CARIBOU BIOSCIENCES®

August 2023

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 additional clinical data from our ongoing ANTLER phase 1 clinical trial for our CB-010 product candidate; plans for meeting with the U.S. Food and Drug Administration (FDA) to discuss a potential pivotal clinical trial for our CB-010 product candidate; the status, progress, and release of clinical data from our ongoing CaMMouflage phase 1 clinical trial for our CB-011 product candidate; expectations relating to the submission of our IND application for our CB-012 product candidate; 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 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 COVID-19 and other 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, 2022, 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 companies' CAR-T cell therapies presented in these slides 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 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 or third-party data in reaching any conclusion or making any investment decision about any securities of the Company. 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, the Company may release additional clinical data from its ongoing ANTLER phase 1 clinical trial and its CaMMouflage phase 1 clinical trial. The Company makes 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 allogeneic cell therapies

- Allogeneic CAR-T and CAR-NK cell therapies **armored for potential improvement in antitumor activity**
  - Checkpoint disruption
  - Immune cloaking
  - Cytokine support
- 6 programs
  - 4 wholly owned
  - 2 for AbbVie in strategic collaboration

Resourced for successful execution

- Experienced, mission-driven leadership
- Strong in-house process development capabilities
- Robust IP portfolio
- $25M Pfizer investment
- >$400M[1] in cash, runway into Q4 2025

chRDNA: CRISPR hybrid RNA-DNA

[1] $292.5M in cash, cash equivalents, and marketable securities as of June 30, 2023, which included the $25.0M proceeds from the Pfizer investment; plus $134.6 million in net proceeds from an underwritten public offering of common stock that closed in the third quarter of 2023.

Pfizer's $25M investment in Caribou highlights potential of programs

$25M investment[1] from premier global pharmaceutical company

- Pfizer investment highlights Caribou's allogeneic CAR-T cell therapy technology
- Use of proceeds to advance CB-011, an immune cloaked allogeneic CAR-T cell therapy
  - CB-011 being evaluated in the ongoing CaMMouflage Phase 1 clinical trial in patients with relapsed or refractory multiple myeloma
  - Pfizer receives a 30-day right of first negotiation for CB-011
- Caribou will maintain full ownership and control of its pipeline of allogeneic CAR-T and CAR-NK cell therapies
- Sriram Krishnaswami, PhD, VP & development head, multiple myeloma, Pfizer Global Product Development, joined Caribou's Scientific Advisory Board

[1] 4.7M shares to Pfizer at $5.33 per share, pursuant to the terms of the Securities Purchase Agreement dated June 29, 2023

Pipeline: allogeneic cell therapies targeting oncology indications

Program	Clinical trial	Target	Indication	Discovery	IND enabling	Phase 1	Phase 2	Phase 3[1]	Designations
CAR-T platform with cell therapies for hematologic indications									
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
CB-012	IND application planned	CLL-1[2]	r/r AML	●	●	○	○	○	
CAR-NK platform with iPSC-derived cell therapies for solid tumor indications									
CB-020		ROR1	solid tumors	●	○	○	○	○	
AbbVie programs under collaboration agreement[3]									
CAR-T program 1						undisclosed			
CAR-T program 2						undisclosed			

IND: investigational new drug; RMAT: Regenerative Medicine Advanced Therapy
[1] Phase 3 may not be required if Phase 2 is pivotal
[2] Also known as CD371
[3] AbbVie has an option for two additional CAR-T cell programs

chRDNA technology

CARIBOU BIOSCIENCES®

chRDNA is a next-generation CRISPR platform with significant advantages

Specificity

Fewer off-target events versus 1st-generation CRISPR

Efficiency

Multiplex editing with high genomic integrity

Versatility

Utility across a multitude of cell types

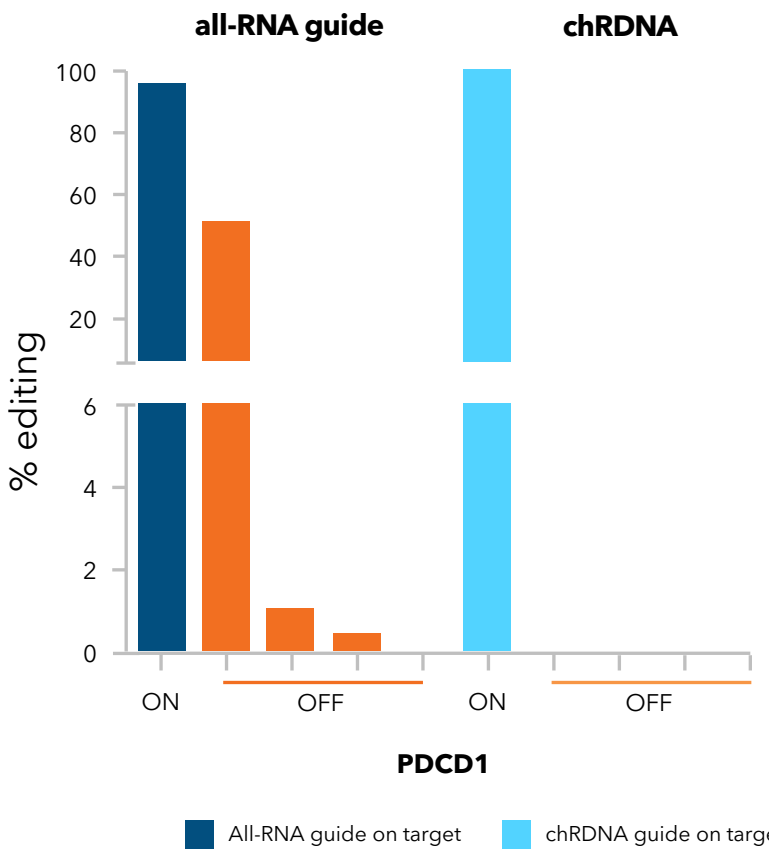
Simplicity

Manufactured via standard chemical synthesis

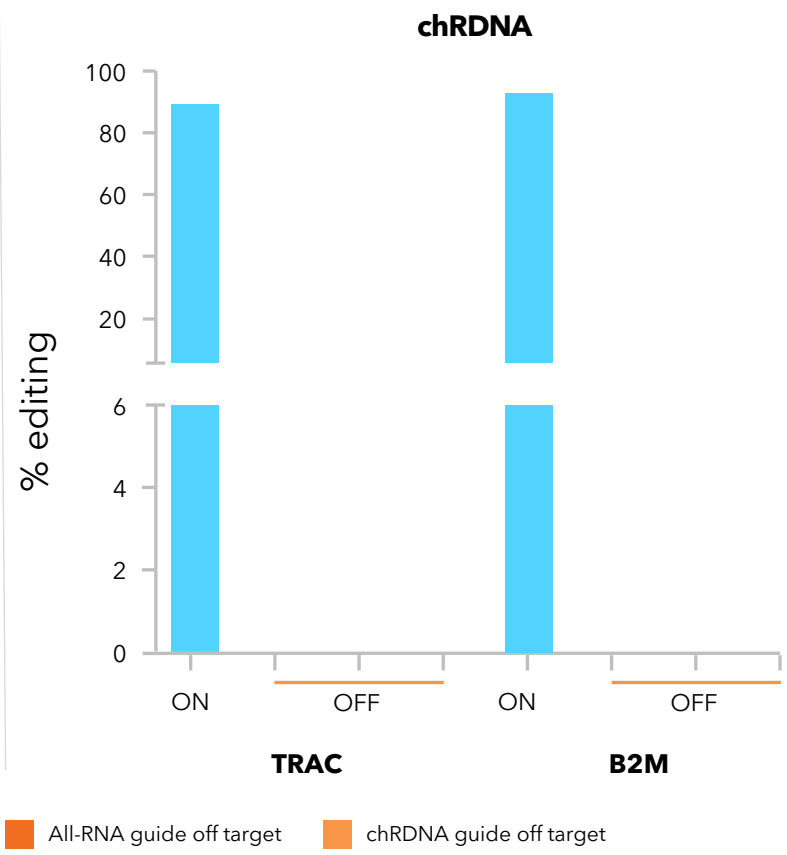
chRDNA guides significantly improve editing specificity

Knockout

Cas9

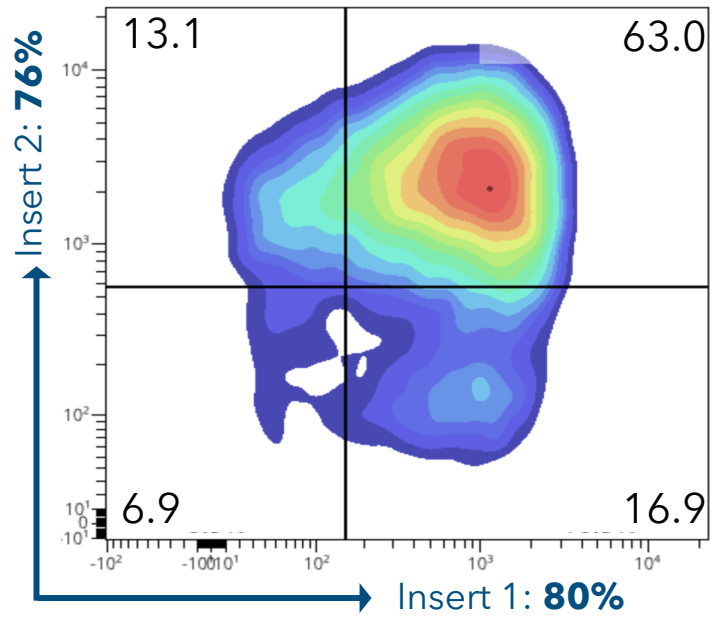


Cas12a



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

Knock-in

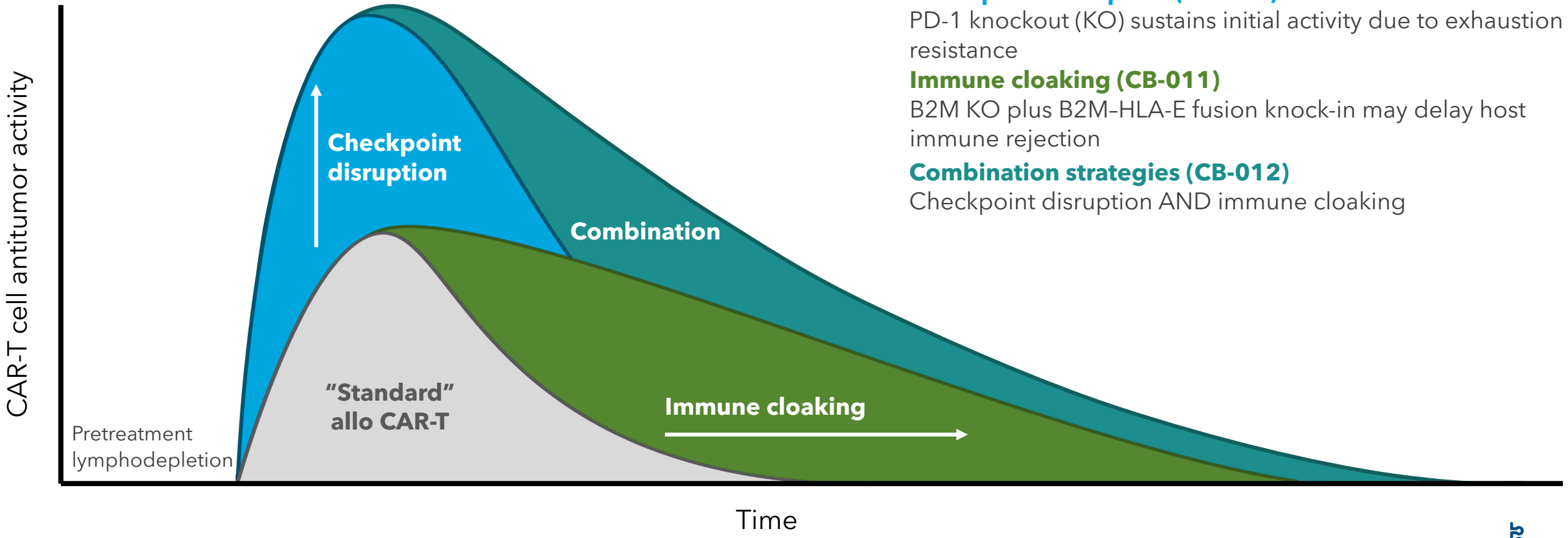


Cas12a chRDNA genome editing + AAV6 transduction leads to >60% of manufacturing-scale engineered T cells with all 4 intended edits

