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 10, 2022

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** **(Address of Principal Executive Offices)**	**94710** **(Zip Code)**

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

(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 10, 2022, Caribou Biosciences, Inc. (the "Company") issued a press release announcing additional initial clinical data from the ongoing ANTLER Phase 1 clinical trial for its allogeneic anti-CD19 CAR-T cell therapy product candidate, CB-010. A copy of the press release is attached hereto as Exhibit 99.1 and incorporated by reference herein.

Also on June 10, 2022, the Company will host a conference call to discuss the additional initial clinical data. A copy of the slide presentation to be used during the Company's conference call is attached hereto as Exhibit 99.2 and incorporated by reference herein. Details for accessing the conference call are included in Exhibit 99.1.

The information in Item 7.01 of this Current Report on Form 8-K (including Exhibit 99.1 and Exhibit 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 otherwise subject to the liabilities of that section, nor shall it be, or be deemed, incorporated by reference in any filings under the Securities Act of 1933, as amended (the "Securities Act"), regardless of any general incorporation language in any such filing or document, unless the Company specifically states that the information is to be considered "filed" under the Exchange Act or incorporates it by reference into a filing under the Securities Act or the Exchange Act.

Item 8.01 Other Events.

On June 10, 2022, the Company presented a poster at the European Hematology Association ("EHA") 2022 Congress containing initial clinical data for six patients in cohort one of the Company's ongoing ANTLER phase 1 clinical trial of its CB-010 product candidate in patients with relapsed or refractory B cell non-Hodgkin lymphoma ("r/r B-NHL"). The initial data indicate that CB-010 was generally well-tolerated and had antitumor activity. As of the May 13, 2022 data cutoff date, six patients had been infused with CB-010 in cohort one at dose level one (40 million CAR-T cells). All patients had completed the 28-day dose-limiting toxicity ("DLT") evaluation period. Among these six patients, most adverse events ("AEs") were Grade 1 or 2. No Grade ≥ 2 cytokine release syndrome ("CRS"), no graft-versus-host disease ("GvHD"), and no Grade 5 AEs were observed. Two patients (33%) experienced Grade 1 CRS, and one patient (17%) experienced Grade 3 immune effector cell-associated neurotoxicity syndrome ("ICANS"), which was characterized as a DLT, for which the patient received tocilizumab and steroids and recovered within 39 hours. This patient went on to achieve a complete response ("CR"). In addition, Grade 3 or 4 treatment-emergent AEs evaluated by clinical investigators to be "probably related" or "related" to CB-010 were observed in four of six patients (67%); three patients (50%) experienced thrombocytopenia and decreased white blood cell counts, while decreased neutrophil counts, decreased lymphocyte counts, and increased LDH levels were each experienced by one patient (17%).

The initial clinical data presented at the EHA 2022 Congress indicate that all six patients in cohort one experienced a CR within 28-63 days following the administration of a single dose of CB-010 at the starting dose level one (40 million CAR-T cells), thus resulting in a 100% CR rate. At six months following the single dose of CB-010, 40% of patients (two of five) remained in CR as of the May 13, 2022 data cutoff date, and, as of this data cutoff date, the longest measured CR was at nine months. As of the data cutoff date, one of the previously assessed CR patients relapsed at their three-month evaluation and two relapsed at their six-month evaluations. One of the six patients from cohort one had not yet reached six months following dosing. After the data cutoff date of May 13, 2022, the first patient treated in the ANTLER trial had their 12-month evaluation and the patient remains in CR. Of the six patients dosed with CB-010 in cohort one, two had diffuse large B cell lymphoma, two had an aggressively behaving form of follicular lymphoma, one had mantle cell lymphoma, and one had primary mediastinal large B cell lymphoma. Based on this initial safety and efficacy profile, the Company's ANTLER phase 1 clinical trial is currently enrolling r/r B-NHL patients in cohort two at dose level two (80 million CAR-T cells).

From time to time, the Company plans to release additional clinical data from its ongoing ANTLER phase 1 clinical trial, including by year end. 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 initial clinical data reported earlier, including the additional data released on June 10, 2022 in connection with the EHA 2022 Congress. Initial, preliminary, or interim clinical trial data are subject to the risk that they will not ultimately be predictive of the safety and/or efficacy of the Company's CB-010 product candidate and that clinical outcomes may differ as additional and long-term clinical data become available. For example, the initial data from the Company's ANTLER trial are based on a limited number of patients (six patients), had a cutoff date of May 13, 2022, and are subject to risks, including that one or more of the clinical outcomes may materially and adversely change as patients continue on study, dose levels change, patient enrollment continues, and additional and long-term data (including, with respect to efficacy, duration of response, and/or safety) become available. For example, of the six patients who achieved CRs in cohort one of the ANTLER trial, three had progressive disease prior to the May 13, 2022 data cutoff date. As the ANTLER trial continues, there may be additional instances of progressive disease and/or adverse events. As a result, topline data should be viewed with caution until final clinical data are available from the ANTLER trial.

The information the Company chooses to disclose publicly regarding preclinical studies or clinical trials is typically a summary of extensive information, and others may not agree with what the Company determines is material or otherwise appropriate information to include in its disclosure, and any information the Company determines not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities, or otherwise regarding a particular product candidate or the Company's

business. If the initial, interim, or preliminary data that the Company reports differ from long-term or final results, or if others, including regulatory authorities, disagree with the conclusions reached, the Company's ability to obtain regulatory approval for, and commercialize, its product candidates may be compromised. For more information regarding the risks relating to initial, preliminary, or interim data from the Company's current and future clinical trials, please see the risk factors in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2021 and in other filings the Company makes with the Securities and Exchange Commission.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press Release dated June 10, 2022
99.2	CB-010 Clinical Program Update Presentation dated June 10, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

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

CARIBOU BIOSCIENCES, INC.

Date: June 10, 2022

By: /s/ Barbara G. McClung

Barbara G. McClung
Chief Legal Officer and
Corporate Secretary

Exhibit 99.1

Caribou Biosciences Reports Positive Additional Data from CB-010 Allogeneic CAR-T Cell Therapy Phase 1 ANTLER Trial at the European Hematology Association (EHA) 2022 Hybrid Congress

-- 100% CR rate (6 of 6 patients), with 40% CR rate (2 of 5 patients) at 6 months, achieved as best response following 1 dose at the initial dose level in patients with aggressive r/r B-NHL --

-- First patient treated in the ANTLER trial remained in CR at 12 months --

-- Based on promising initial safety profile and clinical activity, ANTLER Phase 1 trial enrolling patients at dose level 2 --

-- CB-010 is the 1st allogeneic CAR-T cell therapy in the clinic with a PD-1 knockout, a genome-editing strategy designed to improve the persistence of antitumor activity --

