Caribou Biosciences Reports Positive Clinical Data from Dose Escalation of CB-010 ANTLER Phase 1 Trial in r/r B-NHL

July 13, 2023

-- CB-010 allogeneic CAR-T cell therapy data rival response rates and safety profile of approved autologous CAR-T cell therapies --

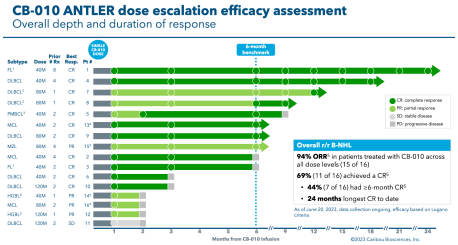
-- 94% overall response rate (ORR), 69% complete response (CR) rate, and 44% CR rate at ≥6 months following a single dose of CB-010; 24 months is the longest CR maintained to date --

-- LBCL patient subgroup had a 50% CR rate at ≥6 months; 18 months is the longest LBCL subgroup CR maintained to date --

-- Actively enrolling second-line LBCL patients in ANTLER dose expansion --

-- Conference call and webcast scheduled for today at 4:30 pm ET --

ANTLER Phase 1 trial of CB-010



94% overall response rate (ORR). 69% of patients achieved a complete response (CR) as best response following a single dose of CB-010 allogeneic CAR-T cell therapy. 44% of patients had a CR at ≥6 months post-CB-010 administration.

BERKELEY, Calif., July 13, 2023 (GLOBE NEWSWIRE) -- Caribou Biosciences, Inc. (Nasdaq: CRBU), a leading clinical-stage CRISPR genome-editing biopharmaceutical company, today reported long-term follow-up data from the dose escalation portion of the ongoing ANTLER Phase 1 trial. The data set includes all 16 patients treated in dose escalation with CB-010, an allogeneic anti-CD19 CAR-T cell therapy being evaluated in patients with relapsed or refractory B cell non-Hodgkin lymphoma (r/r B-NHL).

In ANTLER dose escalation, three dose levels of CB-010 were evaluated ($40x10^6$, $80x10^6$, and $120x10^6$ CAR-T cells) in patients with multiple subtypes of aggressive r/r B-NHL. As of the data cutoff date, results demonstrated:

- CB-010 was generally well tolerated with adverse events consistent with autologous or allogeneic anti-CD19 CAR-T cell therapies; as previously reported, no dose-limiting toxicities (DLTs) were observed at dose levels 2 or 3 following a single DLT at dose level 1.
- 94% overall response rate (ORR; 15 of 16 patients) was observed following a single dose of CB-010.
- 69% of patients (11 of 16) achieved a complete response (CR).
- 44% of patients (7 of 16) had a CR at ≥6 months; 24 months is the longest CR maintained to date.
- For the subset of patients with large B cell lymphoma (LBCL) (N=10):
    - A 90% ORR (9 of 10) was observed.
    - 70% (7 of 10) achieved a CR.
    - 50% (5 of 10) had a CR at ≥6 months; 18 months is the longest CR maintained to date.

Each of the 16 patients had aggressive r/r B-NHL and had received two or more prior lines of chemoimmunotherapy or were primary refractory patients.