Editing assayed in primary human T cells

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

Caribou is implementing multiple armoring strategies



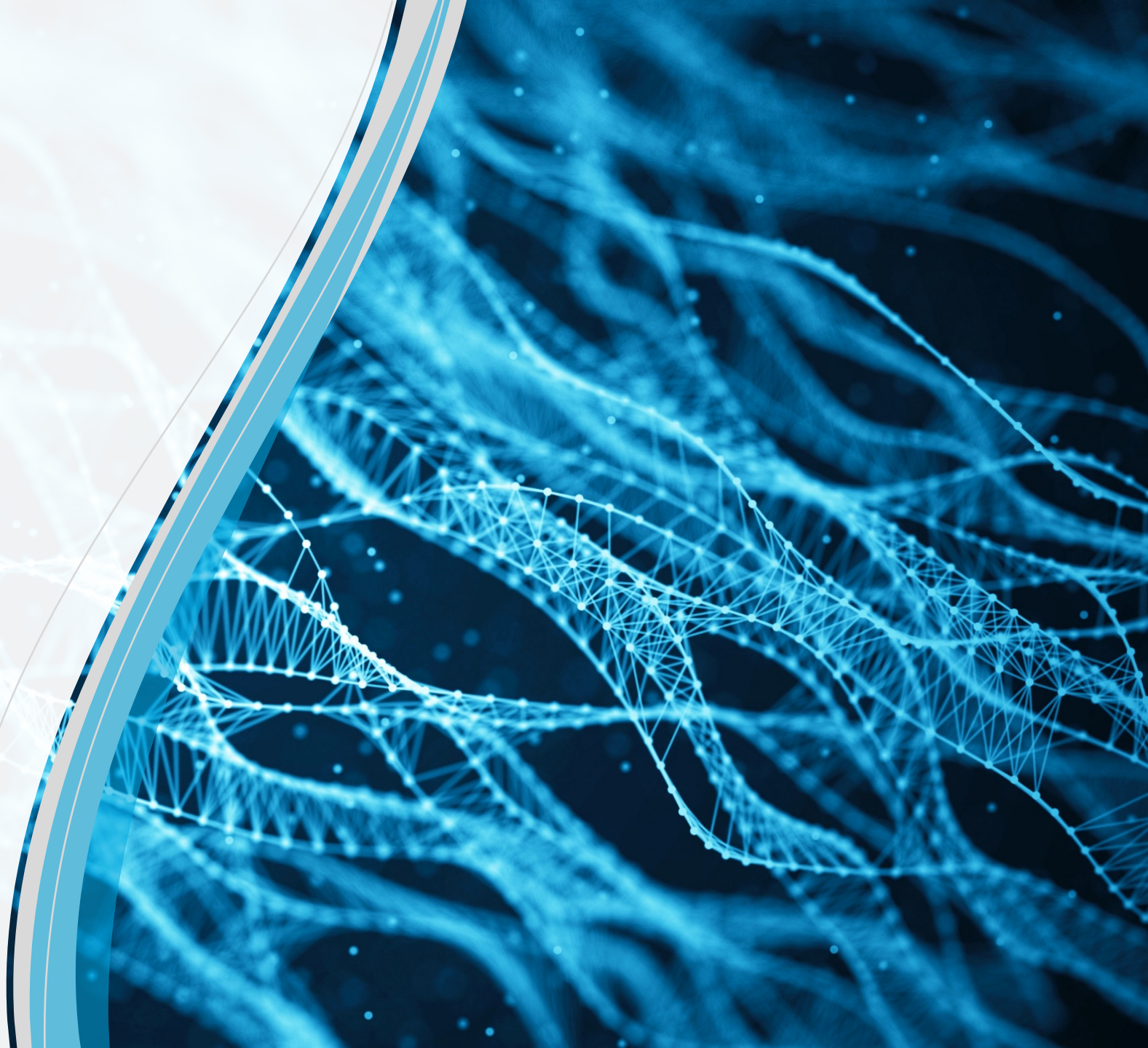
Checkpoint disruption (CB-010)
PD-1 knockout (KO) sustains initial activity due to exhaustion resistance

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

CAR-T platform

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



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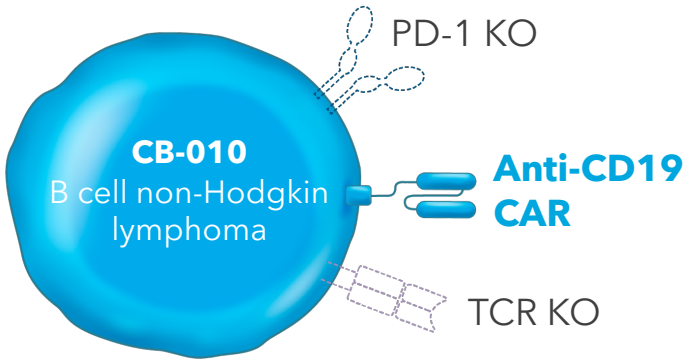
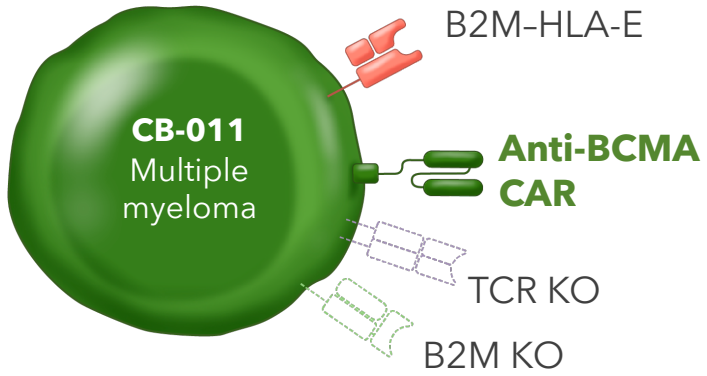
Caribou is a leader in the allogeneic CAR-T cell space with a platform of genome-edited cell therapies

3 Edits



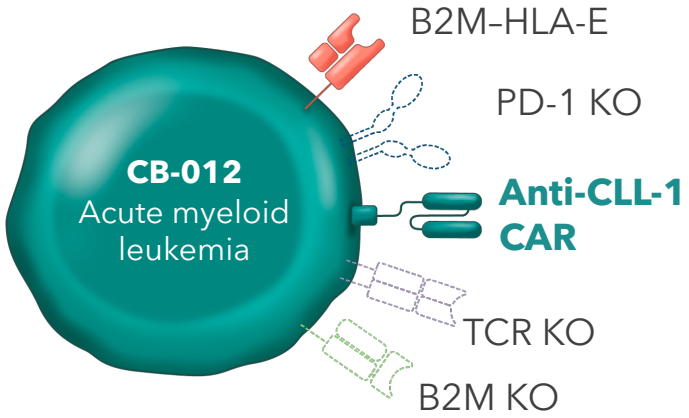
1st allogeneic anti-CD19 CAR-T cell therapy in the clinic with **checkpoint disruption** via PD-1 knockout (KO) to reduce T cell exhaustion

4 Edits



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

5 Edits



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

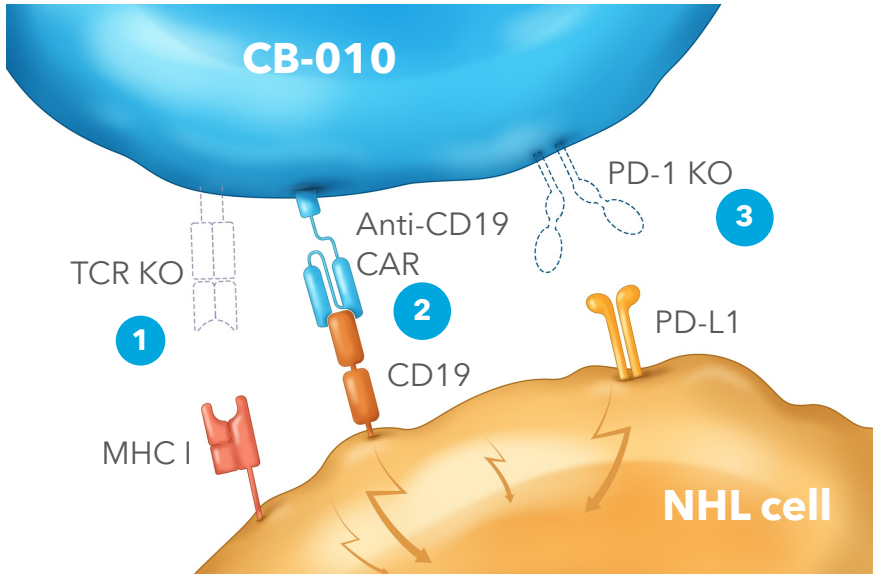
CB-010

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

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

Key attributes	CB-010	Conventional allogeneic anti-CD19 CAR-Ts
Cas9 chRDNA editing for enhanced genomic integrity	✓	✗
• Reduced off-target editing and genomic rearrangements	✓	✗
1 ***TRAC* gene knockout (KO)**	✓	Varies
• Eliminates TCR expression, reduces GvHD risk		
2 **Anti-CD19 CAR site-specific insertion into *TRAC* locus**	✓	Varies
• Eliminates random integration, targets tumor antigen		
3 **PD-1 KO for enhanced antitumor activity**	✓	✗
• Potentially better therapeutic index via initial tumor debulking	✓	✗

CB-010 CAR construct uses an anti-CD19 scFv FMC63 with a 4-1BB costimulatory domain



Program: CB-010

Healthy donor leukapheresis-derived T cells

Tumor antigen: CD19

Indication: r/r B cell non-Hodgkin lymphoma (B-NHL)

Status: ongoing Phase 1 trial enrolling 2L LBCL patients in dose expansion

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

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: 40x10^6 CAR-T cells (N=8, completed[4])
Dose level 2: 80x10^6 CAR-T cells (N=5, completed[4])
Dose level 3: 120x10^6 CAR-T cells (N=3, completed)
Dose expansion: Enrolling patients (approximately 30 total) at dose levels 2 and 3