-- Caribou webcast conference call planned for today at 8:00 am ET --

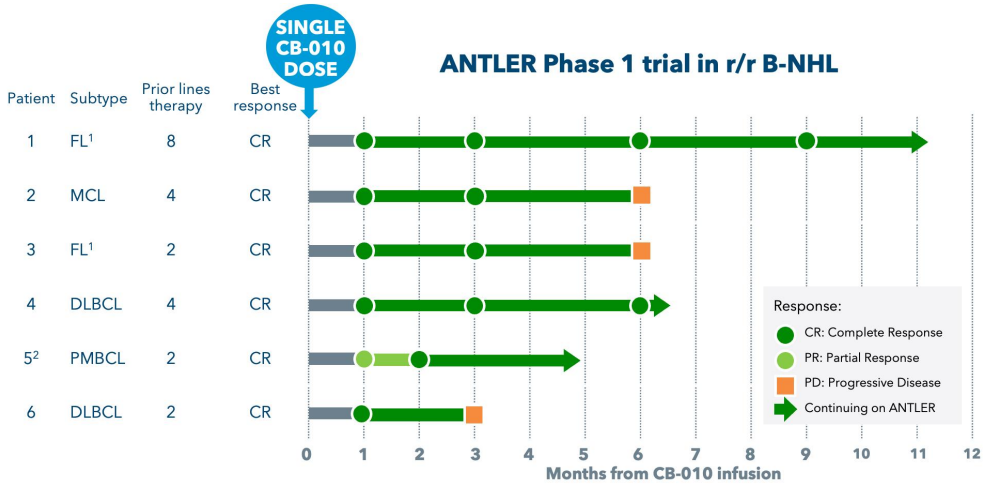
-- Additional ANTLER data expected by year end 2022 --

BERKELEY, CA, June 10, 2022 – Caribou Biosciences, Inc. (Nasdaq: CRBU), a leading clinical-stage CRISPR genome-editing biopharmaceutical company, today announced the presentation of additional initial clinical data from its ANTLER Phase 1 trial for CB-010 in patients with relapsed or refractory B cell non-Hodgkin lymphoma (r/r B-NHL). Following a single dose at the initial dose level of CB-010, a 100% complete response (CR) rate (6 of 6 patients) was observed as best response. At 6 months following the single dose of CB-010, 40% of patients remained in CR (2 of 5 patients) as of the May 13, 2022 data cutoff date. The data are being presented at the European Hematology Association (EHA) 2022 Hybrid Congress, being held in Vienna, Austria, June 9-17, 2022.

“The preliminary safety and efficacy results are promising. All six patients treated with CB-010 at the initial dose level of 40 million CAR-T cells achieved a complete response, and we are now enrolling dose level 2 and look forward to seeing this study mature,” said Loretta J. Nastoupil, M.D., associate professor, Department of Lymphoma/Myeloma in the Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center and the presenting investigator on the ANTLER trial. “CB-010 was generally well-tolerated and the adverse events observed are consistent with autologous or allogeneic CAR-T cell therapies.”

Additional data, which was received after the cutoff date of May 13, 2022 and was not included in the EHA poster, showed the first patient treated in the ANTLER trial remained in CR at their 12-month evaluation.

“We believe the 100% complete response achieved in the ANTLER CB-010 trial is unparalleled for a single, starting dose of cell therapy and represents an important step toward showing the potential of our chRDNA genome-editing platform and pipeline of allogeneic cell therapies,” said Rachel Haurwitz, Ph.D., Caribou’s president and chief executive officer. “As the first allogeneic anti-CD19 CAR-T cell therapy in the clinic with a PD-1 knockout, CB-010 is designed to have sustained antitumor activity by limiting premature CAR-T cell exhaustion in patients with r/r B-NHL. As we enroll patients in cohort 2 at dose level 2 of the ANTLER trial, we are grateful for the patients, caregivers, and investigators who have participated in this clinical trial. We continue to advance CB-010, as our goal is to develop an allogeneic cell therapy that may meaningfully rival autologous cell therapies and extend the potential reach of off-the-shelf treatments for patients.”



FL: follicular lymphoma MCL: mantle cell lymphoma DLBCL: diffuse large B cell lymphoma PMBCL: primary mediastinal large B cell lymphoma
[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
As of May 13, 2022 data cutoff date, data collection ongoing, efficacy based on Lugano criteria

This image is also available at: Patient response rates following treatment with CB-010, single dose at dose level 1, in the ANTLER Phase 1 trial

The EHA poster presentation includes safety, tolerability, and initial antitumor activity data for CB-010 administered at dose level 1 ($40x10^6$ CAR-T cells) to 6 patients with r/r B-NHL who had relapsed after previous treatment with a median of 3 prior therapies (range 2-8).

Following treatment with CB-010, there were no cases of graft versus host disease in the six patients. Grade 3 or 4 treatment emergent adverse events (TEAEs) developed in 5 of 6 patients, see details in accompanying table. Two patients experienced Grade 1 CRS (33%) and one patient experienced Grade 3 ICANS (17%), which was characterized as a dose limiting toxicity (DLT), for which the patient received tocilizumab and steroids and recovered within 39 hours. This patient went on to achieve a CR.

Cohort 1 (N=6)	Any Grade[1] N (%)	Grade ≥ 3 N (%)	Related[2] Grade ≥ 3 N (%)
Total number of TEAEs	**137**	**39**	**17**
Patients with TEAEs	**6 (100)**	**5 (83)**	**4 (67)**
Neutropenia/neutrophil count decreased	5 (83)	5 (83)	1 (17)
Thrombocytopenia/platelet count decreased	4 (67)	4 (67)	3 (50)
Anemia	4 (67)	2 (33)	-
White blood cell count decreased	3 (50)	3 (50)	3 (50)
Lymphocyte count decreased	3 (50)	2 (33)	1 (17)
Lactate dehydrogenase (LDH) increased	2 (33)	1 (17)	1 (17)
Cytokine release syndrome (CRS)	2 (33)	-	-
Blood creatinine increased	2 (33)	-	-
Fatigue	2 (33)	-	-
Hypoalbuminemia	2 (33)	-	-
Hypocalcemia	2 (33)	-	-
Hyponatremia	2 (33)	-	-
ICANS	1 (17)	1 (17)	1 (17)
Febrile neutropenia	1 (17)	1 (17)	-
Syncope	1 (17)	1 (17)	-

[1] TEAE in at least 2 patients of any grade or TEAE in at least 1 patient of Grade ≥ 3 are included
[2] Related TEAEs include TEAEs with relationship to CB-010 of "probably related" or "related" as evaluated by investigator

Image of table available at: Treatment emergent adverse events in the ANTLER Phase 1 trial

Based on promising initial safety and efficacy data from cohort 1 at dose level 1 ($40x10^6$ CAR-T cells), the ANTLER trial is now enrolling patients in cohort 2 at dose level 2 ($80x10^6$ CAR-T cells). Additional data are expected by year end.

Details of the poster presentation at EHA are as follows:
Title: First-in-human trial of CB-010, a CRISPR-edited allogeneic anti-CD19 CAR-T cell therapy with a PD-1 knock out, in patients with relapsed or refractory B cell non-Hodgkin lymphoma (ANTLER study)
Abstract: 3103
Presenter: Loretta J. Nastoupil, M.D., section chief, new drug development; associate professor, Department of Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center
Date and Time: Friday, June 10, 2022, 16:30 – 17:45 CEST (10:30 – 11:45 am ET)
Session Title: Gene therapy, cellular immunotherapy and vaccination - Clinical
Location: Messe Wien Exhibition & Congress Center, Vienna, Austria

The poster is available on the Presentations page of the Investors section of Caribou's website.

