UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 2, 2024

Caribou Biosciences, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-40631**	**45-3728228**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
2929 7th Street, Suite 105 Berkeley, California		**94710**
(Address of Principal Executive Offices)		**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (510) 982-6030

N/A
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	CRBU	NASDAQ Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On June 2, 2024, Caribou Biosciences, Inc. (the "Company") issued a press release announcing updated clinical data from the ongoing ANTLER Phase 1 trial for CB-010, an allogeneic, or off-the-shelf, anti-CD19 CAR-T cell therapy, being evaluated in patients with relapsed or refractory B cell non-Hodgkin lymphoma ("r/r B-NHL"). A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference into this Item 7.01.

The Company hosted a webcast on June 2, 2024, including a discussion with KOLs and Company management, on the CB-010 ANTLER Phase 1 data presentation. The archived audio webcast is available on the Company's website until July 2, 2024. A copy of the slide presentation used during the Company's webcast, which includes a summary of the initial dose expansion results of the ANTLER Phase 1 clinical trial, is attached hereto as Exhibit 99.2 and is incorporated by reference herein.

The information contained in this Item 7.01 and in the accompanying Exhibits 99.1 and 99.2 shall not be deemed filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or incorporated by reference in any filing or other document under the Exchange Act or the Securities Act of 1933, as amended, regardless of any general incorporation language in any such filing or document, except as shall be expressly set forth by specific reference in any such filing or document.

Item 8.01 Other Events.

On June 2, 2024, the Company announced updated clinical data from the ongoing ANTLER Phase 1 trial for CB-010, an allogeneic, or off-the-shelf, anti-CD19 CAR-T cell therapy, being evaluated in patients with r/r B-NHL and hosted a webcast, including a discussion with KOLs and Company management, on the CB-010 ANTLER Phase 1 data presentation. A copy of the slide presentation used during the Company's webcast, which includes a summary of the initial dose expansion results of the ANTLER Phase 1 clinical trial, is attached hereto as Exhibit 99.2 and is incorporated by reference herein.

The clinical results are being presented during a poster presentation at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting on June 3, 2024.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release issued by Caribou Biosciences, Inc. on June 2, 2024
99.2	Caribou Biosciences, Inc. Webcast Slide Presentation dated June 2, 2024 Regarding CB-010 ANTLER Phase 1 Trial Update and KOL Discussion
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Caribou Biosciences, Inc.

Date: June 3, 2024

By: /s/ Rachel E. Haurwitz

Rachel E. Haurwitz
President and Chief Executive Officer

Caribou Biosciences Presents Encouraging Clinical Data from CB-010 ANTLER Phase 1 Trial in Second-line LBCL Patients at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting

-- CB-010 allogeneic CAR-T cell therapy with partial HLA matching has potential to rival efficacy and safety profile of approved autologous CAR-T cell therapies --

-- 14.4 months median PFS in ANTLER patients with partial HLA matching (≥4 alleles) --

-- Plan to enroll ~20 additional 2L LBCL patients in ANTLER to confirm that partial HLA matching improves patient outcomes; initial data expected in H1 2025 --

-- Caribou expects to initiate a pivotal trial for CB-010 in H2 2025, upon confirmation of improved outcomes in partially HLA matched cohort --

-- Off-the-shelf CB-010 is partially HLA matched to patient within current screening timelines --

-- KOL webcast discussion of data from 46 ANTLER patients scheduled for today at 7:00 pm CDT --

BERKELEY, Calif., June 2, 2024 (GLOBE NEWSWIRE) -- Caribou Biosciences, Inc. (Nasdaq: CRBU), a leading clinical-stage CRISPR genome-editing biopharmaceutical company, today presented updated clinical data from the ongoing ANTLER Phase 1 trial that indicates a single dose of CB-010, a readily available, off-the-shelf anti-CD19 CAR-T cell therapy with a PD-1 knockout, has the potential to rival the safety, efficacy, and durability of approved autologous CAR-T cell therapies. The clinical results are being presented during a poster presentation at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting.

“The Phase 1 data from the ANTLER trial continues to be encouraging in terms of both safety and efficacy of an allogeneic CAR-T cell therapy,” said Boyu Hu, MD, director of lymphoma and CLL in the division of hematology and hematologic malignancies at the University of Utah and an investigator on the ANTLER trial. “The partial human leukocyte antigen, or HLA, matching strategy is incredibly intriguing and further evaluation is supported by the ASCO data presentation. As many patients in ANTLER were enrolled due to rapid disease progression that prohibited waiting for an autologous CAR-T cell therapy, I look forward to enrolling patients who will receive partially HLA matched CB-010 in this ongoing trial.”

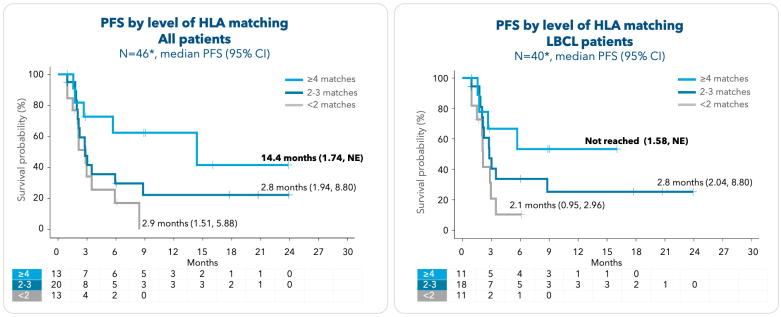
In ANTLER, three dose levels of CB-010 were evaluated ($40x10^6$, $80x10^6$, and $120x10^6$ CAR-T cells) in a total of 46 patients. In dose escalation, 16 patients with multiple subtypes of aggressive relapsed or refractory B cell non-Hodgkin lymphoma (r/r B-NHL) were enrolled, and in dose expansion, 30 patients with second-line large B cell lymphoma (2L LBCL) were enrolled. As of an April 1, 2024 data cutoff date, results demonstrated:

- CB-010 was generally well tolerated. No Grade 3 or higher cytokine release syndrome (CRS) and no graft-versus-host disease (GvHD) was observed.
- A retrospective analysis of all patient data demonstrated that patients who received a dose of CB-010 manufactured from a donor with ≥4 matching HLA alleles (referred to as partial HLA matching) showed improved progression free survival (PFS). Results from patients who received partially HLA matched CB-010 include:
  - Median PFS of 14.4 months (95% CI: 1.74, not estimable [NE]) was observed in patients treated with CB-010 with ≥4 HLA matches (N=13), compared to 2.8 months (95% CI: 2.10, 3.48) for patients treated with CB-010 with ≤3 HLA matches (N=33).
  - In patients with LBCL who received CB-010 with ≥4 HLA matches (N=11, including N=10 2L LBCL and N=1 3L LBCL), median PFS has not been reached (95% CI: 1.58, NE).
- Translational data on CB-010:
  - Pharmacokinetic (PK) data showed that higher numbers of matched HLA alleles between the CB-010 donor and recipient patient correlated with increased CAR-T cell expansion and persistence compared to lower numbers of matched HLA alleles.
  - Pharmacodynamic (PD) data showed that a single dose of CB-010 resulted in extended B cell aplasia (~114 days) and a rapid recovery of the patient's endogenous T and NK cells (~3 weeks).
- Based on the overall safety, efficacy, and translational data analyzed, $80x10^6$ CAR-T cells was selected as the recommended Phase 2 dose (RP2D) for CB-010.

"We are excited to see that patients who receive partially HLA matched CB-010 have improved efficacy and durability outcomes that are on par with approved autologous CAR-T cell therapies," said Rachel Haurwitz, PhD, Caribou's president and chief executive officer. "We next plan to prospectively evaluate this compelling observation by enrolling approximately 20 additional 2L LBCL patients, in either the inpatient or outpatient treatment setting, and we will ensure that they receive a partially matched (≥4 HLA matches) dose of CB-010. We are also excited to open the ANTLER study for the first time to patients who have relapsed following any prior CD19-targeted therapy in a proof-of-concept cohort for up to 10 patients. We expect to report initial data from both the 2L LBCL and CD19 relapsed cohorts in the first half of 2025 and, upon confirmation of improved outcomes in additional patients receiving a partially HLA matched dose of CB-010, we plan to initiate a pivotal Phase 3 clinical trial in 2L LBCL patients, including patients regardless of HLA type, in the second half of 2025."

ANTLER Phase 1 trial of CB-010 – median PFS analyses
A photo accompanying this announcement is available at: https://pr.globenewswire.com/FileDownloader/DownloadFile?source=pnr&fileGuid=893722aa-a457-4e0f-a27e-457bf8b2c0d3

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



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

ANTLER Phase 1 trial of CB-010 – response data

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+)

HLA: human leukocyte antigen; NR: not reached; PFS: progression free survival
ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing

ANTLER Phase 1 trial of CB-010 – response data

	All treated (N=46)	
	Any grade (n, %)	Grade ≥3 (n, %)
Prolonged cytopenias	9 (20)[1]	9 (20)[1]

CRS	26 (57)[2]	0 (0)
Infections	22 (47)[3]	10 (22)[3]
ICANS	10 (22)[4]	3 (7)[5]
Hemophagocytic lymphohistiocytosis (HLH)	1 (2)	0
GvHD	0	0

CRS: cytokine release syndrome; GvHD: graft-versus-host disease; ICANS: immune effector cell-associated neurotoxicity syndrome
There were five patient deaths due to adverse events following CB-010 infusion; 4 were unrelated to CB-010 treatment and 1 death possibly related to CB-010 per investigator due to complications of a bladder perforation in the context of BK virus hemorrhagic cystitis
[1] Prolonged cytopenias are defined as grade 3 or higher events lasting beyond 30 days following CB-010 infusion; 37/46 (80%) of patients recovered from cytopenias to grade ≤2 by day 35 post CB-010 treatment
[2] Median time of onset was 3 days (range 0-22), and median duration was 3 days (range 1-19)
[3] Infection events reported were on or after CB-010 infusion, with highest grade reported per patient; median onset 8 days (range 0-279) and median duration is 14 days (range 1-239)
[4] Median time of onset was 7.5 days (range 6-34), and median duration was 2 days (range 1-27)
[5] 2 Grade 3 and 1 Grade 4; all resolved with supportive care. Median time of onset was 8 days and median duration was 2 days
ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing

Based on these encouraging data, Caribou plans to enroll approximately 20 additional 2L LBCL patients in ANTLER to prospectively confirm that partial HLA matching improves patient outcomes. The patient HLA allele typing occurs within the current screening timelines.

“Integrating the partial HLA matching into manufacturing for CB-010 is straightforward, enabling Caribou to deliver CB-010 as a readily available off-the-shelf CAR-T cell therapy that can serve a broad patient population,” said Tim Kelly, Caribou’s chief technology officer. “In our planned 2L LBCL pivotal Phase 3 trial, we will provide the best possible matched dose of CB-010 to each patient based on lot availability. With at least 13 manufacturing batches of CB-010 on hand, we expect that approximately 90% of all patients who could enroll in our trial would receive a dose of CB-010 with ≥4 matched alleles.”

Webcast conference call Sunday, June 2, at 7:00 pm CDT
Caribou will host a live webcast on Sunday, June 2, at 7:00 pm CDT for a discussion with KOLs and management on the CB-010 ANTLER Phase 1 data presentation. The presenters will include:

- Boyu Hu, MD, director of lymphoma and CLL in the division of hematology and hematologic malignancies, University of Utah
- Mehdi Hamadani, MD, professor of medicine, section chief of hematologic malignancies, Medical College of Wisconsin
- Rachel Haurwitz, PhD, president and chief executive officer, Caribou Biosciences

Additional participants from Caribou Biosciences include:

- Steve Kanner, PhD, chief scientific officer
- Jason O’Byrne, chief financial officer
- Kike Zudaire, PhD, senior vice president, translational sciences and therapeutic discovery
- Tonia Nesheiwat, PharmD, vice president of medical affairs and project leadership

The listen-only webcast with an accompanying presentation will be accessible under Events (https://investor.cariboubio.com/news-events/events) in the Investors section of Caribou’s website. The archived audio webcast will be available on the company’s website following the call and will be available for 30 days.

