Caribou Biosciences Initiates Dose Expansion Portion of CB-010 ANTLER Phase 1 Trial in Second-line LBCL Patients

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-- CB-010 is the first allogeneic CAR-T cell therapy, to Caribou's knowledge, to be evaluated clinically in second-line LBCL patients --

-- Next ANTLER update planned for H2 2023 --

BERKELEY, Calif., March 29, 2023 (GLOBE NEWSWIRE) -- Caribou Biosciences, Inc. (Nasdaq: CRBU), a leading clinical-stage CRISPR genome-editing biopharmaceutical company, today announced initiation of the dose expansion portion of the CB-010 ANTLER Phase 1 trial in second-line patients with large B cell lymphoma (LBCL) following the recent completion of dose escalation. CB-010 is an allogeneic cell therapy being evaluated in patients with relapsed or refractory B cell non-Hodgkin lymphoma (r/r B-NHL).

"The ANTLER trial continues to push boundaries in evaluating the potential of allogeneic CAR-T therapies as we proceed with the dose expansion portion of ANTLER, which will now dose second-line patients with LBCL," said Rachel Haurwitz, PhD, Caribou's president and chief executive officer. "To our knowledge, CB-010 is the first allogeneic CAR-T cell therapy to be evaluated clinically in the second-line setting, where we aim to provide access to greater numbers of patients and potentially impact outcomes earlier in the course of their disease. We remain focused on our goal to develop an allogeneic cell therapy that meaningfully rivals autologous cell therapies and extends the potential reach of cell therapy treatment options for patients."

In ANTLER dose escalation, CB-010 was generally well tolerated at all 3 dose levels evaluated, demonstrating an encouraging safety profile. The observed adverse events were consistent with autologous or allogeneic anti-CD19 CAR-T cell therapies. Most recently, no dose-limiting toxicities (DLTs) were observed in the 3 patients treated with CB-010 at dose level 3 ($120x10^6$ CAR-T cells). As previously reported, at dose level 1 ($40x10^6$ CAR-T cells), 6 of the 6 patients in cohort 1 achieved a complete response as best response, 3 of the 6 patients maintained their complete response at 6 months, and 2 of the 6 patients maintained their complete response at 12 months. In dose escalation, ANTLER enrolled patients following a minimum of two prior lines of therapy as well as primary refractory patients.

"We have heard time and again from the lymphoma community about the challenges of autologous CAR-Ts, such as apheresis, bridging therapy, long wait times for manufacturing, or manufacturing failures. CB-010 addresses these challenges as the therapy is manufactured from healthy donor cells and is available off-the-shelf for eligible clinical trial patients," said Syed Rizvi, MD, Caribou's chief medical officer. "Evaluating CB-010 in the second-line setting places Caribou at the forefront of the off-the-shelf cell therapy field by potentially addressing the unmet needs of patients with a readily available therapeutic option at an earlier stage of their disease."

In the ANTLER dose expansion portion, Caribou plans to evaluate 2 different dose levels of CB-010, each evaluated as a single-dose regimen ($80x10^6$ CAR-T cells and $120x10^6$ CAR-T cells), in approximately 30 total 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, including patients who have failed prior CD19-targeted therapies. Caribou expects the collective data from ANTLER will inform a potential pivotal trial plan. Caribou expects to provide an ANTLER trial safety and efficacy data update in H2 2023, including data from at least 15 patients from dose escalation with a minimum of 6 months of follow up.

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 4 different subtypes of aggressive r/r B-NHL (DLBCL NOS, PMBCL, HGBL, and transformed FL). CB-010 is an allogeneic anti-CD19 CAR-T cell therapy engineered using Cas9 CRISPR hybrid RNA-DNA (chRDNA) technology. CB-010 is the first allogeneic anti-CD19 CAR-T cell therapy in the clinic, to Caribou's knowledge, with a PD-1 knockout (KO), a genome-editing strategy designed to improve antitumor activity by limiting premature CAR-T cell exhaustion. CB-010 is also the first allogeneic CAR-T cell therapy, to Caribou's knowledge, to be evaluated clinically in the second-line setting and has been granted Regenerative Medicine Advanced Therapy (RMAT), Fast Track, and Orphan Drug designations. 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 proprietary 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.

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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 results and updates from its ANTLER Phase 1 clinical trial for CB-010, its plans for dose expansion, its ability to enroll second-line patients, its determination of RP2D, and its enrollment of sufficient patients to inform a potential pivotal trial plan. 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; the risk that preclinical study results we observed will not be borne out in human patients; 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, 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.

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