Caribou Biosciences Announces FDA Clearance of IND Application for CB-011, an Allogeneic Anti-BCMA CAR-T Cell Therapy for the Treatment of Relapsed or Refractory Multiple Myeloma

November 21, 2022

-- CaMMouflage Phase 1 clinical trial to initiate patient enrollment at dose level 1 in early 2023 --

-- CB-011 is engineered with a differentiated immune cloaking strategy, designed to enhance persistence --

-- CB-011 is Caribou's second off-the-shelf CAR-T cell therapy to enter the clinic --

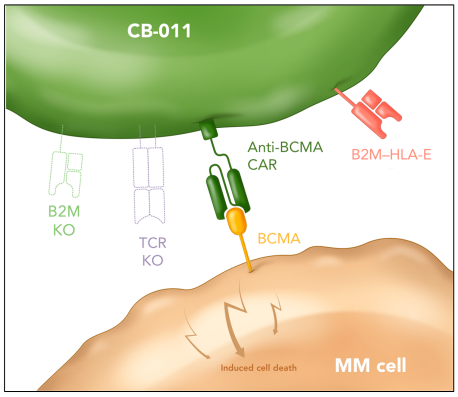
BERKELEY, Calif., Nov. 21, 2022 (GLOBE NEWSWIRE) -- Caribou Biosciences, Inc. (Nasdaq: CRBU), a leading clinical-stage CRISPR genome-editing biopharmaceutical company, today announced that it has received clearance of its Investigational New Drug (IND) application from the U.S. Food and Drug Administration (FDA) for CB-011, a genome-edited allogeneic anti-BCMA CAR-T cell therapy with immune cloaking. The CaMMouflage Phase 1 clinical trial, a multicenter, open-label study to evaluate the safety and efficacy of a single dose of CB-011 in adult patients with relapsed or refractory multiple myeloma (r/r MM), is expected to initiate patient enrollment for treatment at dose level 1 ($50x10^6$ CAR-T cells) in early 2023.

"Clearance of our second IND application represents another key milestone for our pipeline of promising allogeneic cell therapies designed to have enhanced persistence of antitumor activity," said Rachel Haurwitz, Ph.D., Caribou's president and chief executive officer. "CB-011 is designed with an immune cloaking strategy to reduce rejection of the cell therapy by a patient's T and NK cells and we use Caribou's highly precise and specific Cas12a chRDNA genome-editing technology to manufacture this product candidate. We are excited to develop CB-011 as an off-the-shelf cell therapy that may reach a broader number of patients with multiple myeloma than are currently being served, and we look forward to initiating patient enrollment in the CaMMouflage trial in early 2023."

CB-011 is the second allogeneic cell therapy advancing into clinical development from Caribou's CAR-T cell platform targeting hematologic malignancies. Caribou's first allogeneic cell therapy, CB-010, an allogeneic anti-CD19 CAR-T cell therapy with a PD-1 knockout, is being evaluated in the ongoing ANTLER Phase 1 clinical trial in patients with relapsed or refractory B cell non-Hodgkin lymphoma (r/r B-NHL). Encouraging safety and antitumor activity for CB-010 at dose level 1 have been reported from the ANTLER trial.

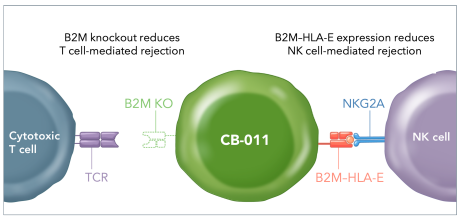
"CAR-T cell therapies have shown great promise for treating patients with relapsed or refractory multiple myeloma," said Sundar Jagannath, M.D., director of the Multiple Myeloma Center of Excellence at Tisch Cancer Institute, Mount Sinai Hospital, New York. "Allogeneic, or 'off-the-shelf,' CAR-T cell therapies would provide a great option for patients with multiple myeloma, helping to overcome the need for bridging therapies as well as variable quality and manufacturing timelines of autologous CAR-T cells."

CB-011



CB-011 is a genome-edited allogeneic anti-BCMA CAR-T cell therapy with immune cloaking.

CB-011 Immune Cloaking



CB-011 is engineered to improve persistence of antitumor response through an immune cloaking genome-editing approach that removes the B2M protein and inserts a B2M–HLA-E fusion protein.

CB-011 is the first allogeneic anti-BCMA CAR-T cell therapy, to Caribou's knowledge, that is engineered to improve persistence of antitumor response through an immune cloaking genome-editing approach that removes the B2M protein and inserts a B2M–HLA-E fusion protein. CB-011 has four edits implemented via Caribou's Cas12a CRISPR hybrid RNA-DNA (chRDNA) technology:

- Edits 1 and 2 – A humanized anti-BCMA CAR is site-specifically inserted into the TRAC gene to target cancer cells, thereby knocking out expression of the T cell receptor to reduce the risk of graft versus host disease (GvHD).
- Edits 3 and 4 – A B2M–HLA-E peptide fusion gene is site-specifically inserted into the B2M gene of the CAR-T cells to prevent recognition and rejection by patient T cells and blunt rejection by NK cells. These edits knock out endogenous B2M expression, eliminating endogenous HLA class I presentation and reducing T cell-mediated rejection, while enabling expression of B2M–HLA-E needed to inhibit NK cell-mediated rejection.

About the CaMMouflage Trial

The CaMMouflage Phase 1 trial is an open-label, multicenter clinical trial designed to evaluate CB-011 in adults with relapsed or refractory multiple myeloma (r/r MM). Part A, a 3+3 dose escalation design, will evaluate the safety and tolerability of CB-011 at multiple dose levels and will be utilized to determine the maximum tolerated dose and/or the recommended Phase 2 dose. Part B is the dose expansion portion with the primary objective of determining tumor response after a single dose of CB-011. CaMMouflage will include patients who have had 3 or more prior lines of therapy and will exclude patients who have received a BCMA-targeted therapy within the last 3 months and/or any prior CAR-T cell therapy.

Caribou plans to initiate patient enrollment in the CaMMouflage trial to treat patients with a single administration of CB-011 at dose level 1 ($50x10^6$ CAR-T cells) in early 2023.

About Multiple Myeloma
Multiple myeloma (MM) is the second most common hematologic malignancy in the United States. According to the National Cancer Institute, an estimated 160,000 people in 2019 were living with MM and an estimated 34,000 individuals are diagnosed with MM each year in the United States. Approximately 50% of patients with MM relapse and have their cancer return after first line treatment or are refractory and do not respond to current treatments.

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 multiple edits at high efficiency, 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.

For more information about Caribou, visit www.cariboubio.com and follow the company @CaribouBio.

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 the timing of the initiation of its CaMMouflage Phase 1 trial for CB-011, the expected timing of patient enrollment for the trial, as well as the results and duration of the trial and expectations and timing regarding the release of clinical data from Caribou's ongoing ANTLER Phase 1 clinical trial for its CB-010 product candidate. 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 development of cell therapy products; uncertainties related to the initiation, cost, timing, progress, and results of 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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Photos accompanying this announcement are available at

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