Exhibit 99.1

Webcast Conference Call Today at 8:00 am ET
Caribou will host a webcast conference call today to discuss the data presented at EHA on the initial ANTLER data for CB-010.

The live webcast and conference call at 8:00 am ET, with an accompanying presentation, will be accessible under Events in the Investors section of the company's website. To participate in the conference call, dial 1-844-862-9351 (domestic) or 1-929-517-0932 (international) and reference conference ID #4657536. The archived audio webcast will be available on Caribou's website following the call and will be available for 30 days.

About CB-010

CB-010 is the lead product candidate from Caribou's allogeneic CAR-T cell therapy platform and is being evaluated in patients with relapsed or refractory B cell non-Hodgkin lymphoma (r/r B-NHL) in the ongoing ANTLER Phase 1 trial. CB-010 is an allogeneic anti-CD19 CAR-T cell therapy engineered using Cas9 CRISPR hybrid RNA-DNA (chRDNA) technology to insert a CD19-specific CAR into the *TRAC* gene and knock out PD-1 to boost the persistence of antitumor activity. CB-010 is the first allogeneic CAR-T cell therapy in the clinic with a PD-1 knock out. Additional information on the ANTLER trial can be found at https://clinicaltrials.gov using identifier 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 Cas12a chRDNA technology to carry out high efficiency multiple edits, including multiplex gene insertions, 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 proprietary Cas12a chRDNA technology, enables superior precision to develop cell therapies that are specifically engineered for enhanced persistence. Caribou is advancing a pipeline of off-the-shelf CAR-T and CAR-NK cell therapies for the treatment of patients with hematologic malignancies and solid tumors.

Follow us @CaribouBio and visit www.cariboubio.com.

Exhibit 99.1

"Caribou Biosciences" and the Caribou logo are registered trademarks of Caribou Biosciences, Inc.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements include, without limitation, statements related to Caribou's strategy, plans, and objectives, and expectations regarding its clinical and preclinical development programs, including its expectations relating to the timing of the release of initial and additional patient data from its ANTLER phase 1 clinical trial for CB-010. 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 current and future research and development programs, preclinical studies, and clinical trials; and the risk that initial 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 more patient data becomes available; 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, 2021, 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.

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Exhibit 99.2

CARIBOU BIOSCIENCES®

ANTLER initial clinical data for CB-010 at EHA 2022

June 10, 2022

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, including but not limited to any statements regarding the initiation, timing, progress, strategy, plans, objectives, expectations, and results of our product candidate preclinical studies, clinical trials, and research programs, including our expectations and timing regarding the initial clinical data from our ANTLER phase 1 clinical trial for our CB-010 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; 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; 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 are forward-looking statements. 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; 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 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, 2021, 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.

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.

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


Introduction
Rachel Haurwitz, PhD
President & CEO
Caribou Biosciences, Inc.
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Today's guests

Loretta J. Nastoupil, MD

Section Chief, New Drug Development

Associate Professor, Department of Lymphoma/Myeloma

The University of Texas MD Anderson Cancer Center

James H. Essell, MD

OHC hematologist, medical oncologist, blood and marrow transplant specialist

Chair, Cellular Therapy, US Oncology Network

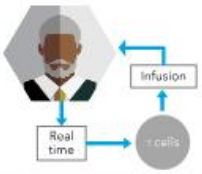
OHC – Specialists in Cancer and Blood Disorders

Aiming to set a new therapeutic bar for patients

Our mission is to develop innovative, transformative therapies for patients with devastating diseases through novel genome editing

Persistence is the key to unlocking the full potential of allogeneic cell therapies

Autologous therapy



Limited patient access
- Long vein-to-vein times
- Not all patients eligible
- Single dose

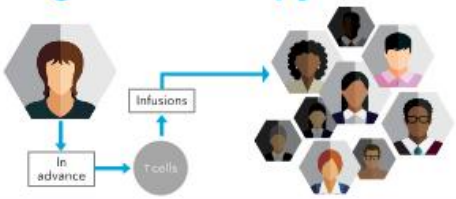
Bridging therapy often required

Manufacturing complexity

High production costs

Variable potency

Allogeneic therapy



Broad patient access
- Immediate availability
- Suitable for many patients
- Repeat dosing possible

Bridging therapy not required

Off-the-shelf availability

More efficient and cost-effective manufacturing

Healthy donor cells genome engineered for potency and persistence

… but efficacy remains a challenge
- Rapid rejection by immune system

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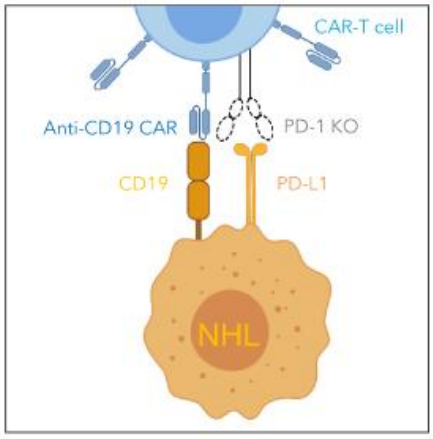
Persistence is the solution

CB-010: anti-CD19 allogeneic CAR-T cell therapy

Key attributes	CB-010	Conventional allo anti-CD19 CAR-Ts
PD-1 KO for enhanced persistence of antitumor activity	▯	X
• Potentially better initial tumor debulking preclinically	▯	X
• Potentially better therapeutic index	▯	X
Site-specific insertion of CAR into *TRAC* locus • Eliminates random integration and reduces risk of GvHD	▯	Varies
Cas9 chRDNA editing for enhanced genomic integrity	▯	X
• Reduced off-target editing and genomic rearrangements	▯	X



Program: CB-010
Tumor antigen: CD19
Healthy donor leukapheresis-derived T cells
Indication: r/r non-Hodgkin lymphoma (NHL)
Status: Phase 1

Source: Caribou data on file
CB-010 Clinical Program Update – 10 June 2022

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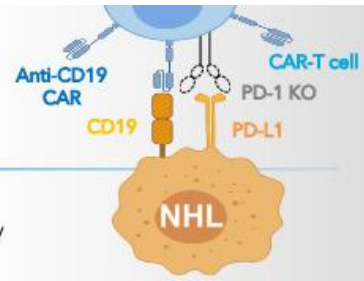
Our goal is to develop CB-010 as a transformative allogeneic cell therapy



- CB-010 is the **1st allogeneic CAR-T cell therapy** in the clinic with a PD-1 KO
- PD-1 KO genome-editing strategy designed to **improve persistence** of antitumor activity

CB-010: 1st allogeneic CAR-T cell therapy to achieve a 100% CR

Single dose at dose level 1* (N=6)

100% CR
6/6 patients

BEST RESPONSE

40% CR
2/5 patients

AT 6 MONTHS
(1 patient has not reached 6-month assessment)

r/r B-NHL patients in ANTLER had aggressive disease (median 3 prior treatments)