ASCO poster presentation on Monday, June 3, 9:00 am-12:00 pm CDT

Details of the ANTLER poster presentation at the 2024 ASCO Annual Meeting are as follows:

Title: A CRISPR-edited allogeneic anti-CD19 CAR-T cell therapy with a PD-1 knockout (CB-010) in patients with relapsed/refractory B cell non-Hodgkin lymphoma (r/r B-NHL): Updated Phase 1 results from the ANTLER trial
Presenter: Boyu Hu, MD, assistant professor, director of lymphoma and CLL, division of hematology and hematologic malignancies, Huntsman Cancer Institute at the University of Utah
Date and time: Monday, June 3, 2024, 9:00 am-12:00 pm CDT
Session: Hematologic Malignancies – Lymphoma and CLL
Location: Hall A, Poster Board 8, McCormick Place, Chicago
Abstract number: 7025

About CB-010
CB-010 is the lead clinical-stage product candidate from Caribou's allogeneic CAR-T cell therapy platform, and it is being evaluated in patients with relapsed or refractory B cell non-Hodgkin lymphoma (r/r B-NHL) in the ongoing ANTLER Phase 1 clinical trial and will be evaluated in patients with lupus nephritis (LN) and extrarenal lupus (ERL) in the GALLOP Phase 1 clinical trial. In ANTLER, Caribou is enrolling second-line patients with large B cell lymphoma (LBCL) comprised of different subtypes of aggressive r/r B-NHL (DLBCL NOS, PMBCL, HGBL, tFL, and tMZL). To Caribou's knowledge, CB-010 is the first allogeneic CAR-T cell therapy in the clinic with a PD-1 knockout, a genome-editing strategy designed to improve activity against diseases by limiting premature CAR-T cell exhaustion. CB-010 is also, to Caribou's knowledge, the first anti-CD19 allogeneic CAR-T cell therapy to be evaluated in the second-line LBCL setting and, for r/r B-NHL, CB-010 has been granted Regenerative Medicine Advanced Therapy (RMAT), Fast Track, and Orphan Drug designations by the FDA. Additional information on the ANTLER trial (NCT04637763) can be found at clinicaltrials.gov (https://clinicaltrials.gov/study/NCT04637763).

About Caribou's novel next-generation CRISPR platform
CRISPR genome editing uses easily designed, modular biological tools to make DNA changes in living cells. There are two basic components of Class 2 CRISPR systems: the nuclease protein that cuts DNA and the RNA molecule(s) that guide the nuclease to generate a site-specific, double-stranded break, leading to an edit at the targeted genomic site. CRISPR systems are capable of editing unintended genomic sites, known as off-target editing, which may lead to harmful effects on cellular function and phenotype. In response to this challenge, Caribou has developed CRISPR hybrid RNA-DNA guides (chRDNAs; pronounced "chardonnays") that direct substantially more precise genome editing compared to all-RNA guides. Caribou is deploying the power of its chRDNA technology to carry out high efficiency multiple edits, to develop CRISPR-edited therapies.

About Caribou Biosciences, Inc.
Caribou Biosciences is a clinical-stage CRISPR genome-editing biopharmaceutical company dedicated to developing transformative therapies for patients with devastating diseases. The company's genome-editing platform, including its Cas12a chRDNA technology, enables superior precision to develop cell therapies that are armored to potentially improve antitumor activity. Caribou is advancing a pipeline of clinical-stage off-the-shelf cell therapies from its CAR-T cell platform as

readily available treatments for patients with hematologic malignancies and autoimmune diseases. Follow us @CaribouBio and visit www.cariboubio.com.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward-looking statements by terms such as “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, although not all forward-looking statements contain these words. These forward-looking statements include, without limitation, statements related to Caribou’s strategy, plans, and objectives, and expectations regarding the timing of status and updates from its ANTLER Phase 1 clinical trial for CB-010, including expectations regarding the enrollment of 20 additional 2L LBCL patients to further study partial HLA matching outcomes, the timing of reporting of initial data from both 2L LBCL and CD 19 relapsed cohorts, the timing of reporting additional dose expansion data from the ANTLER trial, and the timing of initiation of a pivotal Phase 3 clinical trial for CB-010 in 2L LBCL patients, including the conditions to meet that timeline. Management believes that these forward-looking statements are reasonable as and when made. However, such forward-looking statements are subject to risks and uncertainties, and actual results may differ materially from any future results expressed or implied by the forward-looking statements. Risks and uncertainties include, without limitation, risks inherent in the development of cell therapy products; uncertainties related to the initiation, cost, timing, progress, and results of Caribou’s research and development programs, preclinical studies, and clinical trials; and the risk that initial, preliminary, or interim clinical trial data will not ultimately be predictive of the safety and efficacy of Caribou’s product candidates or that clinical outcomes may differ as patient enrollment continues and as more patient data becomes available and is fully evaluated; the ability to obtain key regulatory input and approvals as well as other risk factors described from time to time in Caribou’s filings with the Securities and Exchange Commission, including its Annual Report on Form 10-K for the year ended December 31, 2023 and subsequent filings. In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Except as required by law, Caribou undertakes no obligation to update publicly any forward-looking statements for any reason.

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 this press release have been derived from publicly available reports of clinical trials not conducted by Caribou, and Caribou 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 clinical trials varies in material ways from the design of the ANTLER clinical trial for CB-010, including with respect to patient populations, follow-up times, clinical trial phases, and subject characteristics. As a result, cross-trial comparisons may have no interpretive value on Caribou’s existing or future clinical results. For further information and to understand these material differences, you should read the reports for the other CAR-T cell therapy clinical trials and the sources included in the webcast slide presentation.

