Caribou Biosciences Presents Positive Preclinical Data for Allogeneic Anti-BCMA CAR-T Cell Therapy Candidate CB-011 at the American Association for Cancer Research (AACR) Annual Meeting

April 8, 2022

-- CB-011 is an allogeneic anti-BCMA CAR-T cell therapy immune cloaked to blunt both T- and NK-mediated immune cell rejection, enabling more durable antitumor activity --

-- Data support an expected Investigational New Drug (IND) application submission in 2022 for CB-011, Caribou's second allogeneic cell therapy product candidate --

BERKELEY, Calif., April 08, 2022 (GLOBE NEWSWIRE) -- Caribou Biosciences, Inc. (Nasdaq: CRBU), a leading clinical-stage CRISPR genome-editing biopharmaceutical company, today announced the presentation of positive preclinical data for its allogeneic, immune-cloaked, anti-BCMA CAR-T cell therapy candidate, CB-011, being developed for the treatment of relapsed or refractory multiple myeloma (r/r MM). The data are being presented at the American Association for Cancer Research (AACR) Annual Meeting, April 8-13, 2022, in New Orleans.

The data demonstrate that CB-011 CAR-T cells are cytotoxic against BCMA-expressing tumor cells and are resistant to killing by both allogeneic T cells and natural killer (NK) cells. In a tumor xenograft model of MM, CAR-T cells expressing a CAR containing a proprietary humanized anti-BCMA antibody fragment (scFv) that is used in CB-011 markedly prolonged antitumor activity compared to CAR-T cells expressing a benchmark anti-BCMA CAR. Caribou is conducting Investigational New Drug (IND) application-enabling safety studies to support a planned IND application submission in 2022 for CB-011 in r/r MM.

"The data that will be presented at AACR demonstrate that T cells expressing a CAR deploying Caribou's proprietary anti-BCMA scFv outperform cells expressing a known benchmark CAR," said Steve Kanner, Ph.D., Caribou's chief scientific officer. "The immune-cloaking armoring data confirm the potential value and mechanism of our strategy using multiple genome edits involving HLA class I disruption as an approach to increase the potential therapeutic effect of CB-011. This strategy is enabled by our proprietary Cas12a chRDNA genome-editing technology that reproducibly achieves high specificity genome editing at multiple loci."

Manufacturing CB-011 requires four genome editing steps. Caribou's Cas12a chRDNA technology is used to insert a gene encoding a proprietary, humanized anti-BCMA CAR into the *TRAC* gene of the T cell, which also knocks out expression of the T cell receptor, thereby reducing the risk of graft versus host disease (GvHD). The immune cloaking strategy entails site-specific insertion of a gene encoding a B2M-HLA-E-peptide fusion into the *B2M* gene of the T cell. This edit knocks out B2M expression and eliminates endogenous HLA class I presentation on the surface of the CAR-T cells while enabling expression of the fusion transgene of HLA-E, a minor HLA class I antigen, designed to blunt both T- and NK-cell-mediated rejection of the CAR-T cell therapy by the patient's immune system.

The data demonstrate that, when co-cultured with BCMA-expressing cell lines, CB-011 CAR-T cells proliferate in response to antigen, secrete cytokines consistent with robust T cell activation, and kill BCMA-positive tumor cells. When CB-011 cells are co-cultured with either mismatched CD8+ T cells or NK cells, they are protected from killing, potentially extending their persistence when infused into a patient. In a tumor xenograft model of MM, CB-011 treatment prolonged survival compared to a control. Data generated in this model demonstrated that the anti-BCMA CAR used in CB-011 resulted in superior survival (40% at 80 days) compared to a known benchmark anti-BCMA CAR (0% at 30 days).

"We believe that an off-the shelf approach has the potential to provide an important therapeutic option for people with multiple myeloma, many of whom are not well served by current therapies," said Rachel Haurwitz, Ph.D., Caribou's president and chief executive officer. "We look forward to submitting an IND application in 2022 for CB-011, our second cell therapy candidate. It is an important element of our allogeneic CAR-T cell therapy platform targeting a range of hematologic malignancies."

Details of the poster presentation are as follows:

Title: A BCMA-specific allogeneic CAR-T cell therapy (CB-011) genome engineered to express an HLA-E fusion transgene to prevent immune cell rejection
Presenter: Émilie Degagné, Ph.D.
Date and Time: Sunday, April 10, 2022, 1:30 – 5:00 pm CDT
Location: New Orleans Convention Center

Presentations and posters will be available for registered attendees for on-demand viewing on the AACR website on April 8, 2022 after 1:00 pm EDT. The poster is available on the Presentations page of the Investors section of Caribou's website.

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 Type II 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 occasionally edit 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 chRDNAs (pronounced "chardonnays"), RNA-DNA hybrid guides 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 genome 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.
"Caribou Biosciences" and the Caribou logo are registered trademarks of Caribou Biosciences, Inc.

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 but not limited to, its timing expectations relating to the submission of an IND application for CB-011. 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 the risks inherent in drug development such as those associated with being in preclinical development, and with the initiation, cost, timing, progress, and results of current and future research and development programs, preclinical studies, and clinical trials, 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. 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.

Caribou Biosciences, Inc.
Contacts:
Amy Figueroa, CFA
Investor Relations and Corporate Communications
afigueroa@cariboubio.com

Investors:
Elizabeth Wolffe, Ph.D., and Sylvia Wheeler
Wheelhouse LSA
lwolffe@wheelhouselsa.com
swheeler@wheelhouselsa.com

Media:
Greg Kelley
Ogilvy
gregory.kelley@ogilvy.com
617-461-4023