NCT04637763
[1] Subtypes include: DLBCL, HGBL, tFL, PMBCL, FL, MZL, MCL (Note, FL subtype is aggressively behaving, with POD24 (high risk))
[2] LBCL subtypes include: DLBCL, HGBL, PMBCL, tFL
[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

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

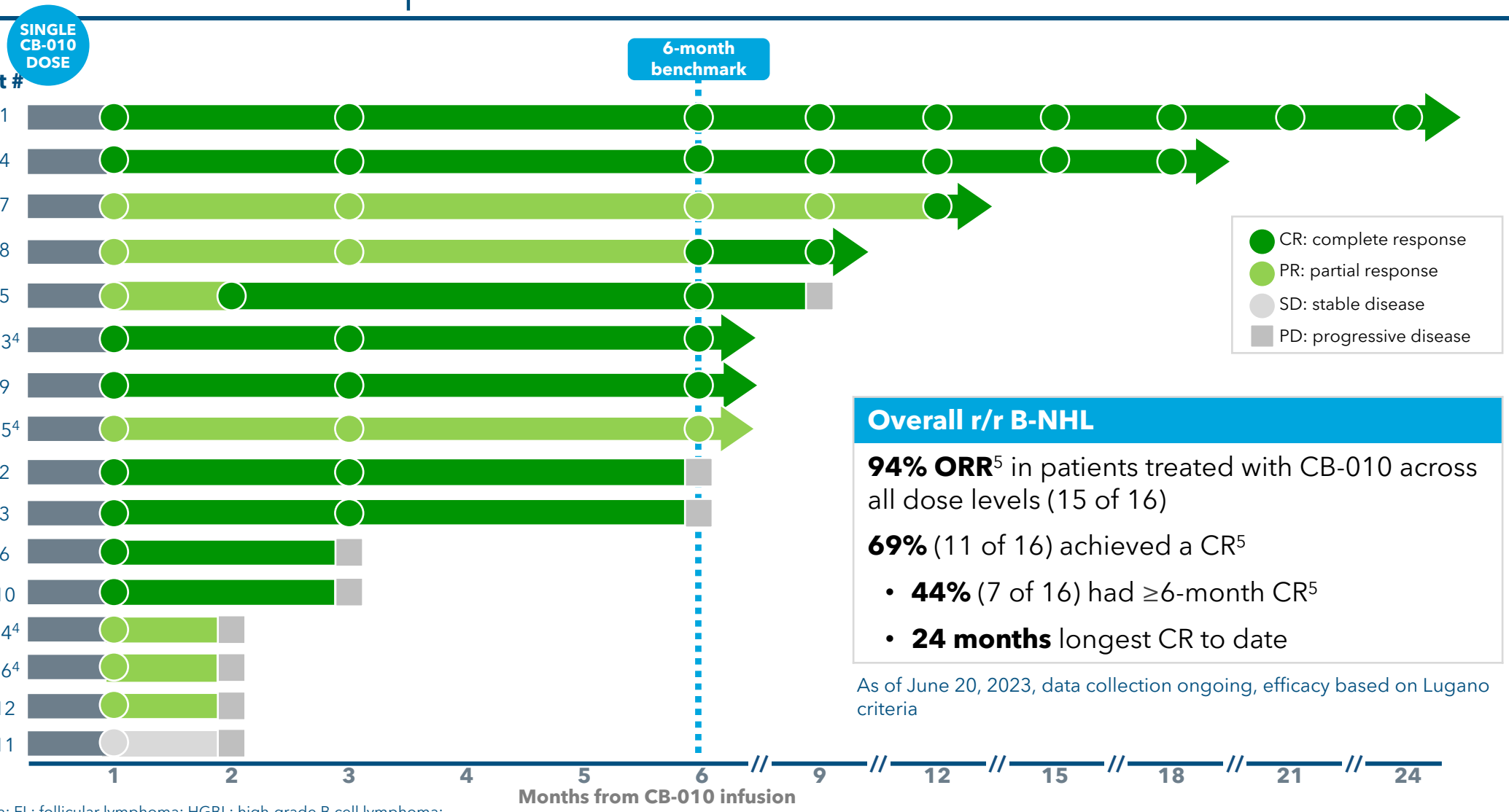
As of May 4, 2023 data cutoff date

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]

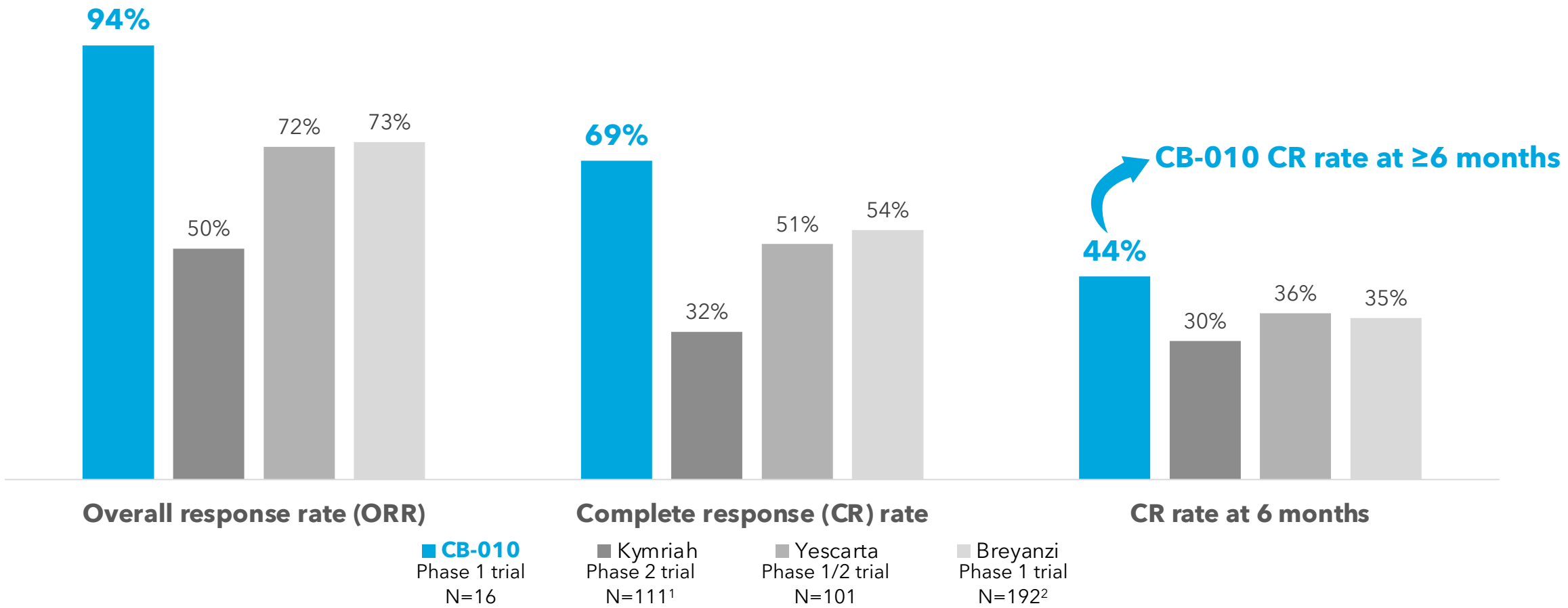
- **44%** (7 of 16) had ≥6-month CR[5]
- **24 months** longest CR to date

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 converted from a CR or PR to PD at various assessment time points as indicated in the chart above

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.

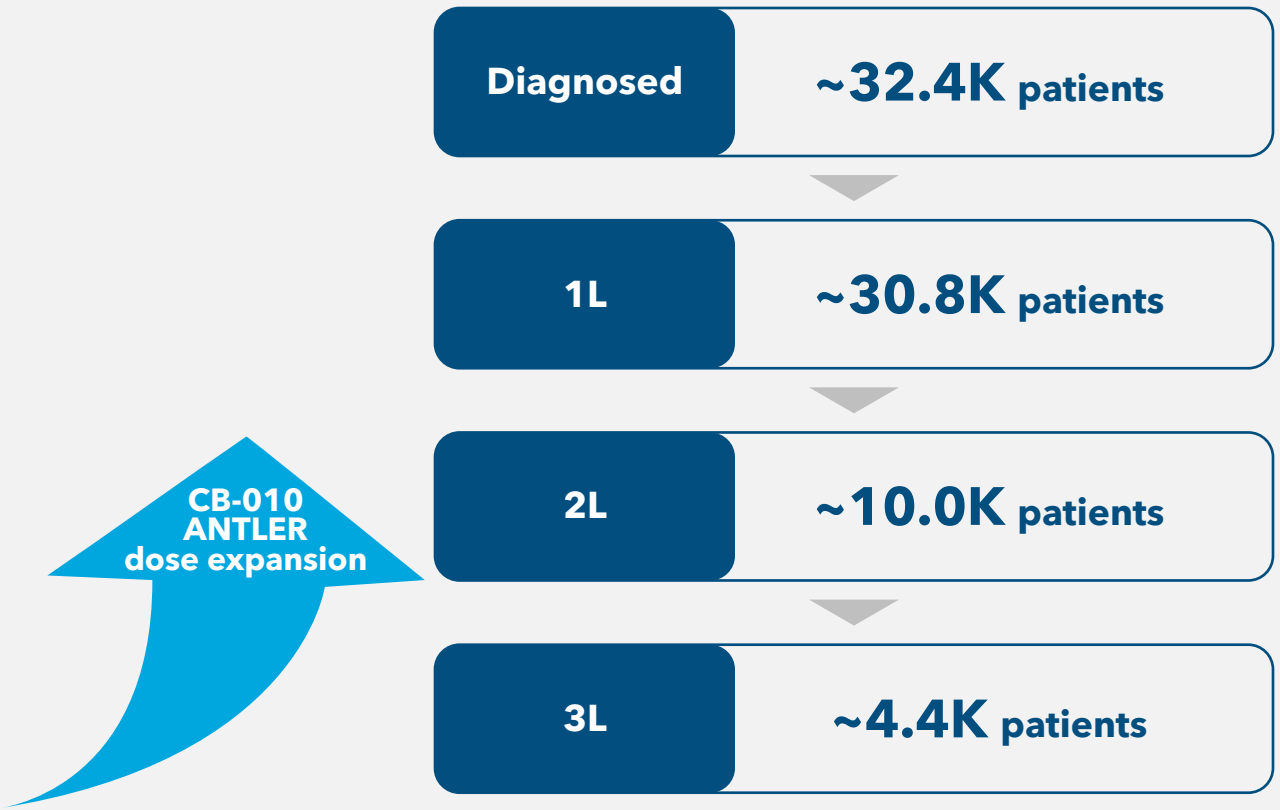
Subgroup efficacy profile supports 2L LBCL clinical development

