CARIBOU BIOSCIENCES®

May 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 the release of dose expansion clinical data, emerging translational data, and follow up dose escalation data from our ongoing ANTLER phase 1 clinical trial for our CB-010 product candidate, disclosure of the recommended Phase 2 dose for CB-010, and the possibility of improved clinical outcomes by utilizing partial human leukocyte antigen matching; the status, progress, and expectations relating to the timing of release of clinical data from our ongoing CaMMouflage phase 1 clinical trial for our CB-011 product candidate; the status, progress, and expectations relating to the timing of release of clinical data from our ongoing AMpLify phase 1 clinical trial for our CB-012 product candidate; the timing for the initiation of our GALLOP phase 1 clinical trial for adults 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 separate product candidates. 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 companies' 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 its ongoing ANTLER phase 1 clinical trial, its CaMMouflage phase 1 clinical trial, its AMpLify phase 1 clinical trial, and its 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 and CAR-NK cell therapies **armored for enhanced activity**
  - Checkpoint disruption
  - Immune cloaking
  - Cytokine support
- **4 clinical-stage trials** targeting hematologic malignancies and autoimmune diseases

Resourced for successful execution

- Experienced, mission-driven leadership
- Strong in-house process development capabilities
- Robust IP portfolio
- $346M[1] in cash, runway into Q1 2026

chRDNA: CRISPR hybrid RNA-DNA

[1] $345.9M in cash, cash equivalents, and marketable securities as of March 31, 2024.

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

Program	Clinical trial	Target	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Designations
Hematologic malignancies								
CB-010	ANTLER Dose expansion	CD19	r/r B-NHL					RMAT, Fast Track, Orphan Drug
CB-011	CaMMouflage Dose escalation	BCMA	r/r MM					Fast Track, Orphan Drug
CB-012	AMpLify Dose escalation	CLL-1*	r/r AML					
Autoimmune diseases								
CB-010	GALLOP Site activation	CD19	LN and ERL					

ERL: extrarenal lupus; LN: lupus nephritis, RMAT: Regenerative Medicine Advanced Therapy
*Also known as CD371

2024 clinical catalysts

Program	Clinical milestone	Expected timing
CB-010	Present initial dose expansion data, RP2D, and translational data from the ANTLER Phase 1 clinical trial	ASCO June 2024
CB-011	Present initial dose escalation data from CaMMouflage Phase 1 trial	YE 2024
CB-010	Initiate GALLOP Phase 1 trial	YE 2024

chRDNA technology

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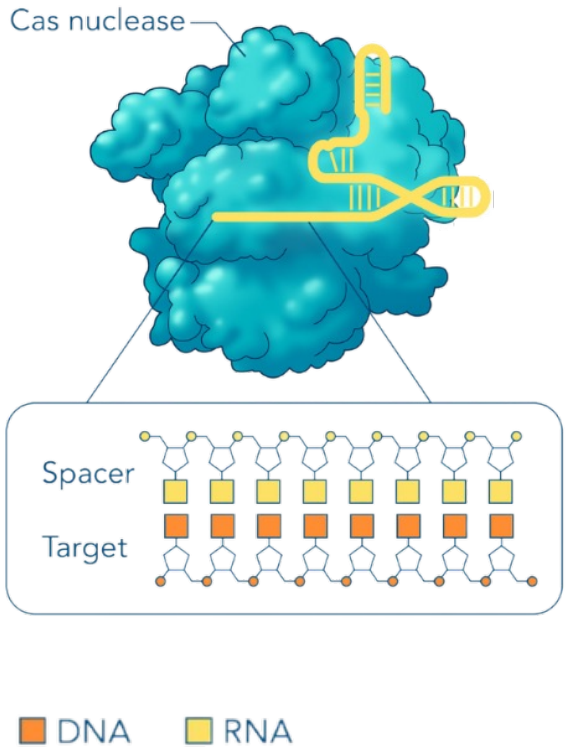
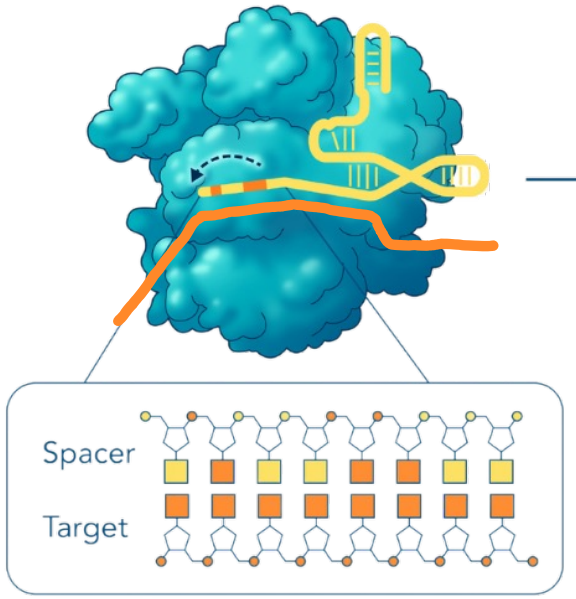
chRDNA guides promote on-target and reduce off-target edits

