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): December 12, 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		**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 December 12, 2022, Caribou Biosciences, Inc. (the "Company") issued two press releases.

In the first press release, the Company announced new 12-month clinical data from cohort 1 (six patients) in the ongoing ANTLER Phase 1 clinical trial of its allogeneic anti-CD19 CAR-T cell product candidate, CB-010, at the initial dose level 1 ($40x10^6$ CAR-T cells) in patients with relapsed or refractory B cell non-Hodgkin lymphoma ("r/r B-NHL"). The Company also provided information on the status of dose level 2 ($80x10^6$ CAR-T cells) and dose level 3 ($120x10^6$ CAR-T cells) in the ANTLER Phase 1 trial. The Company also reported that it was presenting a trial-in-progress poster at the 64th Annual American Society of Hematology ("ASH") meeting on December 12, 2022 with details of the design and objectives of the ANTLER Phase 1 trial. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and also is incorporated by reference into this Item 7.01.

In the second press release, the Company announced that it had selected receptor tyrosine kinase like orphan receptor 1 ("ROR1") as the target for its CB-020 product candidate, the Company's first off-the-shelf induced pluripotent stem cell ("iPSC")-derived allogeneic CAR-NK cell therapy targeting solid tumors. The Company also reported that it was presenting preclinical data on the selection of the CB-020 target as well as armoring strategies for its CAR-NK cell platform on December 12, 2022 at the 12th American Association for Cancer Research and Japanese Cancer Association Joint Conference ("AACR-JCA"). A copy of the press release is furnished as Exhibit 99.2 to this Current Report on Form 8-K and also is incorporated by reference into this Item 7.01.

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.

CB-010

On December 12, 2022, the Company announced new 12-month clinical data from cohort 1 (six patients) in the ANTLER Phase 1 clinical trial of its CB-010 product candidate at the initial dose level 1 ($40x10^6$ CAR-T cells) in patients with r/r B-NHL. Cohort 1 results show:

- Six of six patients achieved a complete response ("CR") as best response;
- Three of six patients maintained a durable CR at six months;
- Two of six patients maintain a long-term CR at the 12-month scan and remain on the trial;
- 18 months is the longest CR maintained to date in ANTLER, achieved by the first patient dosed with CB-010; and
- CB-010 was generally well tolerated with adverse events consistent with autologous or allogeneic anti-CD19 CAR-T cell therapies.

In addition, the Company reported that it has observed a promising safety profile for CB-010 at dose level 2 ($80x10^6$ CAR-T cells) with no dose-limiting toxicities ("DLTs") in the three patients treated in dose level 2 and that the Company is currently enrolling patients at dose level 3 ($120x10^6$ CAR-T cells).

CB-020 and CAR-NK cell platform

On December 12, 2022, the Company also announced that it had selected ROR1 as the target for CB-020, its iPSC-derived allogeneic CAR-NK cell therapy targeting solid tumors. ROR1 is a cell signaling receptor that is overexpressed on the surface of several solid tumor types and has been shown to promote tumor cell growth, survival, and metastasis. Preclinical data to be presented at AACR-JCA show that a single dose of iPSC-derived anti-ROR1 CAR-NK cells, administered in a tumor xenograft model, significantly reduced tumor burden compared to iPSC-derived NK cells without an anti-ROR1 CAR.

The Company also announced armoring strategies for its CAR-NK cell platform, including a Casitas B-Lineage lymphoma proto-oncogene-B knockout ("CBLB"), a beta 2 microglobulin ("B2M") knockout with a beta-2-microglobulin–human-leukocyte-antigen-E–peptide transgene ("B2M–HLA-E") insertion, and a membrane-bound IL-15/IL-15RA fusion protein insertion. Preclinical data will be presented at AACR-JCA on these armoring strategies in iPSC-derived CAR-NK cells.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release Issued by Caribou Biosciences, Inc. on December 12, 2022
99.2	Press Release Issued by Caribou Biosciences, Inc. on December 12, 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, 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: December 12, 2022

By: /s/ Rachel E. Haurwitz

Rachel E. Haurwitz
President and Chief Executive Officer

Caribou Biosciences Reports CB-010 ANTLER Phase 1 Trial Progress

-- Long-term durability observed for CB-010 allogeneic cell therapy at dose level 1 in ANTLER trial for r/r B-NHL --

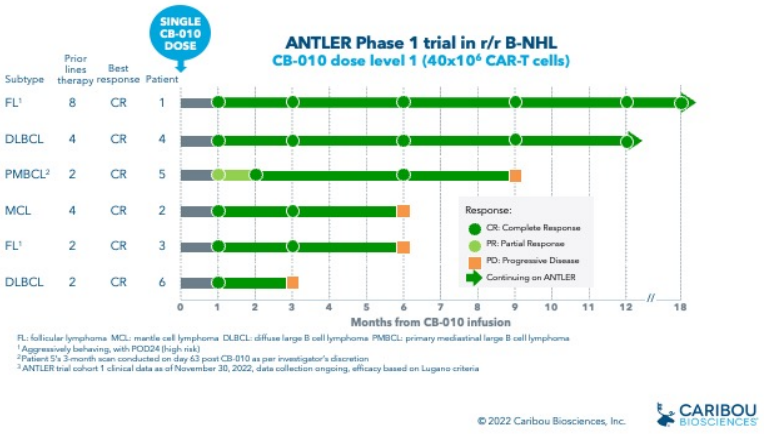
-- ANTLER trial enrolling patients at dose level 3 --