Generally well tolerated with AEs as expected for autologous/allogeneic anti-CD19 CAR-T cell therapies

Additional ANTLER data expected by YE 2022

Enrolling patients at dose level 2† → planning for future development

* $40x10^6$ CAR-T cells ; † $80x10^6$ CAR-T cells
† All data as of May 13, 2022 data cutoff date, data collection ongoing, efficacy measured by Lugano criteria
Source: Poster from European Hematology Association (EHA) 2022 Hybrid Congress

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With gratitude for patients, caregivers, investigators

- **MD Anderson Cancer Center, Houston**
- **Chao Family Comprehensive Cancer Center / University of California Irvine, Orange**
- **Oncology Hematology Care, Cincinnati**
- **Baylor Chares A. Sammons Cancer Center, Dallas**
- **HonorHealth, Scottsdale**
- **University of California San Diego Moores Cancer Center, La Jolla**
- **Additional sites coming soon**

THANK YOU

for your contributions toward Caribou's mission to develop innovative, transformative therapies for patients with devastating diseases through novel genome editing


ANTLER Phase 1 trial initial data for CB-010
EHA 2022
Loretta J. Nastoupil, MD
Section Chief, New Drug Development
Associate Professor, Department of Lymphoma/Myeloma
The University of Texas MD Anderson Cancer Center
CARIBOU
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Disclosures

LJN has received honorarium for participation in advisory boards from ADC Therapeutics, BMS, Caribou Biosciences, Epizyme, Genentech/Roche, Genmab, Gilead/Kite, Janssen, MorphoSys, Novartis, and Takeda.

LJN has received research support from BMS, Caribou Biosciences, Epizyme, Genentech/Roche, Gilead/Kite, Janssen, IGM Biosciences, Novartis, and Takeda.

LJN serves on data safety monitoring boards for DeNovo, Genentech, MEI, and Takeda.

CB-010 ANTLER Phase 1 trial design

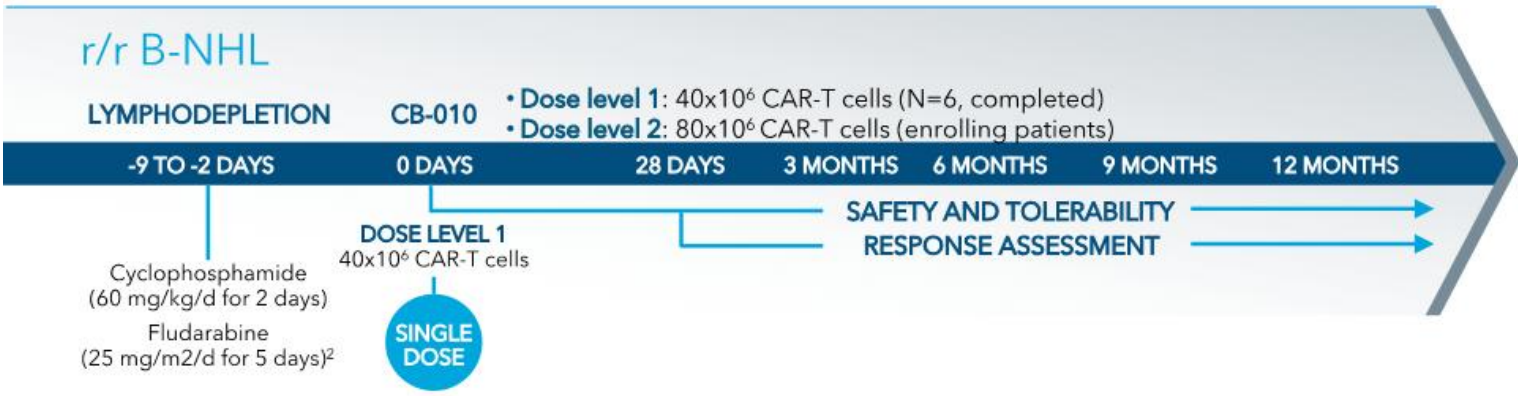
Patients with aggressive disease

- **r/r B-NHL** (DLBCL, HGBL, tFL, PMBCL, FL[1], MZL, MCL)
- ≥2 prior lines of chemoimmunotherapy
- Exclusion: prior CD19-targeted therapy

Part A: 3+3 dose escalation
Objective: safety, determine MTD, RP2D

Part B: dose expansion
Objective: tumor response

r/r B-NHL



MTD: maximum tolerated dose RP2D: recommended Phase 2 dose

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

[2] Clin Cancer Res. 2011 July 1; 17(13): 4550-4557. doi:10.1158/1078-0432.CCR-11-0116

Clinicaltrials.gov NCT#04637763

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ANTLER patients' baseline and disease characteristics

Characteristics	Cohort 1 (N=6)
Median age (range), years	65 (62-68)
Male, n (%)	5 (83)
ECOG performance status, n (%) 0 1	 5 (83) 1 (17)
Time since first diagnosis, years Median (range)	 6.0 (0.7-16)
Non-Hodgkin lymphoma subtype DLBCL FL[1] MCL PMBCL	 2 2 1 1
CD19+ disease, n (%)	6 (100)
Prior systemic therapies, median number (range)[2]	3 (2-8)

[1] Aggressively behaving, with POD24 (high risk)
[2] Patients are CD19 CAR-T naïve

Treatment emergent adverse events (TEAE)

Event Cohort 1 (N=6)	Any Grade[1] N (%)	Grade ≥ 3 N (%)	Related[2] Grade ≥ 3 N (%)
Total number of TEAEs	**137**	**39**	**17**
Patients with TEAEs	**6 (100)**	**5 (83)**	**4 (67)**
Neutropenia/neutrophil count decreased	5 (83)	5 (83)	1 (17)
Thrombocytopenia/platelet count decreased	4 (67)	4 (67)	3 (50)
Anemia	4 (67)	2 (33)	-
White blood cell count decreased	3 (50)	3 (50)	3 (50)
Lymphocyte count decreased	3 (50)	2 (33)	1 (17)
Lactate dehydrogenase (LDH) increased	2 (33)	1 (17)	1 (17)
Cytokine release syndrome (CRS)	2 (33)	-	-
Blood creatinine increased	2 (33)	-	-
Fatigue	2 (33)	-	-
Hypoalbuminemia	2 (33)	-	-
Hypocalcemia	2 (33)	-	-
Hyponatremia	2 (33)	-	-
ICANS	1 (17)	1 (17)	1 (17)
Febrile neutropenia	1 (17)	1 (17)	-
Syncope	1 (17)	1 (17)	-

[1] TEAE in at least 2 patients of any grade or TEAE in at least 1 patient of Grade ≥ 3 are included
[2] Related TEAEs include TEAEs with relationship to CB-010 of "probably related" or "related" as evaluated by investigator
As of May 13, 2022 data cutoff date

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AEs of special interest

Event	Cohort 1 (N=6)
CRS[1], n (%)	
Any grade	2 (33)
Grade 1	2 (33)
Grade ≥ 2	0 (0)
Median time to onset, days (range)	4 (1-7)
Median duration of events, days (range)	8 (7-8)

[1] 1 CRS required treatment. Patient received tocilizumab (8mg x 2) and antibiotics and was hospitalized