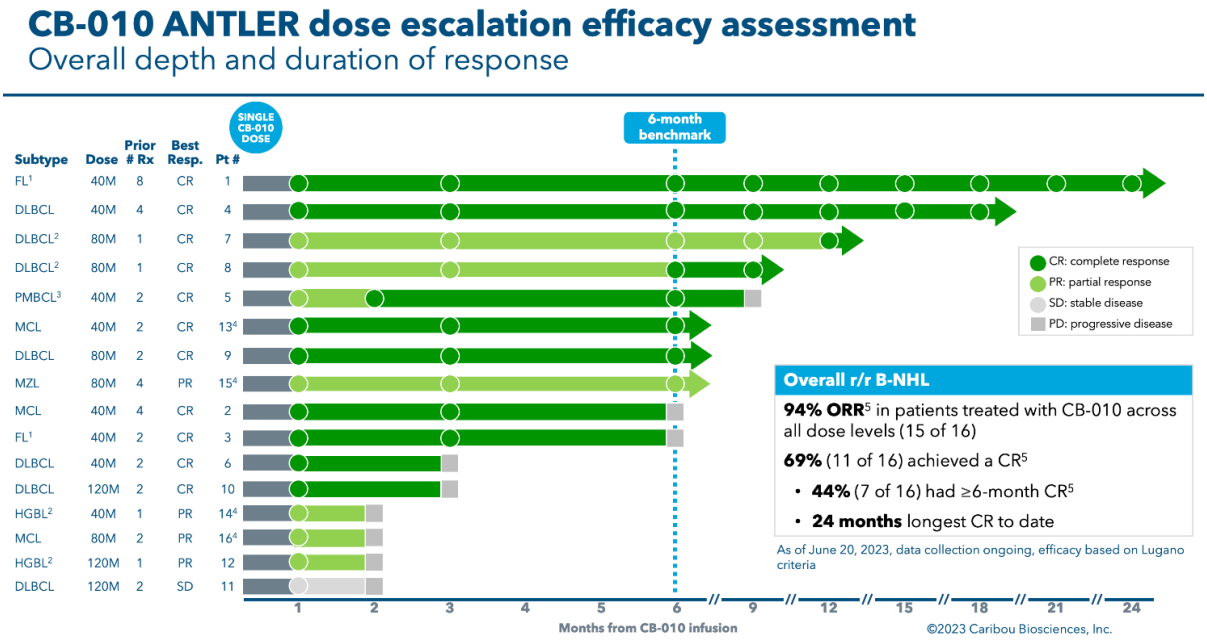
Based on these positive data, Caribou is enrolling second-line patients with LBCL in the ongoing dose expansion portion of the ANTLER clinical trial. In expansion, the mid dose and the high dose from escalation ($80x10^6$ and $120x10^6$ CAR-T cells) are being evaluated in approximately 30 second-line patients (approximately 15 patients per dose level) to determine the recommended Phase 2 dose (RP2D). Once the RP2D is determined, Caribou may enroll additional patients in ANTLER. Caribou plans to report initial dose expansion data from the ongoing ANTLER trial in H1 2024.

“I am excited to see the initial and durable response rates for patients following a single dose of CB-010 in the ANTLER Phase 1 clinical trial. The data are promising and may offer a clinical advantage as an off-the-shelf option compared with approved autologous CAR-T cell therapies,” said Loretta J. Nastoupil, MD, deputy chair and associate professor in the department of lymphoma/myeloma at the University of Texas MD Anderson Cancer Center in Houston and investigator on the ANTLER trial. “In addition to encouraging antitumor activity, CB-010 could provide greater access to patients, including those who are not eligible for or cannot wait for an autologous CAR-T cell therapy. As the field of cell therapy moves to earlier lines of treatment, I look forward to being part of CB-010’s development as an off-the-shelf treatment option for patients with LBCL in the second-line clinical setting.”

To Caribou’s knowledge, CB-010 is the first allogeneic anti-CD19 CAR-T cell therapy in the clinic to be evaluated in second-line LBCL patients and CB-010 is also the first allogeneic anti-CD19 CAR-T cell therapy in the clinic with a PD-1 knockout, a genome-editing strategy designed to enhance antitumor activity by limiting premature CAR-T cell exhaustion.

“CB-010 dose escalation data rival the responses from autologous cell therapies and demonstrate the potential utility of an off-the-shelf CAR-T cell therapy that could, if approved, provide greater access to patients in need,” said Rachel Haurwitz, PhD, Caribou’s president and chief executive officer. “We are actively enrolling patients in dose expansion to gain a better understanding of the safety and antitumor activity of CB-010 in a greater number of patients. We look forward to determining a recommended Phase 2 dose of CB-010, engaging with the FDA on next steps, and reporting ANTLER dose expansion data in the first half of 2024.”

ANTLER Phase 1 trial of CB-010
A photo accompanying this announcement is available at
https://www.globenewswire.com/NewsRoom/AttachmentNg/659312ff-d77b-4b83-9813-b2368d5a22c2



DLBCL: diffuse large B cell lymphoma; FL: follicular lymphoma; HGBL: high-grade B cell lymphoma; MCL: mantle cell lymphoma; MZL: marginal zone lymphoma; PMBCL: primary mediastinal large B cell lymphoma.
[1] Aggressively behaving, with POD24 (high risk). [2] Primary refractory disease. [3] Patient 5's 3-month scan conducted on day 63 post CB-010 as per investigator's discretion. [4] Patients 13-16 are backfill patients at 40M and 80M. [5] Certain patients converted from a CR or PR to PD at various assessment time points as indicated in the chart above.

