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

December 12, 2022

-- 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, Calif., 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 webpage.

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.

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 its timing and expectations relating to the target selection for CB-020 and armoring strategies for the company's CAR-NK cell platform. 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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