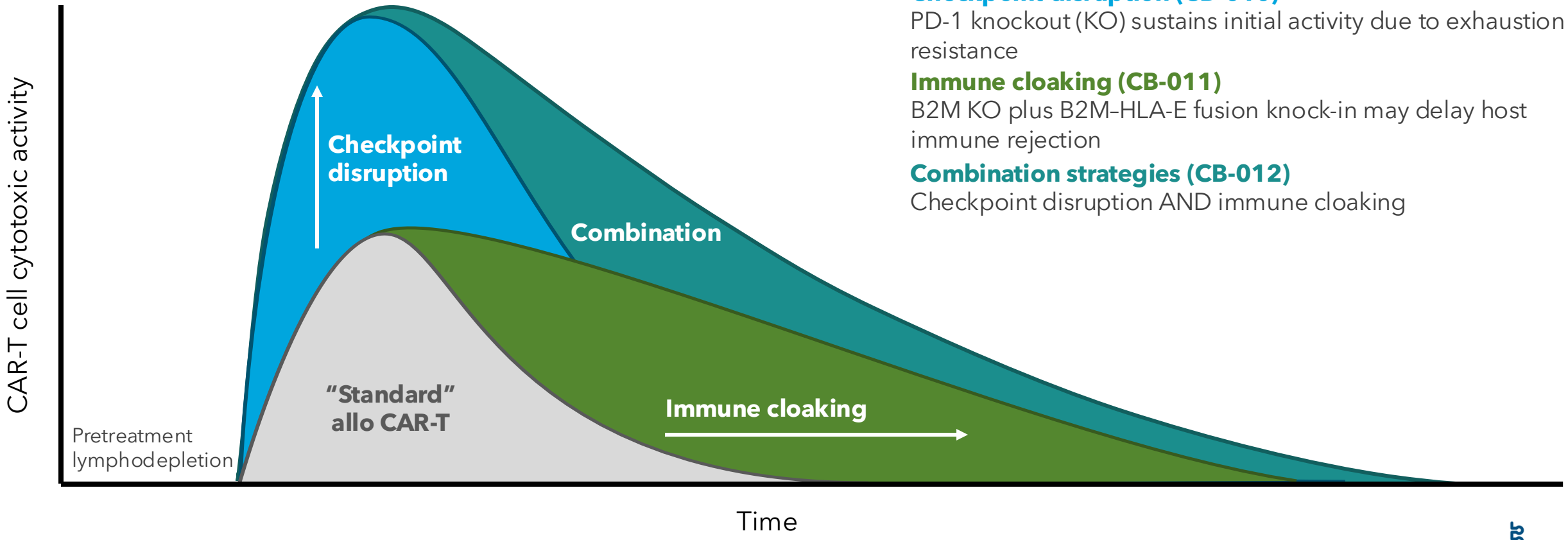
Advancing pipeline of clinical-stage allogeneic CAR-T cell therapies for hematologic malignancies and autoimmune diseases

Program	Target	Indication	Designations	Pre-Clinical	Phase 1	Phase 2	Phase 3	Upcoming milestones
Hematologic malignancies								
CB-010 **ANTLER**	CD19	r/r B-NHL	RMAT, Fast Track, Orphan Drug					H1 2025: partial HLA matching data from 2 cohorts (2L and CD19 relapsed LBCL)
CB-011 **CaMMouflage**	BCMA	r/r MM	Fast Track, Orphan Drug					H1 2025: dose escalation data
CB-012 **AMpLify**	CLL-1	r/r AML	Fast Track, Orphan Drug					
Autoimmune diseases								
CB-010 **GALLOP**	CD19	LN and ERL	Fast Track					YE 2024: initiate Phase 1 trial

LN: lupus nephritis; ERL: extrarenal lupus; RMAT: Regenerative Medicine Advanced Therapy

Engineering for improved activity against disease is key to unlocking the full potential of allogeneic cell therapies

Caribou is implementing multiple armoring strategies



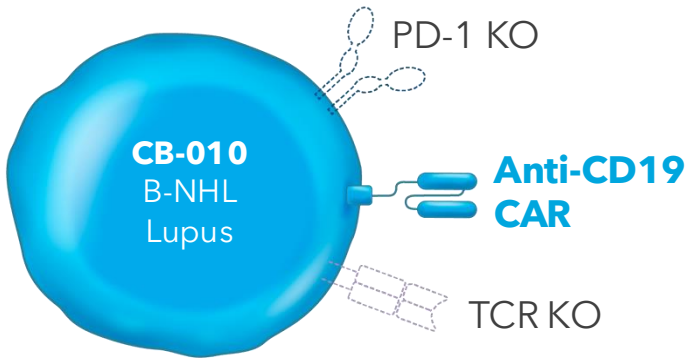
Checkpoint disruption (CB-010)
PD-1 knockout (KO) sustains initial activity due to exhaustion resistance

Immune cloaking (CB-011)
B2M KO plus B2M–HLA-E fusion knock-in may delay host immune rejection

Combination strategies (CB-012)
Checkpoint disruption AND immune cloaking

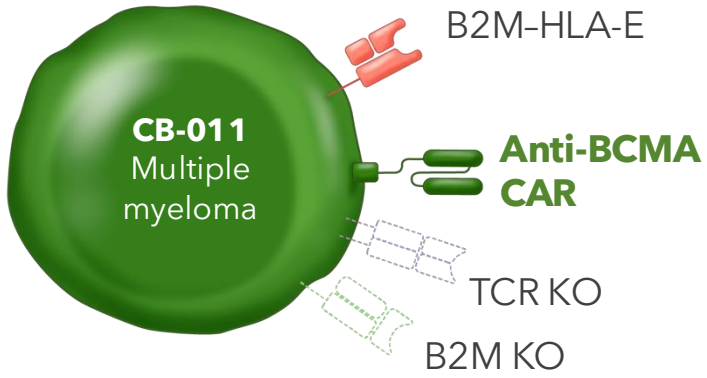
Caribou is a leader in the allogeneic CAR-T cell space with a platform of genome-edited cell therapies

3 Edits



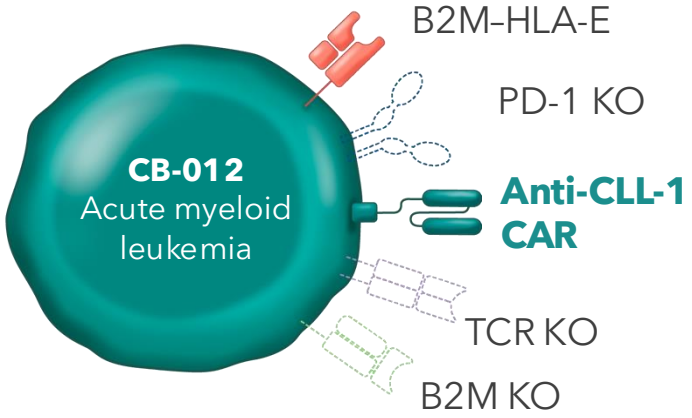
1st allogeneic anti-CD19 CAR-T cell therapy in the clinic with **checkpoint disruption** via PD-1 knockout (KO)[1] to reduce CAR-T cell exhaustion

4 Edits



1st allogeneic anti-BCMA CAR-T cell therapy with **immune cloaking** via *B2M* KO and insertion of B2M–HLA-E fusion protein[1]

5 Edits



1st allogeneic CAR-T cell therapy with both **checkpoint disruption** and **immune cloaking**[1]

[1] To Caribou's knowledge

Patients shouldn't have to wait for treatment

Allogeneic therapy
N=many
per batch

Screening + HLA typing

Product shipment

Days | **Lymphodepletion**

The future of cell therapy is off-the-shelf

Autologous therapy
N=1
per batch

Screening

Queuing, leukapheresis scheduling

Leukapheresis

Sample shipment

Manufacturing, product failure identification

Bridging therapy

Product shipment

Weeks to months[1] | **Lymphodepletion**

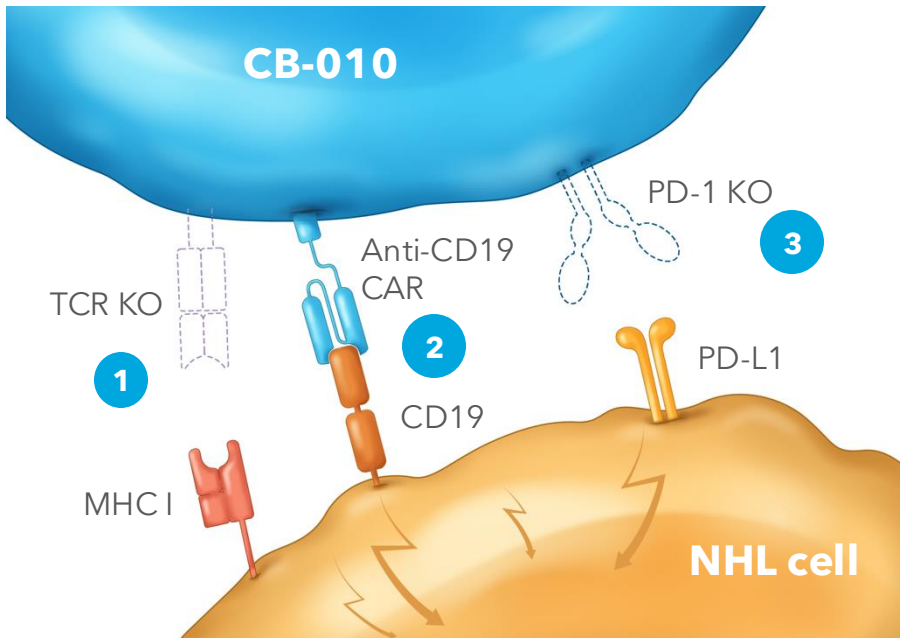
[1] Mikhael, J. et al. JCO Oncology Practice 2022 18:12, 800-807

CB-010

Allogeneic anti-CD19 CAR-T cell therapy with a PD-1 knockout for r/r B cell non-Hodgkin lymphoma (B-NHL)

CARIBOU BIOSCIENCES®

CB-010 has a PD-1 KO designed to reduce CAR-T cell exhaustion



Armored with 3 genome edits

1. ***TRAC* gene knockout (KO)**
   - Eliminates TCR expression, reduces GvHD risk
2. **Anti-CD19 CAR site-specific insertion into *TRAC* locus**
   - Eliminates random integration, targets tumor antigen
3. **PD-1 KO for enhanced antitumor activity**
   - Reduces CAR-T cell exhaustion
   - Potentially contributes to initial tumor debulking

- 1st CAR-T in the clinic with **checkpoint disruption** via PD-1 KO[1]
- Cas9 chRDNA editing for **reduced off-target editing** and enhanced genomic integrity
- **Anti-CD19** scFv FMC63 with a 4-1BB costimulatory domain

CAR: chimeric antigen receptor; KO: knockout; CD: cluster of differentiation; chRDNA: CRISPR hybrid RNA-DNA; CRISPR: clustered regularly interspaced short palindromic repeats; PD-1: programmed cell death protein 1; TCR: T cell receptor; *TRAC*: T cell receptor alpha constant; scFv: single-chain variable fragment

[1] To Caribou's knowledge.