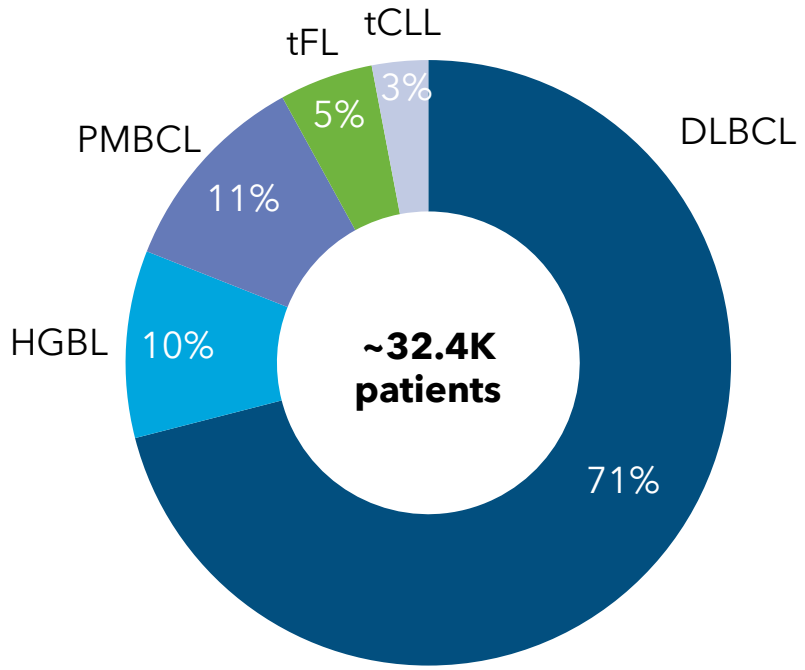
	r/r B-NHL	r/r LBCL[2]	2L LBCL[3]
Endpoints N, (%)	**All patients** (N=16)	**Subgroup** (N=10)	**Subgroup** (N=4)
Overall response rate (ORR)[1]	15 (94%)	9 (90%)	4 (100%)
Complete response (CR) rate[1]	11 (69%)	7 (70%)	2 (50%)
≥6-month CR rate[1]	7 (44%)	5 (50%)	2 (50%)
CR at longest duration to date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

[1] Certain patients converted from a CR or partial response (PR) to progressive disease (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.

Potential to address high unmet medical need in 2L LBCL

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





Source: market research on file

Dose escalation data support ANTLER dose expansion

CB-010 single dose allogeneic CAR-T cell therapy

- Response rates rival approved autologous CAR-T cell therapies
- Generally well-tolerated safety profile
- Off-the-shelf, readily-available
- 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 converted from a CR or PR to progressive disease (PD) at various assessment time points.

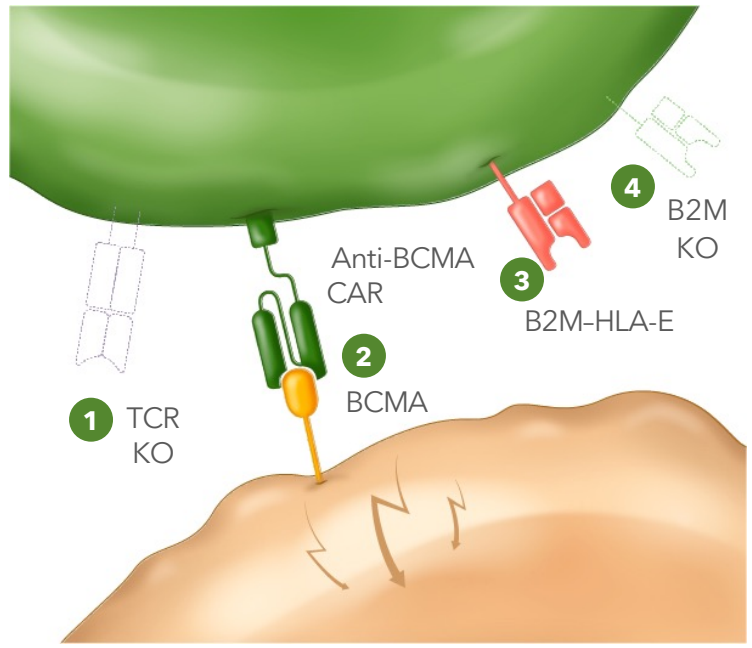
CB-011

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

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

Key attributes	CB-011	Conventional allogeneic anti-BCMA CAR-Ts
Cas12a chRDNA editing for enhanced genomic integrity • Reduced off-target editing and enhanced insertion rates	✓	✗
1 ***TRAC* gene knockout (KO)** • Eliminates TCR expression, reduces GvHD risk	✓	Varies
2 **Humanized anti-BCMA CAR site-specifically inserted into *TRAC* gene** • Eliminates random integration, targets tumor antigen	✓	Varies
3 **B2M-HLA-E-peptide fusion site-specifically inserted into *B2M* gene** • Blunts NK cell-mediated rejection	✓	✗
4 ***B2M* gene KO** • Reduces HLA class I presentation and T cell-mediated rejection	✓	✗

CB-011 uses a patented[1], potent, humanized anti-BCMA scFv with a 4-1BB costimulatory domain



Program: CB-011

Healthy donor leukapheresis-derived T cells

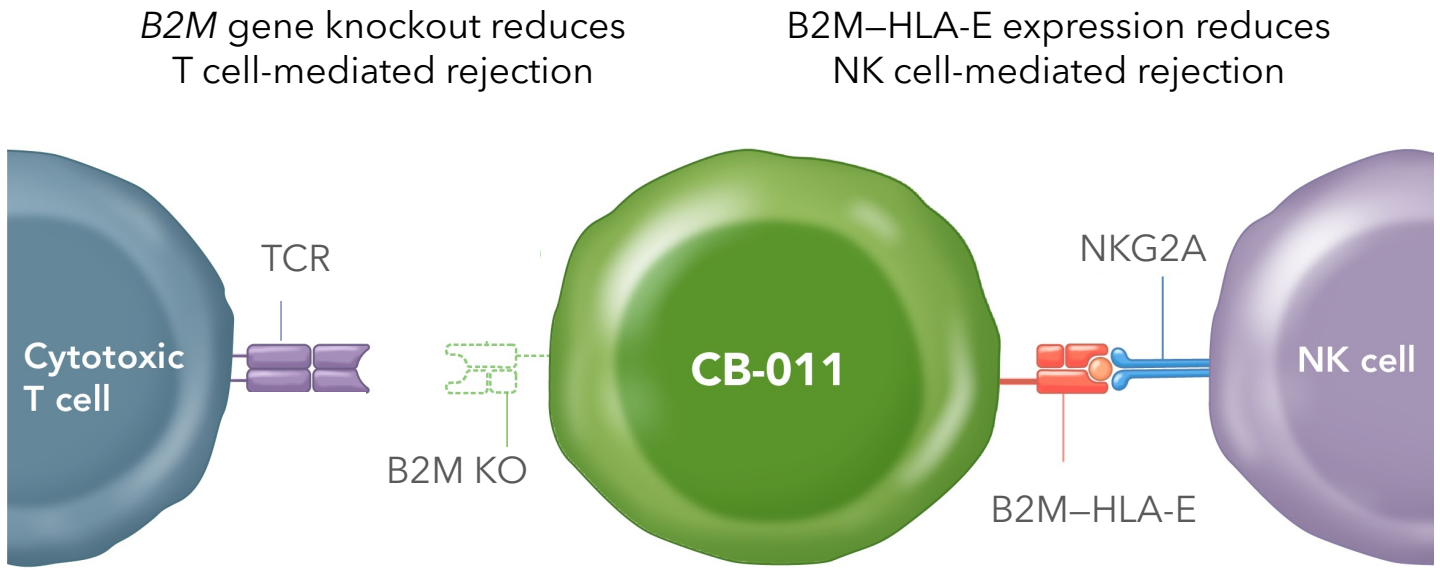
Tumor antigen: BCMA

Indication: r/r multiple myeloma (MM)

Status: ongoing Phase 1 trial enrolling patients in dose escalation

[1] 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

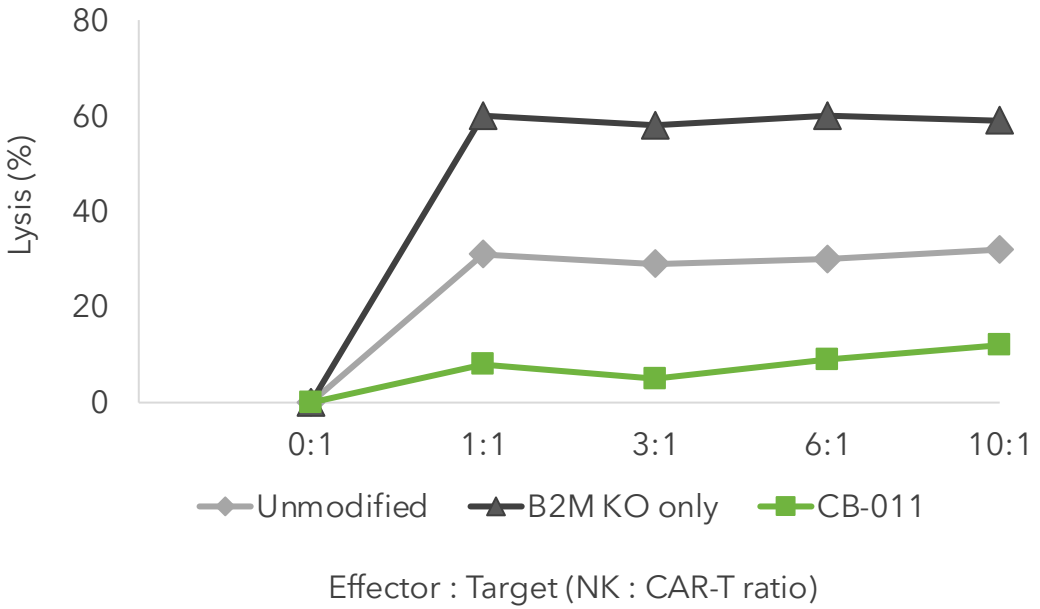


- *B2M* KO removes all endogenous HLA class I presentation to **reduce T cell-mediated rejection**
- B2M–HLA-E-peptide fusion insertion **blunts NK cell-mediated rejection**
- The **Cas12a chRDNA** editing platform achieves **high insertion efficiencies** facilitating the insertion of the B2M–HLA-E-peptide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

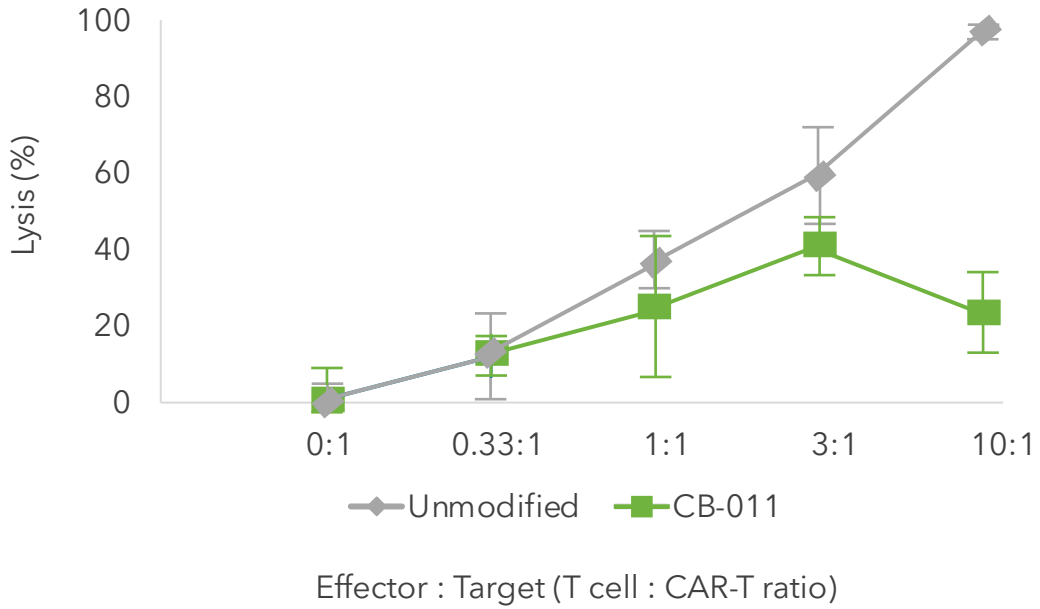
B2M–HLA-E fusion enables CB-011 cells to resist killing by NK cells