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Peggy Vorwald, PhD
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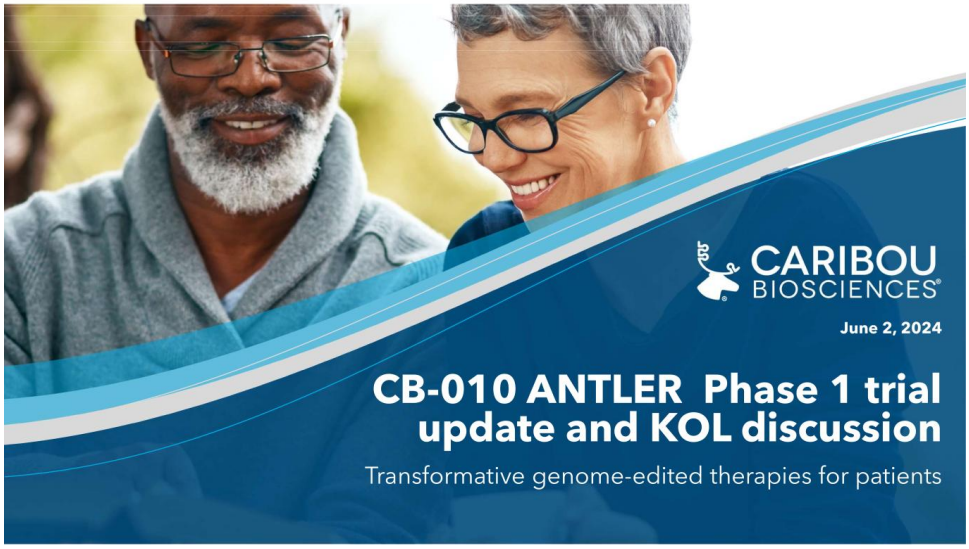

CARIBOU
BIOSCIENCES
June 2, 2024
CB-010 ANTLER Phase 1 trial update and KOL discussion
Transformative genome-edited therapies for patients

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, and emerging translational 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 an updated timeline for our planned phase 3 pivotal trial for CB-010 in second-line large B cell lymphoma patients (and the conditions to meet that timeline); 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 in patients with multiple myeloma; 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 in patients with acute myeloid leukemia; 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 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.


The future of CAR-T cell therapies is off-the-shelf
CB-010 ANTLER Phase 1 trial
Rachel Haurwitz, PhD
President & CEO
Caribou Biosciences, Inc.
CARIBOU BIOSCIENCES

Today's guests

Boyu Hu, MD

Assistant professor, director of lymphoma and CLL in the division of hematology and hematologic malignancies

Huntsman Cancer Institute
University of Utah

Mehdi Hamadani, MD

Professor of medicine and section chief of hematologic malignancies

Medical College of Wisconsin

Patients shouldn't have to wait for treatment

Allogeneic therapy
N=many
per batch

Screening | Product shipment

Days | Lymphodepletion

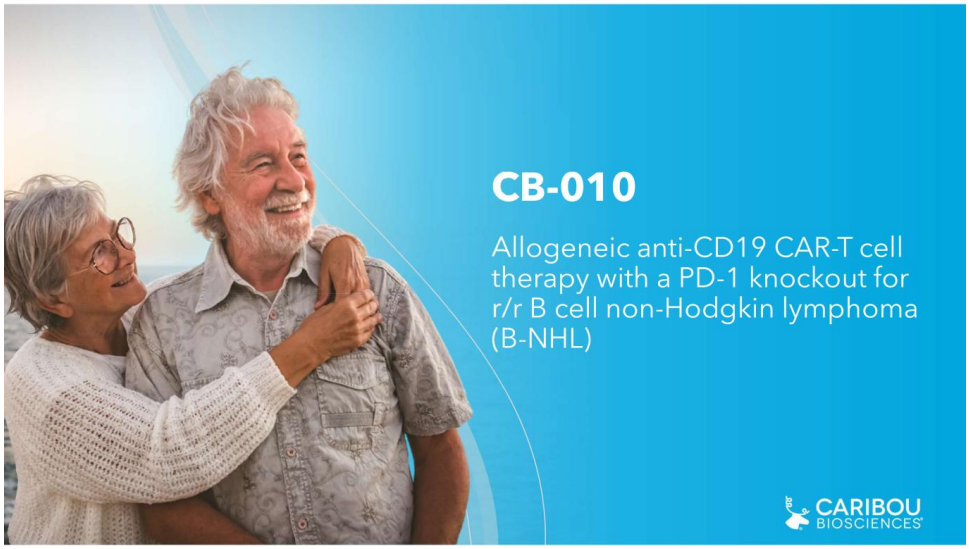
The future of cell therapy is off-the-shelf

Autologous therapy
N=1
per batch

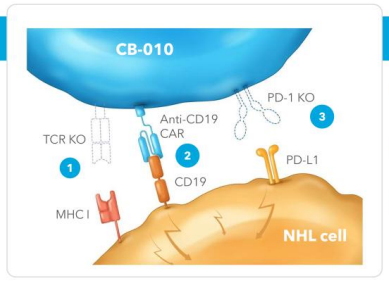
Screening | Queuing, leukapheresis scheduling | Leukapheresis | Sample shipment | Manufacturing, product failure identification | Bridging therapy | Product shipment

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)
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

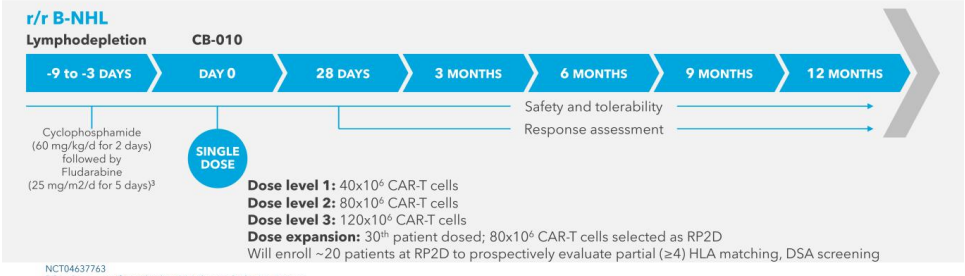
CAR: chimeric antigen receptor; KO: knockout; CD: cluster of differentiation; chRDNA: CRISPR hybrid RNA-DNA; CRISPR: clustered regularly interspaced short palindromic repeats; PD-1: programmed cell death protein 1; TCR: T cell receptor; *TRAC*: T cell receptor alpha constant; scFv: single-chain variable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

[1] To Caribou's knowledge.