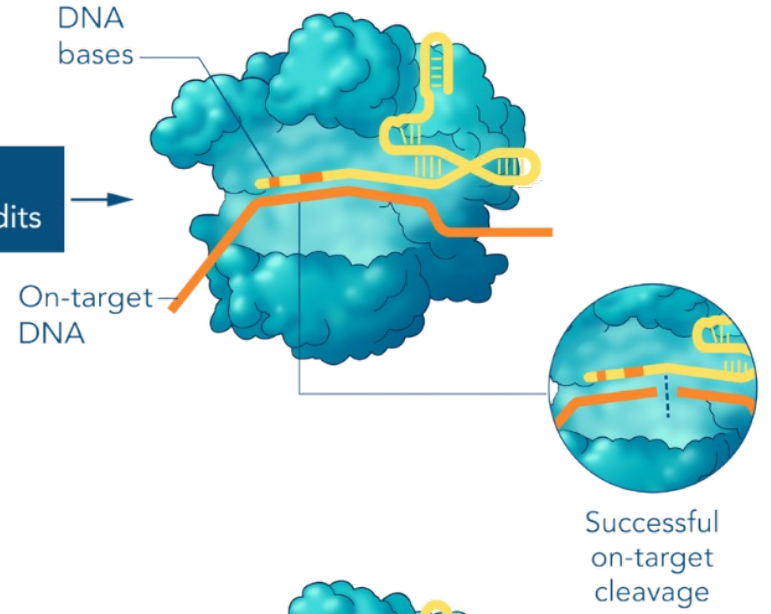
First-generation
all-RNA CRISPR-Cas



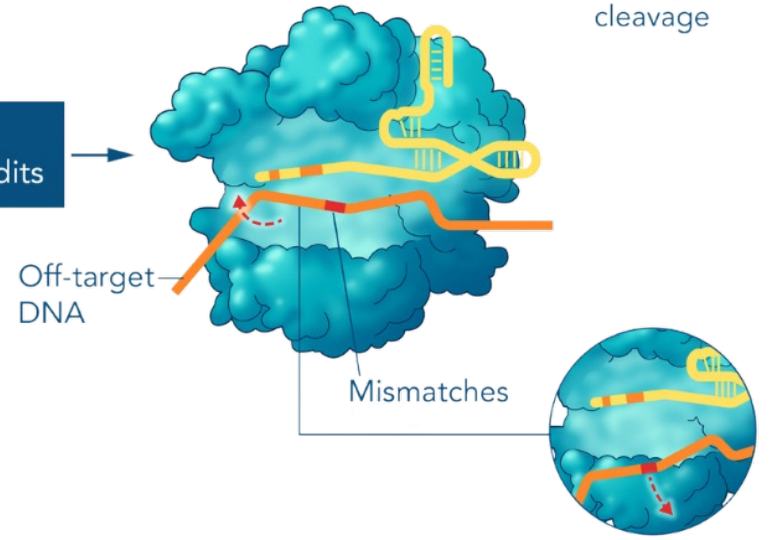
chRDNA
CRISPR hybrid RNA-DNA



Promotes on-target edits



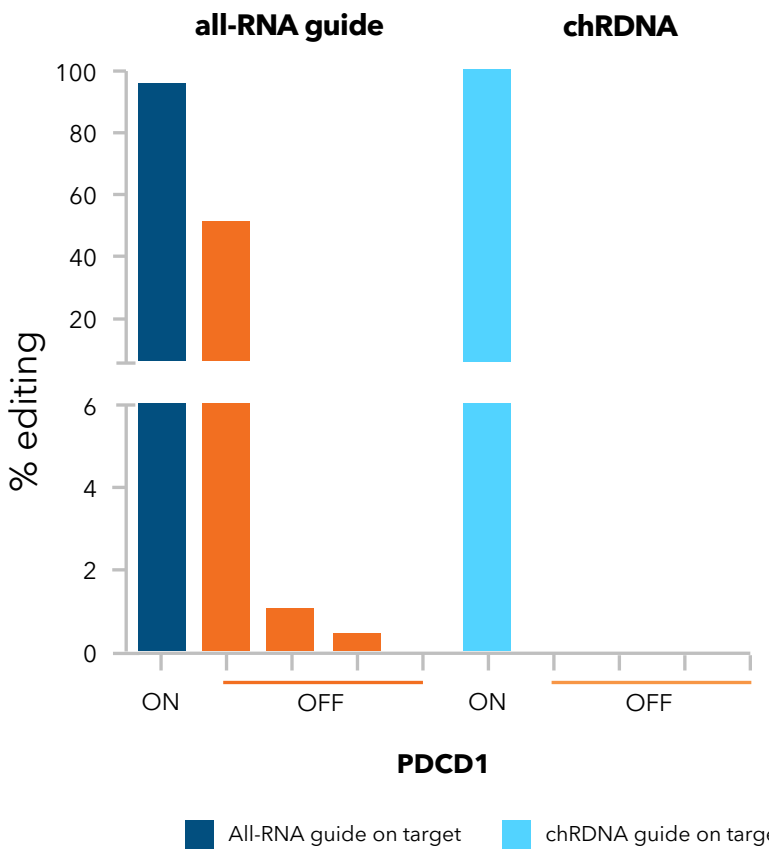
Reduces off-target edits



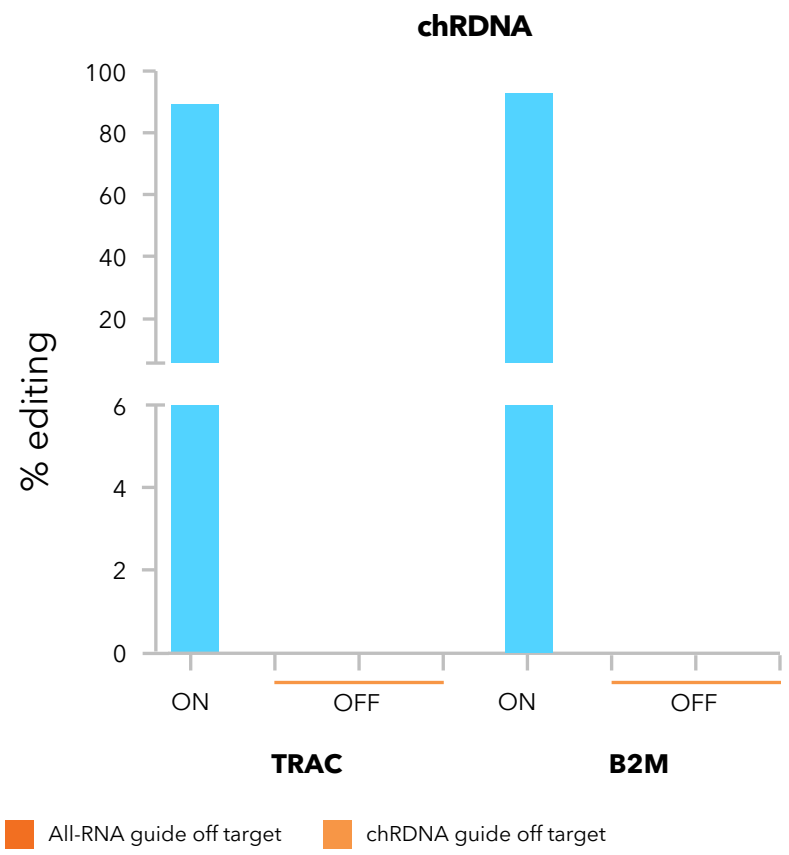
chRDNA guides significantly improve editing specificity

Knockout

Cas9

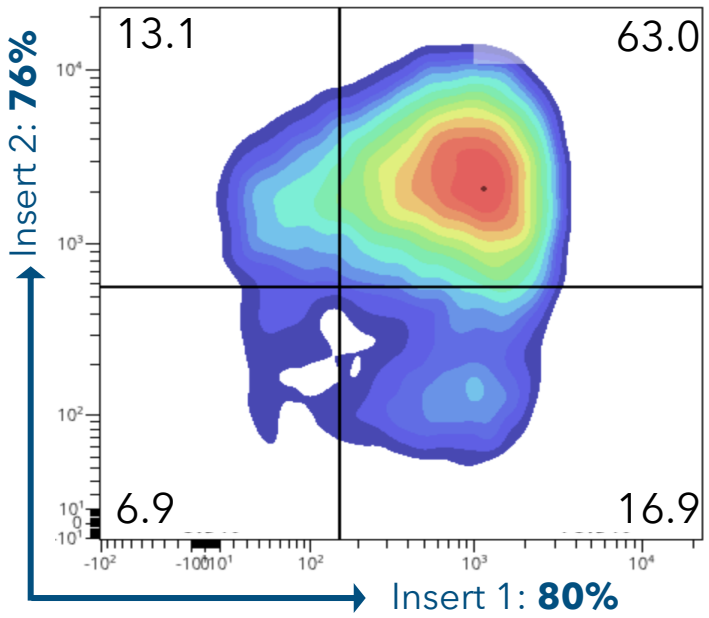


Cas12a



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

Knock-in

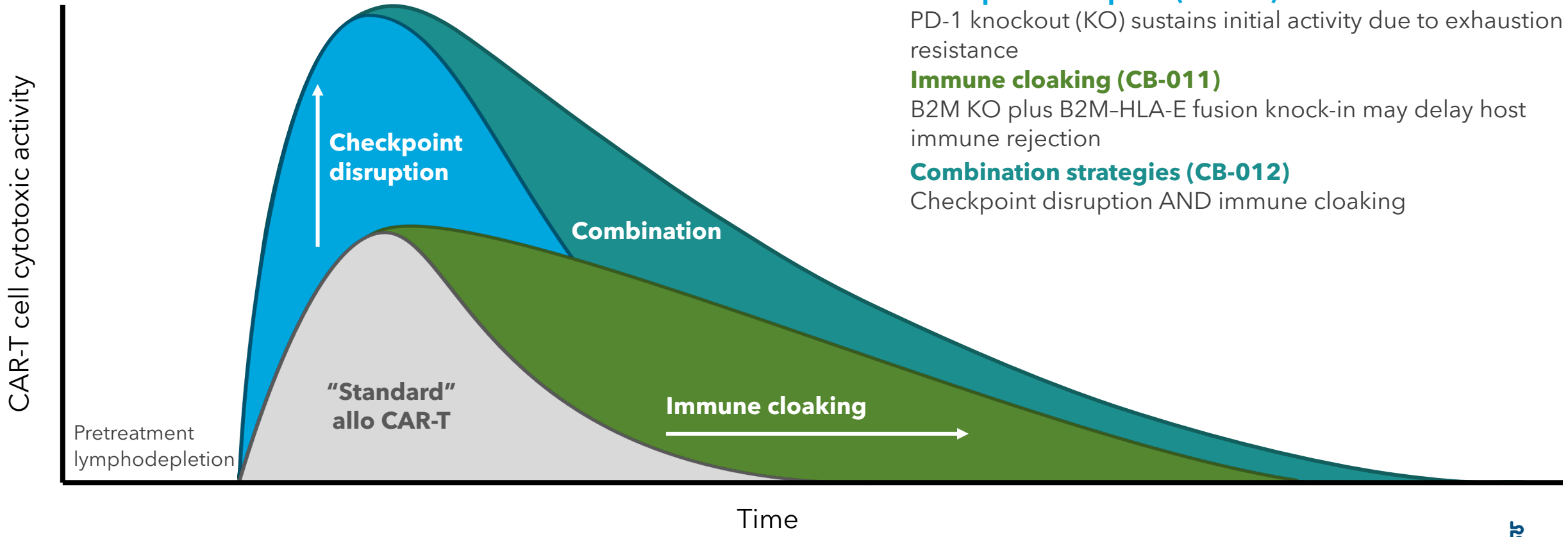


Cas12a chRDNA genome editing + AAV6 transduction leads to >60% of manufacturing-scale engineered T cells with all 4 intended edits

8 Editing assayed in primary human T cells.

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

Caribou is implementing multiple armoring strategies



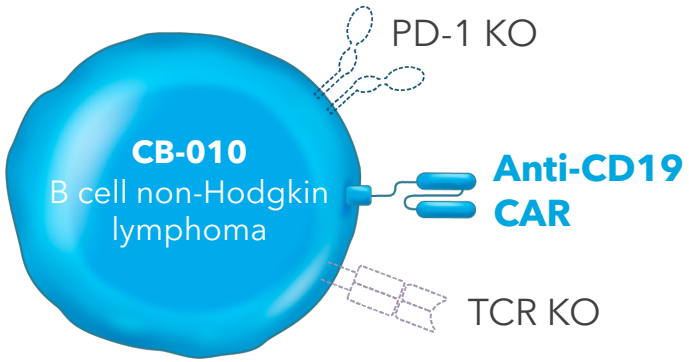
Checkpoint disruption (CB-010)
PD-1 knockout (KO) sustains initial activity due to exhaustion resistance

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

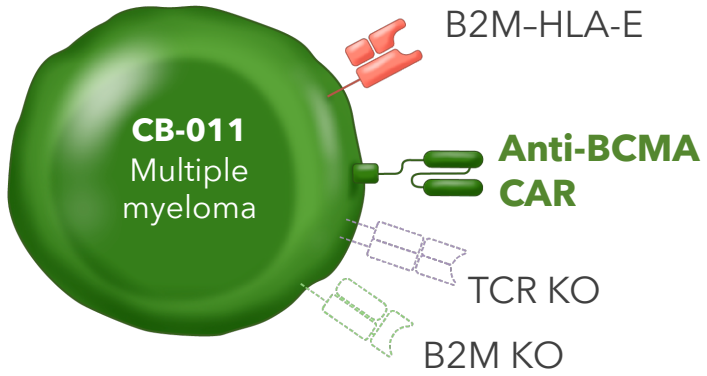
Caribou is a leader in the allogeneic CAR-T cell space with a platform of genome-edited cell therapies

3 Edits



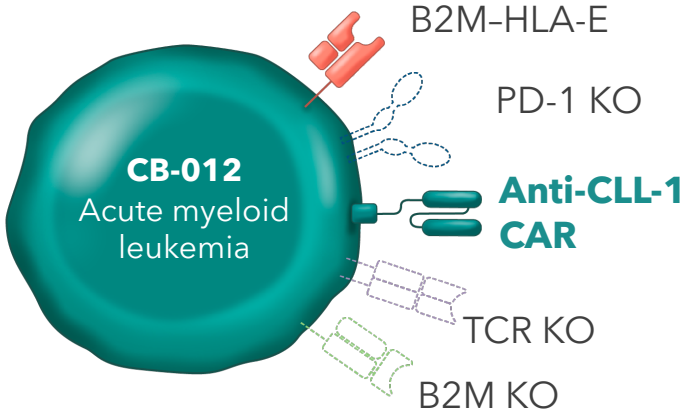
1st allogeneic anti-CD19 CAR-T cell therapy in the clinic with **checkpoint disruption** via PD-1 knockout (KO)[1] to reduce CAR-T cell exhaustion

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

Off-the-shelf CAR-T cell therapy programs

- CB-010 for r/r B-NHL
- CB-010 for lupus
- CB-011 for r/r MM
- CB-012 for r/r AML

Patients shouldn't have to wait for treatment

Allogeneic therapy
N=many
per batch

Screening | **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)