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*

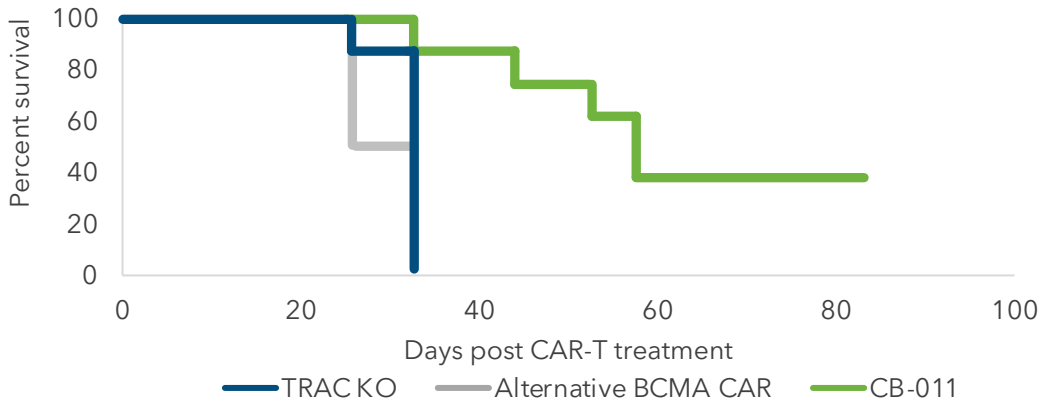


**In vitro* cytotoxicity measured 24 hours after co-incubation

CB-011 enhanced long-term survival in preclinical studies

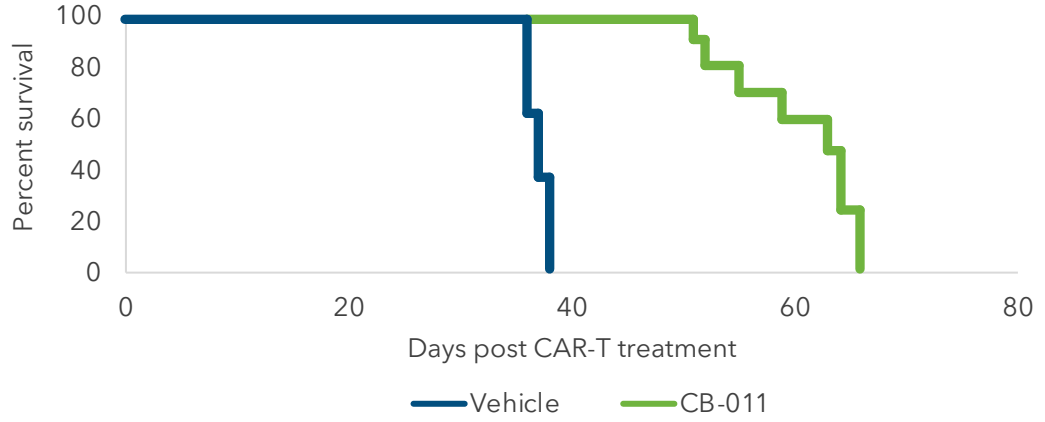
CB-011 led to statistically significant and longer survival of tumor-bearing mice
relative to an alternative anti-BCMA CAR-T cell therapy after a single dose

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



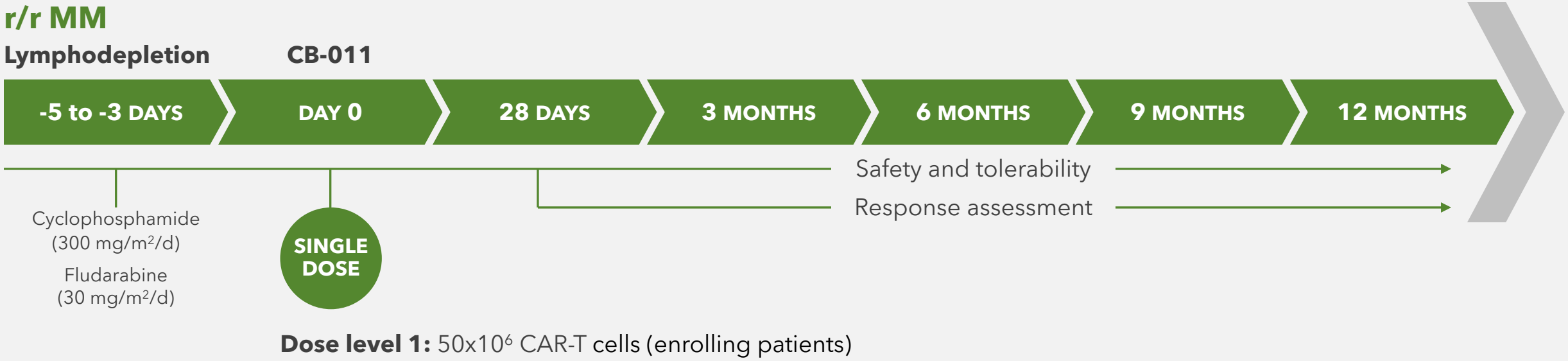
- Established orthotopic MM tumor xenograft
- Single dose CAR-T cell treatment

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, RP2D

Part B: dose expansion
- Objective: antitumor response



Dose level 1: 50x10⁶ CAR-T cells (enrolling patients)

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

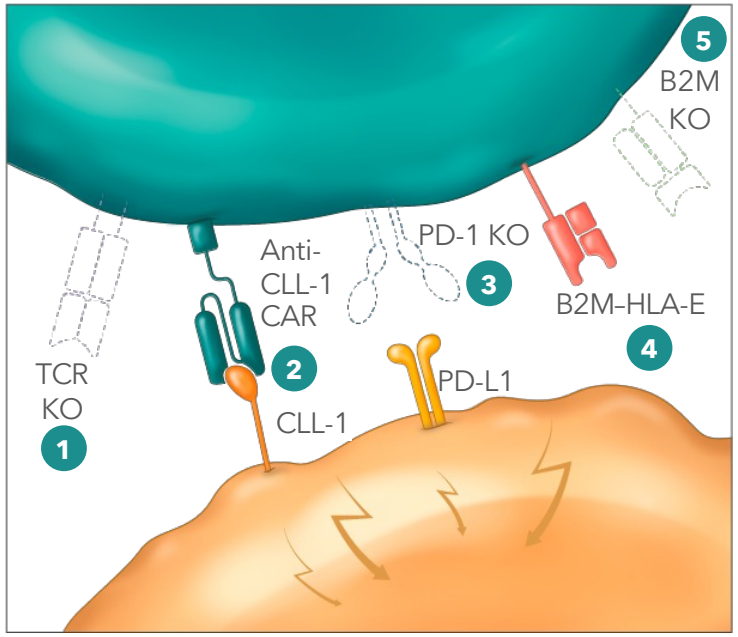
CB-012

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

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

Key attributes	CB-012	Other allogenic CAR-Ts for AML
Cas12a chRDNA editing for enhanced genomic integrity • Reduced off-target editing and enhanced insertion rates	✓	✗
1 ***TRAC* gene knockout (KO)** • Eliminates TCR expression, reduces GvHD risk	✓	Varies
2 **Human anti-CLL-1 CAR site-specifically inserted into *TRAC* gene** • Eliminates random integration, targets tumor antigen	✓	Varies
3 **PD-1 KO for enhanced antitumor activity** Potentially better therapeutic index via initial tumor debulking	✓	✗
4 **B2M-HLA-E-peptide fusion site-specifically inserted into *B2M* gene** • Blunts NK cell-mediated rejection	✓	✗
5 ***B2M* gene KO** • Reduces HLA class I presentation and T cell-mediated rejection	✓	✗

CB-012 uses a potent, fully human anti-CLL-1 scFv[1] with a CD28 costimulatory domain



Program: CB-012

Healthy donor leukapheresis-derived T cells

Tumor antigen: CLL-1 (also known as CD371)

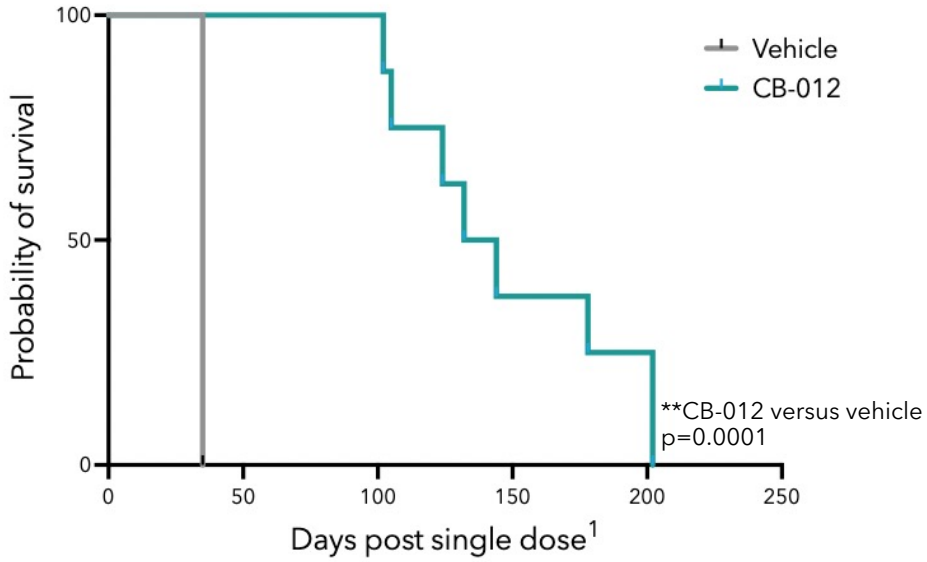
Indication: r/r acute myeloid leukemia (AML)

Status: IND planned for H2 2023

[1] Anti-CLL-1-specific scFv exclusively licensed from Memorial Sloan Kettering Cancer Center for allogeneic cell therapies