CB-010 ANTLER Phase 1 trial in 2L LBCL

✓ **Dose escalation**
r/r B-NHL[1]
- ✓ 16 patients dosed
- ✓ Generally well tolerated at all dose levels

✓ **Dose expansion**
2L LBCL[2]
- ✓ 30 patients dosed
- ✓ $80x10^6$ CAR-T cells selected as RP2D

Enrolling in ongoing Phase 1 trial

Cohort 1: 2L LBCL[2]
- Enrolling ~20 patients
- Confirmatory cohort of CB-010 with HLA matching strategy

Cohort 2: Relapsed after CD19 therapy LBCL
- Enrolling ~10 patients
- Evaluate safety and efficacy of CB-010 in patients after relapse with prior CD19 treatment

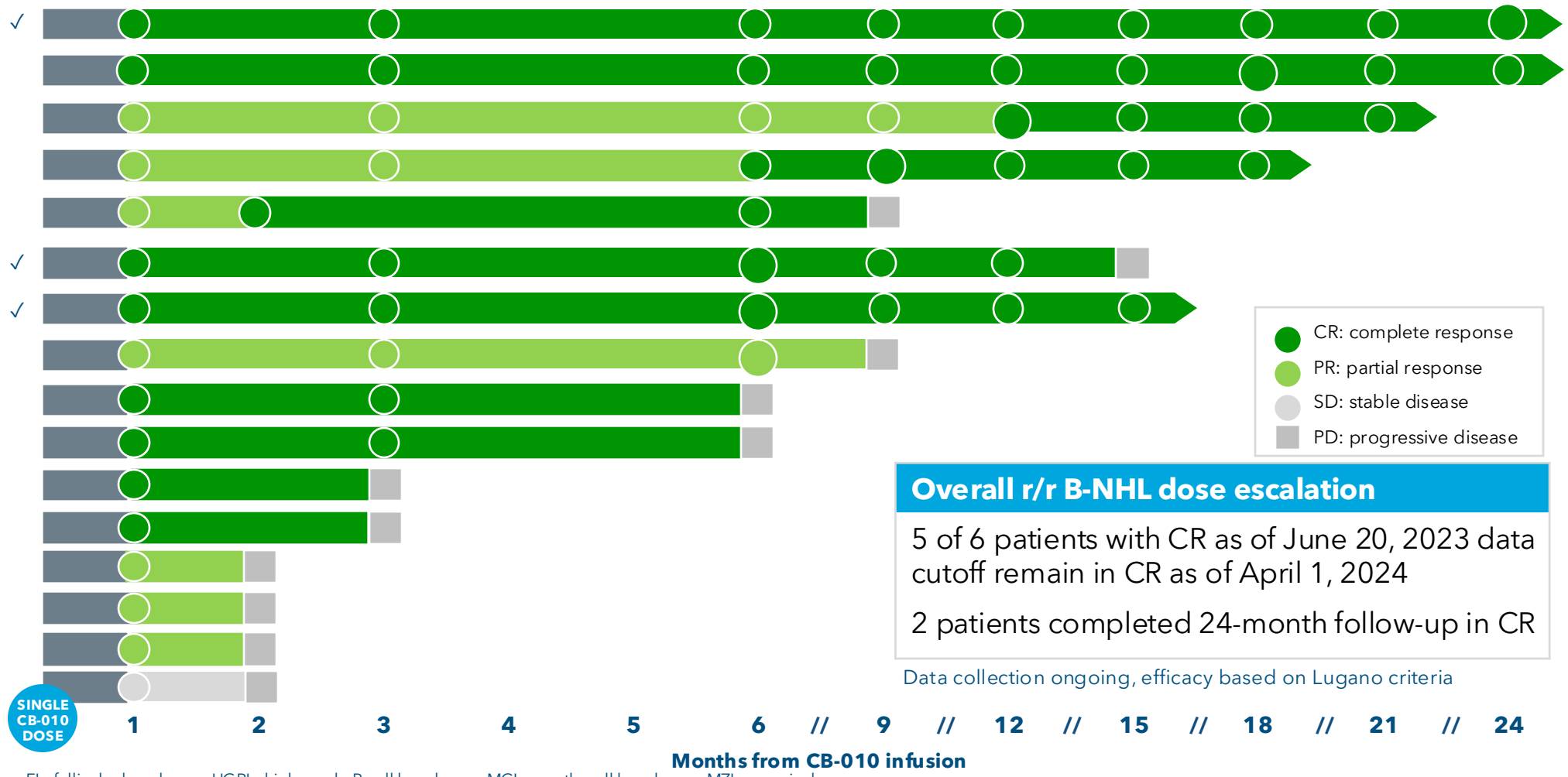
ANTLER trial design for all cohorts

NCT04637763
HLA: human leukocyte antigen
[1] Subtypes include: DLBCL (diffuse large B cell lymphoma), HGBL (high-grade B cell lymphoma), tFL (transformed DLBCL from follicular lymphoma, PMBCL (primary mediastinal large B cell lymphoma), FL (follicular lymphoma, aggressively behaving with POD24 (high risk)), MZL (marginal zone lymphoma)
[2] LBCL subtypes include: DLBCL NOS (DLBCL not otherwise specified), HGBL, transformed DLBLC from FL or MZL, and PMBCL
[3] Clin Cancer Res. 2011 July 1; 17(13): 4550–4557. doi:10.1158/1078-0432.CCR-11-0116

CB-010's foundational data: durable responses in dose escalation

4 of 4 DLBCL patients remain in CR since last data cutoff June 20, 2023

Subtype	Dose	PLoT	Pt #	≥4 HLA
FL[1]	40M	8	1	✓
DLBCL	40M	4	4	
DLBCL	80M	1	7	
DLBCL	80M	1	8	
PMBCL[2]	40M	2	5	
MCL	40M	2	13	✓
DLBCL	80M	2	9	✓
MZL	80M	4	15	
MCL	40M	4	2	
FL[1]	40M	2	3	
DLBCL	40M	2	6	
DLBCL	120M	2	10	
HGBL	40M	1	14	
MCL	80M	2	16	
HGBL	120M	1	12	
DLBCL	120M	2	11	



Overall r/r B-NHL dose escalation

5 of 6 patients with CR as of June 20, 2023 data cutoff remain in CR as of April 1, 2024

2 patients completed 24-month follow-up in CR

Data collection ongoing, efficacy based on Lugano criteria

DLBCL: diffuse large B cell lymphoma; FL: follicular lymphoma; HGBL: high-grade B cell lymphoma; MCL: mantle cell lymphoma; MZL: marginal zone lymphoma; PLoT: prior lines of therapy (#); PMBCL: primary mediastinal large B cell lymphoma

✓ = patients with ≥4 HLA (human leukocyte antigen) matches (all other patients have ≤3 HLA matches)

[1] Aggressively behaving, with POD24 (high risk)

[2] Patient 5's 3-month scan conducted on day 63 post CB-010 as per investigator's discretion

ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing

CB-010 with partial HLA matching shows safety, efficacy, and durability can potentially rival autologous CAR-T cell therapies

1 dose per patient,
3 dose levels evaluated,
all generally well tolerated

RP2D selected
80x10^6 CAR-T cells

2L LBCL at RP2D
CR rate: 50%
Median duration of CR: NR

Median PFS
14.4 months
(95% CI: 1.7-NE)
observed in 13 patients with partial (≥4) HLA matching[1]

Enrolling in ANTLER with HLA matching strategy in 2L LBCL

2L: second-line; 3L: third-line; B-NHL: B cell non-Hodgkin's lymphoma; CI: confidence interval; CR: complete response; HLA: human leukocyte antigen; LBCL: large B cell lymphoma; NE: not estimable; NR: not reached; PFS: progression free survival; partial HLA matching: patient has ≥4 HLA alleles that match donor T cells used for CB-010 manufacturing; RP2D: recommended Phase 2 dose
[1]Retrospective analysis in 13 patients with ≥4 HLA allele matching; subset includes: 2L LBCL (N=10), 3L LBCL (N=1), and 3L+ BNHL (N=2) ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing

Patients in ANTLER all had aggressive r/r B-NHL

Patient and disease characteristics	All treated (N=46)	Dose escalation (N=16)	Dose expansion (N=30)
Age, years, median (range)	65.0 (21-82)	66.0 (55-82)	63.0 (21-78)
Men, n (%)	36 (78.3)	14 (87.5)	22 (73.3)
ECOG performance status, n (%)			
0	21 (45.7)	6 (37.5)	15 (50.0)
1	25 (54.3)	10 (62.5)	15 (50.0)
Time since diagnosis, months, median (range)	10.6 (2.9-196.4)	29.0 (2.9-196.4)	9.5 (4.9-79.6)
NHL subtype, n (%)			
LBCL			
DLBCL	26 (56.5)	7 (43.8)	19 (63.3)
HGBL	8 (17.4)	2 (12.5)	6 (20.0)
tFL	4 (8.7)	0	4 (13.3)
PMBCL	2 (4.3)	1 (6.3)	1 (3.3)
Other B-NHL			
MCL	3 (6.5)	3 (18.8)	0
FL[1]	2 (4.3)	2 (12.5)	0
MZL	1 (2.2)	1 (6.3)	0
Prior systemic therapies, median (range)[2]	1 (1-8)	2 (1-8)	1 (1-1)
IPI score at screening, n (%)[3]			
0 or 1	11 (23.9)	4 (25.0)	7 (23.3)
2	8 (17.4)	2 (12.5)	6 (20.0)
≥3	18 (39.1)	3 (18.8)	15 (50.0)
Maximum lesion diameter ≥7.5 cm, n (%)	10 (21.7)	3 (18.8)	7 (23.3)
LDH at screening, U/L, median (range)	216 (126-1799)	202 (126-710)	233.5 (140-1799)
Baseline LDH > ULN, n (%)	23 (50.0)	5 (31.3)	18 (60.0)
LDH >2 x ULN, n (%)	7 (15.2)	1 (6.3)	6 (20.0)

DLBCL: diffuse large B cell lymphoma; FL: follicular lymphoma; HGBL: high-grade B cell lymphoma; IPI: International Prognostic Index; LDH: lactate dehydrogenase; MCL: mantle cell lymphoma; MZL: marginal zone lymphoma; PMBCL: primary mediastinal large B cell lymphoma; tFL: transformed follicular lymphoma; ULN: upper limit of normal

[1] Aggressively behaving, with POD24 (high risk)

[2] Patients are CD19 CAR-T naïve

[3] IPI scores were not recorded for all patients

As of April 1, 2024 cutoff date

CB-010 has a generally well-tolerated safety profile

No Grade ≥3 CRS, no GvHD observed (N=46)

	All CB-010 treated (N=46)		Yescarta (N=170)	
	Any grade (n, %)	Grade ≥3 (n, %)	Any grade (n, %)	Grade ≥3 (n, %)
Prolonged cytopenias	9 (20)[1]	9 (20)[1]	49 (29)[2]	49 (29)[2]
CRS	26 (57)[3]	0 (0)	157 (92)	11 (6)
Infections	22 (47)[4]	10 (22)[4]	76 (45)	28 (17)
ICANS	10 (22)[5]	3 (7)[6]	102 (60)	36 (21)
Hemophagocytic lymphohistiocytosis (HLH)	1 (2)	0	NR	NR
GvHD	0	0	NR	NR

FOR ILLUSTRATIVE PURPOSES ONLY: The results of other CAR-T cell therapies presented on this slide have been derived from publicly available reports of a clinical trial run independently of Caribou. The Company has not performed any head-to-head trials comparing any other CAR-T cell therapies with CB-010. As such, the results of other clinical trials may not be comparable to clinical results for CB-010. The design of other trials varies in material ways from the design of the clinical trial for CB-010, including with respect to patient populations, follow-up times, the clinical trial phase, and subject characteristics. As a result, cross-trial comparisons may have no interpretive value on the Company's existing or future results. For further information and to understand these material differences, you should read the reports for the other trial at the sources included below.

CRS: cytokine release syndrome; GvHD: graft-versus-host disease; ICANS: immune effector cell–associated neurotoxicity syndrome; NR: not reported

[1] Prolonged cytopenias are defined as grade 3 or higher events lasting beyond 30 days following CB-010 infusion; 37/46 (80%) recovered from cytopenias to grade ≤2 by day 35 post CB-010 treatment

[2] Prolonged cytopenias of grade 3 or higher that were present at or after 30 days from Yescarta infusion

[3] Median time of onset was 3 days (range 0-22) and median duration was 3 days (range 1-19)

[4] Infection events reported were on or after CB-010 infusion, with highest grade reported per patient; median onset 8 days (range 0-279) and media duration is 14 days (range 1-239)

[5] Median time of onset was 7.5 days (range 6-34) and median duration was 2 days (range 1-27)

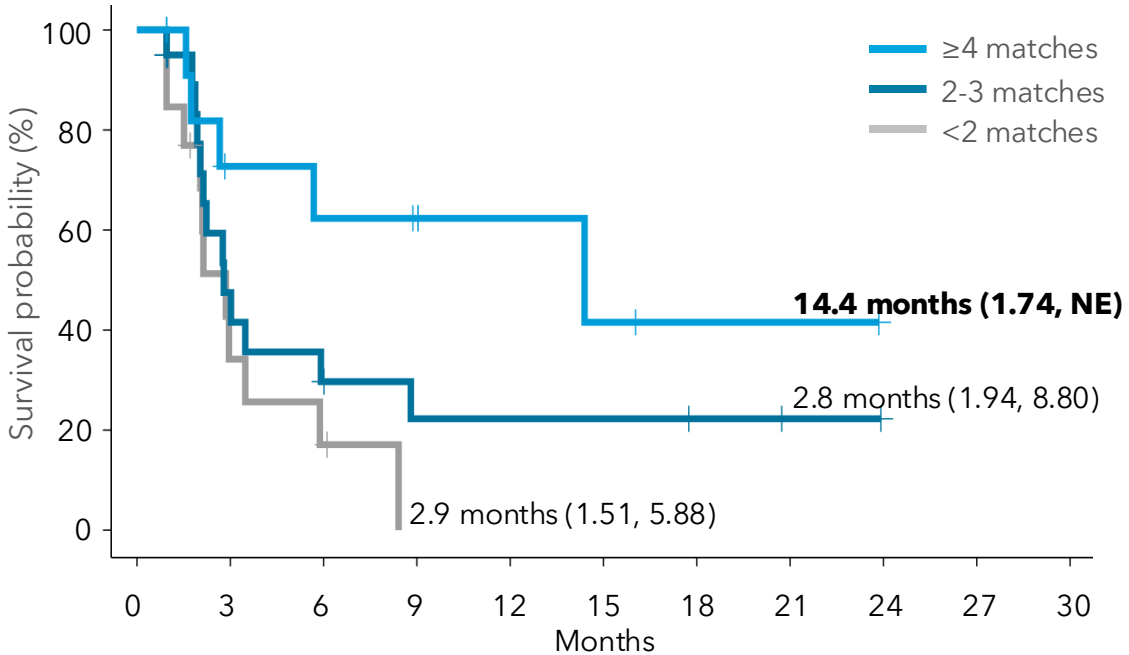
[6] 2 Grade 3 and 1 Grade 4; all resolved with supportive care. Median time of onset was 8 days and median duration 2 days

ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing

Source: ZUMA-7, Locke et al, NEJM, 2022 (prolonged cytopenia at 30 days), Westin et al, NEJM, 2023 (CRS, infections, ICANS/neurological events)

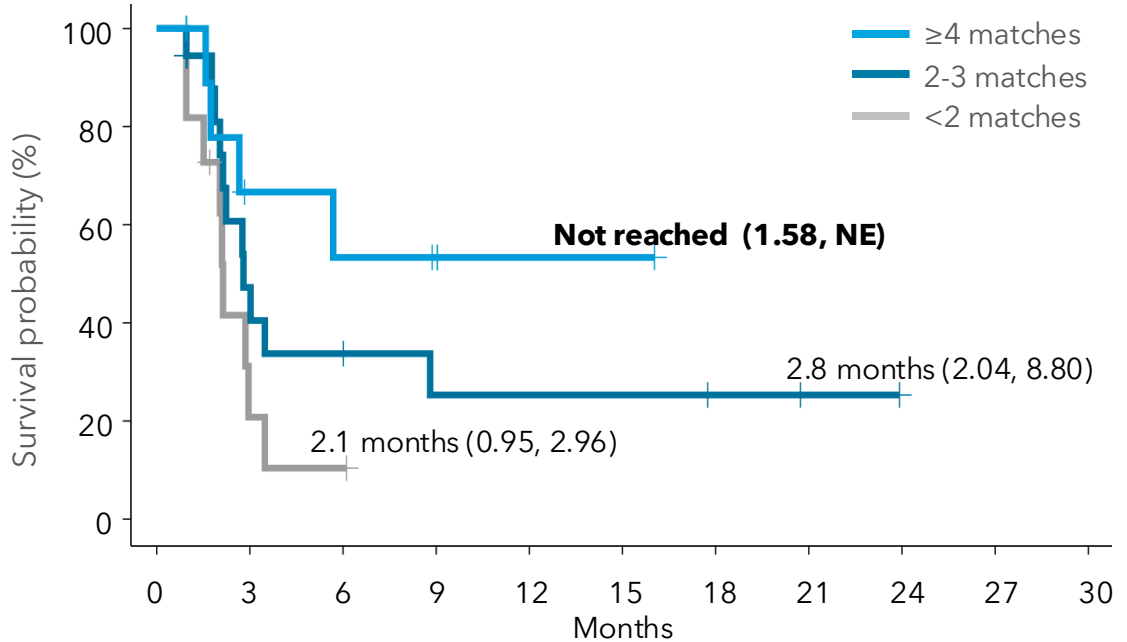
Improved PFS for all patients treated with CB-010 from a donor with partial HLA matching

PFS by level of HLA matching
All patients
N=46*, median PFS (95% CI)



≥4	13	7	6	5	3	2	1	1	0		
2-3	20	8	5	3	3	3	2	1	0		
<2	13	4	2	0							

PFS by level of HLA matching
LBCL patients
N=40*, median PFS (95% CI)



≥4	11	5	4	3	1	1	0				
2-3	18	7	5	3	3	3	2	1	0		
<2	11	2	1	0							

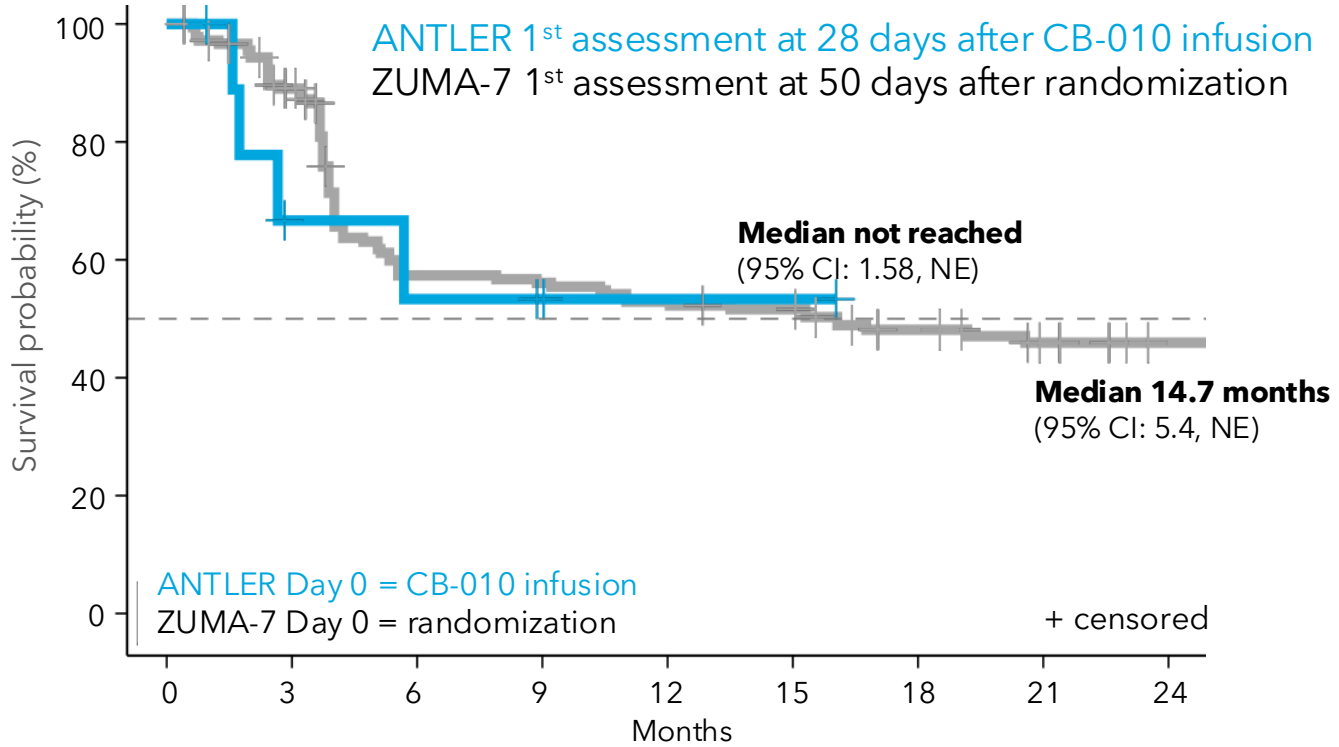
CI: confidence interval; HLA: human leukocyte antigen; NE: not estimable; partial HLA matching: patient has ≥4 HLA alleles that match donor T cells used for CB-010 manufacturing

*Retrospective analysis of HLA allele matching for class I and class II antigens

ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing

Preliminary PFS with partial HLA matching has potential to be on par with an approved autologous CAR-T cell therapy

ANTLER LBCL patients with partial HLA matching and Yescarta ZUMA-7 trial



CB-010[1]	11	5	4	3	1	1	0		
Yescarta	180	147	90	88	83	80	56	35	12

FOR ILLUSTRATIVE PURPOSES ONLY: The results of other CAR-T cell therapies presented on this slide have been derived from publicly available reports of clinical trials run independently of Caribou and the data has been digitally recreated from publicly available original sources to compare approximations of the findings. The Company has not performed any head-to-head trials comparing any of these other CAR-T cell therapies with CB-010. As such, the results of these other clinical trials may not be comparable to clinical results for CB-010. The design of these other trials vary in material ways from the design of the clinical trials for CB-010, including with respect to patient populations, follow-up times, the clinical trial phase, and subject characteristics. As a result, cross-trial comparisons may have no interpretive value on the Company's existing or future results. For further information and to understand these material differences, you should read the reports for the other trials at the sources included below.

Source: ZUMA-7, Locke et al, NEJM, 2022

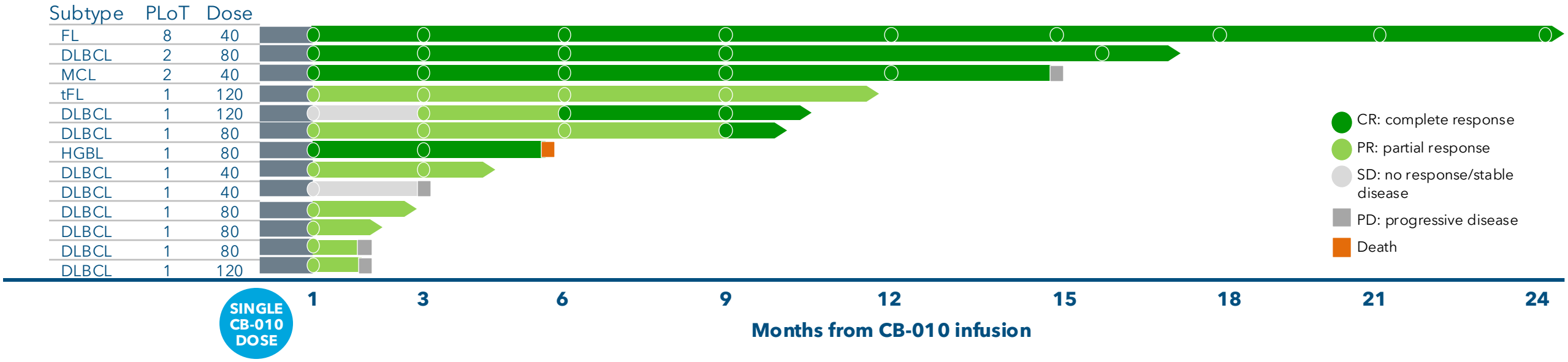
PFS: progression free survival; 2L: second-line; 3L: third-line; LBCL: large B cell lymphoma; HLA: human leukocyte antigen; NE: not estimable; partial HLA matching: patient has ≥4 HLA alleles that match donor T cells used for CB-010 manufacturing

[1] N=11 ≥4 HLA matching subset includes: 2L LBCL patients (N=10) and 3L LBCL patient (N=1).

ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing.

CB-010 ANTLER efficacy assessment for patients with ≥4 HLA matching

(N=13)



Median PFS	CR[1] rate	Median duration of CR
14.4 months	**46%**	**Not reached**

DLBCL: diffuse large B cell lymphoma; CR: complete response; HGBL: high-grade B cell lymphoma; PFS: progression free survival; PMBCL: primary mediastinal large B cell lymphoma; tFL: transformed DLBCL from follicular lymphoma; PLoT: prior lines of therapy

[1] 46% CR rate measures the number of patients (6 of 13) achieving a CR at any time point after treatment with CB-010.

As of April 1, 2024, data collection ongoing, efficacy based on Lugano criteria.

CB-010 ANTLER efficacy assessment with and without partial HLA matching

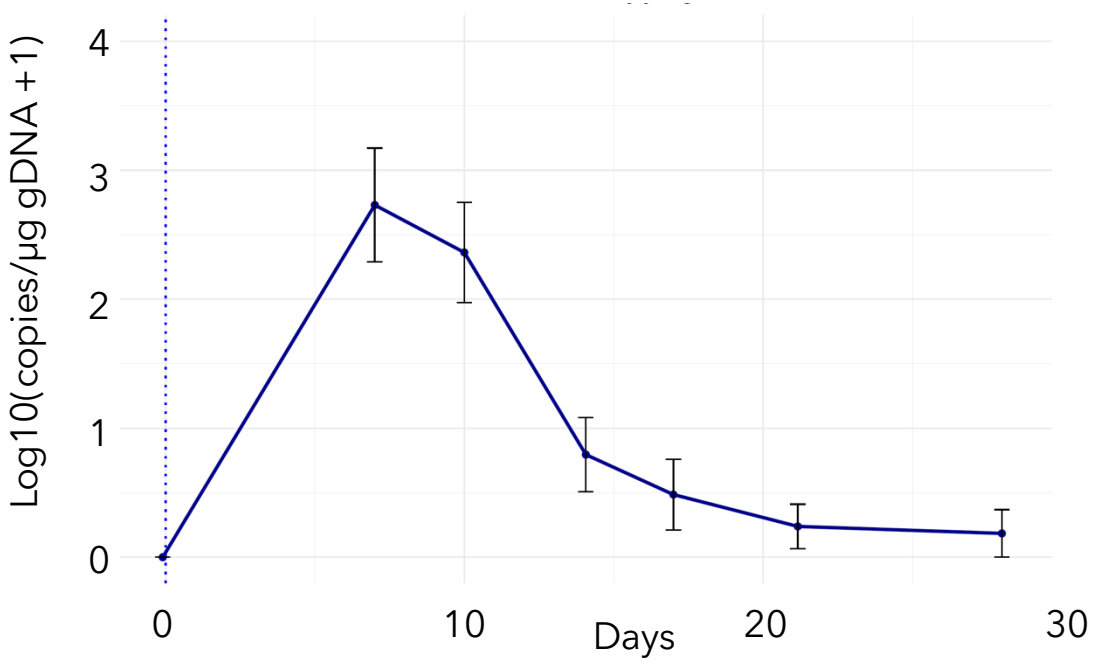
Endpoints (N, %)	All patients ≤3 HLA matches (N=33)	All patients ≥4 HLA matches (N=13)	LBCL ≥4 HLA matches (N=11)
Overall response rate (ORR)	23 (69%)	12 (92%)	10 (91%)
Duration of response (DoR), median months (range)	2.0 (1-23+)	13.5 (1-23+)	NR (1-15+)
Complete response (CR) rate	15 (45%)	6 (46%)	4 (36%)
Duration of CR, median months (range)	5.0 (1-23+)	NR (5-23+)	NR (5-15+)
6-month PFS	25%	62%	53%
PFS, median months (range)	2.8 (1-24+)	14.4 (2-24+)	NR (2-16+)

+ censored observation

18 HLA: human leukocyte antigen; partial HLA matching: patient has ≥4 HLA alleles that match donor T cells used for CB-010 manufacturing; NR: not reached
ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing.