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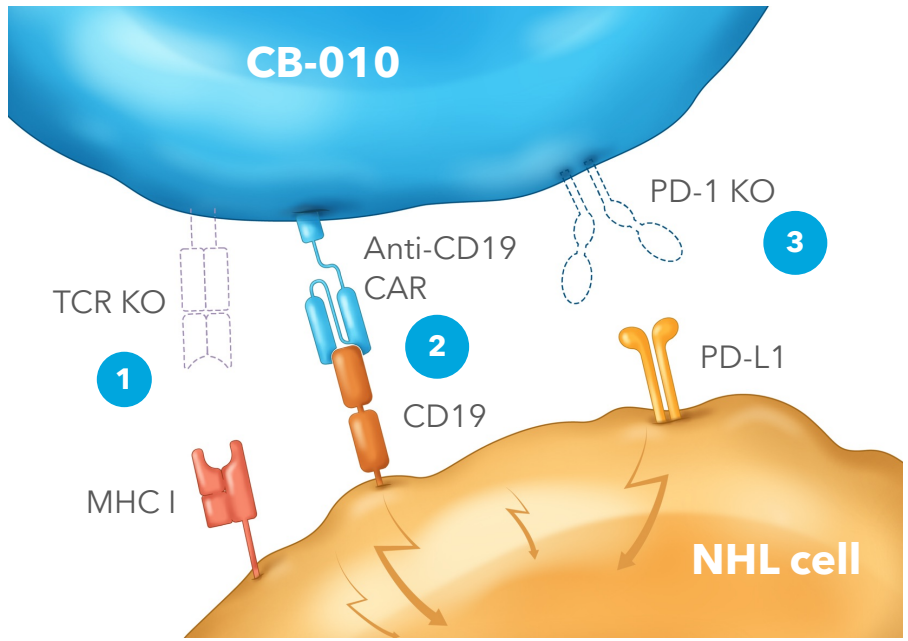
CB-010 has a PD-1 KO designed to reduce CAR-T cell exhaustion



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: dose expansion in 2L LBCL underway

Part A: 3+3 dose escalation – completed (N=16)
- Eligibility: aggressive r/r B-NHL[1] with ≥2 prior lines of chemoimmunotherapy or primary refractory
- Exclusion: prior CD19-targeted therapy

Part B: dose expansion – enrolling
- Eligibility: 2nd line LBCL[2]
- Exclusion: prior CD19-targeted therapy
- Objective: tumor response, RP2D

r/r B-NHL

Lymphodepletion **CB-010**

-9 to -2 DAYS | DAY 0 | 28 DAYS | 3 MONTHS | 6 MONTHS | 9 MONTHS | 12 MONTHS

Safety and tolerability

Response assessment

Cyclophosphamide (60 mg/kg/d for 2 days) followed by Fludarabine (25 mg/m²/d for 5 days)[3]

SINGLE DOSE

Dose level 1: 40x10⁶ CAR-T cells (N=8, completed[4])
Dose level 2: 80x10⁶ CAR-T cells (N=5, completed[4])
Dose level 3: 120x10⁶ CAR-T cells (N=3, completed)
Dose expansion: Enrolling patients (30th patient dosed; enrolling approximately 20 additional patients to prospectively evaluate partial HLA matching, DSA screening)

NCT04637763
DSA: donor-specific antibodies; 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
[4] Includes 2 backfill patients at dose level 1 and 2 backfill patients at dose level 2

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

Patients' baseline and disease characteristics

Characteristics	Total (N=16)
Median age, years (range)	66 (55-82)
Male, n (%)	14 (88)
ECOG performance status, n (%)	
0	6 (38)
1	10 (62)
Time since first diagnosis, years	
Median (range)	2.4 (0.2-16.4)
Non-Hodgkin lymphoma subtype, n (%)	
LBCL	10 (63)
DLBCL	7 (44)
HGBL	2 (13)
PMBCL	1 (6)
Other B-NHL	6 (38)
MCL	3 (19)
FL[1]	2 (13)
MZL	1 (6)
$CD19^+$ disease, n (%)	16 (100)
Prior systemic therapies, median number (range)[2]	2 (1-8)

DLBCL: diffuse large B cell lymphoma; FL: follicular lymphoma; HGBL: high-grade B cell lymphoma; MCL: mantle cell lymphoma; MZL: marginal zone lymphoma; PMBCL: primary mediastinal large B cell lymphoma

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

[2] Patients are CD19 CAR-T naïve

As of May 4, 2023 cutoff date

CB-010 has generally well-tolerated safety profile

No DLTs at dose level 2 or dose level 3, no Grade 3+ CRS, no GvHD observed (N=16)

AEs of special interest	ANTLER dose escalation (N=16)		
	CRS	ICANS[1]	Infections[2, 3]
Any grade, N (%)	7 (44%)	4 (25%)	7 (44%)
Grade 1	4 (25%)	2 (13%)	2 (13%)
Grade 2	3 (19%)	-	4 (25%)
Grade 3	-	1 (6%)	1 (6%)[3]
Grade 4	-	1 (6%)	-
Median time to onset, days (range)	3.5 (1,7)	7.5 (5,10)	27.0 (0, 279)
Median duration, days (range)	3.0 (1,9)	2.0 (1,34)	14.0 (2,63)

	CRS Gr 3+	ICANS Gr 3+	Infections Gr 3+
CB-010 ANTLER Phase 1	**0%**	**13%**	**6%**
Kymriah Phase 2[4]	23%	15%	41%
Yescarta Phase 1/2[5]	13%	31%	29%
Breyanzi Phase 1[6]	4%	12%	23%

AE: adverse event; CRS: cytokine release syndrome; DLT: dose-limiting toxicity; GvHD: graft-versus-host disease; ICANS: immune effector cell–associated neurotoxicity syndrome; TEAE: treatment-emergent adverse event

[1] Four total events, 2 Grade 1; 2 Grade 3+ at dose level 1, both with complete resolution of symptoms with supportive care.

[2] Infection events reported were on or after CB-010 infusion, with highest grade reported per patient.

[3] Grade 3 cellulitis (right antecubital) occurred after CB-010 infusion and was unrelated to CB-010 per the investigator.

[4] Kymriah: USPI, NCT02445248, Schuster NEJM 2019, N=111

[5] Yescarta: USPI, NCT02348216, N=101

[6] Breyanzi: USPI, NCT02631044, N=192

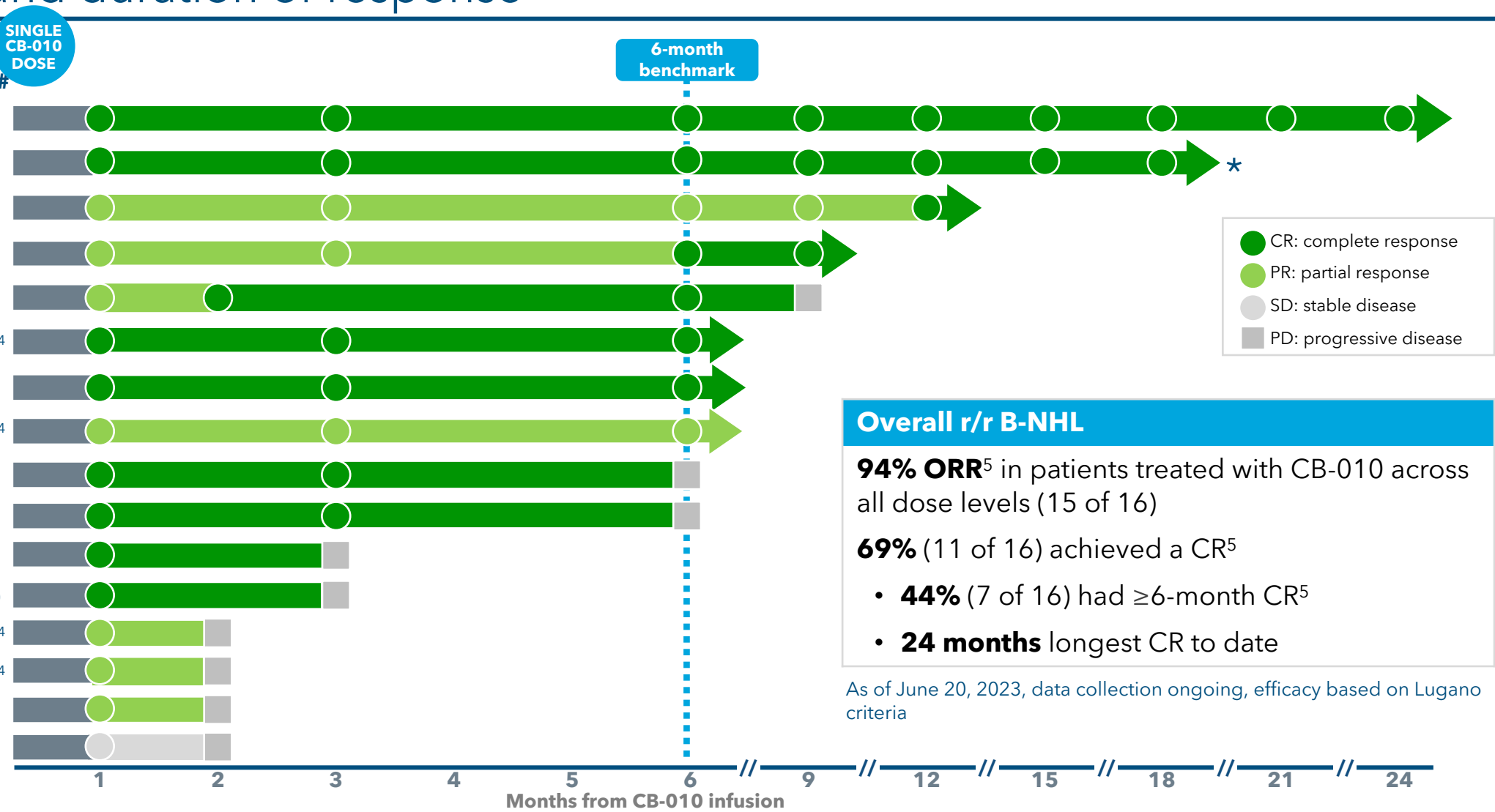
As of May 4, 2023 data cutoff date

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 in footnotes 4-6 of this slide.