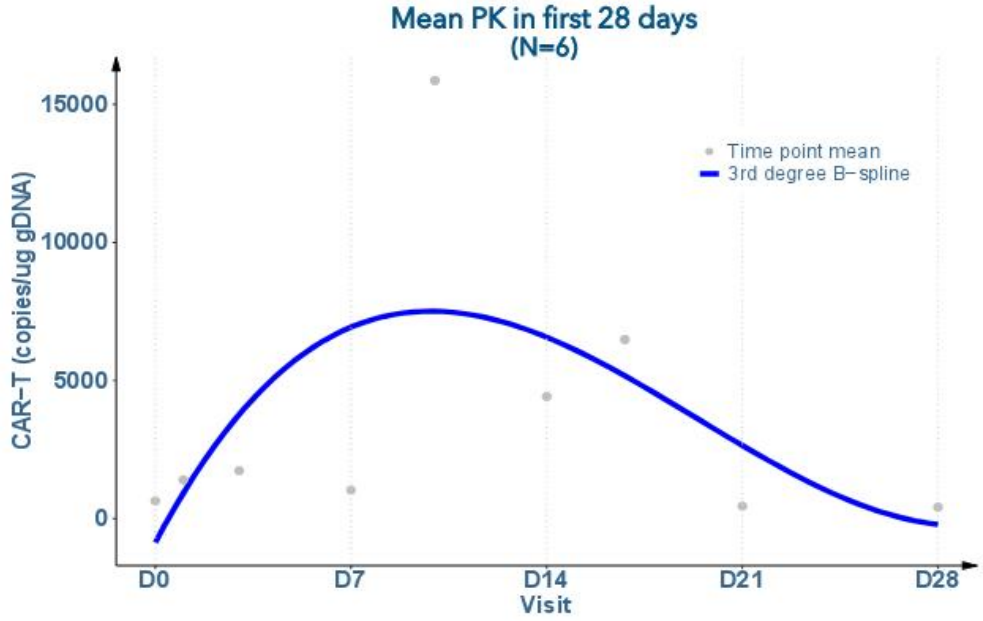
Event	Cohort 1 (N=6)
ICANS[2], n (%)	
Any grade	1 (17)
Grade 3	1 (17)
Grade ≥ 4	0 (0)
Time to onset, days	8
Duration of event, days	<2 (~39 hrs)

[2] Patient received dexamethasone (10mg x 2 and 20mg x 4) and was hospitalized

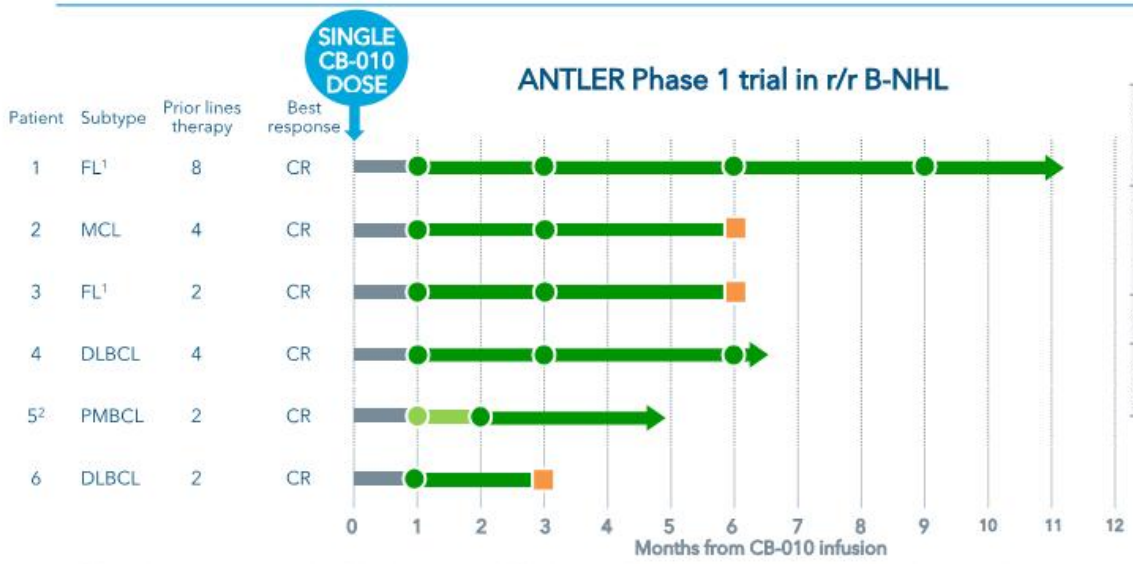
Event	Cohort 1 (N=6)
Infections[3], n (%)	
Any grade	2 (33)
Grade 1	0 (0)
Grade 2	1 (17)
Grade 3	1 (17)
Median time to onset, days (range)	8.5 (2-140)
Median duration of events, days (range)	5 (1-56)

[3] Grade 3, pre-CB-010 infusion. Grade 2, post-CB-010 infusion. None were related to CB-010

Kinetics of CB-010



CB-010: preliminary efficacy



6 patients treated with a single infusion at dose level 1 ($40x10^6$ CAR-T cells)

6 patients evaluable for efficacy[3]
- 100% CR (6/6, best response)
- 40% CR (2/5) at 6 months

9 months was longest measured CR

CRs measured by investigator assessment and central read

Response:
- CR: Complete Response
- PR: Partial Response
- PD: Progressive Disease
- Continuing on ANTLER

FL: follicular lymphoma MCL: mantle cell lymphoma DLBCL: diffuse large B cell lymphoma PMBCL: primary mediastinal large B cell lymphoma
[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
[3] As of May 13, 2022 data cutoff date, data collection ongoing, efficacy based on Lugano criteria