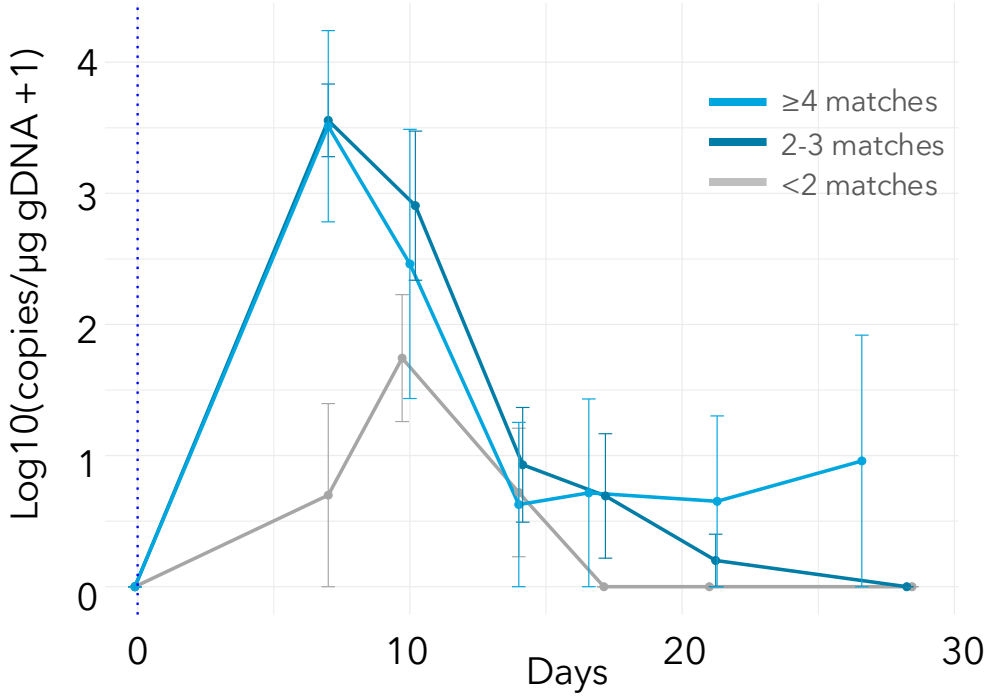
Partial HLA matching improves exposure of CB-010

Pharmacokinetic (PK) exposure



- Peak expansion (C_{max}) occurred 7 to 10 days post infusion
- Persistence was observed up to ~30 days
- PK consistent for three dose levels evaluated

Partial HLA matching impact on PK



- Higher numbers of HLA matched alleles demonstrate more expansion and persistence vs. lower numbers

LLOQ: lower limit of quantification
Mean values represented by dots with standard error shown; values below LLOQ converted to 0; Includes all available data from the V2 ddPCR assay; visits up to D28 shown; D0 values represent pre-infusion level set to 0.
N=35 total number of patients included in PK analysis based on samples analyzed as of data cutoff of April 1, 2024.

CB-010 with partial HLA matching shows safety, efficacy, and durability can potentially rival autologous CAR-T cell therapies[1]

- Advancing CB-010 to establish new standard of care for 2L LBCL and broaden patient access
- Generally well-tolerated safety profile
- Off-the-shelf, readily-available single dose cell therapy
- RMAT and Fast Track designations enable FDA interactions
- Safety and efficacy profile supports clinical development for 2L LBCL and lupus patients and in outpatient setting

Progression free survival

14.4 months

median (95% CI: 1.7-NE)
all patients with ≥4 HLA matches

NR

median (95% CI: 1.6-NE)
all LBCL patients with ≥4 HLA matches

2L: second-line; LBCL: large B cell lymphoma; PFS: progression free survival; HLA: human leukocyte antigen
[1]To be confirmed with additional clinical data.
ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing.

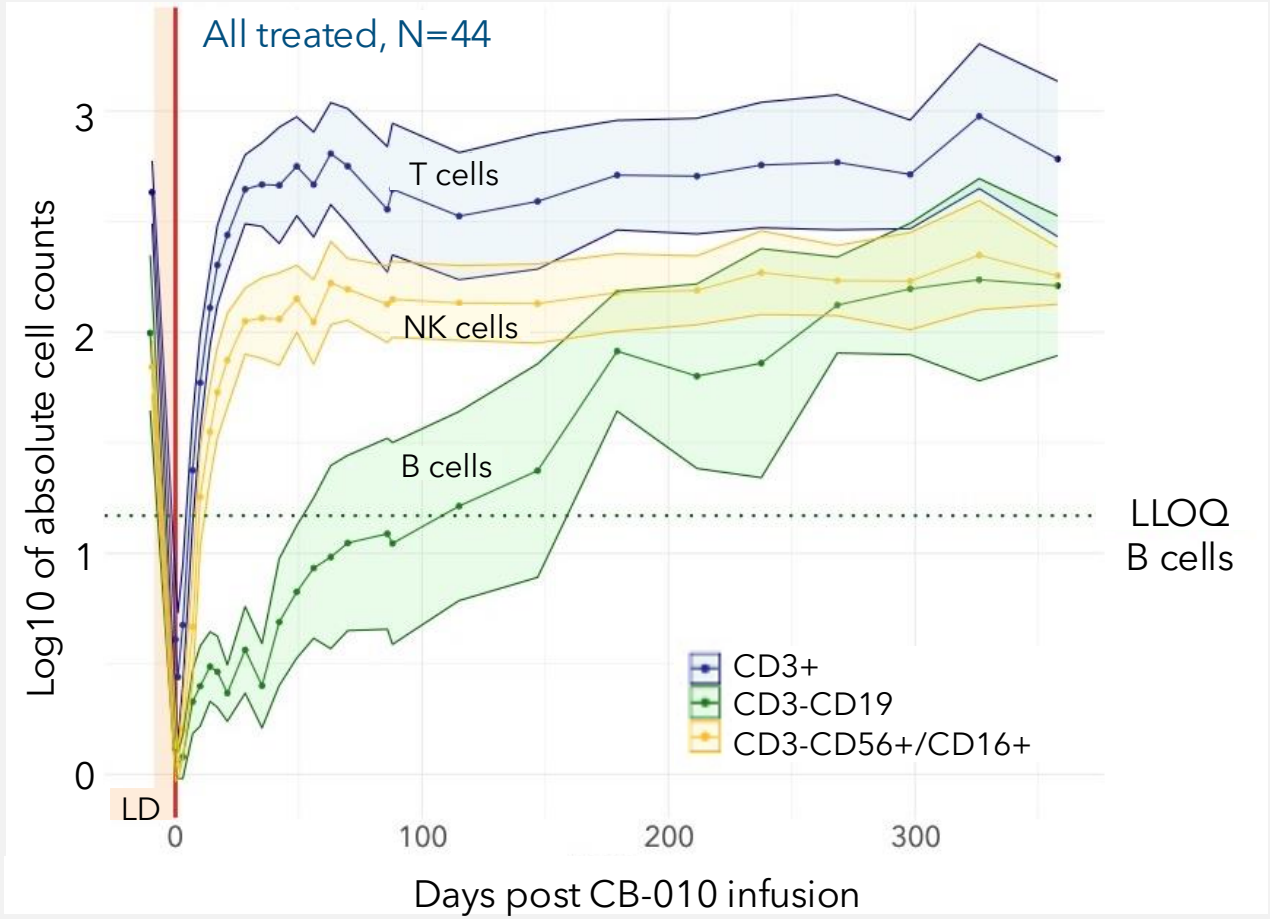
CB-010

Allogeneic anti-CD19 CAR-T cell therapy with a PD-1 knockout for lupus

CARIBOU BIOSCIENCES

Single dose of CB-010 results in extended B cell aplasia and rapid recovery of immune cells

B cell, T cell, and NK cell depletion and recovery



- CB-010 specifically targets B cells, resulting in extended B cell aplasia for ~114 days
- B cells recover to normal levels by ~268 days
- T cells and NK cells recovered ~3 weeks after LD regimen

22 LD: lymphodepletion; LLOQ: lower limit of quantification
Baseline B cells absolute levels calculated with samples of 10 cells/µl or above.

CB-010 duration of B cell aplasia is similar to lupus case studies

Duration of B cell aplasia Days	
CB-010 N=44	114 Mean (IQR 42-150)
Müller et al N=14[1]	112 Mean (IQR 72-153)

FOR ILLUSTRATIVE PURPOSES ONLY: The results of other CAR-T cell therapies presented on this slide have been derived from publicly available reports of clinical trials run independently of Caribou. The Company has not performed any head-to-head trials comparing any of these other CAR-T cell therapies with CB-010. As such, the results of these other clinical trials may not be comparable to clinical results for CB-010. The design of these other trials vary in material ways from the design of the clinical trials for CB-010, including with respect to patient populations, follow-up times, the clinical trial phase, and subject characteristics. As a result, cross-trial comparisons may have no interpretive value on the Company's existing or future results. For further information and to understand these material differences, you should read the reports for the other trials at the sources included below.

[1] Patient population included severe SLE (8 patients), idiopathic inflammatory myositis (3 patients), or systemic sclerosis (3 patients) who received a single infusion of CD19 chimeric antigen receptor (CAR) T cells after preconditioning with fludarabine and cyclophosphamide.
Source: Müller et al , NEJM, 2024; B cell aplasia defined as being below the limit of quantification.

CB-010 GALLOP Phase 1 trial design

Eligibility and matching

- Refractory to glucocorticoids and at least 2 immunosuppressive therapies
- Excludes active CNS involvement
- Partial HLA matching and absence of baseline donor-specific antibody (DSAs)

Treatment and objective

- Single dose level of CB-010 following LD
- Primary endpoint: safety and tolerability
- Secondary and exploratory endpoints: pharmacokinetics, pharmacodynamics, and efficacy

Patient cohorts

Cohort 1: Lupus nephritis
Class III/IV glomerulonephritis,
24 h UPCR ≥ 0.8 mg/mg

Cohort 2: Extrarenal lupus
SLEDAI-2K ≥ 8

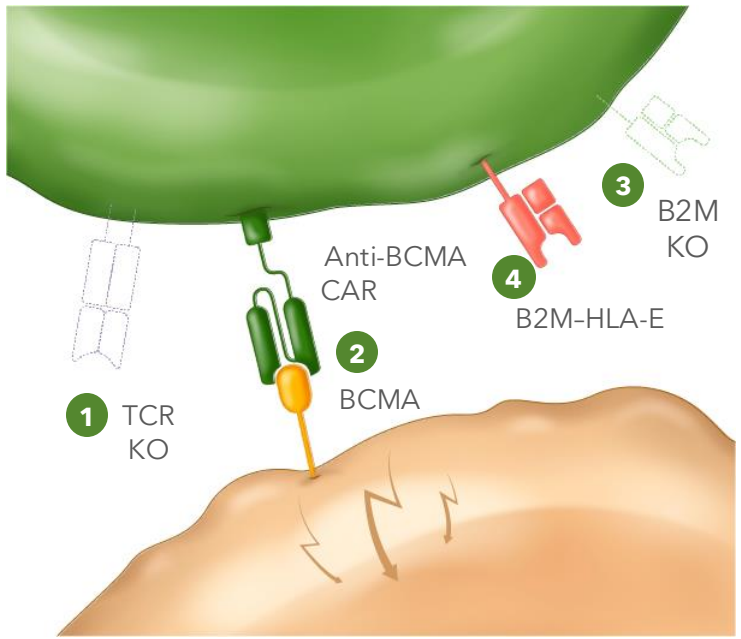
HLA: human leukocyte antigen; LD: lymphodepletion; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index