BERKELEY, CA, December 12, 2022 – Caribou Biosciences, Inc. (Nasdaq: CRBU), a leading clinical-stage CRISPR genome-editing biopharmaceutical company, today reported new 12-month clinical data from cohort 1 in the ongoing ANTLER Phase 1 trial, which show long-term durability following a single infusion of CB-010 at the initial dose level 1 (40x10^6 CAR-T cells). Cohort 1 results show:

- 6 of 6 patients achieved a complete response (CR) as best response
- 3 of 6 patients maintained a durable CR at 6 months
- 2 of 6 patients maintain a long-term CR at the 12-month scan and remain on the trial
- 18 months is the longest CR maintained to date in ANTLER, achieved by the first patient dosed with CB-010
- CB-010 was generally well tolerated with adverse events consistent with autologous or allogeneic anti-CD19 CAR-T cell therapies

Based on promising initial data, the U.S. Food and Drug Administration (FDA) granted CB-010 both Regenerative Medicine Advanced Therapy (RMAT) and Fast Track designations. In addition, Caribou has observed an encouraging safety profile for CB-010 at dose level 2 (80x10^6 CAR-T cells) with no dose-limiting toxicities (DLTs) in the 3 patients treated and is currently enrolling patients at dose level 3 (120x10^6 CAR-T cells). Caribou expects to provide an ANTLER trial update in 2023.

Image: ANTLER Phase 1 trial of CB-010 at dose level 1



"With next-generation CRISPR genome-editing technology, the promise of allogeneic cell therapies has advanced significantly, and the early results seen in the ANTLER trial to date are a reflection of

that potential," said Rachel Haurwitz, Ph.D., Caribou's president and chief executive officer. "The long-term durability at dose level 1 is comparable to autologous cell therapies and we believe CB-010 has the potential to set a new therapeutic bar for what allogeneic anti-CD19 CAR-T cell therapies can achieve. We are further encouraged by receiving RMAT and Fast Track designations for CB-010 from the FDA, which is a testament to both the encouraging initial ANTLER data and the need for novel therapies for patients with relapsed or refractory B-NHL."

CB-010 is the first allogeneic anti-CD19 CAR-T cell therapy in the clinic with a PD-1 knockout, a genome-editing strategy designed to improve the persistence of antitumor activity by limiting premature CAR-T cell exhaustion.

"Patients with relapsed or refractory B cell non-Hodgkin lymphoma are in need of treatments that are immediately available and do not require burdensome or ineffective bridging therapies," said Susan O'Brien, M.D., professor of medicine, Chao Family Comprehensive Cancer Center at University of California, Irvine, CA, and presenting investigator on the ANTLER clinical trial. "The early results from the ANTLER trial are promising and I look forward to enrolling additional patients in this trial to learn more about the potential of CB-010 as an off-the-shelf treatment option for patients with aggressive B-NHL who have a high unmet medical need."

ANTLER is a Phase 1, open-label, multicenter clinical trial (NCT04637763) evaluating the safety and efficacy of the company's lead allogeneic cell therapy, CB-010, in patients with r/r B-NHL. The trial includes Part A, a 3+3 dose escalation phase designed to evaluate safety of CB-010 at multiple dose levels and establish the recommended Phase 2 dose, and Part B, a dose expansion phase with the primary objective to determine tumor response after a single dose of CB-010. As permitted by the protocol, backfilling patients has begun at doses deemed well tolerated to increase the understanding of CB-010's safety profile and antitumor activity and provide additional data for establishing a recommended Phase 2 dose.

ANTLER Trial-in-Progress Poster at ASH 2022
Today at the 64th Annual ASH meeting, a trial-in-progress poster is being presented to provide details of the design and objectives of the ANTLER Phase 1 trial for CB-010 in r/r B-NHL. Details of the poster presentation are as follows:

Title: A First-in-Human Phase 1, Multicenter, Open-Label Study of CB-010, a Next-Generation CRISPR-Edited Allogeneic Anti-CD19 CAR-T Cell Therapy with a PD-1 Knockout, in Patients with Relapsed/Refractory B Cell Non-Hodgkin Lymphoma (ANTLER Study)
Presenter: Susan O'Brien, M.D., professor of medicine, Chao Family Comprehensive Cancer Center at University of California, Irvine, CA
Session Name: 626. Aggressive Lymphomas: Prospective Therapeutic Trials: Poster III
Session Date: Monday, December 12, 2022
Presentation Time: 6:00 pm - 8:00 pm CST
Location: Ernest N. Morial Convention Center, Hall D
Abstract number: 4257

The poster presentation will be available for registered attendees on the ASH website and on Caribou's website under Scientific Publications (www.cariboubio.com/technology/#pubs) on Monday, December 12, 2022 at 9:00 am CST.