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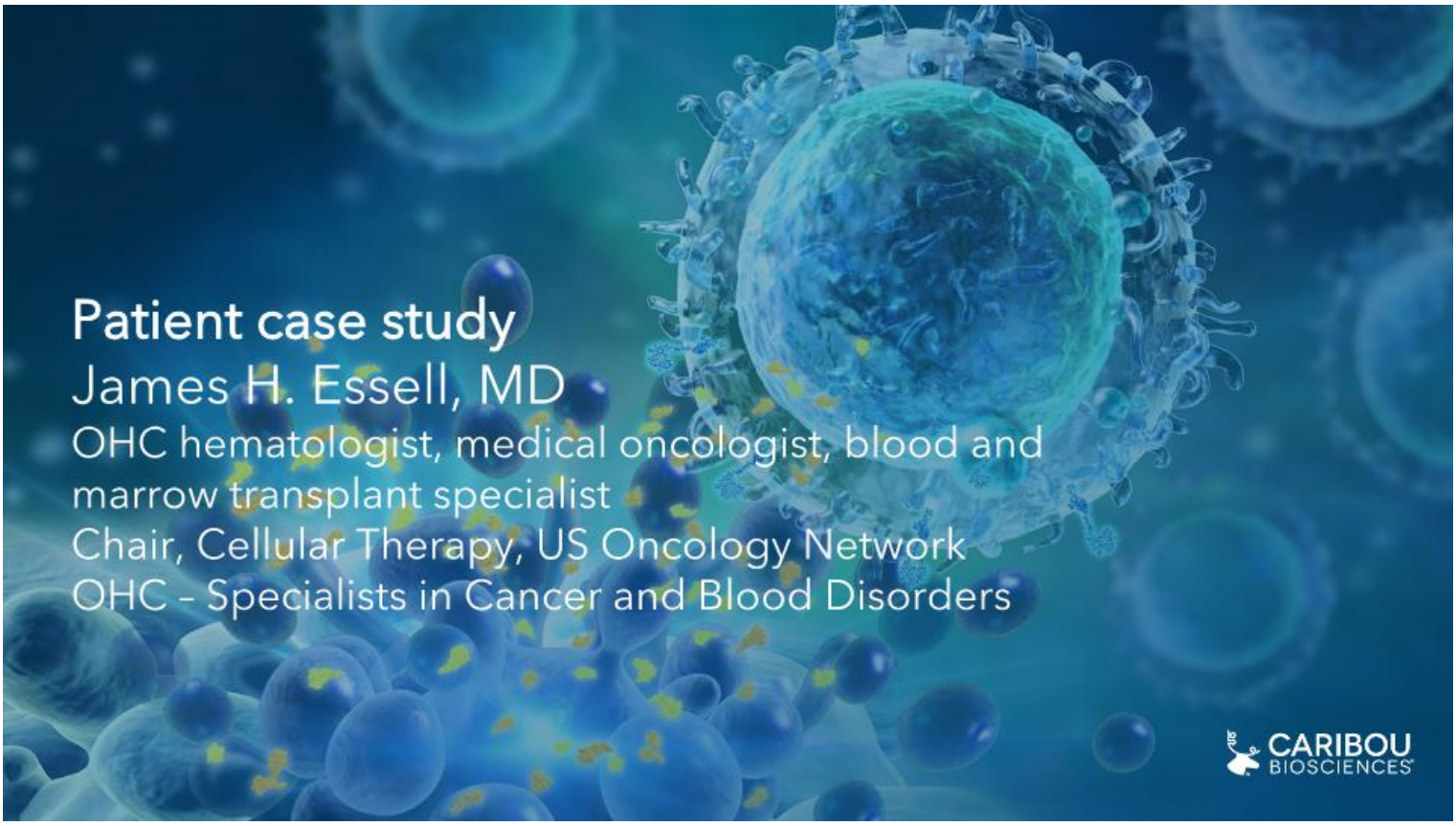
Patient case study
James H. Essell, MD
OHC hematologist, medical oncologist, blood and marrow transplant specialist
Chair, Cellular Therapy, US Oncology Network
OHC – Specialists in Cancer and Blood Disorders
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CASE STUDY
ANTLER Phase 1 trial

Patient #1[1]

Age: 66

Gender: M

BMI: 25.4

Original prognosis

Tumor subtype: FL (aggressively behaving, with POD24)

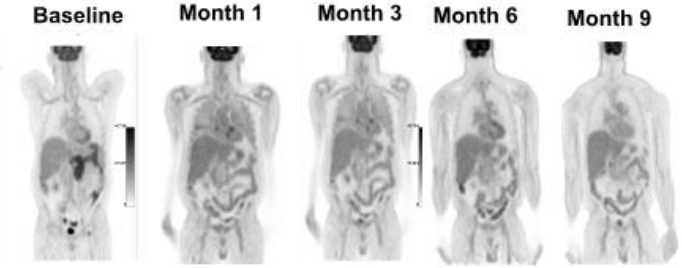
Stage: IV

Years since diagnosis: 8

Lines of prior therapy: 8

History: multiple relapses and progressive disease, then enrolled on ANTLER trial

PET-CT scans[2]



Significant disease burden with 10 cm abdominal mass

CR CR CR CR

After CB-010 dose level 1 treatment[3]

Days since CB-010 infusion: 329

Best ORR: confirmed CR from Day 28 post-infusion to Month 9

Tolerability: Grade ≥ 3 related AE: 1

Status: continuing on study

[1] The information presented in this patient case study relates to one patient and may not be reflective of any of the other patients in the ANTLER Phase 1 trial. In addition, initial or interim clinical trial data is subject to the risk that it will not ultimately be predictive of the safety and efficacy of the product candidates and that clinical outcomes may differ as more and longer-term clinical data become available.
[2] Responses evaluated by investigator assessment and independent radiologist
[3] As of May 13, 2022 data cutoff date, data collection ongoing, efficacy based on Lugano criteria

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Fireside chat
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Fireside chat with Dr. Nastoupil and Dr. Essell

Loretta J. Nastoupil, MD

Section Chief, New Drug Development

Associate Professor, Department of Lymphoma/Myeloma

The University of Texas MD Anderson Cancer Center

James H. Essell, MD

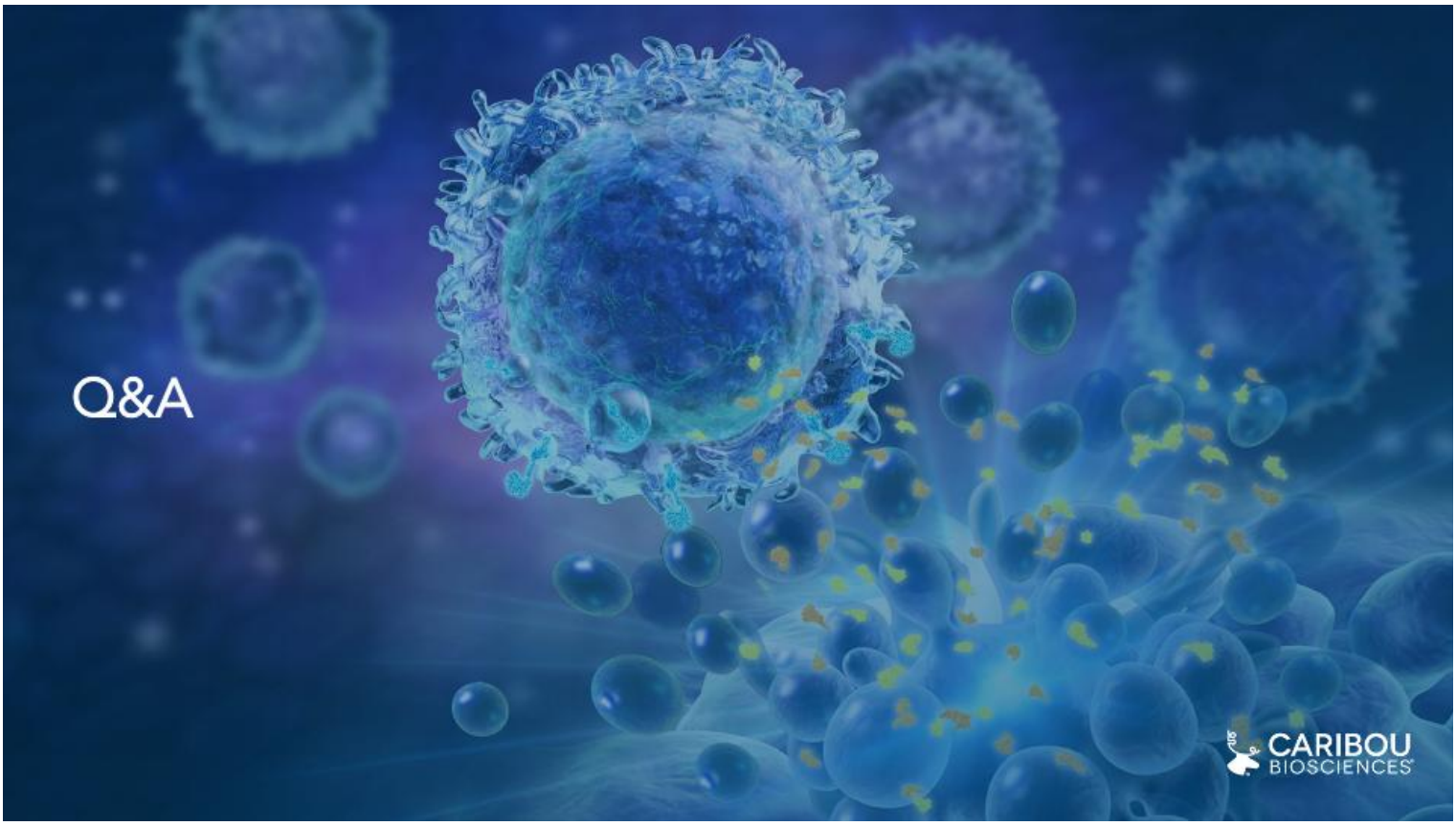
OHC hematologist, medical oncologist, blood and marrow transplant specialist