CB-010 ANTLER dose escalation efficacy assessment

Overall depth and duration of response

Subtype	Dose	Prior # Rx	Best Resp.	Pt #
FL[1]	40M	8	CR	1
DLBCL	40M	4	CR	4
DLBCL[2]	80M	1	CR	7
DLBCL[2]	80M	1	CR	8
PMBCL[3]	40M	2	CR	5
MCL	40M	2	CR	13[4]
DLBCL	80M	2	CR	9
MZL	80M	4	PR	15[4]
MCL	40M	4	CR	2
FL[1]	40M	2	CR	3
DLBCL	40M	2	CR	6
DLBCL	120M	2	CR	10
HGBL[2]	40M	1	PR	14[4]
MCL	80M	2	PR	16[4]
HGBL[2]	120M	1	PR	12
DLBCL	120M	2	SD	11



Overall r/r B-NHL

94% ORR[5] in patients treated with CB-010 across all dose levels (15 of 16)

69% (11 of 16) achieved a CR[5]

- **44%** (7 of 16) had ≥6-month CR[5]
- **24 months** longest CR to date

As of June 20, 2023, 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; PMBCL: primary mediastinal large B cell lymphoma

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

[2] Primary refractory disease

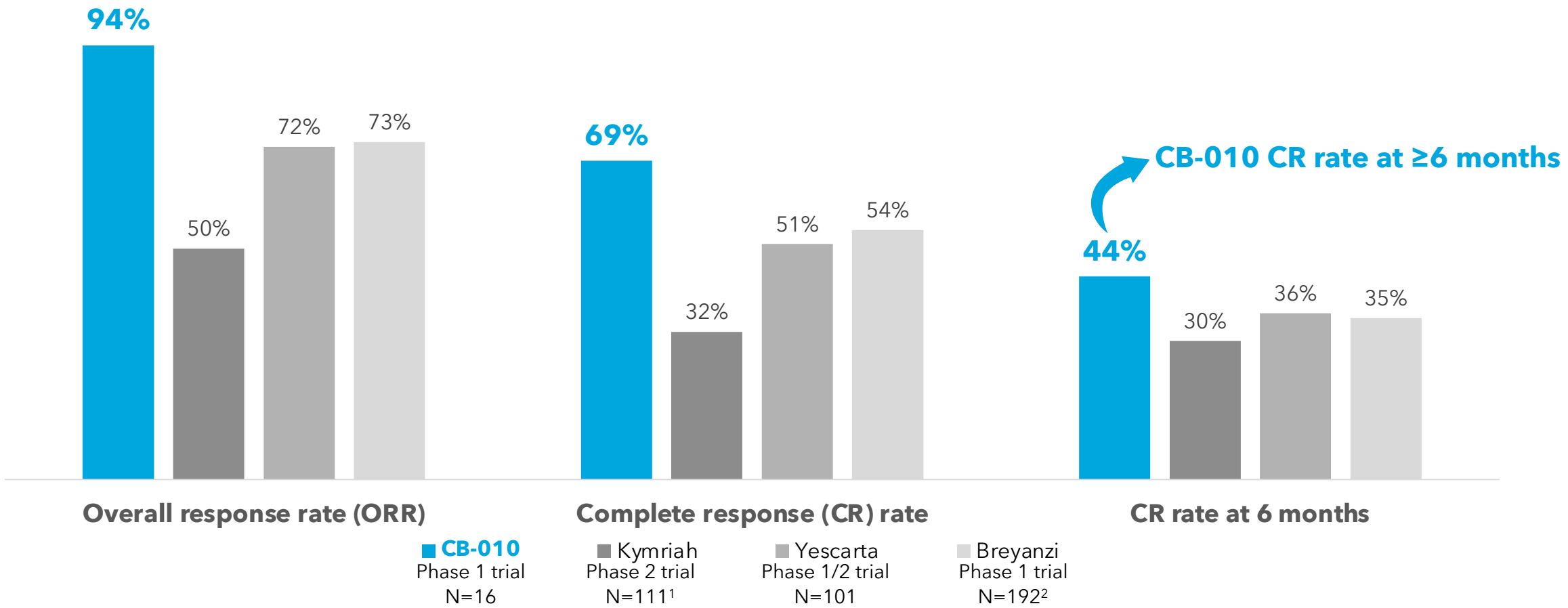
[3] Patient 5's 3-month scan conducted on day 63 post CB-010 as per investigator's discretion

[4] Patients 13-16 are backfill patients at 40M and 80M

[5] Certain patients with initial CR or PR progressed to PD at various assessment time points as indicated in the chart above

* Update on patient 4 presented at Lymphoma Leukemia & Myeloma Congress 2023; CR ongoing through month 21

CB-010 drives durable CRs that rival autologous CAR-T cell therapies



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Sources / patients enrolled
Kymriah: USPI, NCT02445248, Schuster NEJM 2019 / DLBCL NOS (78%) and tFL (22%)
Yescarta: USPI, NCT02348216, Focused on the Cure, Kite Pharma Corporate Presentation, March 2017 / DLBCL (76%), tFL (16%) and PMBCL (8%)
Breyanzi: USPI, NCT02631044 / DLBCL NOS (53%), DLBCL transformed from indolent lymphoma (25%), HGBL (14%), PMBCL (7%) and FL grade 3B (1%)
[1] ORR and CR rates shown are based on a 68-patient sub-group retrospectively identified as patients who were evaluable for the major efficacy outcome measures
[2] Enrolled population was 299; 6-month CR rate shown are patients who received treatment with Breyanzi

Subgroup efficacy profile supports 2L LBCL clinical development

	r/r B-NHL	r/r LBCL[2]	2L LBCL[3]
Endpoints N, (%)	**All patients** (N=16)	**Subgroup** (N=10)	**Subgroup** (N=4)
Overall response rate (ORR)[1]	15 (94%)	9 (90%)	4 (100%)
Complete response (CR) rate[1]	11 (69%)	7 (70%)	2 (50%)
≥6-month CR rate[1]	7 (44%)	5 (50%)	2 (50%)
CR at longest duration to date	24 months	18 months	12 months[4]

[1] Certain patients with initial CR or PR progressed to PD at various assessment time points
[2] Subgroup includes patients #4, 5, 6, 7, 8, 9, 10, 11, 12, and 14
[3] Four primary refractory patients were enrolled in dose escalation; subgroup includes patients #7, 8, 12, and 14.
[4] Patient #7 had a CR at 12 months, which converted from PR at the prior efficacy assessment

Advancing CB-010 to establish new standard of care for 2L LBCL and broaden patient access

- Response rates rival approved autologous CAR-T cell therapies
- 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 in second-line LBCL patients

94%

overall response rate (ORR)[1]

69%

complete response (CR) rate[2]

44%

complete response (CR) rate ≥6 months[3]

[1] 94% ORR measures number of patients (15 of 16) achieving either a CR or partial response (PR) at any time point after treatment with CB-010
[2] 69% CR rate measures the number of patients (11 of 16) achieving a CR at any time point after treatment with CB-010
[3] 44% CR rate measures number of patients (7 of 16) with a CR at 6-month or greater time point; includes one patient who converted from PR to CR at 12-month assessment
[1, 2, 3] Certain patients with initial CR or PR progressed to PD at various assessment time points

CB-010

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

CARIBOU BIOSCIENCES®

Lupus is a chronic, inflammatory autoimmune disease driven by autoantibody-producing B cells

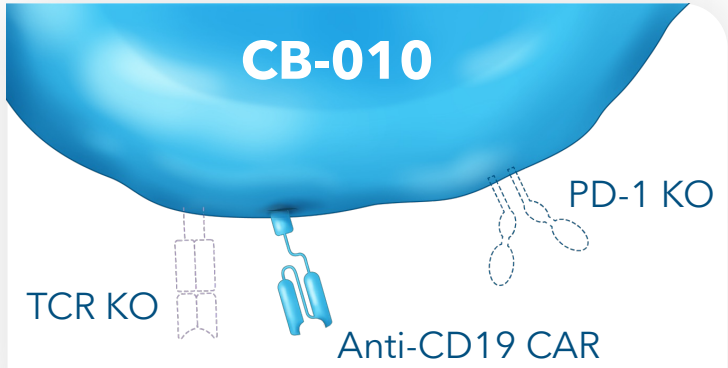
Lupus is a chronic disease affecting **~320,000** individuals in the US[1]

- Lupus is caused by B cell production of autoantibodies that drive damage of healthy tissue
- Lupus can cause widespread organ damage, increase cardiovascular risk, and significantly impair patient quality of life
- Urgent unmet need for new treatment options that can offer sustained, drug-free remission

[1]Li D, et al. Rheumatology (Oxford). 2020 Mar 1;59(3):495-504.

CB-010 is an allogeneic CAR-T cell therapy that targets autoantibody-producing B cells

Anti-CD19 CAR targets autoantibody-producing B cells



Engineered for improved activity

chRDNA genome editing enables **precision engineering** and **reduced off-target** edits

CB-010 is **engineered with a PD-1 KO[1]** to potentially enhance anti-B cell activity and may drive **sustained remission**

Encouraging clinical data

Encouraging initial safety and efficacy demonstrated for CB-010 in ANTLER Phase 1 trial

ANTLER **B cell depletion is on par** with depletion data published on autologous CAR-T cells in lupus[2]

[1] To Caribou's knowledge, CB-010 is the first allogeneic CAR-T in the clinic with checkpoint disruption via PD-1 KO
[2] Müller F, et al. N Engl J Med. 2024

CB-010 GALLOP Phase 1 trial design

Eligibility and matching

- Non-responsive to glucocorticoids and have tried and failed at least 2 defined immunosuppressive therapies
- Excludes cardiac and CNS involvement
- Partial HLA matching and absence of baseline DSAs

Treatment and objective

- Single dose level of CB-010 following LD
- Primary endpoint: safety

Patient cohorts

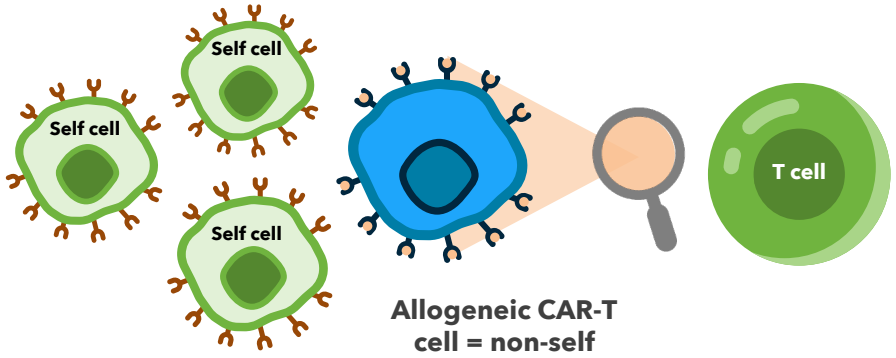
Cohort 1: Lupus nephritis (LN)
Renal SLEDAI ≥ 8 or Class III/IV glomerular nephritis

Cohort 2: Extrarenal lupus (ERL)
SLEDAI ≥ 8

Cy: cyclophosphamide; DSAs: donor-specific antibodies; Flu: fludarabine; HLA: human leukocyte antigen; LD: lymphodepletion; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index

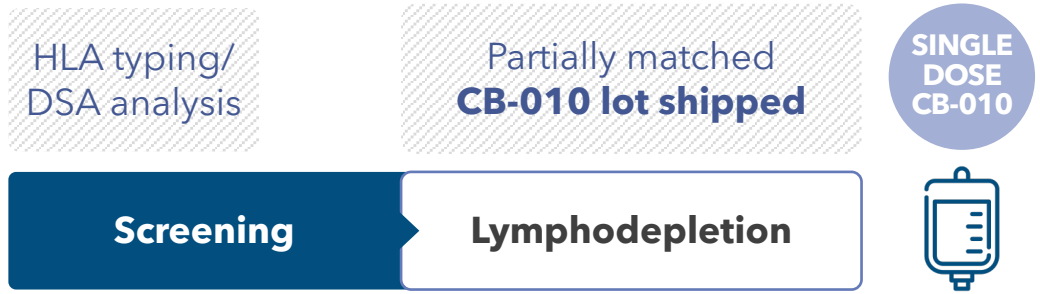
Partial HLA matching to potentially improve patient outcomes

How does HLA matching work?