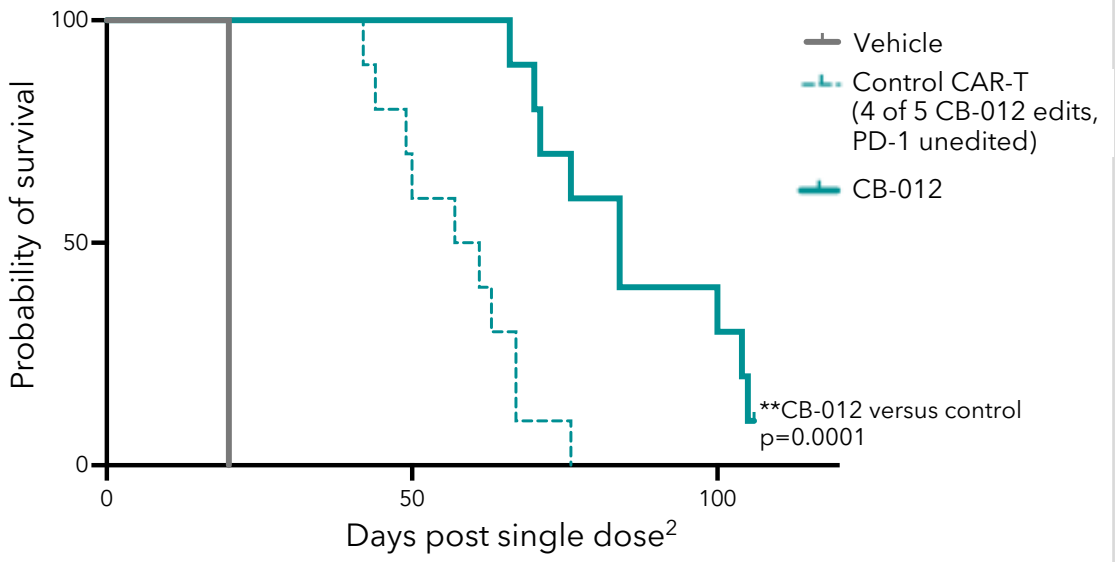
CB-012 significantly reduced tumor burden and increased overall survival in preclinical studies

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

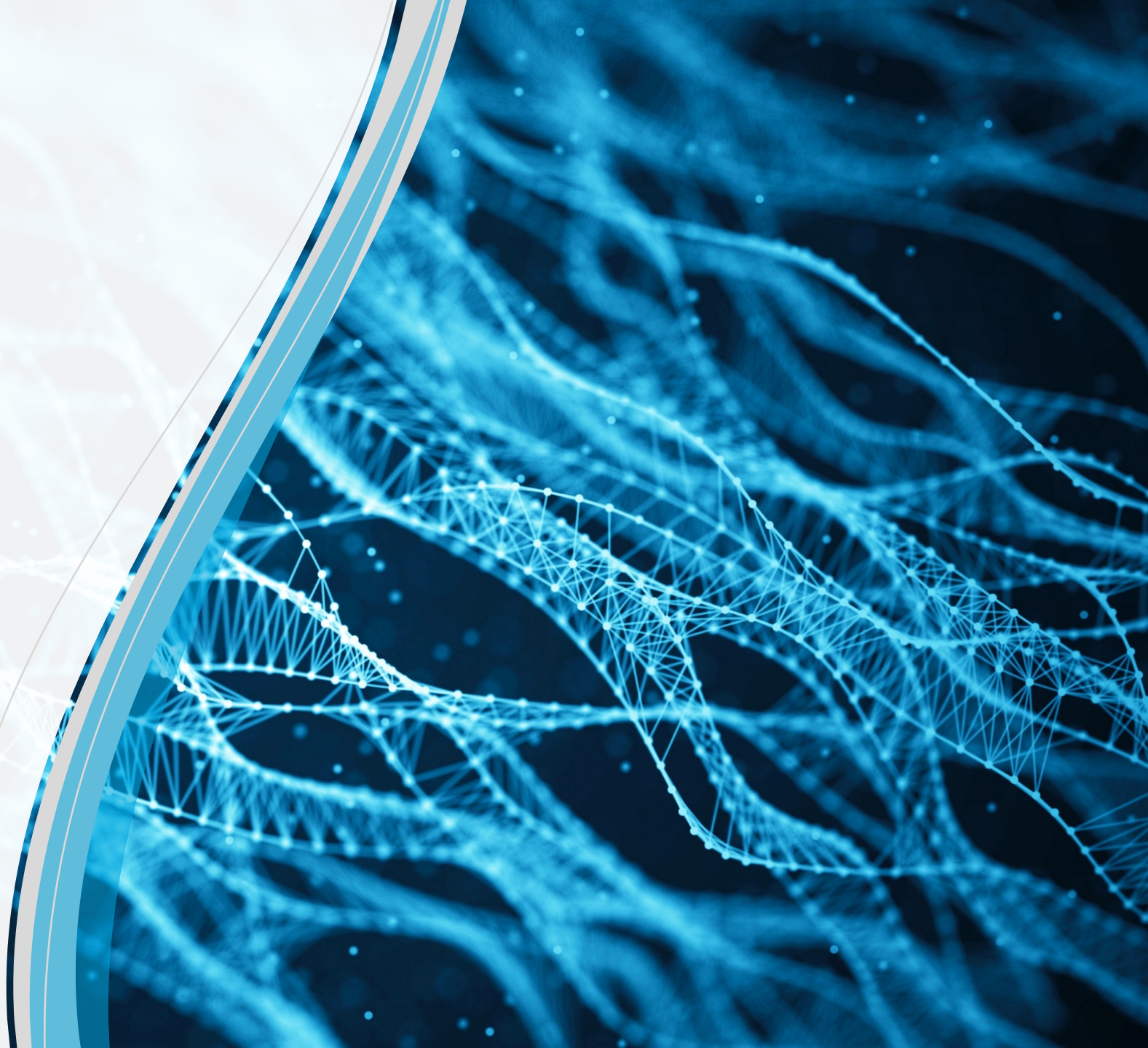


Addition of PD-1 KO in genome-editing strategy **increased overall survival** compared to control CAR-T cell without PD-1 KO

[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

CAR-NK platform:

- CB-020 for solid tumors



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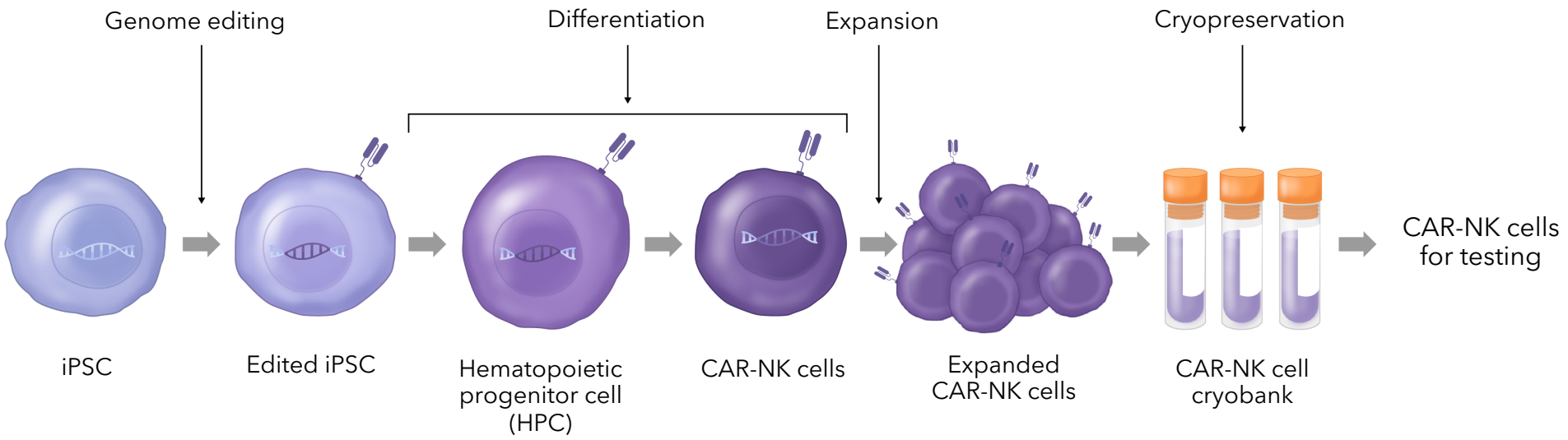
Caribou has a robust iPSC to NK differentiation protocol

CAR-T cells generally have not demonstrated broad, robust antitumor activity in solid tumors

Natural killer (NK) cells are allogeneic and inherently target solid tumors and metastases

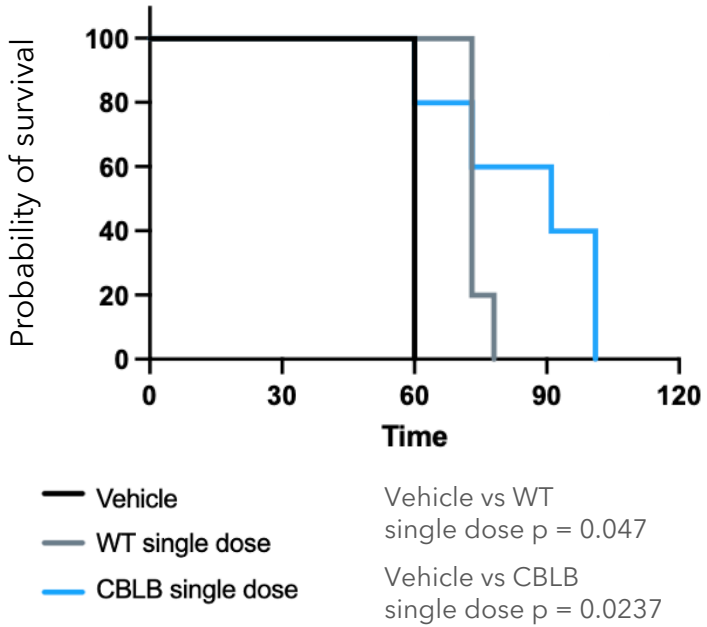
Edited iPSC-derived CAR-NK cell therapies are a compelling platform for solid tumor-targeting cell therapy development

Caribou has developed robust differentiation and expansion protocols to derive NKs from iPSCs



Multiple armoring strategies in development for CAR-NK platform

Enhanced antitumor activity

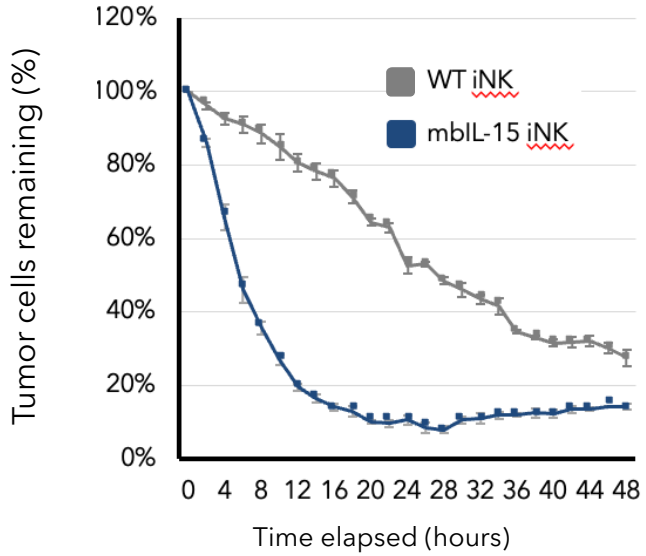


Vehicle vs WT single dose p = 0.047

Vehicle vs CBLB single dose p = 0.0237

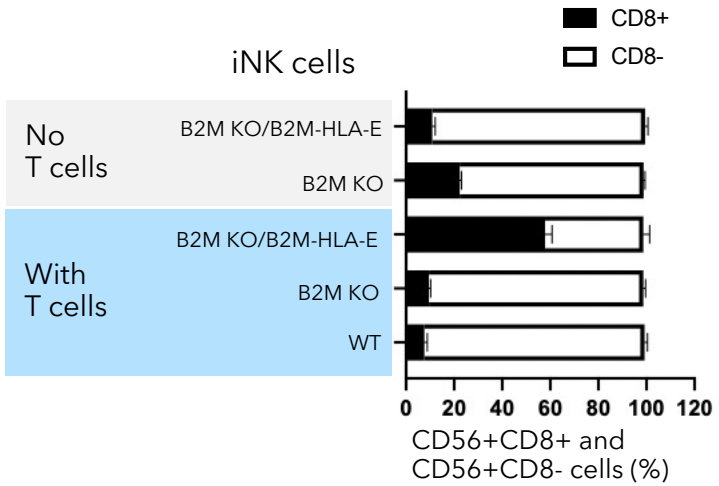
iNK cells with ***CBLB* knockout** exhibit significant enhancement in antitumor activity compared to WT iNK cells in a solid tumor xenograft model