CB-011

Allogeneic anti-BCMA CAR-T cell therapy with immune cloaking for r/r multiple myeloma (MM)

CARIBOU BIOSCIENCES®

CB-011: anti-BCMA allogeneic CAR-T cell therapy with immune cloaking to blunt rejection



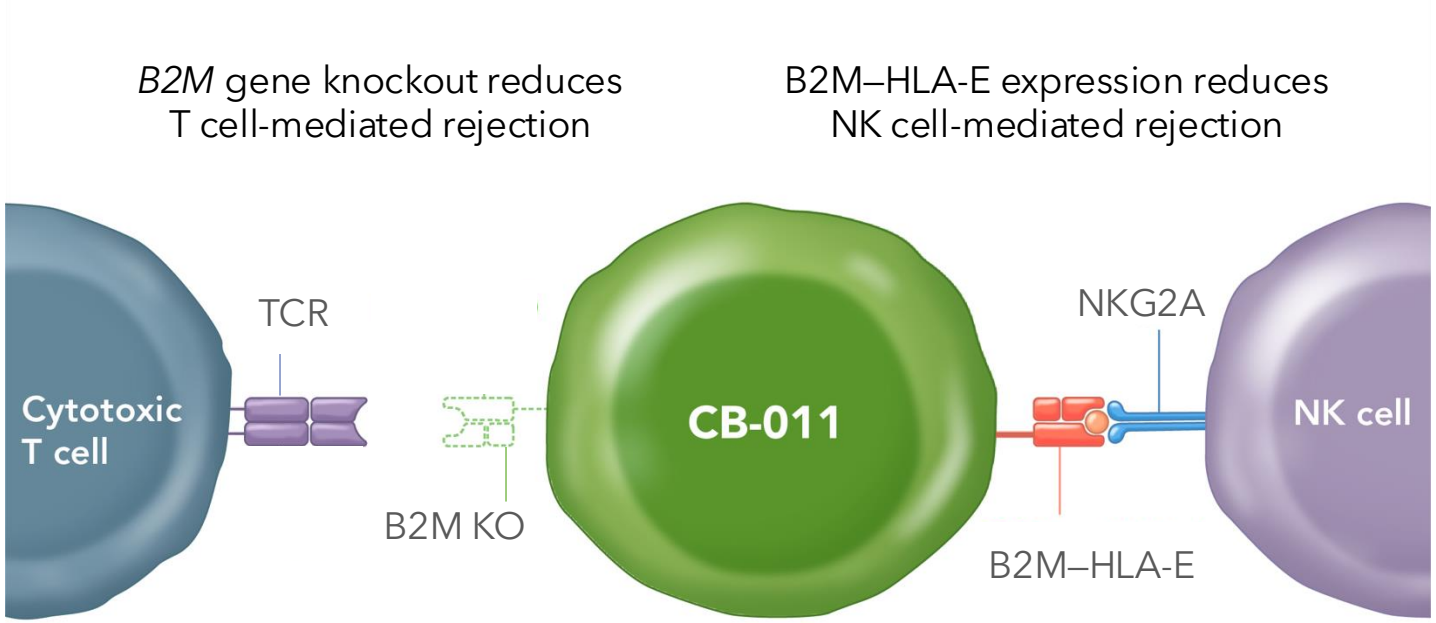
Armored with 4 genome edits

1. ***TRAC* gene knockout (KO)**
   - Eliminates TCR expression, reduces GvHD risk
2. **Humanized anti-BCMA CAR site-specifically inserted into *TRAC* gene**
   - Eliminates random integration, targets tumor antigen
3. **B2M gene KO**
   - Reduces HLA class I presentation and T cell-mediated rejection
4. **B2M–HLA-E-peptide fusion site-specifically inserted into B2M gene**
   - Blunts NK cell-mediated rejection

- 1st CAR-T in the clinic with **immune cloaking** using a B2M KO and B2M–HLA-E-peptide fusion insertion[1]
- Cas12a chRDNA editing for reduced off-target editing and **enhanced insertion rates**
- Patented[2], potent, humanized **anti-BCMA** scFv with a 4-1BB costimulatory domain

[1] To Caribou's knowledge
[2] Four U.S. patents granted to date covering CB-011 scFv

CB-011 editing strategy designed to reduce both T cell- and NK cell-mediated rejection

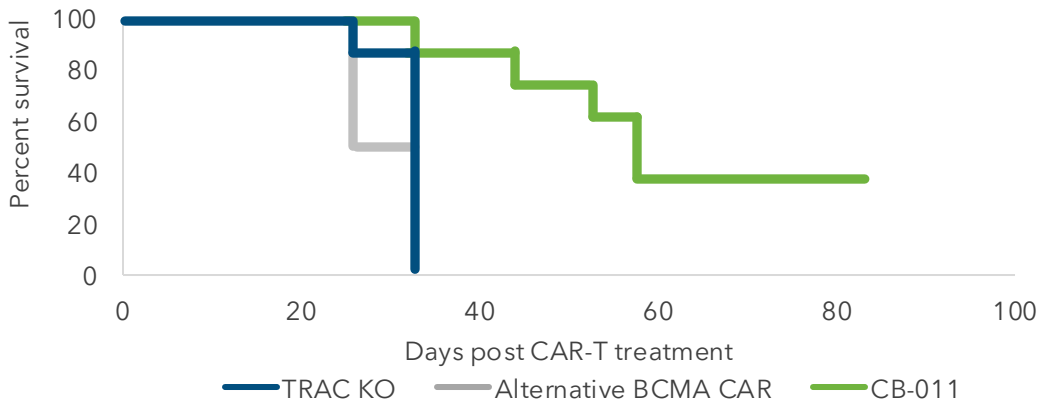


- *B2M* KO removes all endogenous HLA class I presentation to **reduce T cell-mediated rejection**
- B2M–HLA-E-peptide fusion insertion **blunts NK cell-mediated rejection**
- The **Cas12a chRDNA** editing platform achieves **high insertion efficiencies** facilitating the insertion of the B2M–HLA-E-peptide fusion and CAR into different genomic locations

CB-011 enhanced long-term survival in preclinical studies

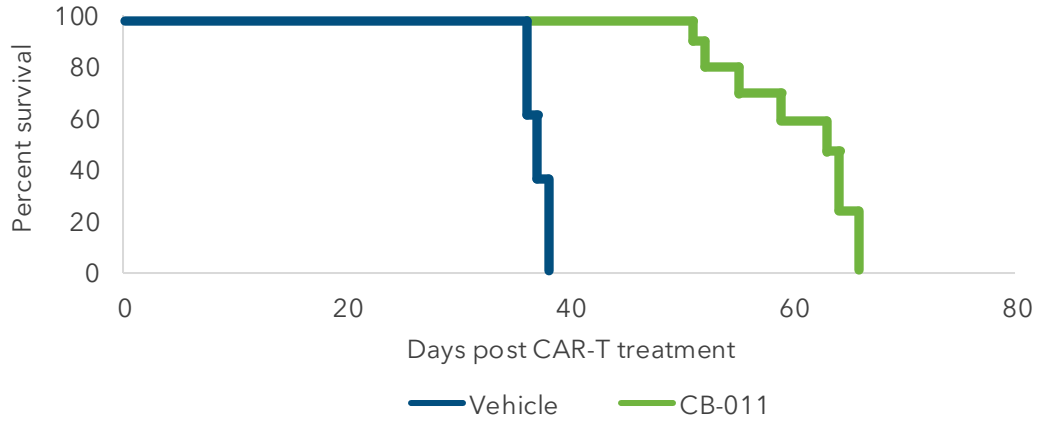
CB-011 led to statistically significant and longer survival of tumor-bearing mice
relative to an alternative anti-BCMA CAR-T cell therapy after a single dose

CB-011 vs alternative BCMA CAR
p=0.0006



- Established subcutaneous MM tumor xenograft
- Single dose CAR-T cell treatment

CB-011 vs vehicle
p=0.0001



- Established orthotopic MM tumor xenograft
- Single dose CAR-T cell treatment

Degagné É, et al. Cancer Immunol Res. s; 12(4) April 2024.

CB-011 CaMMouflage Phase 1 trial design

Patients with r/r MM
- ≥3 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 antibody
- Exclusions: prior CAR-T cell therapy and/or BCMA-targeted therapy within last 3 months

Part A: 3+3 dose escalation
- Objective: safety, determine MTD, RDE

Part B: dose expansion
- Objective: antitumor response, RP2D

Dose level		LD regimen[1]	Status
1	$50x10^6$ CAR-T cells	300 cy	Completed
2	$150x10^6$ CAR-T cells	300 cy	Completed
3a	$450x10^6$ CAR-T cells	300 cy	Completed
3b	$450x10^6$ CAR-T cells	500 cy	Enrolling backfill patients
4	$800x10^6$ CAR-T cells	500 cy	Enrolling patients

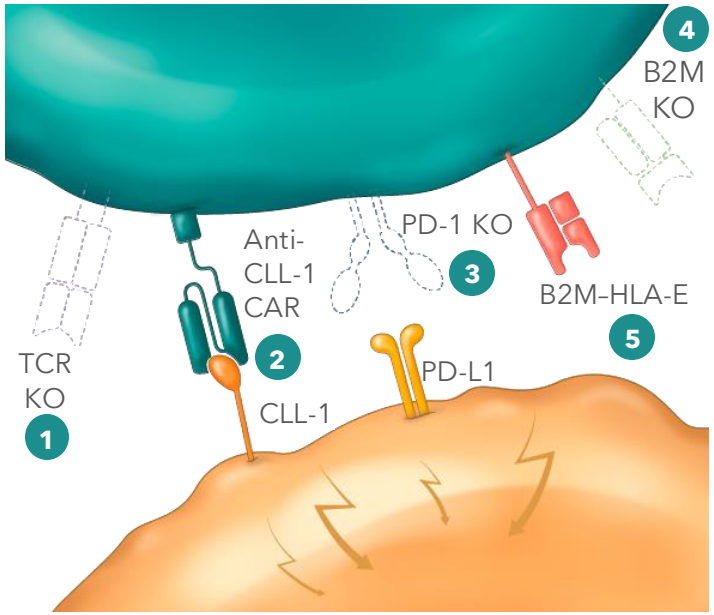
NCT05722418
[1] DL1, DL2, and DL3a LD regimen: 300 mg/m^2 cy and flu 30 mg/m^2 daily x 3 days;
DL3b and DL4 LD regimen: 500 mg/m^2 cy and flu 30 mg/m^2 daily x 3 days
IMiD: immunomodulatory drug; mAb: monoclonal antibody; MM: multiple myeloma; MTD: maximum tolerated dose;
PI: proteasome inhibitor; RDE: recommended dose for expansion; RP2D: recommended Phase 2 dose

CB-012

Allogeneic anti-CLL-1 CAR-T cell therapy with a PD-1 knockout and immune cloaking for r/r acute myeloid leukemia (AML)

CARIBOU BIOSCIENCES®

CB-012: anti-CLL-1 allogeneic CAR-T cell therapy with a PD-1 knockout and immune cloaking



Armored with 5 genome edits

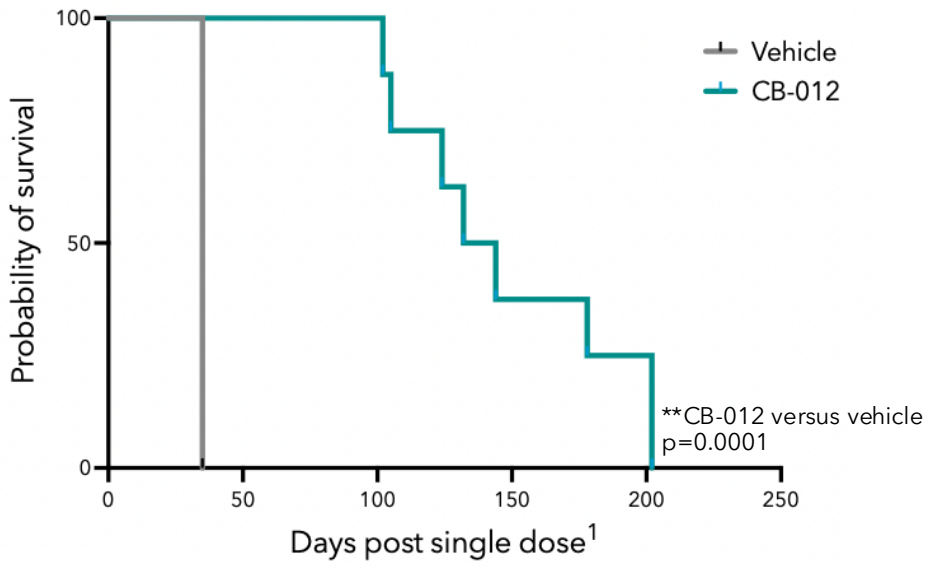
1. ***TRAC* gene knockout (KO)**
   - Eliminates TCR expression, reduces GvHD risk
2. **Human anti-CLL-1 CAR site-specifically inserted into *TRAC* gene**
   - Eliminates random integration, targets tumor antigen
3. **PD-1 KO for enhanced antitumor activity**
   - Potentially better therapeutic index via initial tumor debulking
4. ***B2M* gene KO**
   - Reduces HLA class I presentation and T cell-mediated rejection
5. **B2M–HLA-E-peptide fusion site-specifically inserted into *B2M* gene**
   - Blunts NK cell-mediated rejection