CB-010 ANTLER Phase 1 trial in 2L LBCL

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

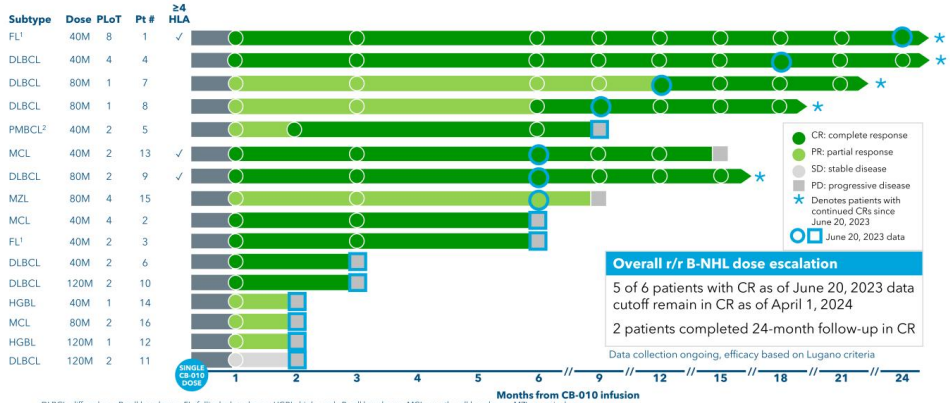


Dose level 1: 40x10^6 CAR-T cells
Dose level 2: 80x10^6 CAR-T cells
Dose level 3: 120x10^6 CAR-T cells
Dose expansion: 30th patient dosed; 80x10^6 CAR-T cells selected as RP2D
Will enroll ~20 patients at RP2D to prospectively evaluate partial (≥4) HLA matching, DSA screening

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.

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



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

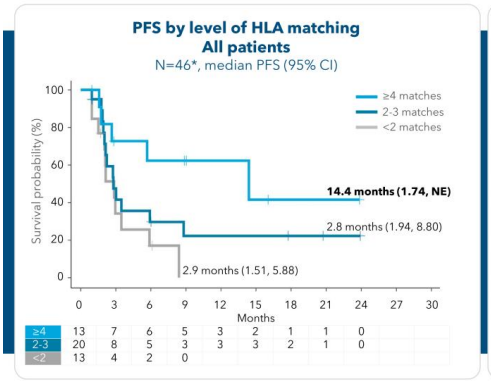
Median PFS
14.4 months
(95% CI: 1.7-NE)
observed in 13 patients with partial (≥4) HLA matching[1]

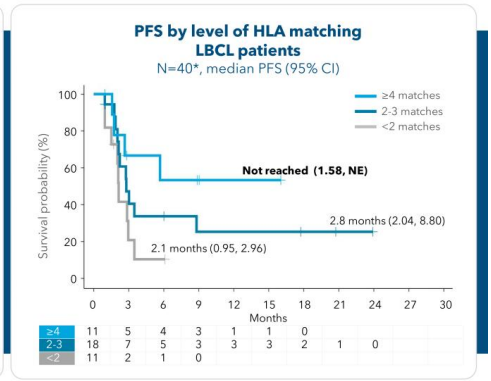
Advancing CB-010 with partial HLA matching
in 2L LBCL and lupus
Phase 1 clinical trials

2L: second-line; 3L: third-line; B-NH: 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; CR: complete response; NR: not reached

[1]Retrospective analysis in 13 patients with ≥4 HLA allele matching; subset includes: 2L LBCL (N=10), 3L LBCL (N=1), and 3L+ B-NHL (N=2). ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing.

Improved PFS for all patients treated with CB-010 from a donor with partial (≥4) HLA matching





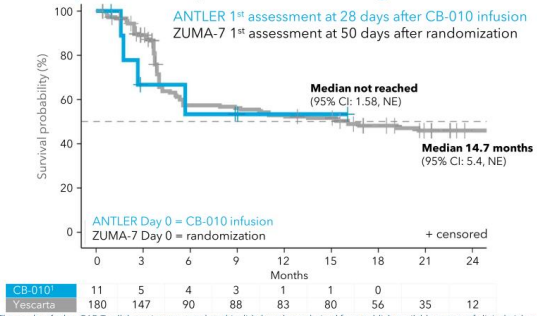
CI: confidence interval; HLA: human leukocyte antigen; NE: not estimable; partial HLA matching: patient has ≥4 HLA alleles that match donor T cells used for CB-010 manufacturing

*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.


ANTLER Phase 1 trial initial dose expansion data
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CARIBOU BIOSCIENCES

Disclosures

Consulting: Novartis, Bristol Meyers Squibb, Eli Lilly, GenMab, ADC Therapeutics, ImmPACT Bio, Seattle Genetics, Regeneron, Caribou Biosciences, Abbvie

Research Funding: Genentech, Celgene, CRISPR Therapeutics, Morphosys AG, Caribou Biosciences, Repare Therapeutics, Artiva Biotherapeutics, Newave, AstraZeneca, ImmPACT Bio

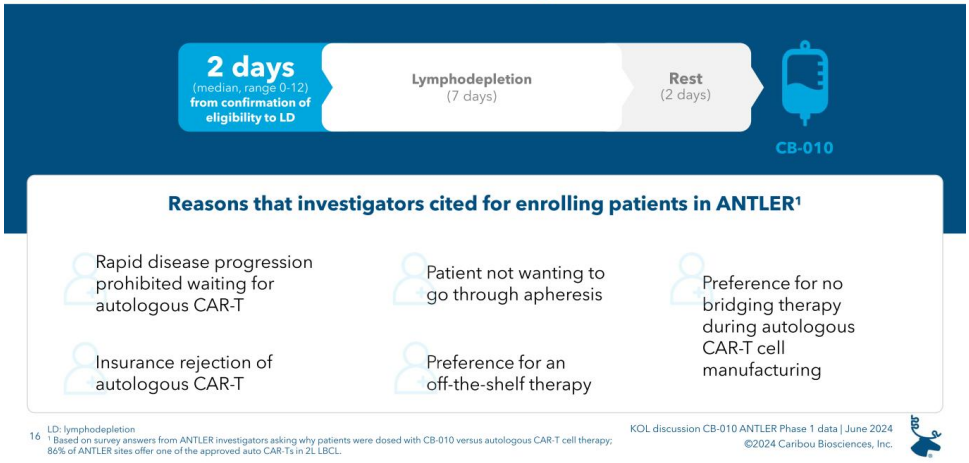
Patients in ANTLER all had aggressive r/r B-NHL

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; MCL: mantle cell lymphoma; MZL: marginal zone lymphoma; PMBCL: primary mediastinal large B cell lymphoma; IPI: International Prognostic Index; LDH: lactate dehydrogenase; 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.