- Human leukocyte antigens (HLAs) help the immune system identify "self" from "non-self"
- Patient's immune cells recognize allogeneic CAR-T cells as "non-self" and initiate rejection

HLA matching and DSA screening for ANTLER and GALLOP Phase 1 trials



- HLA typing and DSA analysis occur within screening timeline
- Partial HLA matching could result in enhanced outcomes for patients[1]

DSA: donor-specific antibodies
[1]Based on data from the ANTLER Phase 1 trial in r/r B-NHL and to be confirmed in the trials; initial data to be presented at ASCO 2024

Advancing CB-010 for autoimmune disease

Allogeneic CAR-T cell therapies are derived from healthy donor T cells and offer readily-available, single dose treatment

Expansion of CB-010 development to include autoimmune disease

- Encouraging initial safety and efficacy in r/r B-NHL
- CB-010-driven depletion of B cells on par with published B cell depletion data[1]
- B cell depletion could reset immune system and lead to sustained, drug-free remission
- Enhanced patient outcomes possible with partial HLA matching and DSA screening

Engineered with chRDNA precision genome-editing technology

- PD-1 knockout designed to prevent CAR-T cell exhaustion
- No lentiviral or retroviral vectors

HLA: human leukocyte antigens; DSA: donor-specific antibodies

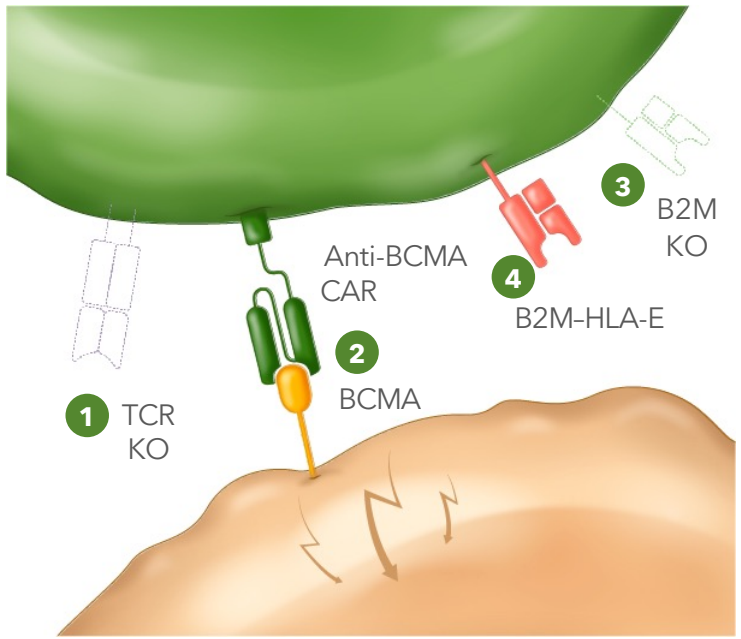
[1]Müller et al. N Engl J Med. 2024 Feb 22;390(8):687-700

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



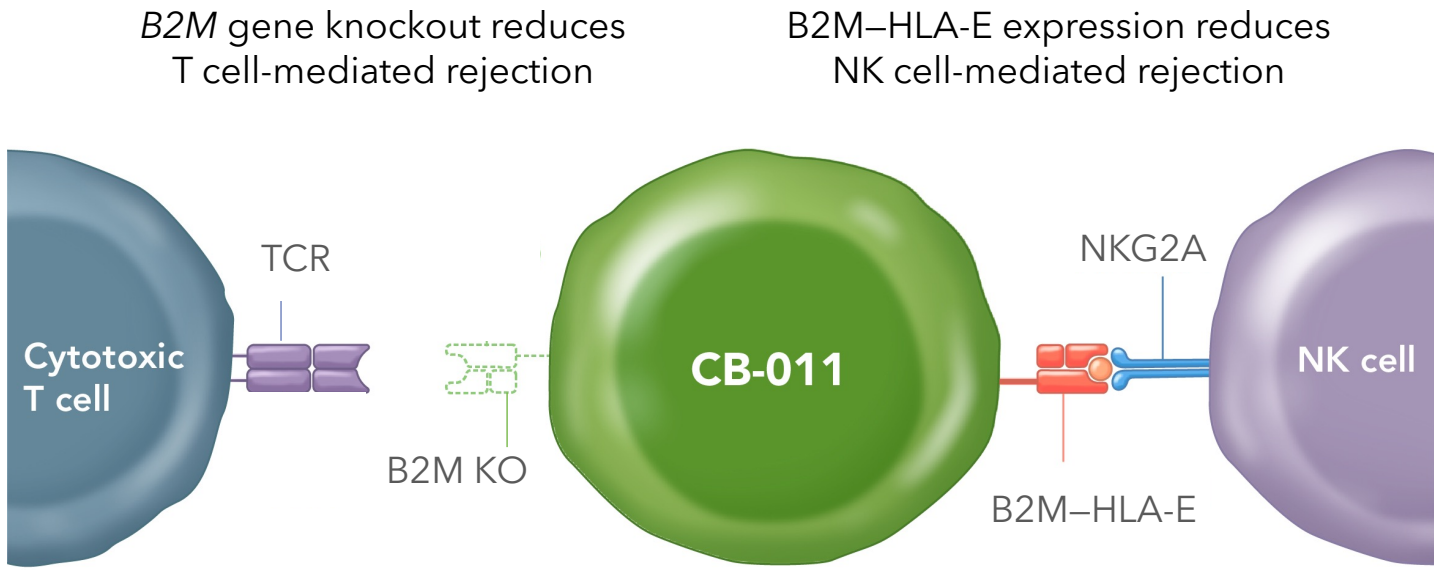
Armored with 4 genome edits

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

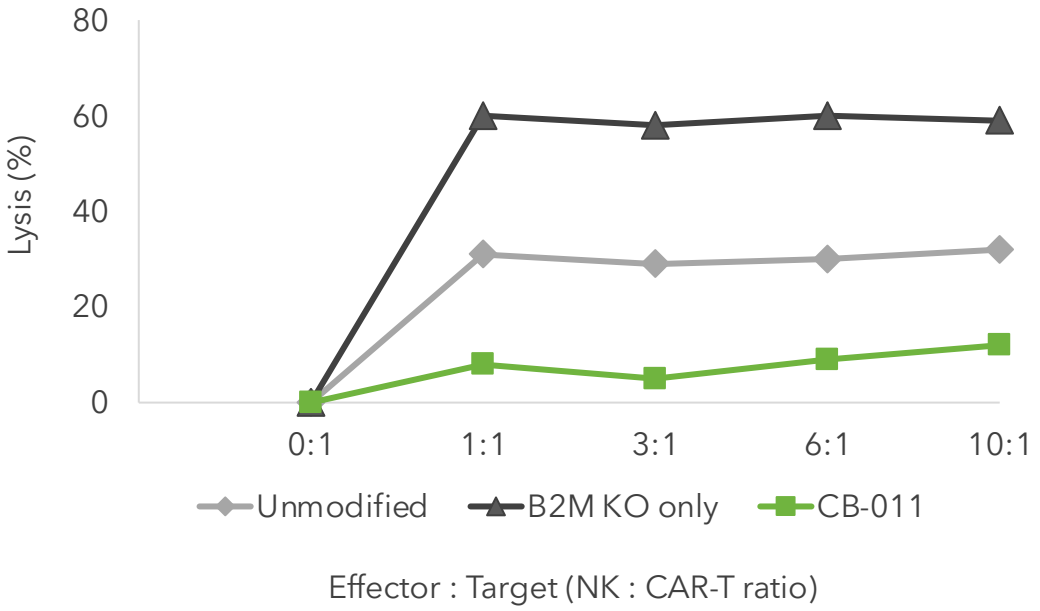


- *B2M* KO removes all endogenous HLA class I presentation to **reduce T cell-mediated rejection**
- B2M–HLA-E-peptide fusion insertion **blunts NK cell-mediated rejection**
- The **Cas12a chRDNA** editing platform achieves **high insertion efficiencies** facilitating the insertion of the B2M–HLA-E-peptide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

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

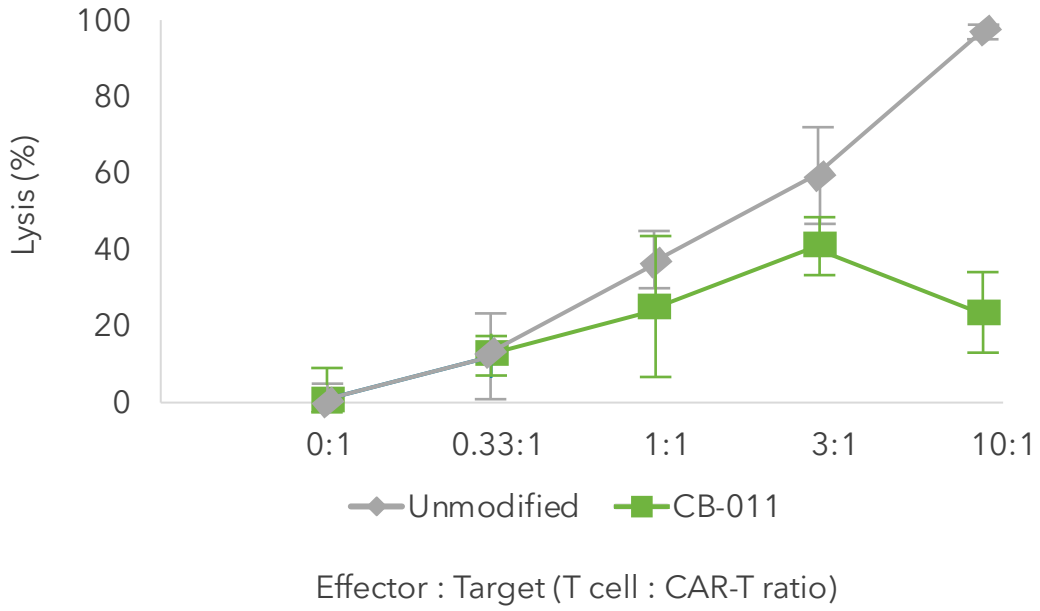
B2M–HLA-E fusion enables CB-011 cells to resist killing by NK cells