- 1st CAR-T with **checkpoint inhibition and immune cloaking** (PD-1 KO, B2M KO + B2M–HLA-E-peptide fusion) to enter the clinic[1]
- Cas12a chRDNA editing for reduced off-target editing and **enhanced insertion rates**
- Potent, fully human **anti-CLL-1** scFv[2] with a CD28 costimulatory domain

[1] To Caribou's knowledge
[2] Anti-CLL-1-specific scFv exclusively licensed from Memorial Sloan Kettering Cancer Center for allogeneic cell therapies

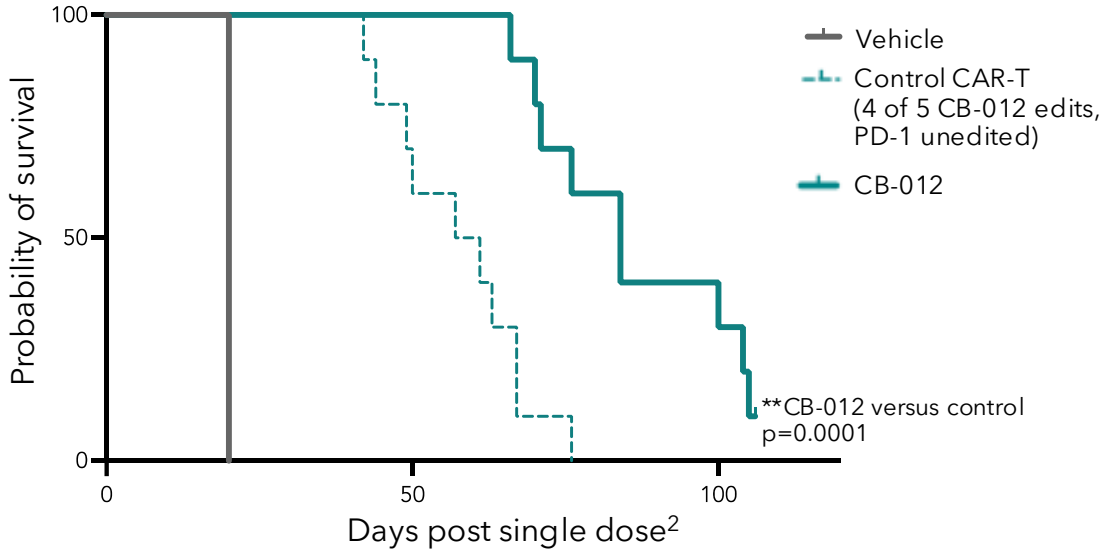
CB-012 significantly reduced tumor burden and increased overall survival in preclinical studies

Overall survival analysis



Single dose of CB-012 **significantly reduced tumor burden** over a longer duration compared to vehicle treatment in an AML xenograft model

Overall survival analysis



Addition of PD-1 KO in genome-editing strategy **increased overall survival** compared to control CAR-T cell without PD-1 KO

[1] Orthotopic engraftment of HL-60 CLL-1-expressing AML model in NSG mice
[2] Orthotopic engraftment of U937 CLL-1- and PD-L1-expressing cell line in NSG mice

CB-012 AMpLify Phase 1 trial design

Patients with r/r AML
- Relapsed or refractory AML patients should have received at least 1 but not more than 3 prior lines of therapy
- Patients with prior allo or auto SCT are allowed
- Exclusions: prior CAR-T cell therapy and/or CLL-1-targeted therapy

Part A: 3+3 dose escalation – enrolling
- Objective: safety, determine MTD/RDE

Part B: dose expansion
- Objective: antitumor response, determine RP2D, safety

AML: acute myeloid leukemia; SCT: stem cell transplant; MTD: maximum tolerated dose; RDE: recommended dose or doses for expansion; RP2D: recommended phase 2 dose

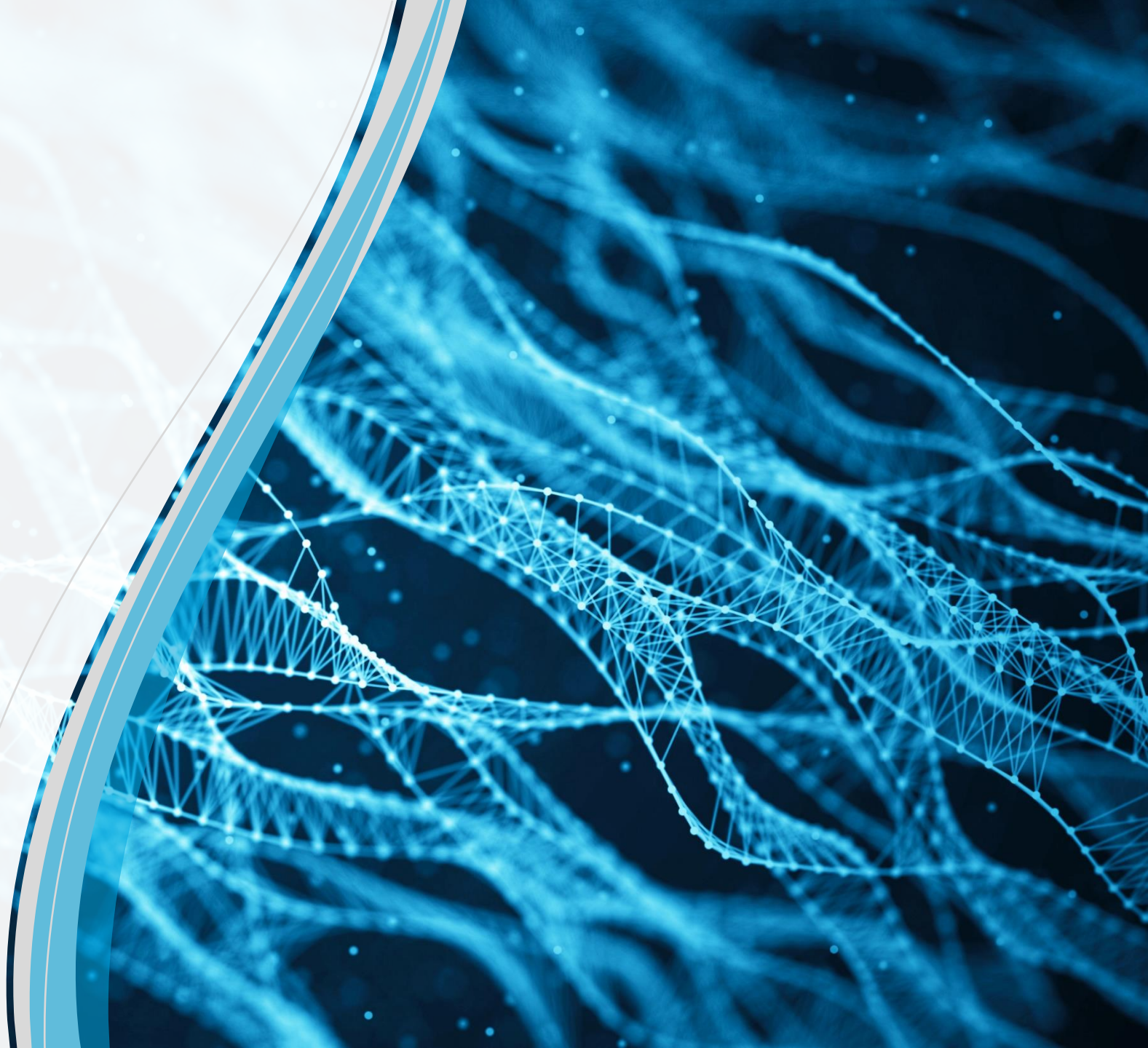
Upcoming clinical catalysts

Program	Clinical milestone	Expected timing
CB-010 2L LBCL	Present initial data on partial HLA matching (~20 patients, some outpatient), CD19 relapsed (~10 patients) from the ANTLER Phase 1 clinical trial	H1 2025
	Initiate pivotal Phase 3 trial	H2 2025
CB-011 r/r MM	Present dose escalation data from CaMMouflage Phase 1 trial	H1 2025
CB-010 LN/ERL	Initiate GALLOP Phase 1 trial	YE 2024

Thank you

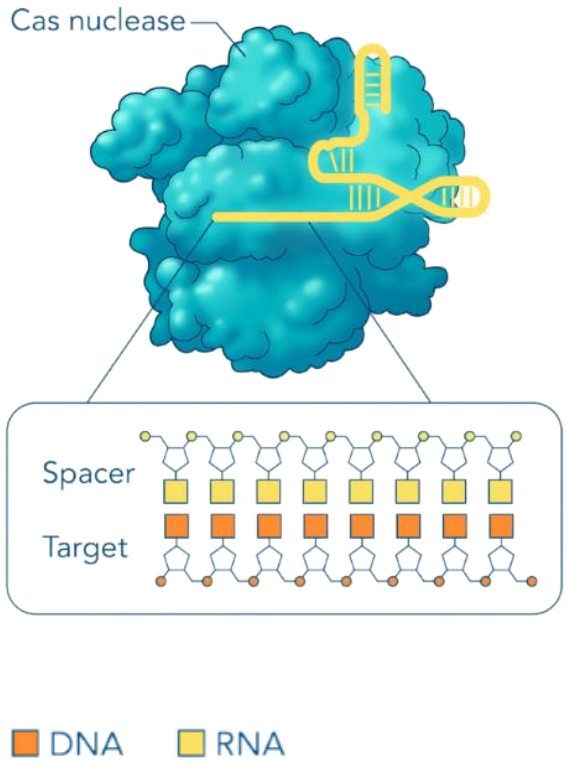
https://cariboubio.com
info@cariboubio.com