Chair, Cellular Therapy, US Oncology Network

OHC – Specialists in Cancer and Blood Disorders

Rachel Haurwitz, PhD
President and CEO

Caribou Biosciences


Q&A
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Open to your questions

Loretta J. Nastoupil, MD

Section Chief, New Drug Development

Associate Professor, Department of Lymphoma/Myeloma

The University of Texas MD Anderson Cancer Center

James H. Essell, MD

OHC hematologist, medical oncologist, blood and marrow transplant specialist

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Rachel Haurwitz, PhD
President and CEO
Director

Caribou Biosciences

Syed Rizvi, MD
Chief Medical Officer

Caribou Biosciences

Steve Kanner, PhD
Chief Scientific Officer

Caribou Biosciences


Closing remarks
Rachel Haurwitz, PhD
President & CEO
Caribou Biosciences, Inc.
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Initial ANTLER data are an important step toward validating Caribou's chRDNA genome-editing platform

- **100% CR rate[1] (6/6, best response), 40% CR rate[1] (2/5) at 6 months from a single dose of CB-010 at dose level 1**
  1st allogeneic CAR-T cell therapy to achieve 100% CR rate, best response
  Promising initial safety profile
- **Currently enrolling patients in ANTLER Phase 1 trial at dose level 2**
- **Additional ANTLER data expected by YE 2022**
- **Goal to develop CB-010 as an allogeneic cell therapy that can meaningfully rival autologous cell therapies to reach broader groups of patients globally who need off-the-shelf cell therapy**
- **CB-010 is Caribou's lead program and part of a pipeline of precision genome-edited allogeneic CAR-T and CAR-NK cell therapies**
- **Experienced team and capital[2] to execute on our mission**

[1] As of May 13, 2022 data cutoff date, data collection ongoing, efficacy based on Lugano criteria
[2] $391M in cash, cash equivalents, and marketable securities as of March 31, 2022

Pipeline: initial focus on allogeneic cell therapy programs for solid and liquid tumors

Program	Target	Editing	Indications	Discovery	IND enabling	Phase 1	Phase 2	Phase 3[1]	Anticipated milestone
CAR-T platform with cell therapies for hematologic indications									
CB-010	CD19	CAR into TRAC; armoring: PD-1 KO	r/r B-NHL	●	●	●	○	○	Additional data expected YE 2022
CB-011	BCMA	CAR into TRAC; armoring: B2M KO, B2M-HLA-E insertion	r/r MM	●	●	○	○	○	IND submission H2 2022
CB-012	CD371[2]	CAR into TRAC; armoring: undisclosed	r/r AML	●	○	○	○	○	IND submission 2023
CAR-NK platform with iPSC-derived cell therapies for solid tumor indications									
CB-020	undisclosed	armoring: undisclosed	solid tumors	●	○	○	○	○	target selection Q4 2022
AbbVie programs under collaboration agreement[3]									
CAR-T Program 1	undisclosed	undisclosed	undisclosed	●	○	○	○	○	
CAR-T Program 2	undisclosed	undisclosed	undisclosed	●	○	○	○	○	

[1] Phase 3 may not be required if Phase 2 is registrational
[2] Also known as CLL-1
[3] AbbVie has an option to include up to two additional CAR-T cell programs


Thank you
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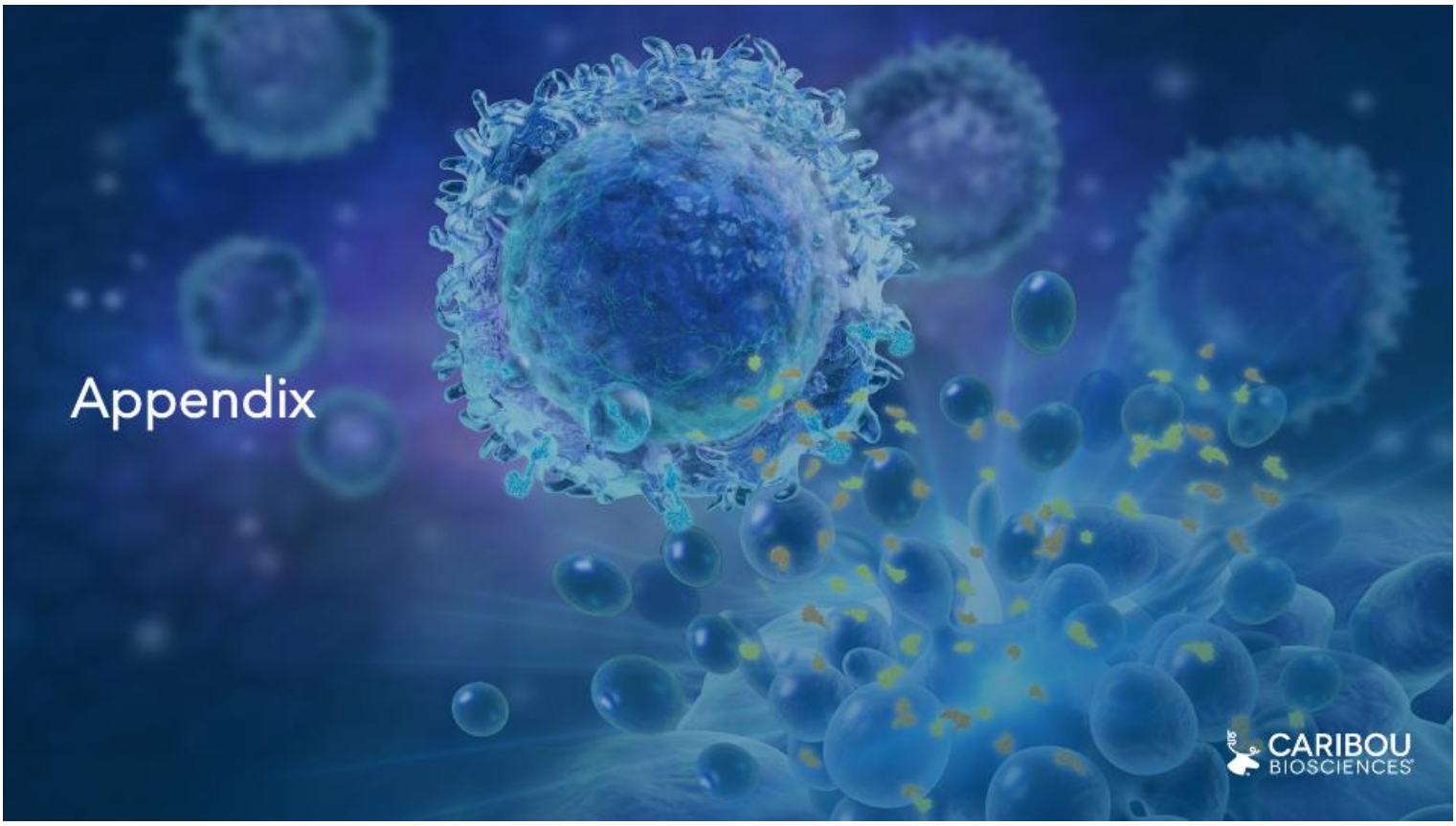
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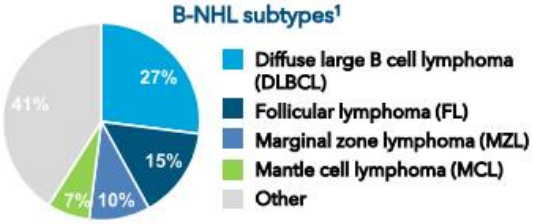
r/r B-NHL: high unmet need globally for off-the-shelf cell therapy