Rapid timeline to treatment key to patients choosing CB-010 over approved autologous CAR-T cell therapies



Reasons that investigators cited for enrolling patients in ANTLER[1]

- Rapid disease progression prohibited waiting for autologous CAR-T
- Patient not wanting to go through apheresis
- Preference for no bridging therapy during autologous CAR-T cell manufacturing
- Insurance rejection of autologous CAR-T
- Preference for an off-the-shelf therapy

LD: lymphodepletion
[1] Based on survey answers from ANTLER investigators asking why patients were dosed with CB-010 versus autologous CAR-T cell therapy; 86% of ANTLER sites offer one of the approved auto CAR-Ts in 2L LBCL.

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 has 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

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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).

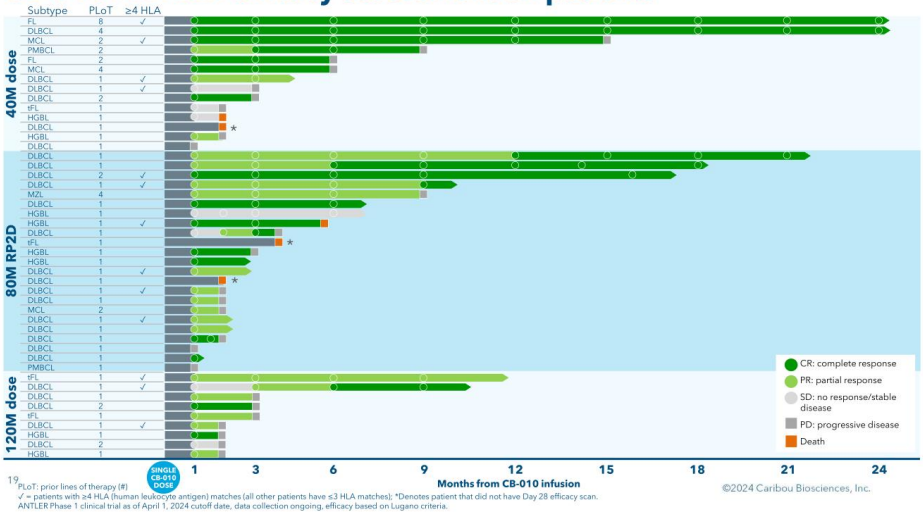
[5] Median time of onset was 7.5 days (range 6-34) and median duration was 2 days (range 1-27).

[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)

CB-010 ANTLER efficacy assessment all patients



19

PLoT: prior lines of therapy (#)
✓ = patients with ≥4 HLA (human leukocyte antigen) matches (all other patients have ≤3 HLA matches); *Denotes patient that did not have Day 28 efficacy scan.
ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing, efficacy based on Lugano criteria.

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.

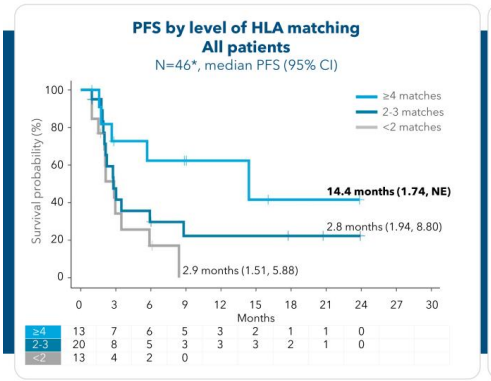
CB-010 ANTLER efficacy assessment with and without partial HLA matching

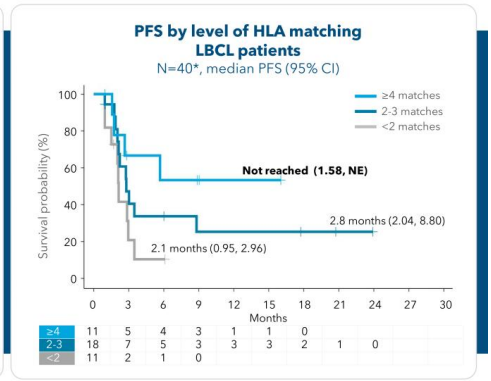
Endpoints (N, %)	All patients ≤3 HLA matches (N=33)	All patients ≥4 HLA matches (N=13)	LBCL ≥4 HLA matches (N=11)
Overall response rate (ORR)	23 (69%)	12 (92%)	10 (91%)
Duration of response (DoR), median months (range)	2.0 (1-23+)	13.5 (1-23+)	NR (1-15+)
Complete response (CR) rate	15 (45%)	6 (46%)	4 (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

21 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.

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





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

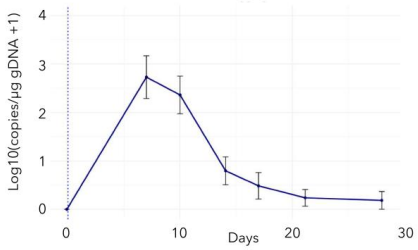
*Retrospective analysis of HLA allele matching for class I and class II antigens.

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


CB-010 translational research data
Kike Zudaire, PhD
SVP of translational sciences and therapeutic discovery
Caribou Biosciences
CARIBOU BIOSCIENCES

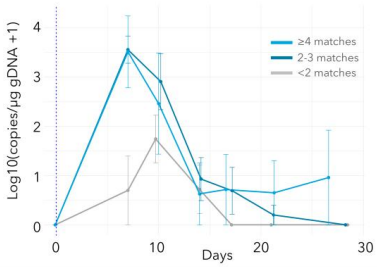
Partial HLA matching improves exposure of CB-010

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

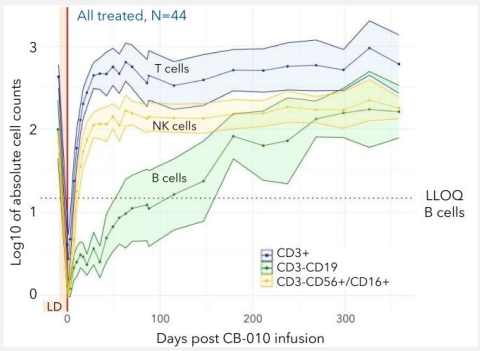
LLOQ: lower limit of quantification

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.