CARIBOU BIOSCIENCES®

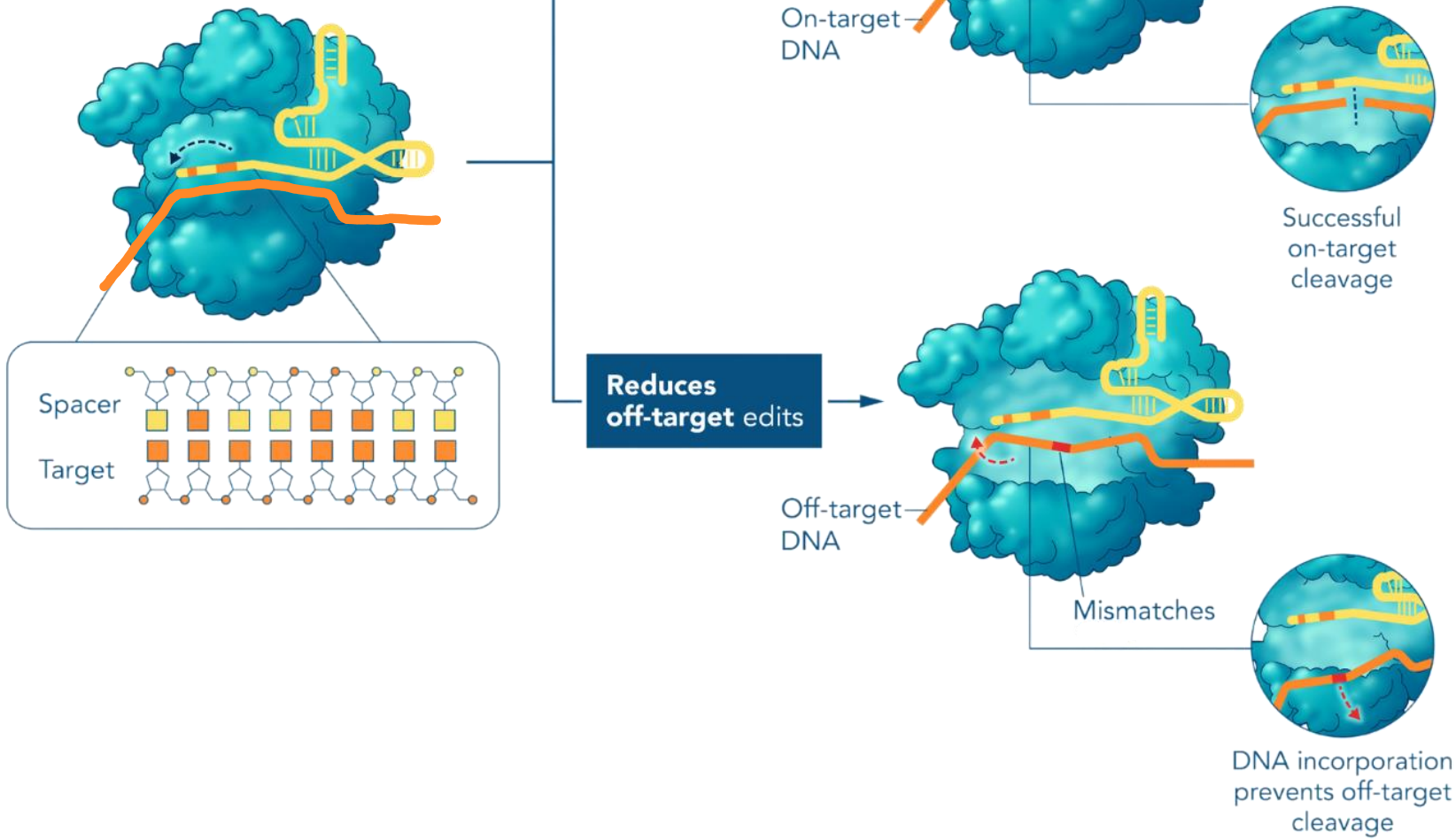


chRDNA guides promote on-target and reduce off-target edits

First-generation
all-RNA CRISPR-Cas



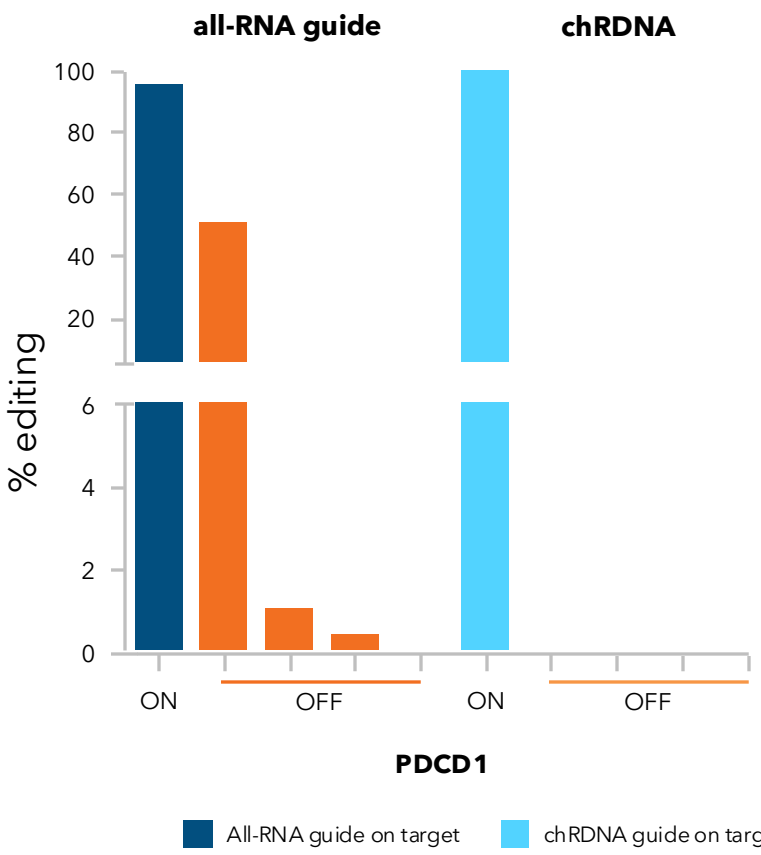
chRDNA
CRISPR hybrid RNA-DNA



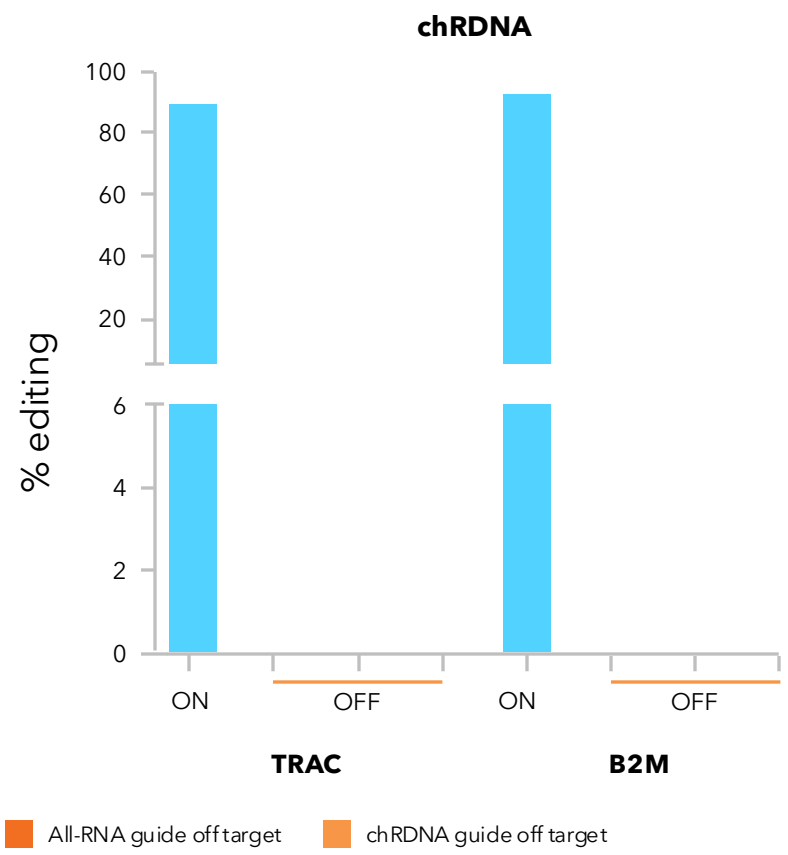
chRDNA guides significantly improve editing specificity

Knockout

Cas9

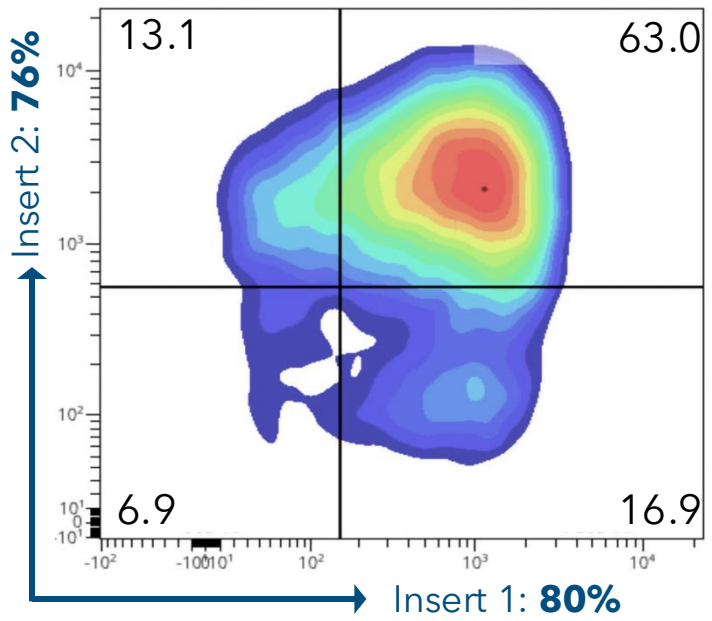


Cas12a



All-RNA guide on target | chRDNA guide on target | All-RNA guide off target | chRDNA guide off target

Knock-in



Cas12a chRDNA genome editing + AAV6 transduction leads to >60% of manufacturing-scale engineered T cells with all 4 intended edits

Editing assayed in primary human T cells.

CB-010 is generally well tolerated

Treatment-emergent adverse events (TEAE[1]) in ≥20% of all patients

System organ class, n (%) Preferred term, n (%)	All treated (N = 46)			LBCL subgroup (N=40)			2L LBCL RP2D subgroup (N=20)		
	Any grade	Grade ≥3	Related grade ≥3	Any grade	Grade ≥3	Related grade ≥3	Any grade	Grade ≥3	Related grade ≥3
Any TEAE	46 (100)	41 (89)	23 (50)	40 (100)	35 (88)	20 (50)	20 (100)	18 (90)	10 (50)
Thrombocytopenia	30 (65)	29 (63)	15 (33)	26 (65)	25 (63)	13 (33)	12 (60)	11 (55)	6 (30)
Anemia	27 (59)	24 (52)	10 (22)	24 (60)	22 (55)	10 (25)	13 (65)	11 (55)	6 (30)
Neutropenia	22 (48)	19 (41)	7 (15)	18 (45)	15 (38)	6 (15)	10 (50)	8 (40)	4 (20)
White blood cell count decreased	15 (33)	14 (30)	6 (13)	14 (35)	13 (33)	5 (13)	9 (45)	8 (40)	2 (10)
CRS	26 (57)	0	0	23 (58)	0	0	13 (65)	0	0
Infections	22 (48)	10 (22)	4 (9)	19 (48)	8 (20)	4 (10)	9 (45)	6 (30)	3 (15)
Hypokalemia	11 (24)	0	0	9 (23)	0	0	4 (20)	0	0
Pyrexia	11 (24)	0	0	10 (25)	0	0	2 (10)	0	0
ICANS	10 (22)	3 (7)	3 (7)	8 (20)	2 (5)	2 (5)	5 (25)	1 (5)	1 (5)
Diarrhea	10 (22)	0	0	7 (18)	0	0	3 (15)	0	0

Five patients died due to adverse events following CB-010 infusion (4 unrelated, 1 possibly related[2] to CB-010)

CRS: cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome

[1] TEAEs are defined as adverse events (AEs) with a start date on or after the CB-010 infusion date.

[2] One death possibly related to CB-010 per investigator due to complications of a bladder perforation in the context of BK virus hemorrhagic cystitis. As of April 1, 2024 cutoff date.

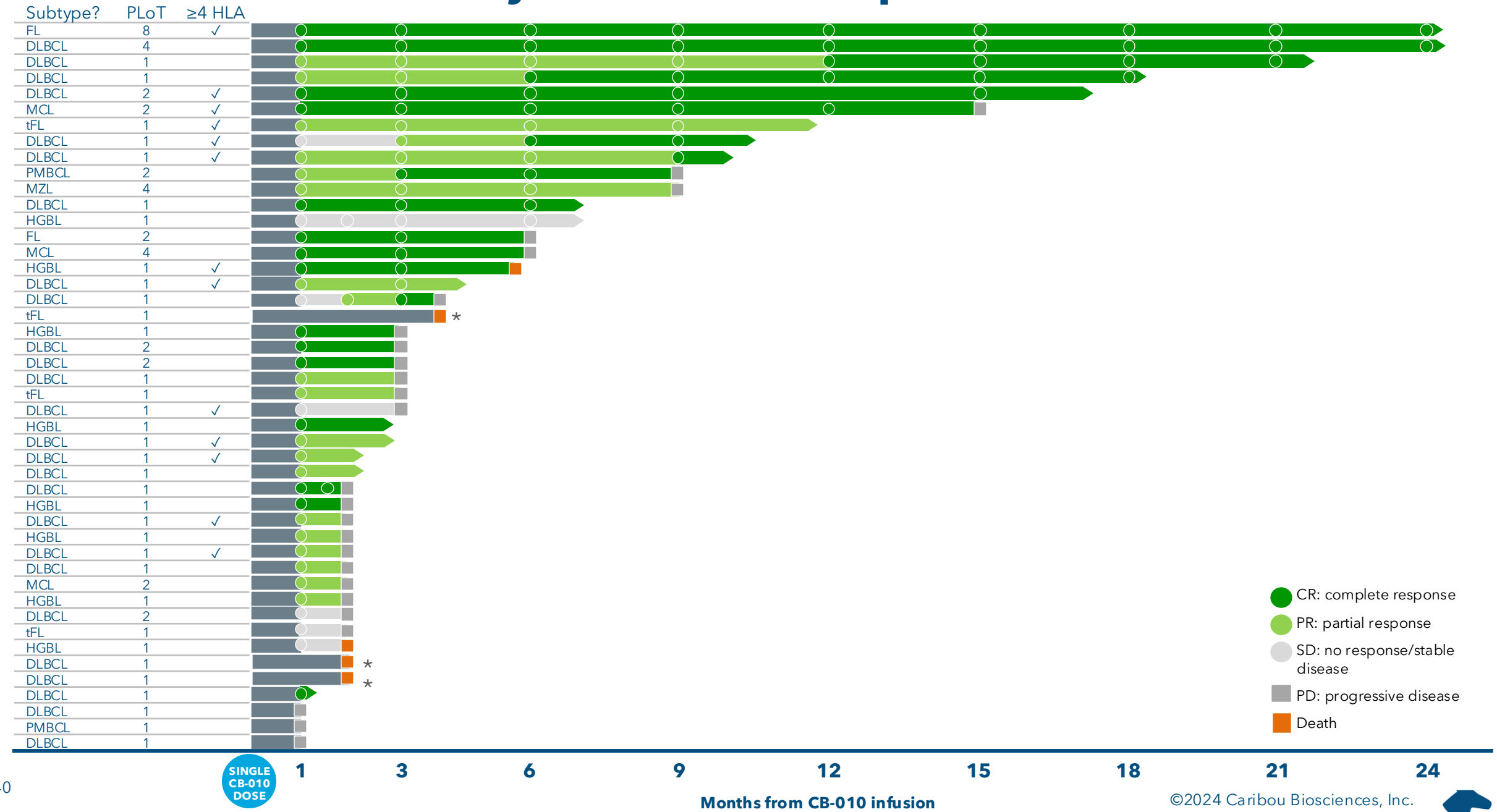
CB-010 ANTLER efficacy assessment by all patients and LBCL subgroups