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. CB-010 has been granted Regenerative Medicine Advanced Therapy (RMAT), Fast Track, and Orphan Drug designations. Additional information on the ANTLER trial can be found at www.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.

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 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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Caribou Biosciences Selects ROR1 as the Target for CB-020, an iPSC-derived Allogeneic CAR-NK Cell Therapy

-- Data supporting selection of ROR1 for CB-020 and armoring strategies for Caribou's CAR-NK cell platform to be presented at AACR-JCA Conference today --

-- Caribou is using its chRDNA next-gen CRISPR technology to engineer and advance both CAR-NK and CAR-T cell therapy programs --

BERKELEY, CA, Dec. 12, 2022 (GLOBE NEWSWIRE) -- Caribou Biosciences, Inc. (Nasdaq: CRBU), a leading clinical-stage CRISPR genome-editing biopharmaceutical company, today announced target selection for CB-020, an induced pluripotent stem cell (iPSC)-derived allogeneic anti-ROR 1 (receptor tyrosine kinase like orphan receptor 1) CAR-NK cell therapy. Preclinical data on the selection of the CB-020 CAR construct and armoring strategies for Caribou's CAR-NK cell platform will be presented today at the 12th American Association for Cancer Research and Japanese Cancer Association (AACR-JCA) Joint Conference.

"ROR1 has been selected as the target for CB-020, Caribou's first off-the-shelf iPSC-derived CAR-NK cell therapy, and the preclinical data presented at AACR-JCA shows that ROR1 may be a promising target for several solid tumor indications," said Steve Kanner, Ph.D., Caribou's chief scientific officer. "We are leveraging our chRDNA genome-editing technology across our allogeneic CAR-T and CAR-NK cell programs to address disease-specific challenges. For solid tumors, we are exploring several armoring strategies for our allogeneic CAR-NK cell therapy platform, including a *CBLB* knockout, a B2M knockout with a B2M–HLA-E fusion protein insertion, and a membrane-bound IL-15 insertion/IL-15RA fusion protein to help overcome the complex tumor microenvironment that has challenged previous cell therapies."

iPSC-derived NK cells innately exhibit potent antitumor activity against solid tumors. CB-020 is being engineered using Caribou's Cas12a chRDNA genome-editing technology to express a ROR1-specific CAR, which can enhance the innate NK cell antitumor activity by increasing specificity and function. ROR1 is a cell signaling receptor that is overexpressed on the surface of several solid tumor types and has been shown to drive tumor cell growth, survival, and metastasis. Preclinical data to be presented at AACR-JCA show that a single dose of iPSC-derived anti-ROR1 CAR-NK cells, administered in a tumor xenograft model, significantly reduced tumor burden compared to iPSC-derived NK cells without an anti-ROR1 CAR.

Multiple armoring strategies are being developed for Caribou's CAR-NK cell platform to enhance tumor targeting, allogeneic CAR-NK cell survival, and persistence of antitumor activity. Results from the company's preclinical studies suggest iPSC-derived NK cells with a knockout of *CBLB* (Casitas B-Lineage lymphoma proto-oncogene-B), a ubiquitin ligase that negatively regulates NK cell function, results in reduced tumor burden and increased overall survival in an *in vivo* solid tumor xenograft model, compared to unedited iPSC-derived NK cells. Additionally, results show that iPSC-derived NK cells were not killed by donor-derived T cells and NK cells when harboring a knockout of B2M and an insertion of a BM2–HLA-E fusion protein. This strategy may induce more potent NK activity and help prevent CAR-NK cells from killing each other, which is a common problem with NK cell therapies. In addition, results from iPSC-derived NK cells with an insertion of membrane-bound IL-15/IL-15RA

fusion protein, which is shown to enhance NK cell antitumor activity, demonstrated high cytotoxicity against tumor cells compared to unedited iPSC-derived NK cells. Together, these preclinical data demonstrate Caribou's genome-editing technology has the potential to be used to implement a variety of armoring strategies in iPSC-derived CAR-NK cells to address many of the challenges associated with treating solid tumors.

Details of the poster presentation at the AACR-JCA Joint Conference are as follows:

Title: CB-020, an iPSC-derived allogeneic CAR-NK cell therapy
Speaker: Rudy Gonzalez, Ph.D., executive director of stem cell therapeutics, Caribou Biosciences, Berkeley, CA
Date and time: Monday, December 12 at 5:30 pm HST
Abstract number: B06
Location: Hyatt Regency Maui, Monarchy Ballroom

The full poster is available on Caribou's Scientific Publications (www.cariboubio.com/technology/#pubs) webpage.

About Caribou's Novel Next-Generation CRISPR Platform
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For more information about Caribou, visit www.cariboubio.com and follow the company @CaribouBio.

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