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

25 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

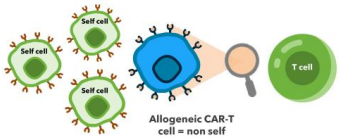
Duration of B cell aplasia Days	
CB-010 N=44	114 Mean (IQR 42-150)
Müller et al N=14[1]	112 Mean (IQR 72-153)

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.

Partial HLA matching does not impact time to treatment

How does HLA matching work?



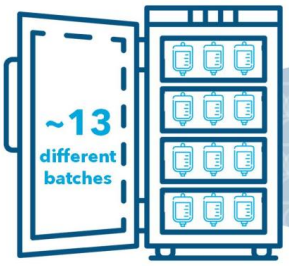
- Human leukocyte antigens (HLAs) help the immune system identify "self" from "non-self"
- Patient's immune cells recognize allogeneic CAR-T cells as "non-self" and initiate rejection

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

- HLA typing and DSA analysis occur within screening timeline and does not impact time to receive treatment
- Partial HLA matching could result in enhanced outcomes for patients[1]

27 DSA: donor-specific antibodies
[1] Based on data from the ongoing ANTLER Phase 1 trial in r/r B-NHL and to be confirmed in the ANTLER and GALLOP Phase 1 trials.

CB-010 is an off-the shelf CAR-T cell therapy that is easily matched to 2L LBCL 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


Advancing CB-010 development
Tonia Nesheiwat, PharmD
VP of medical affairs and project leadership
Caribou Biosciences
CARIBOU BIOSCIENCES

Broadening patient access through outpatient administration and expanding into an additional population of unmet need

New protocol amendment enables outpatient administration

Sites have the option to provide outpatient administration of both lymphodepletion and CB-010 treatment

Proof-of-concept cohort to evaluate CB-010 for patients who have relapsed following prior CD19-targeted therapy

Assess safety, efficacy, durability in patients who relapsed following any prior CD19-directed therapy (N=10)

Advancing CB-010 for 2L LBCL patients

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 DLBCL from FL or MZL, and PMBCL.


Fireside chat
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Fireside chat with leaders in hematologic malignancies

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President and CEO
Caribou Biosciences

Boyu Hu, MD
Assistant professor, director of lymphoma and CLL in the division of hematology and hematologic malignancies
Huntsman Cancer Institute
University of Utah

Mehdi Hamadani, MD
Professor of medicine and section chief of hematologic malignancies
Medical College of Wisconsin


Q&A
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Open to your questions

Rachel Haurwitz, PhD
President and CEO

Steve Kanner, PhD
CSO

Jason O'Byrne
CFO

Kike Zudaire, PhD
SVP, translational sciences and therapeutic discovery

Tonia Nesheiwat, PharmD
VP, medical affairs and project leadership

Boyu Hu, MD

Assistant professor, director of lymphoma and CLL in the division of hematology and hematologic malignancies

Huntsman Cancer Institute University of Utah

Mehdi Hamadani, MD

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

- With partial HLA matching, safety, efficacy, durability has the potential to rival approved autologous CAR-T cell therapies[1]
- 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.

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

Future: planned pivotal Phase 3 trial

~13 manufacturing batches allow for partial (≥4) HLA matching for **~90% of 2L LBCL patients**

KOL discussion CB-010 ANTLER Phase 1 data | June 2024

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 initial dose escalation data from CaMMouflage Phase 1 trial	YE 2024
CB-010 LN/ERL	Initiate GALLOP Phase 1 trial	YE 2024

With gratitude for patients, caregivers, investigators contributing to CB-010's clinical development

ANTLER Phase 1 trial: 29 active sites in US, Australia, and Israel

Alabama
University of Alabama Birmingham (Mehta)

Arizona
HonorHealth Cancer Institute (Kanate)
University of Arizona (Husnain)
Banner MD Anderson (Nath)

California
University of California Irvine (O'Brien)
University of California San Diego (Hamdan)

Florida
Advent Health (Patel)

Georgia
Augusta (Kota)
BMT of Georgia (Sohl)

Iowa
University of Iowa (Farooq)

Kentucky
University of Kentucky (Yalniz)
Norton Cancer Institute (Stevens)

New Jersey
Morristown Memorial Hospital (Cherry)
Hackensack (Feldman)

New York
Montefiore (Kornblum)
NYU Langone (Diefenbach)

Ohio
Oncology Hematology Care (Essell)

Pennsylvania
University of Pennsylvania (Nasta)

Tennessee
Vanderbilt University (Oluwole)

Texas
Baylor Charles A. Sammons (Holmes)
MD Anderson Cancer Center (Nastoupil)

Utah
Huntsman Cancer Institute (Hu)

Washington
Swedish Cancer Institute (Patel)

Wisconsin
Medical College of Wisconsin (Hamadani)

Australia
Westmead Hospital
Epworth Hospital

Israel
Hadassah University Hospital
Rabin Medical Center
Tel Aviv Sourasky Medical Center


Thank you
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Appendix
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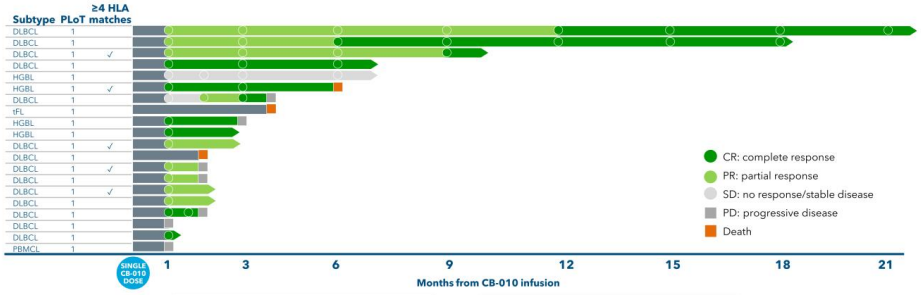
CB-010 ANTLER efficacy assessment in 2L LBCL at RP2D