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*

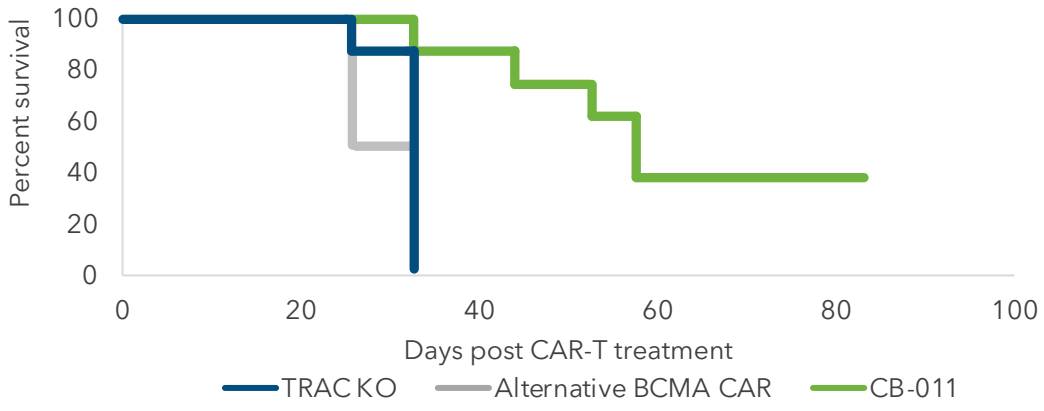


**In vitro* cytotoxicity measured 24 hours after co-incubation
Degagné É, et al. Cancer Immunol Res. s; 12(4) April 2024.

CB-011 enhanced long-term survival in preclinical studies

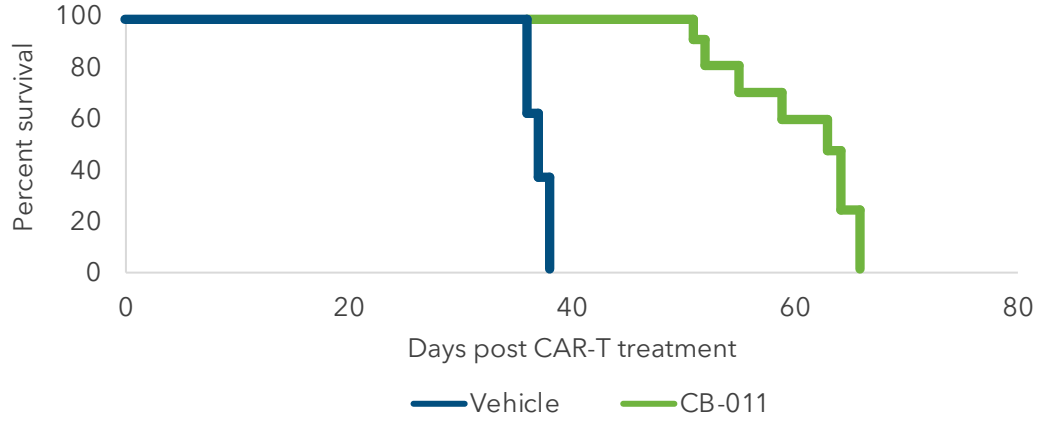
CB-011 led to statistically significant and longer survival of tumor-bearing mice
relative to an alternative anti-BCMA CAR-T cell therapy after a single dose

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

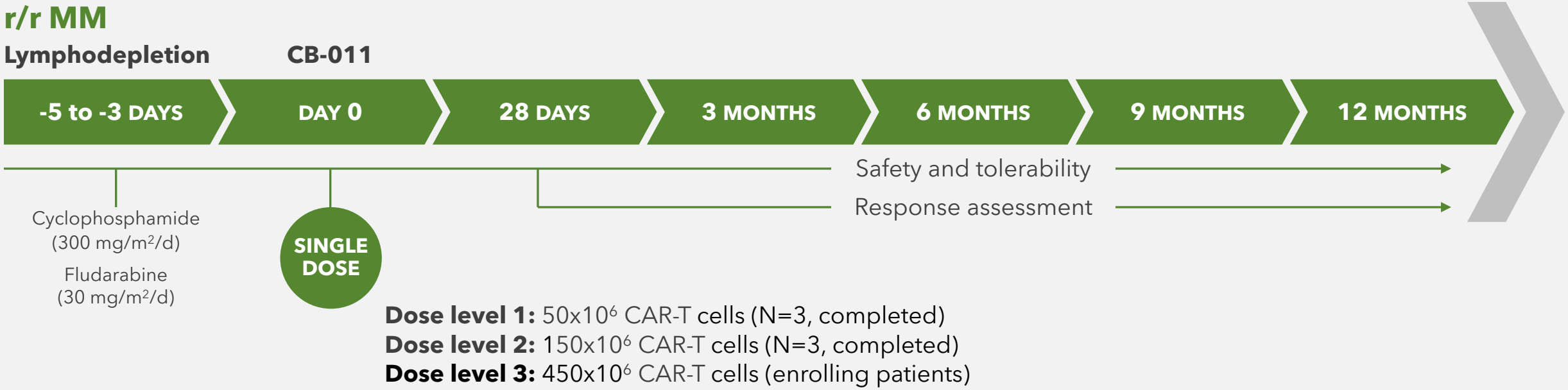
Degagné É, et al. Cancer Immunol Res. s; 12(4) April 2024.

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



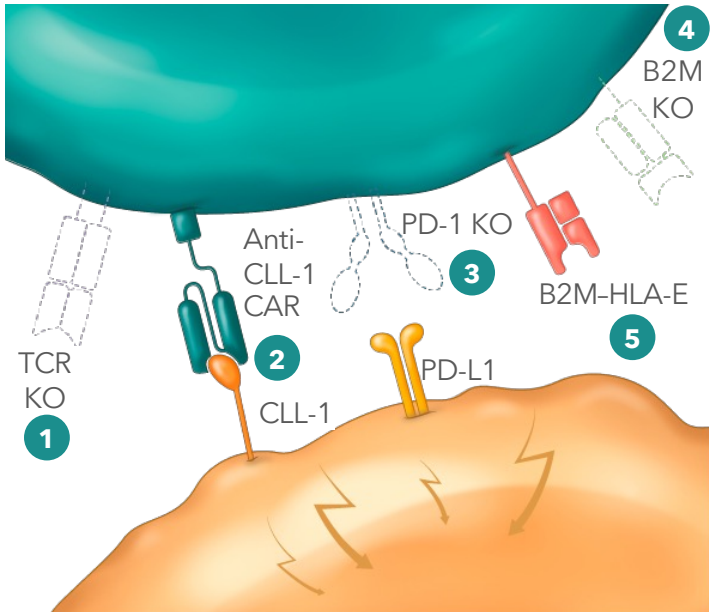
NCT05722418
IMiD: immunomodulatory drug; mAb: monoclonal antibody; MM: multiple myeloma; MTD: maximum tolerated dose; PI: proteasome inhibitor; RDE: recommended dose for expansion; RP2D: recommended Phase 2 dose

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

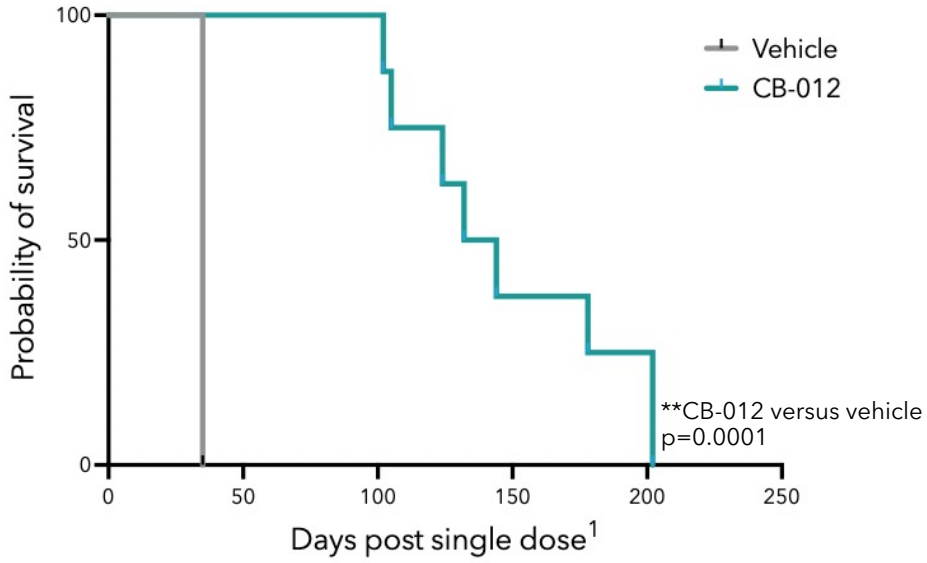
1. ***TRAC* gene knockout (KO)**
   - Eliminates TCR expression, reduces GvHD risk
2. **Human anti-CLL-1 CAR site-specifically inserted into *TRAC* gene**
   - Eliminates random integration, targets tumor antigen
3. **PD-1 KO for enhanced antitumor activity**
   - Potentially better therapeutic index 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

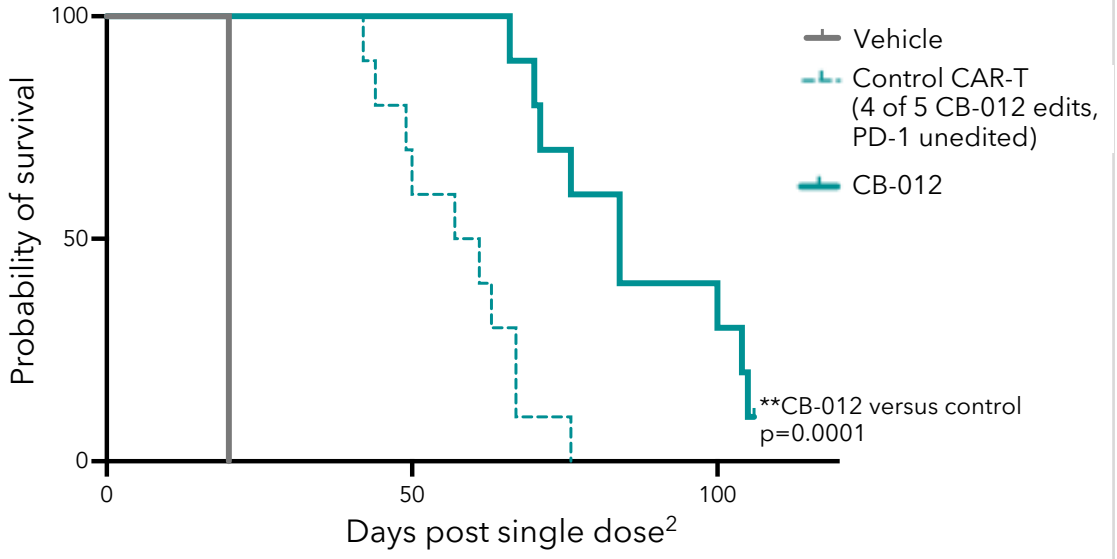
CB-012 significantly reduced tumor burden and increased overall survival in preclinical studies