- NHL is the most common hematologic malignancy in the U.S.
- Mature B cell lymphomas (B-NHL) are 80-85% of all NHL cases
- ~34% of B-NHL cases are considered relapsed or refractory (r/r)[1]
- Current autologous CAR-T cell therapies have limited patient access with complex manufacturing and high production costs

B-NHL subtypes[1]



Worldwide NHL incidence[2]

US incidence[1]: ~82,900 | **EU incidence: ~101,000** | **China incidence: ~97,500** | **Japan incidence: ~33,600**

B-NHL 5-year post-diagnosis survival rates[3]

[1] National Cancer Institute, Leukemia & Lymphoma Society, Lymphoma Research Foundation
[2] Evaluate Pharma, May 2022, www.evaluate.com
[3] Cancer Research U.K.

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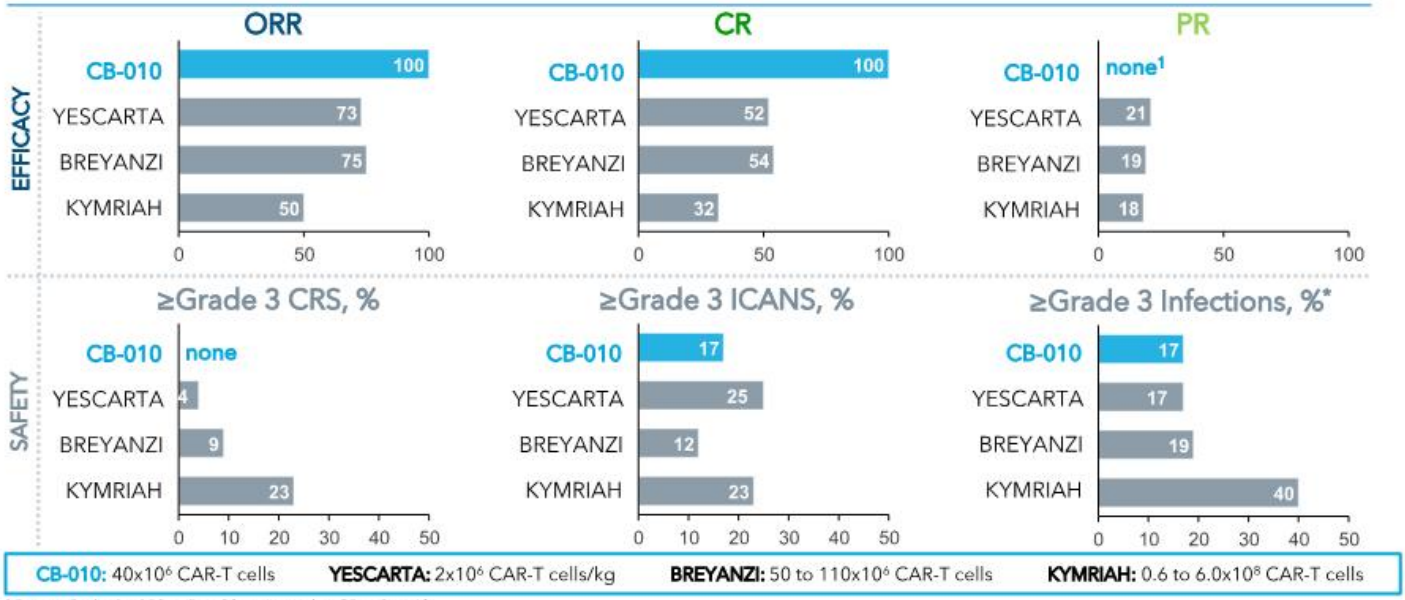
CB-010: an allogeneic cell therapy that may rival autologous anti-CD19 cell therapies



CB-010: 40x10⁶ CAR-T cells **YESCARTA:** 2x10⁶ CAR-T cells/kg **BREYANZI:** 50 to 110x10⁶ CAR-T cells **KYMRIAH:** 0.6 to 6.0x10⁸ CAR-T cells

[1] Patient 5 who had PR at Day 28 converted to CR at Day 63
* 1 patient with 2 Grade 3 infections recorded prior to CB-010 infusion
Sources: package inserts for YESCARTA, BREYANZI, KYMRIAH

Information regarding competitors and their results may be based on different stages of trials, different trial designs, and may be based on different assumptions or estimates. Caution should be used when evaluating competitor results presented against CB-010 and the reader should not place undue reliance on this comparative information.

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Deeper lymphodepletion protocol does not result in 100% ORR in B-NHL patients

Clinical autologous CAR-T cell response rates following intensive LD regimens in B-NHL[1]

LD regimen prior to autologous anti-CD19 CAR-T cell therapy infusion	N=	Objective response rate (ORR)	Complete response (CR) rate
Cy 60 mg/kg/day + Flu 25 mg/kg^2/day x 3-5 days	28	67%	42%

B-NHL: B cell non-Hodgkin lymphoma Cy: cyclophosphamide Flu: fludarabine LD: lymphodepletion

[1] Turtle CJ et al. *Blood*. 2015;126(23):184