Enhanced persistence



Membrane-bound **IL-15/IL-15RA fusion** (mbIL-15) engineered iNK cells demonstrate enhanced cytotoxicity against a solid tumor cell line

Immune cloaking



B2M KO/B2M-HLA-E knock-in reduces T cell-mediated iNK cell killing and prevents fratricide (NK cell self-killing)

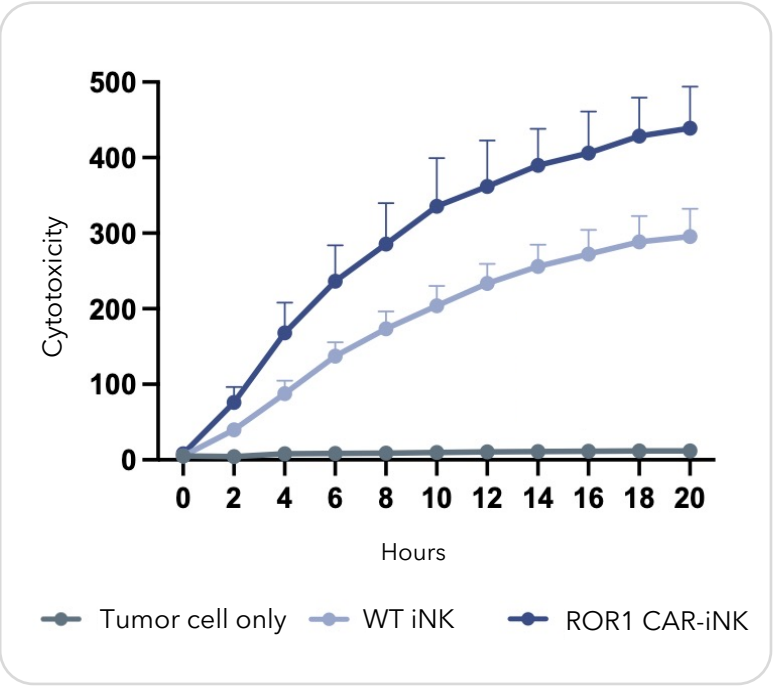
iNK: induced pluripotent stem cell-derived NK cell; PBMC: peripheral blood mononuclear cell
Data presented at American Association for Cancer Research and Japanese Cancer Association (AACR-JCA) Conference, December 12, 2022

CB-020

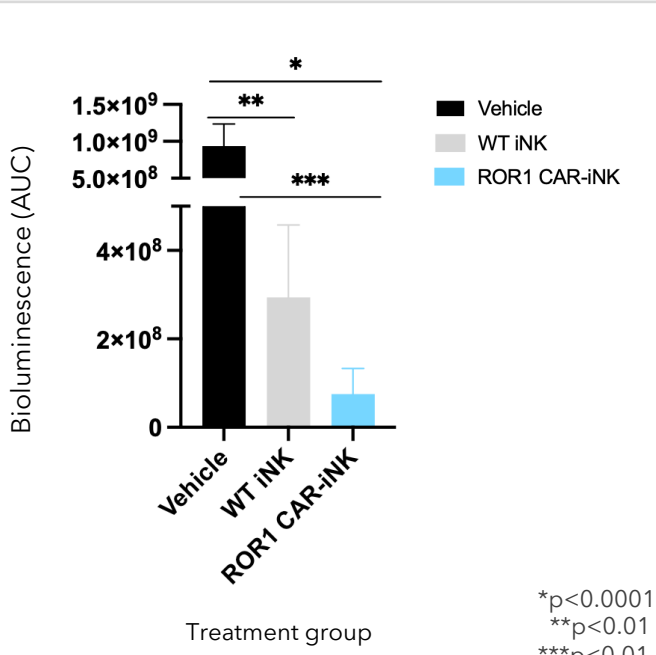
Allogeneic iPSC-derived anti-ROR1 CAR-NK cell therapy for solid tumors

CB-020: Anti-ROR1 CAR-NK exhibits increased tumor cell killing in *in vitro* and *in vivo* models

In vitro cytotoxicity of anti-ROR1 CAR-NK



In vivo anti tumor activity of anti-ROR1 CAR-NK



iPSC-derived anti-ROR1 CAR-NK cells demonstrated enhanced cell killing and led to reduced tumor burden compared to iPSC-derived NK cells without a CAR

iNK: induced pluripotent stem cell-derived NK cell
Data presented at American Association for Cancer Research and Japanese Cancer Association (AACR-JCA) Conference, December 12, 2022

The momentum continues in 2023

Recent accomplishments

CB-010
Positive dose escalation data
Enrolling 2L LBCL patients in dose expansion
RMAT, Fast Track designations

CB-011
CaMMouflage trial initiated
First patient dosed
Fast Track designation

CB-012
Presented
AACR poster with preclinical AML data

Well capitalized
>$400M[1] in cash
Runway extended into Q4 2025

Future anticipated milestones

CB-010
Feedback from FDA by YE 2023
ANTLER dose expansion data H1 2024

CB-011
CaMMouflage dose escalation updates

CB-012
IND submission planned in H2 2023

IND: investigational new drug, RMAT: Regenerative Medicines Advanced Therapy

[1] $292.5M in cash, cash equivalents, and marketable securities as of June 30, 2023, which included the $25.0M proceeds from the Pfizer investment; plus $134.6 million in net proceeds from the sale of common stock in an underwritten public offering that closed in the third quarter of 2023.

Thank you

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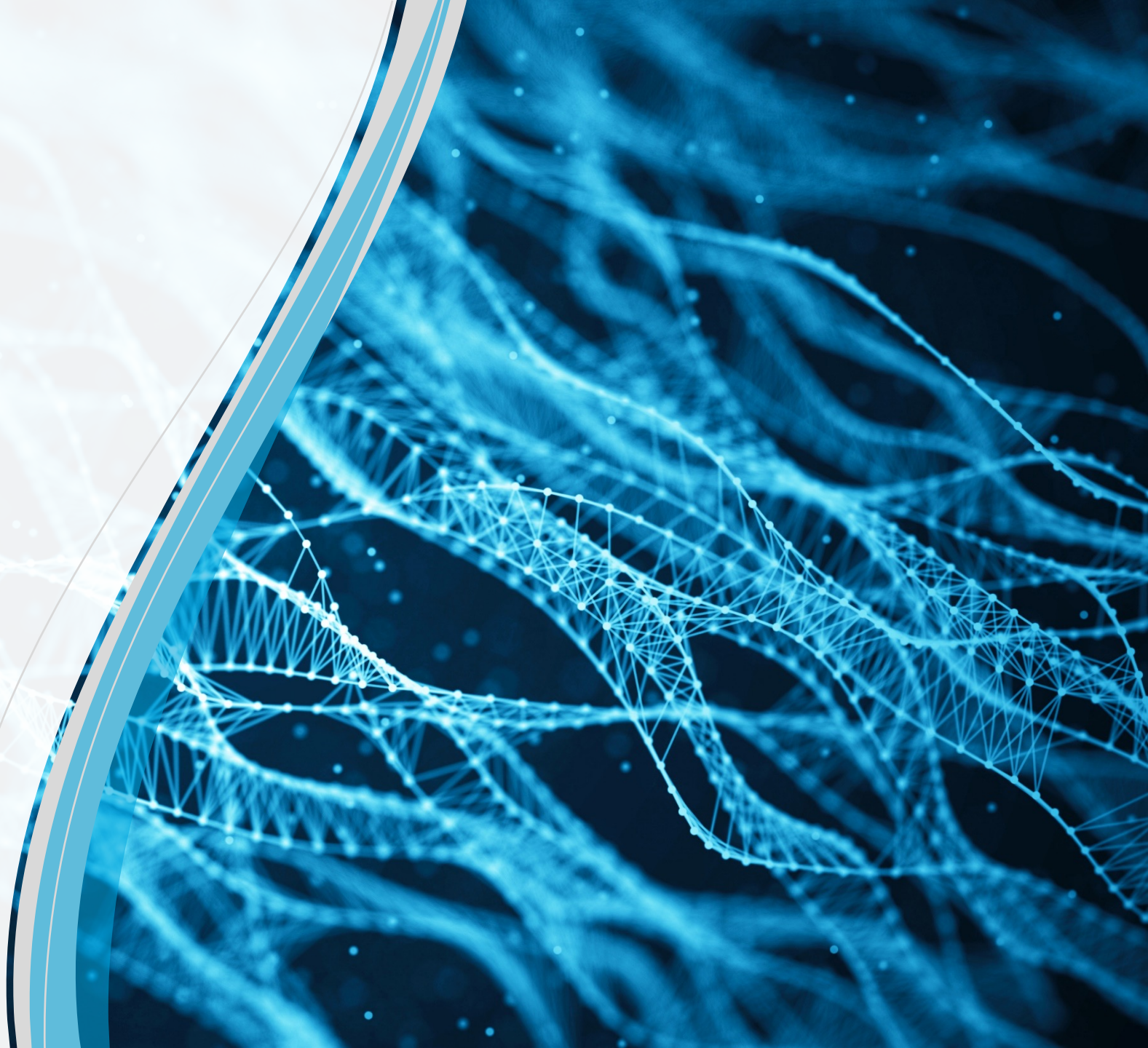
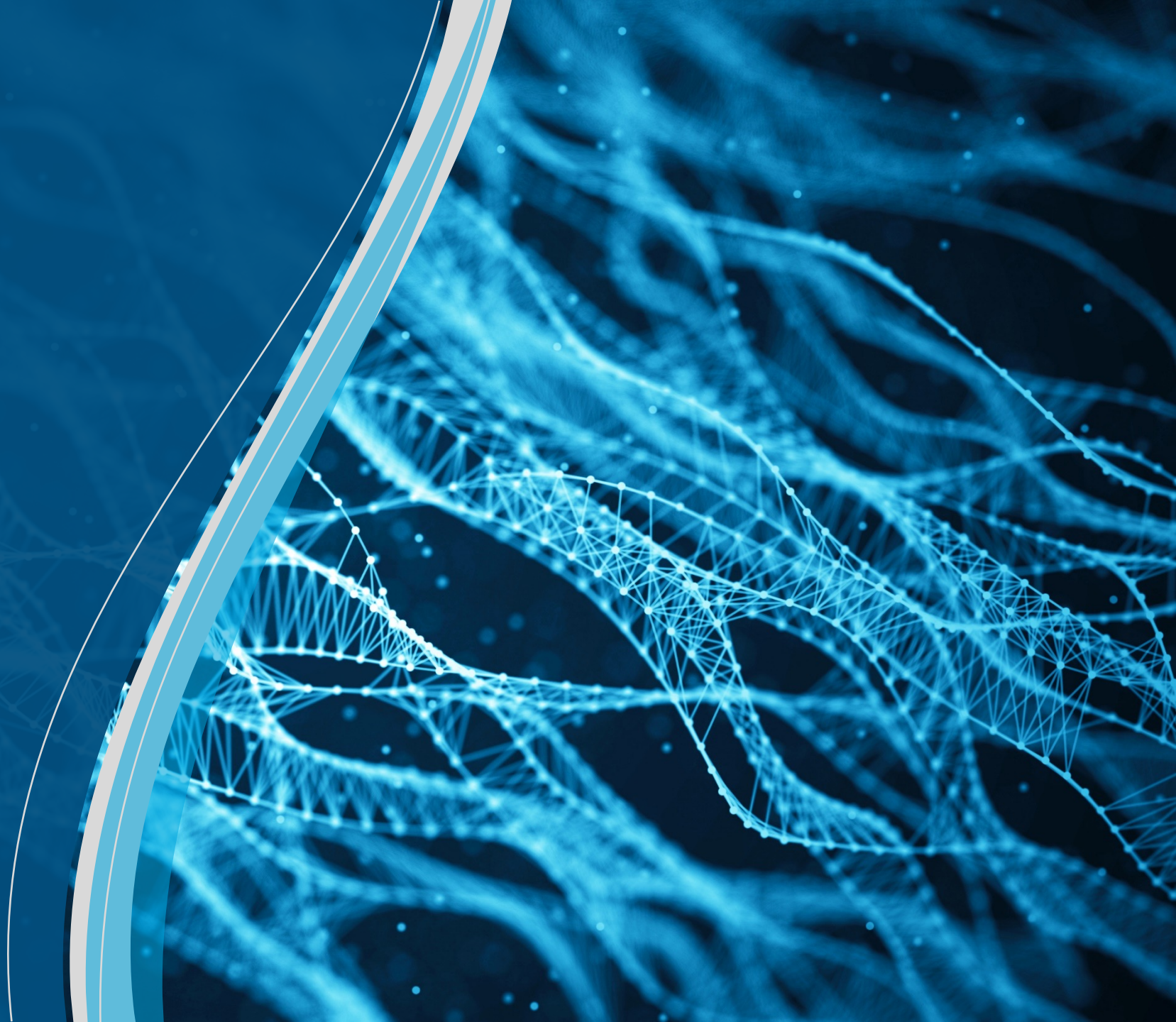