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

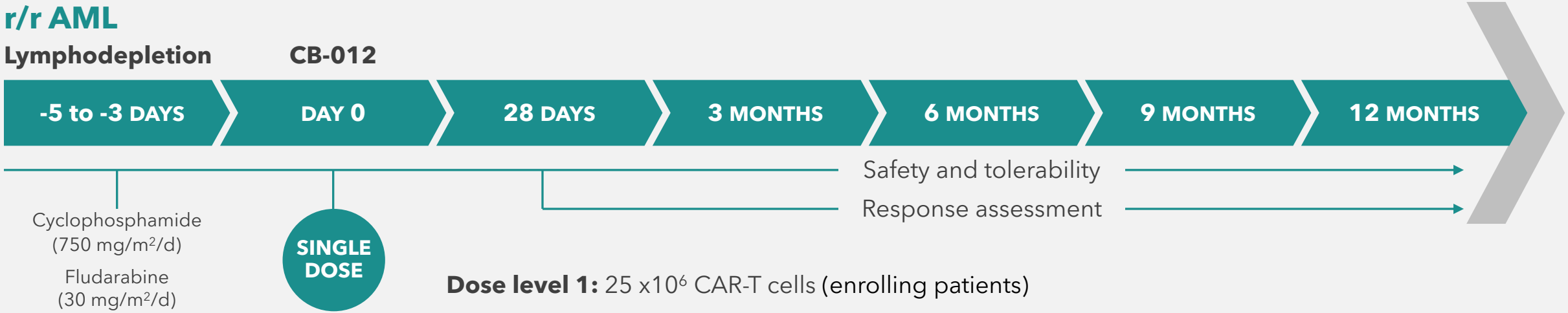
- Relapsed or refractory AML patients should have received at least 1 but not more 3 prior lines of therapy
- Patients with prior allo or auto SCT are allowed
- Exclusions: prior CAR-T cell therapy and/or CLL-1-targeted therapy

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

2024 accomplishments and upcoming milestones

Hematologic malignancies

CB-010 in 2L LBCL

○ Present initial dose expansion data from ANTLER Phase 1 trial in 2L LBCL, RP2D	ASCO June 2024

CB-011 in r/r MM

○ Present initial dose escalation data from CaMMouflage Phase 1 trial	YE 2024

CB-012 in r/r AML

✓ Dosed first patient in the AMpLify Phase 1 trial	

Autoimmune disease

CB-010 in LN and ERL

○ Initiate GALLOP Phase 1 trial	YE 2024

Corporate and financial

Well capitalized

- ✓ ~$346M[1] in cash
- ✓ Runway into Q1 2026

[1]$345.9M in cash, cash equivalents, and marketable securities as of March 31, 2024

Thank you

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

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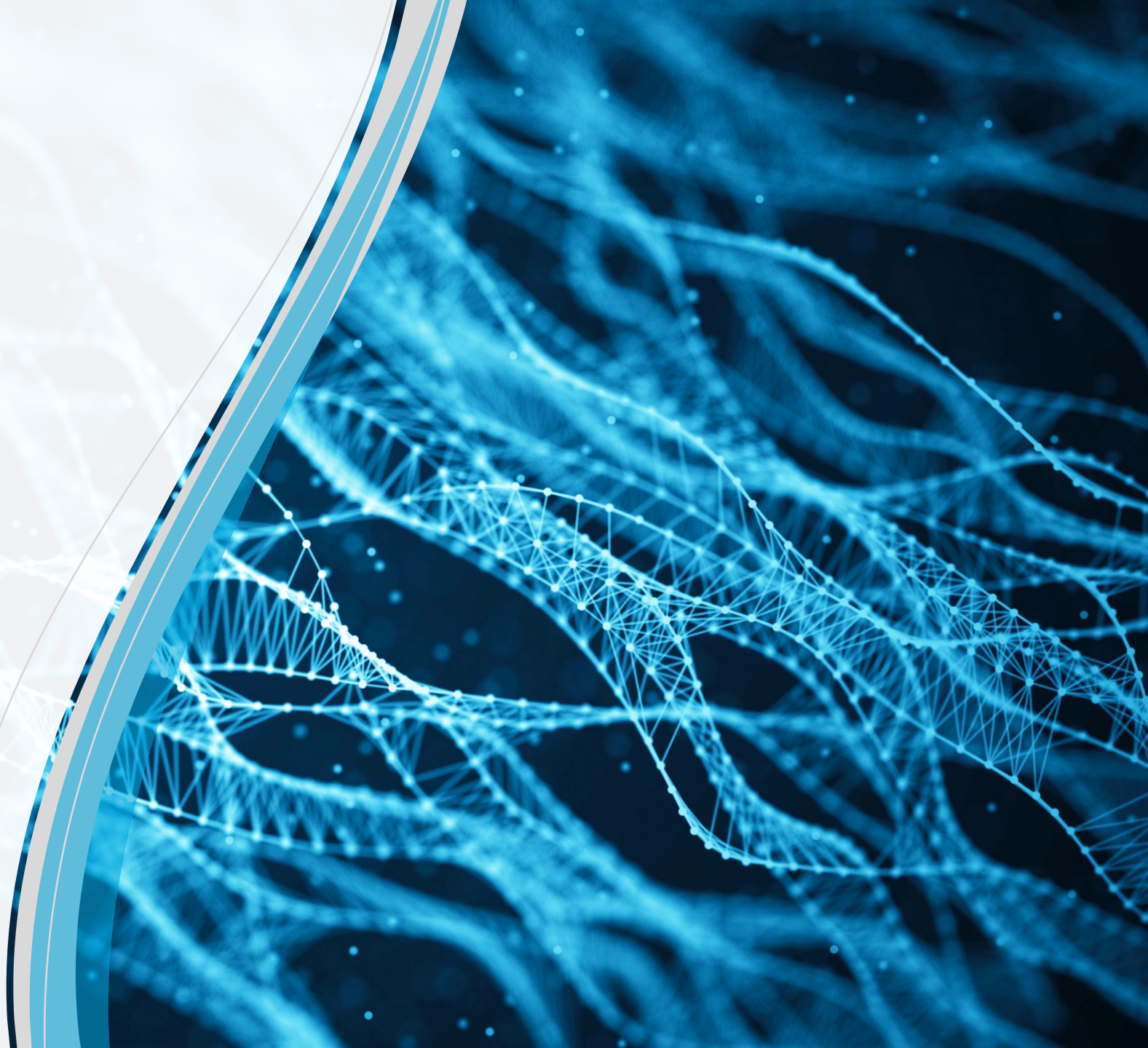
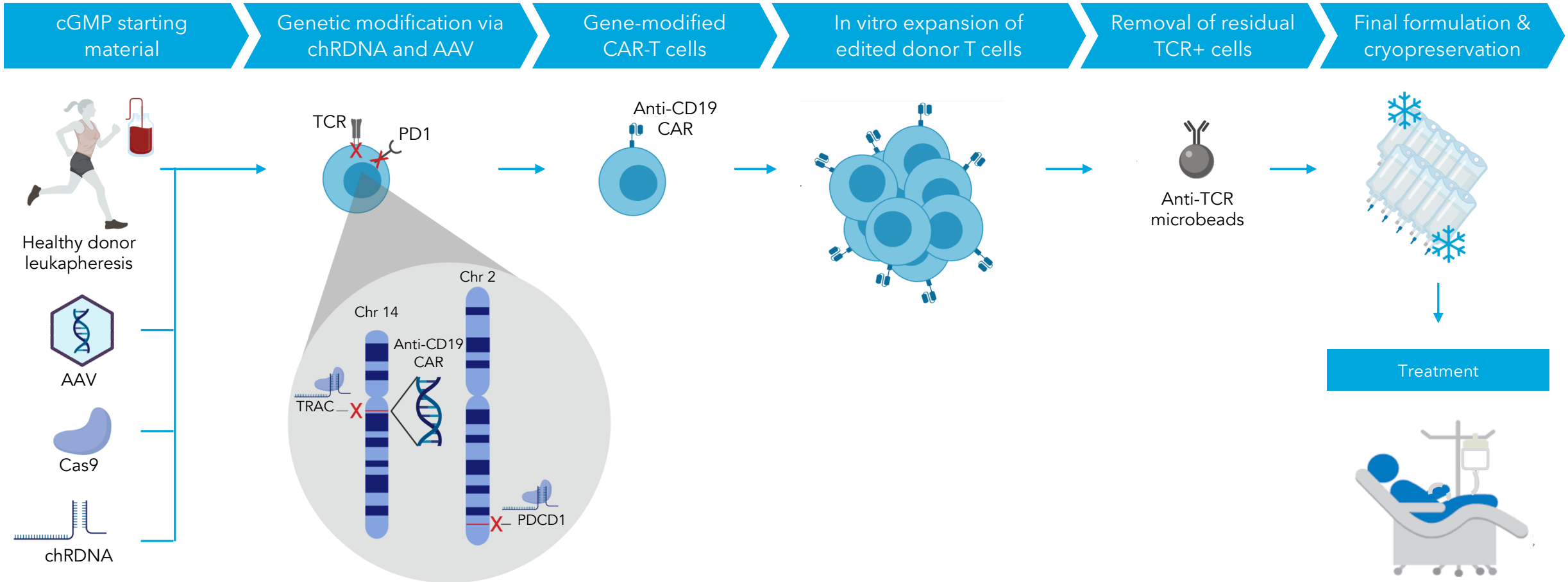


Allogeneic CAR-T cell manufacturing process overview for CB-010

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



CB-010 ANTLER dose escalation efficacy assessment

Overall, r/r, and 2L LBCL subgroups, by dose level

	r/r B-NHL	r/r LBCL[2]	2L LBCL[3]	CB-010 dose level		
Endpoints (N, %)	**All patients** (N=16)	**Subgroup** (N=10)	**Subgroup** (N=4)	**40M** (N=8)	**80M** (N=5)	**120M** (N=3)
Overall response rate (ORR)[1]	15 (94%)	9 (90%)	4 (100%)	8 (100%)	5 (100%)	2 (67%)
Complete response (CR) rate[1]	11 (69%)	7 (70%)	2 (50%)	7 (88%)	3 (60%)	1 (33%)
≥6-month CR rate[1]	7 (44%)	5 (50%)	2 (50%)	4 (50%)	3 (60%)	0
CR at longest duration	24 months	18 months	12 months[4]	24 months	12 months	28 days

[1] Certain patients with initial CR or PR progressed to PD at various assessment time points.
[2] Subgroup includes patient #4, 5, 6, 7, 8, 9, 10, 11, 12, and 14.
[3] Four primary refractory patients were enrolled in dose escalation. Subgroup includes patient #7, 8, 12, and 14.
[4] Patient #7 had a CR at 12 months, which converted from PR at the prior efficacy assessment.