Overall depth and duration of response in 2L LBCL at 80x10⁶ CAR-T cells (N=20)



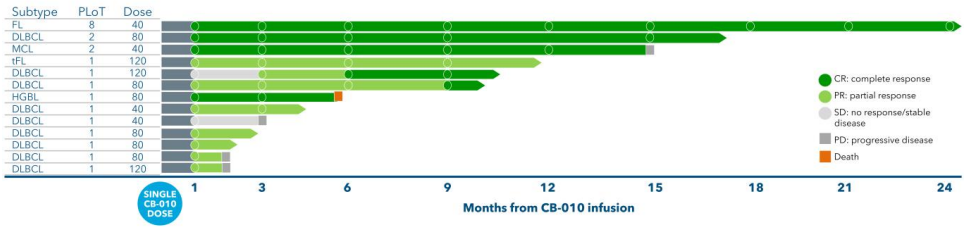
CR[1] rate
50%

Median duration of CR
Not reached

DLBCL: diffuse large B cell lymphoma; CR: complete response; HGBL: high-grade B cell lymphoma; PMBCL: primary mediastinal large B cell lymphoma; tFL: transformed DLBCL from follicular lymphoma; PLoT: prior lines of therapy; HLA: human leukocyte antigen
[1]50% CR rate measures the number of patients (10 of 20) 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 for patients with ≥4 HLA matching

(N=13)



Median PFS
14.4 months

CR[1] rate
46%

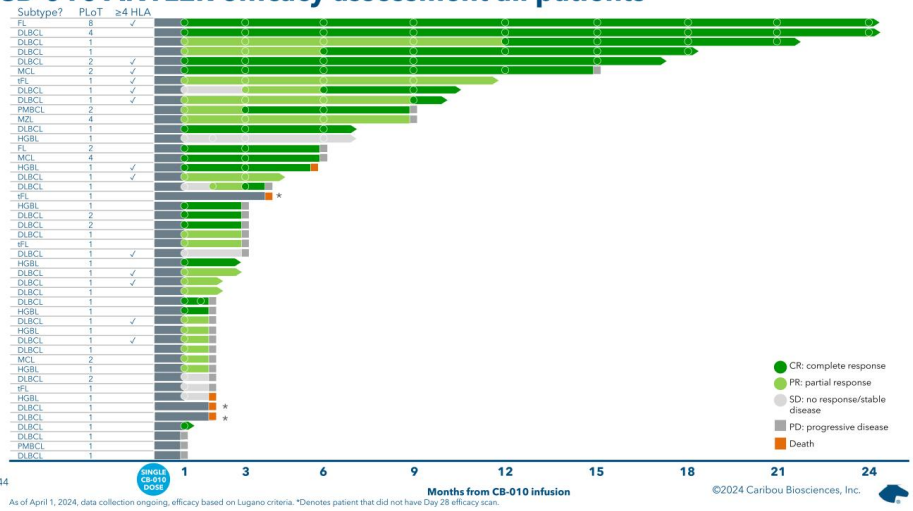
Median duration of CR
Not reached

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 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 ANTLER efficacy assessment by dose level

80x10^6 selected as RP2D

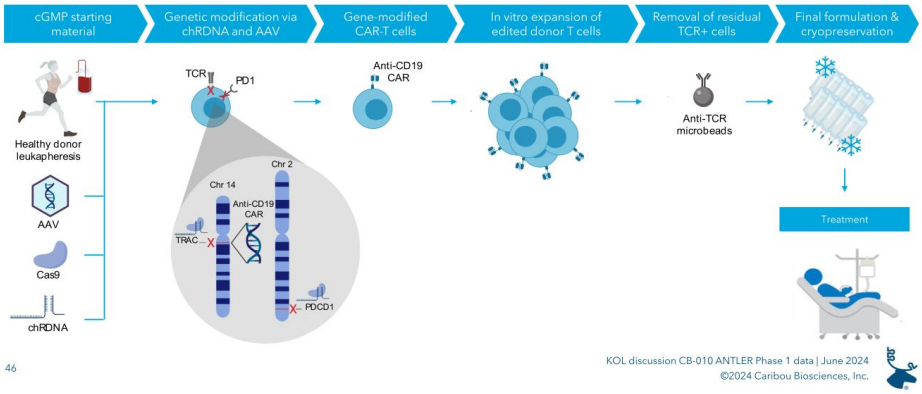
	r/r B-NHL	CB-010 dose level		
Endpoints (N, %)	**All patients** (N=46)	**40M** (N=14)	**80M** (N=23)	**120M** (N=9)
Overall response rate (ORR)	35 (76%)	9 (64%)	18 (78%)	8 (89%)
Duration of response (DoR), median months (range)	5 (1-23+)	7.9 (1-23+)	7.4 (1-20+)	1.9 (1-8+)
Complete response (CR) rate	21 (46%)	7 (50%)	11 (48%)	3 (33%)
Duration of CR, median months (range)	7 (1-23+)	6.7 (2-23+)	NR (1-15+)	1.8 (1-3+)
6-month PFS	35%	33%	43%	22%

+ censored observation

M: million cells per dose; NR: not reached; PFS: progression free survival; RP2D: recommended Phase 2 dose
ANTLER Phase 1 clinical trial as of April 1, 2024 cutoff date, data collection ongoing.

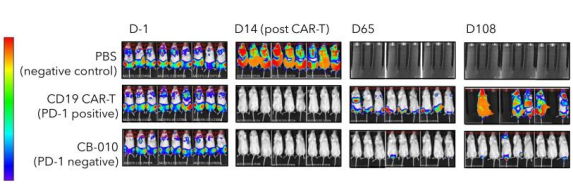
Allogeneic CAR-T cell manufacturing process overview for CB-010

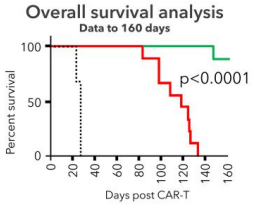
Caribou's process development team created the manufacturing process and transferred it to a CMO to generate phase 1 cGMP clinical material



CB-010 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