Appendix



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Patients shouldn't have to wait for treatment

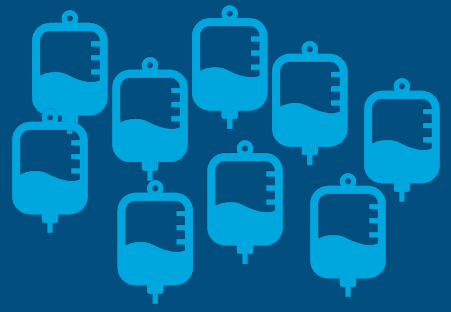
Allogeneic therapy
N=many per batch

Screening

Product shipment

Days

Lymphodepletion



The future of cell therapy is off-the-shelf

Autologous therapy
N=1

Screening

Queuing, leukapheresis scheduling

Leukapheresis

Sample shipment

Manufacturing, product failure identification

Bridging therapy

Product shipment

Lymphodepletion

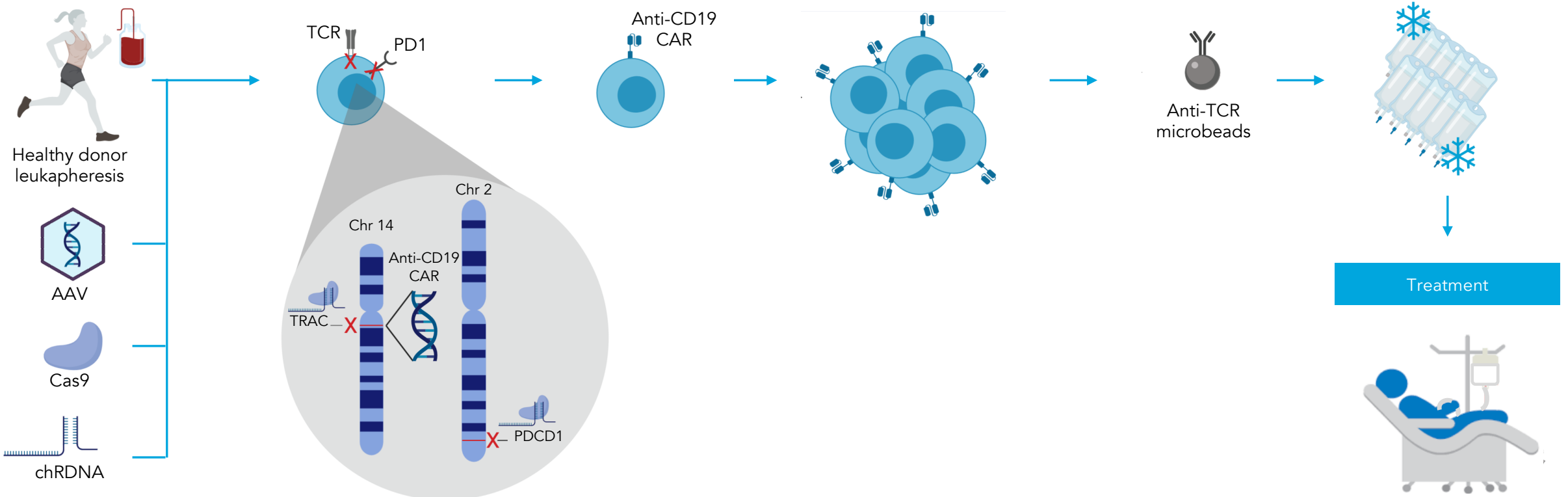
Weeks to months[1]

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

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



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 converted from a CR or partial response (PR) to progressive disease (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 converted from a CR or partial response (PR) to progressive disease (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

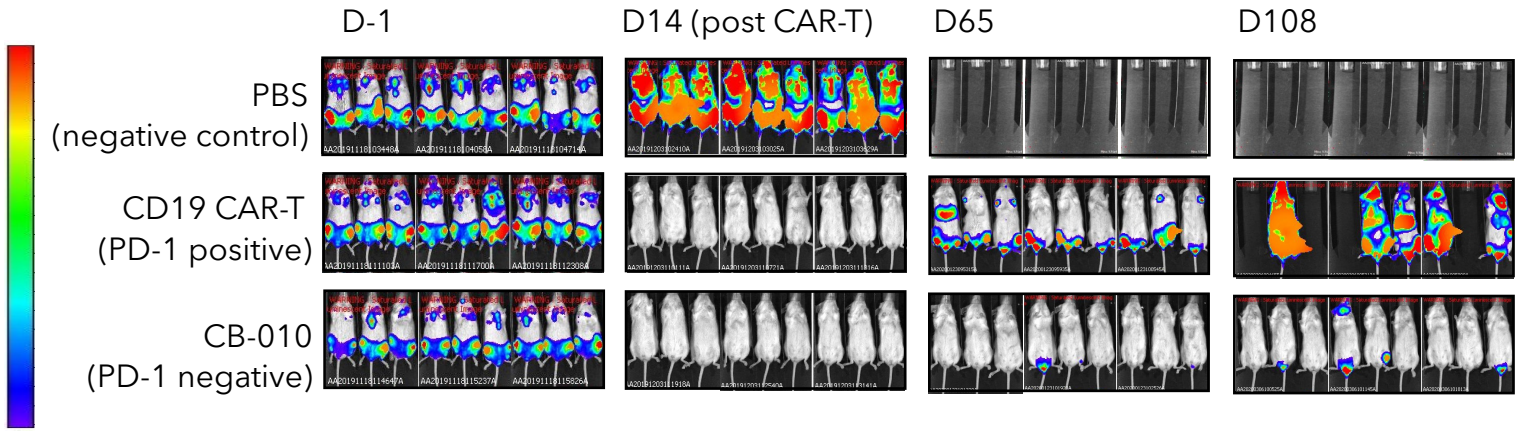
Treatment-emergent adverse events (TEAE)

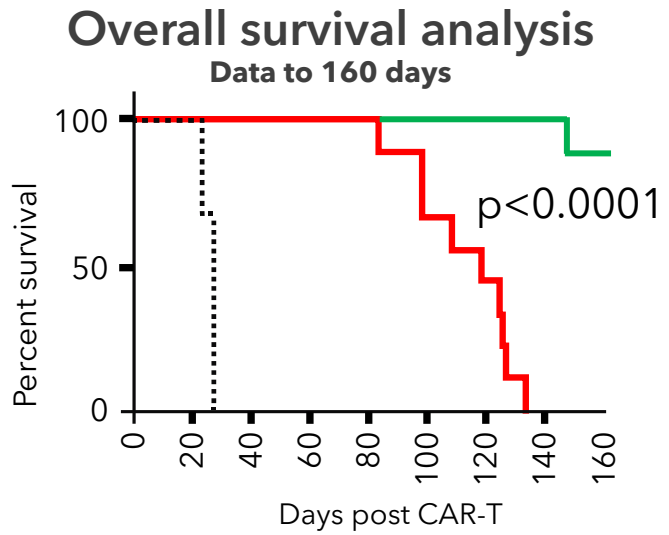
Event (N=16)	Any Grade[1] N (%)	All Grade 3+ N (%)	Related Grade 3+ N (%)
Total number of TEAEs, N	**348**	**96**	**28**
Subjects with TEAE, n (%)	**15 (94)**	**14 (88)**	**8 (50)**
Thrombocytopenia/platelet count decreased	11 (69)	11 (69)	5 (31)
Anemia	11 (69)	8 (50)	1 (6)
Neutropenia/Neutrophil count 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

Caribou's technologies offer broad applications to enable transformational therapies

Initial focus on allogeneic cell therapies with:

Potential for improved antitumor activity through **diverse genome-editing strategies**

Checkpoint disruption

Immune cloaking

Enhanced cytotoxic activity

Future potential applications:

Ex vivo

Leverage the power of precision cell therapies into disease areas **beyond oncology**

Expand engineered iPSC-derived therapies **beyond NK cells**

In vivo

Apply the Cas12a chRDNA platform to ***in vivo*** **applications**

Experienced management team

Rachel Haurwitz, PhD

President and CEO
Director

Steve Kanner, PhD

Chief scientific officer

Jason O'Byrne

Chief financial officer

Syed Rizvi, MD

Chief medical officer

Barbara McClung, JD

Chief legal officer and corporate secretary

Ruhi Khan

Chief business officer