ANTLER Phase 1 trial of CB-010 - response data
Dose escalation (N=16)

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

[1] Subgroup includes patient #4, 5, 6, 7, 8, 9, 10, 11, 12, and 14. [2] Four primary refractory patients were enrolled in dose escalation. Subgroup includes patient #7, 8, 12, and 14. [3] Patient #7 had a CR at 12 months, which converted from PR at the prior efficacy assessment. These efficacy data are as of the June 20, 2023 efficacy data cutoff date.

CB-010 was generally well tolerated with adverse events consistent with autologous or allogeneic anti-CD19 CAR-T cell therapies. No grade 3+ cytokine release syndrome (CRS) and no graft-vs-host disease (GvHD) cases were observed. The most common adverse events included thrombocytopenia (69% Grade 3+), neutropenia (56% Grade 3+), and anemia (50% Grade 3+).

ANTLER Phase 1 trial of CB-010 – safety data

Treatment-emergent adverse events (TEAE) of special interest		
	All patients (N=16)	
Adverse event N, (%)	**All Grades**	**Grade 3+**
CRS	7 (44%)	-
ICANS[1]	4 (25%)	2 (13%)
Infections[2]	7 (44%)	1 (6%)[3]

CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity. [1] Four total events, 2 Grade 1; 2 Grade 3+ at dose level 1, both with complete resolution of symptoms with supportive care.
[2] Infection events reported were on or after CB-010 infusion, with highest grade reported per patient. [3] Grade 3 cellulitis (right antecubital) occurred

after CB-010 infusion and was unrelated to CB-010 per the investigator. These safety data are as of May 4, 2023 safety data cutoff date.

Webcast conference call today at 4:30 pm ET
Caribou will host a live conference call and webcast today at 4:30 pm ET to discuss the ANTLER dose escalation data for CB-010. The webcast presenters will include:

- Loretta J. Nastoupil, MD, deputy chair and associate professor in the department of lymphoma/myeloma at the University of Texas MD Anderson Cancer Center in Houston
- Rachel Haurwitz, PhD, president and chief executive officer of Caribou
- Syed Rizvi, MD, chief medical officer of Caribou
- Steven Kanner, PhD, chief scientific officer of Caribou

If you would like the option to ask a question on the live conference call, please use this link to register to receive a personal PIN to access the conference call and to ask a question.

The listen-only webcast with an accompanying presentation will be accessible under 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.

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, Caribou is enrolling second-line patients with large B cell lymphoma (LBCL) comprising four different subtypes of aggressive r/r B-NHL (DLBCL NOS, PMBCL, HGBL, and tFL). CB-010 is an allogeneic anti-CD19 CAR-T cell therapy engineered using Cas9 CRISPR hybrid RNA-DNA (chRDNA) technology. 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 antitumor activity by limiting premature CAR-T cell exhaustion. To Caribou's knowledge, CB-010 is also the first anti-CD19 allogeneic CAR-T cell therapy to be evaluated in the second-line LBCL setting and 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.

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 Cas12a chRDNA technology, enables superior precision to develop cell therapies that are armored to potentially improve antitumor activity. Caribou is advancing a pipeline of off-the-shelf cell therapies from its CAR-T and CAR-NK platforms as readily available treatments for 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 updates from, and strategy, safety, efficacy, and potential advantages of, its ANTLER Phase 1 clinical trial for CB-010, and the potential of Caribou's product candidates to generate durable complete responses and safety results similar to approved autologous CAR-T cell therapies. Management believes that these forward-looking statements are reasonable as and when made. However, such forward-looking statements are subject to risks and uncertainties, which may cause actual results to differ materially from any future results expressed or implied by the forward-looking statements. These 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; the risk that preclinical study results observed will not be borne out in human patients; as well as other risk factors described from time to time under the heading "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Caribou's filings with the Securities and Exchange Commission, including its Annual Report on Form 10-K for the year ended December 31, 2022 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.

In addition, caution should be exercised when interpreting results from separate trials involving separate product candidates. Clinical trials of other companies' CAR-T cell therapies referenced in this press release were run independently of Caribou and Caribou has only reviewed publicly available reports of those trials. 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 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 Caribou's existing or future results. For further information and to understand these material differences, you should read the reports for the other companies' clinical trials.

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