CB-010's responses rival autologous CAR-T cell therapies

	CB-010 dose escalation Phase 1 % (n/N)	Kymriah Phase 2 % (n/N)	Yescarta Phase 1/2 % (n/N)	Breyanzi Phase 1 % (n/N[2])
Overall response rate (ORR)[1]	94% (15/16)	50% (34/68)	72% (73/101)	73% (141/192)
Complete response (CR) rate[1]	69% (11/16)	32% (22/68)	51% (52/101)	54% (104/192)
CR rate at 6 months[1]	44% (7/16)[3]	30% (33/111)	36% (36/101)	35% (68/192)
CRS (Grade 3+)	0% (0/16)	23%	13%	4%
ICANS (Grade 3+)	13% (2/16)	15%	31%	12%
Infections (Grade 3+)	6% (1/16)	41%	29%	23%

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.

Sources / patients enrolled
Kymriah: USPI, NCT02445248, Schuster NEJM 2019 / DLBCL NOS (78%) and tFL (22%)
Yescarta: USPI, NCT02348216 / Locke, et al, AACR 2017 ZUMA-1 presentation / DLBCL (76%), tFL (16%) and PMBCL (8%)
Breyanzi: USPI, NCT02631044 / DLBCL NOS (53%), DLBCL transf. from ind. lymphoma (25%), HGBL (14%), PMBCL (7%) and FL grade 3B (1%)

[1] Certain patients with initial CR or PR progressed to PD at various assessment time points.
[2] Enrolled population was 299; 6-month CR rate shown are patients who received treatment with Breyanzi.
[3] CR rate ≥6 months.

CB-010 is generally well tolerated

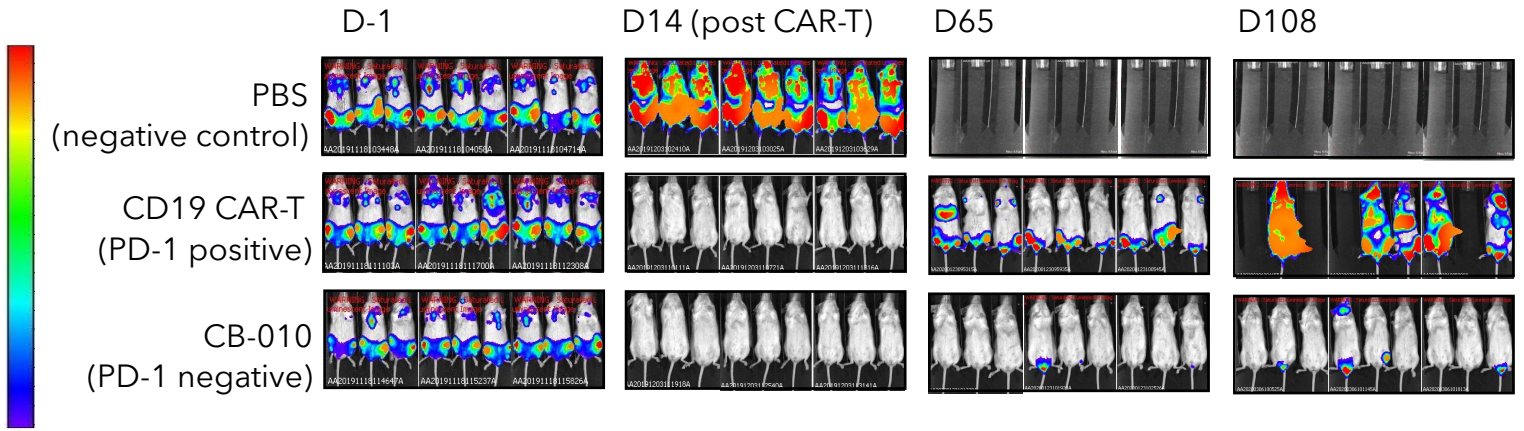
Treatment-emergent adverse events (TEAE)

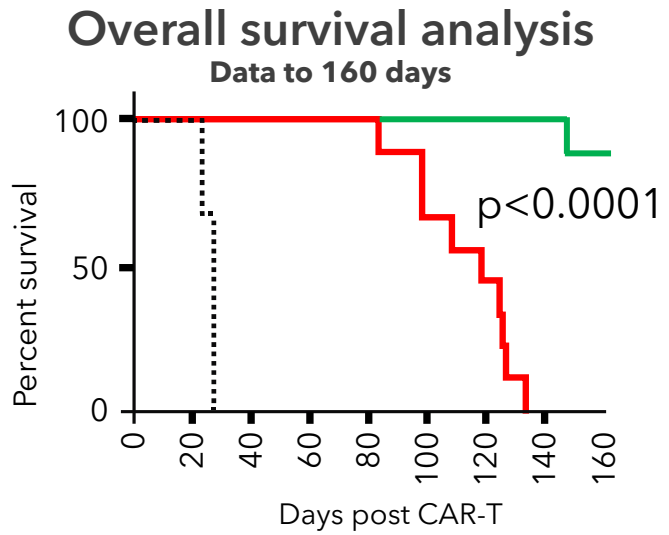
Event (N=16)	Any Grade[1] N (%)	All Grade 3+ N (%)	Related Grade 3+ N (%)
Total number of TEAEs, N	**348**	**96**	**28**
Subjects with TEAE, n (%)	**15 (94)**	**14 (88)**	**8 (50)**
Thrombocytopenia/platelet count decreased	11 (69)	11 (69)	5 (31)
Anemia	11 (69)	8 (50)	1 (6)
Neutropenia/Neutrophil count decreased	10 (63)	9 (56)	1 (6)
Cytokine release syndrome	7 (44)	-	-
White blood cell count decreased	7 (44)	7 (44)	4 (25)
Fatigue	4 (25)	-	-
Lymphocyte count decreased	4 (25)	3 (19)	1 (6)
Blood creatinine increased	4 (25)	-	-
ICANS (immune effector cell–associated neurotoxicity)	4 (25)	2 (13)	2 (13)
Fall	3 (19)	-	-
Diarrhea	3 (19)	-	-
Hypoalbuminemia	2 (13)	-	-
Hypocalcemia	2 (13)	-	-
Hyponatremia	2 (13)	-	-
Muscular weakness	2 (13)	-	-
Febrile neutropenia	2 (13)	2 (13)	1 (6)
Syncope	2 (13)	2 (13)	-
Pulmonary embolism	2 (13)	1 (6)	-
Atrial fibrillation	1 (6)	1 (6)	1 (6)
Acute kidney injury	1 (6)	1 (6)	-
Cellulitis	1 (6)	1 (6)	-
Encephalopathy[2]	1 (6)	1 (6)	1 (6)
Hyperglycemia	1 (6)	1 (6)	-

[1] TEAEs are defined as adverse events (AEs) with a start date on or after the CB-010 infusion date.
[2] Encephalopathy and Grade 4 ICANS events were related and occurred in same patient.
Table includes AEs with at least 2 subjects at any single dose level or at least 1 subject with a higher than Grade 3 TEAE.
As of May 4, 2023 data cutoff date.

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

Potential to address high unmet medical need in 2L LBCL

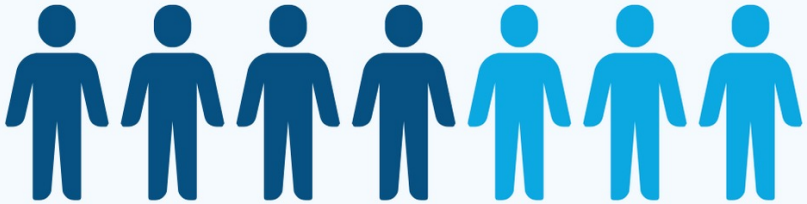
LBCL patient treatment journey
(U.S. incidence 2022)

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

ANTLER dose expansion

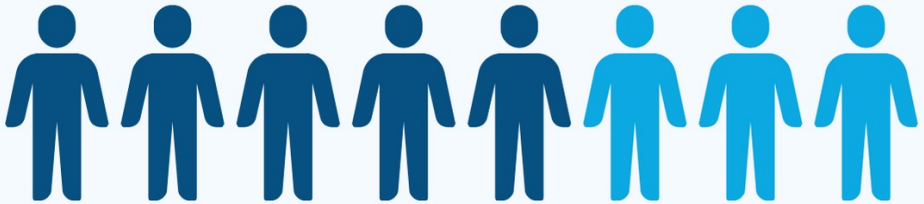
Herd diversity

EXECUTIVE LEADERSHIP



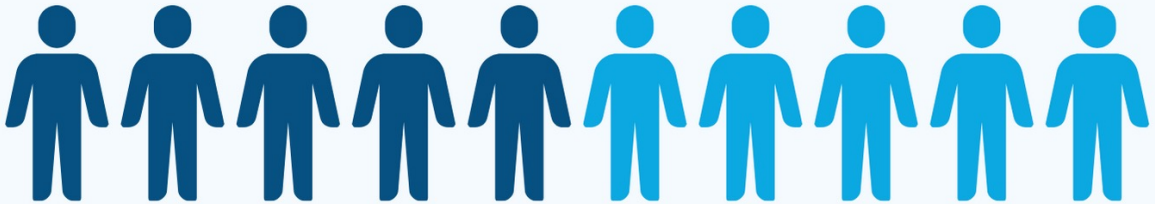
57% FEMALE

BOARD OF DIRECTORS



62% FEMALE

ALL EMPLOYEES



51% FEMALE