Endpoints (N, %)	All patients (N=46)	LBCL (N=40)	2L LBCL 80M (N=20)
Overall response rate (ORR)[1]	35 (76%)	29 (73%)	15 (75%)
DoR, median months (range)	5 (1-23+)	2 (1-23+)	5 (1-20+)
Complete response (CR) rate[1]	21 (46%)	17 (43%)	10 (50%)
Duration of CR, Median months (range)	7 (1-23+)	7 (1-23+)	NR (1-12+)
6-month PFS	35%	28%	38%
PFS, median months (range)	3 (1-24+)	3 (1-24+)	3.5 (1-21+)

+ censored observation

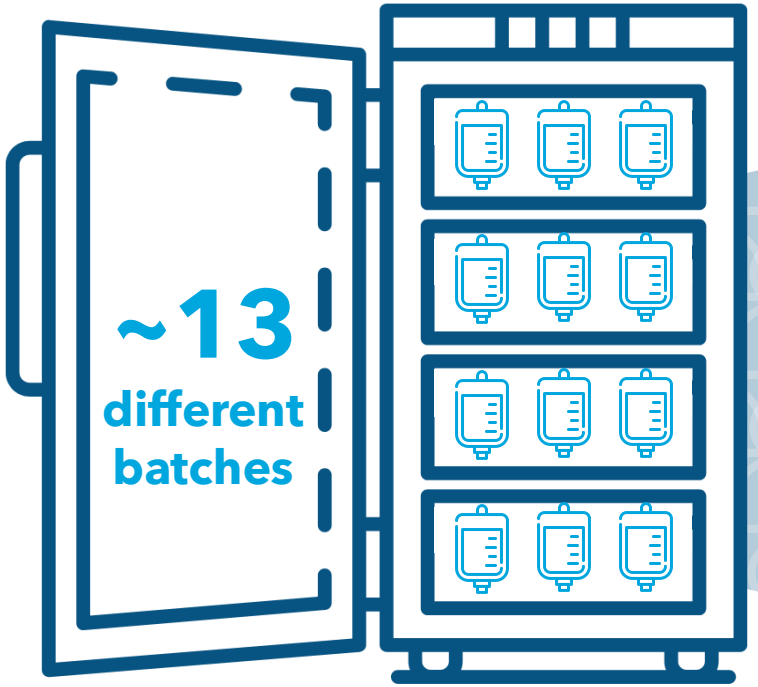
As of April 1, 2024 cutoff date.

CB-010 ANTLER efficacy assessment all patients



As of April 1, 2024, data collection ongoing, efficacy based on Lugano criteria. *Denotes patient that did not have Day 28 efficacy scan.

CB-010 is an off-the shelf CAR-T cell therapy that is easily matched to patients



~90%

of 2L LBCL patients for planned Phase 3 clinical trial[1] are expected to receive ≥4 HLA matched product

Only a small number of manufacturing batches are needed to provide partially HLA matched CB-010 to ~90% of patients

HLA: human leukocyte antigen; partial HLA match: patient has ≥4 HLA alleles that match donor T cells used for CB-010 manufacturing

[1] Planned pivotal Phase 3 intends to enroll CD19 naïve 2L LBCL patients who will be dosed with best matched CB-010

Potential to address high unmet medical need in 2L LBCL

LBCL patient treatment journey
(U.S. incidence 2022)

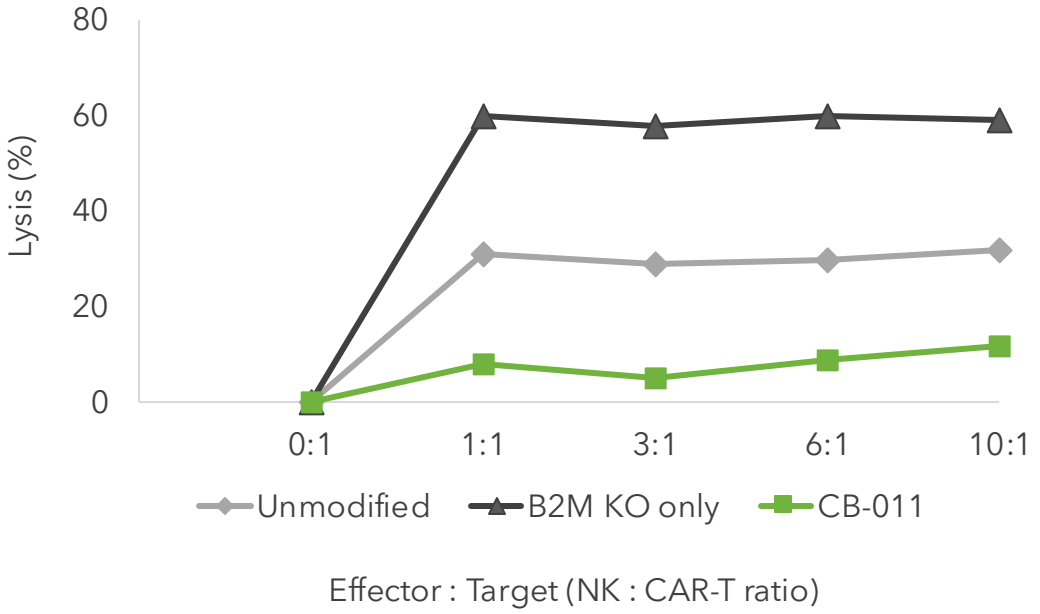
Diagnosed	~32.4K patients
1L	~30.8K patients
2L	~10.0K patients
3L	~4.4K patients

ANTLER dose expansion

B2M KO and B2M–HLA-E fusion strategy protects CB-011 CAR-T cells from NK and T cell-mediated lysis

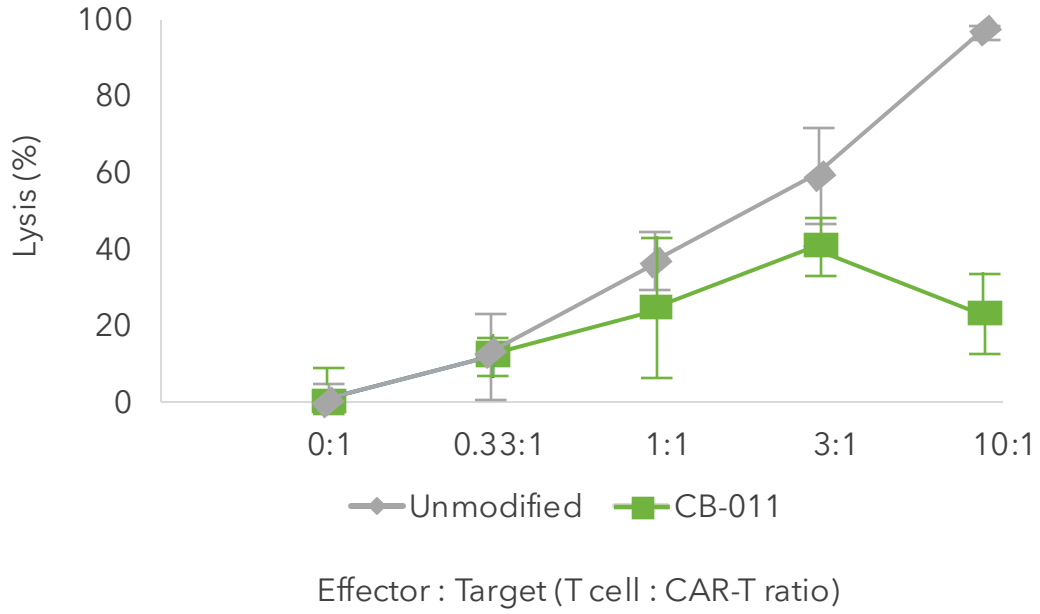
B2M–HLA-E fusion enables CB-011 cells to resist killing by NK cells

CAR-T cell co-incubation with NK-92 cells*



B2M KO enables CB-011 cells to resist killing by T cells

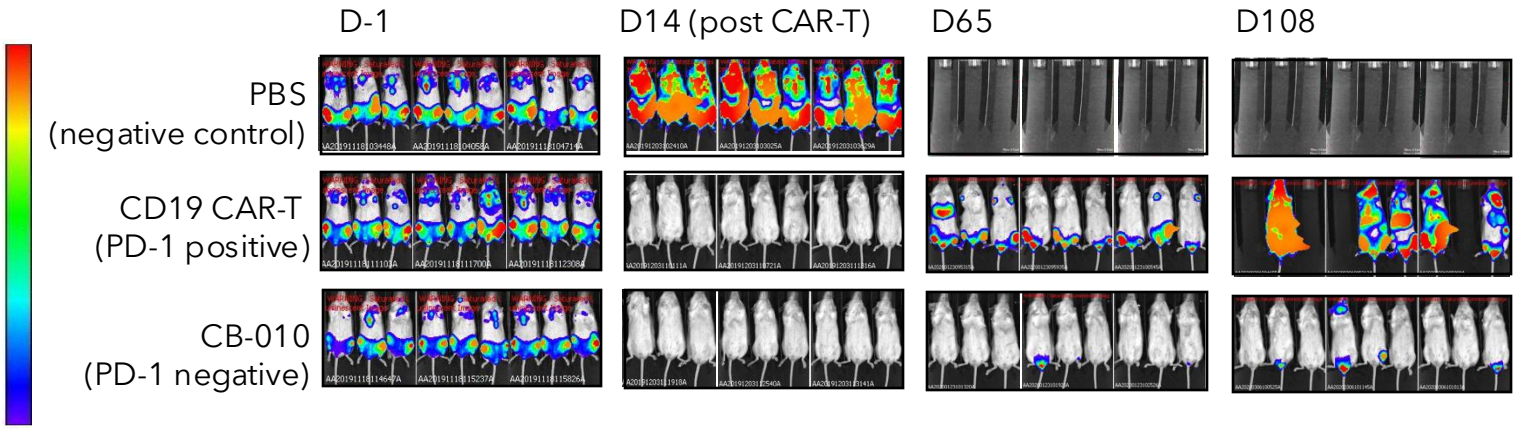
CAR-T cell co-incubation with PBMC-derived $CD8^+$ T cells*

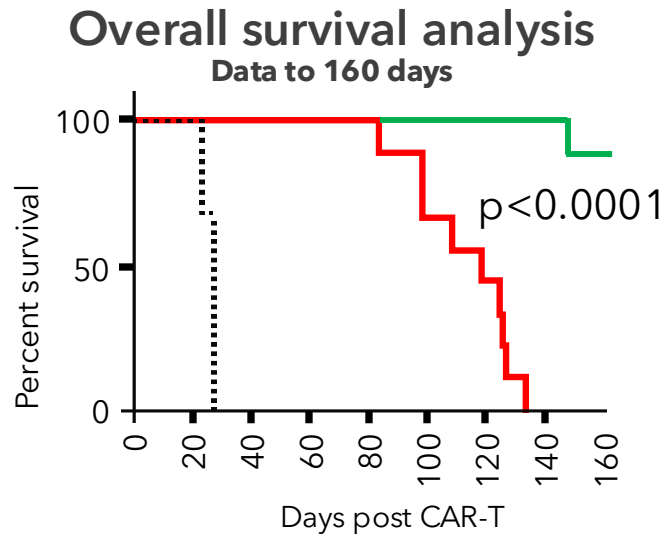


**In vitro* cytotoxicity measured 24 hours after co-incubation
Degagné É, et al. Cancer Immunol Res. s; 12(4) April 2024.

CB-010 demonstrated differentiated, long-term antitumor activity in preclinical studies

A single dose of CB-010 resulted in profound tumor regression of metastatic CD19⁺ tumor xenografts and led to a significantly longer antitumor response and survival
vs. conventional CD19-specific allogeneic CAR-T cells (expressing PD-1)





- NALM-6/PD-L1⁺ B-ALL tumors were established by IV engraftment for 23 days (Day -1)
- A single dose treatment was administered by IV on Day 24 (PBS or 10^7 cells where indicated)

Lau E, et al. *Cytotherapy*. 2023;25(7):750

Allogeneic CAR-T cell manufacturing process overview for CB-010

Caribou's process development team created the manufacturing process and transferred it to a CMO to generate phase 1 cGMP clinical material

cGMP starting material → Genetic modification via chRDNA and AAV → Gene-modified CAR-T cells → In vitro expansion of edited donor T cells → Removal of residual TCR+ cells → Final formulation & cryopreservation