



Caribou Biosciences Announces Publication of Data Demonstrating High Specificity Genome Editing with its Proprietary chRDNA Technology

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Data published in Molecular Cell provide a mechanistic framework to explain the enhanced specificity and key differentiation of Caribou's proprietary chRDNA technology for therapeutic applications

BERKELEY, Calif., Sept. 02, 2021 (GLOBE NEWSWIRE) -- [Caribou Biosciences, Inc.](#) (Nasdaq:CRBU), a leading clinical-stage CRISPR genome-editing biopharmaceutical company, announced today the publication of data demonstrating that its proprietary CRISPR hybrid RNA-DNA (chRDNA) guide technology provides significantly improved specificity compared to all-RNA guides, thereby enabling high levels of intended genomic edits in cells while eliminating or minimizing inadvertent off-target events. Higher specificity is a key advantage in the development of therapeutics and of critical importance in therapies that contain multiple genome edits.

The data, which provide a mechanistic framework to elucidate the specificity of chRDNA guides, were published in an article entitled, "[Conformational control of Cas9 by CRISPR hybrid RNA-DNA guides mitigates off-target activity in T cells](#)," in the journal *Molecular Cell*.

"Caribou is currently developing unique allogeneic CAR-T cell therapies with multiple genome edits designed to enhance their persistence in patients," said Steve Kanner, Ph.D., Caribou's chief scientific officer. "By altering the position and number of DNA residues in our chRDNA guides, we readily achieve optimal on-target editing and minimize unintended off-target edits that may be problematic in therapeutic applications."

"These data demonstrate that our chRDNA editing platform provides an efficient and highly customizable approach to develop sophisticated allogeneic CAR-T cells for the treatment of hematologic malignancies," said Rachel Haurwitz, Ph.D., Caribou's president and chief executive officer. "The first of Caribou's multiplex-edited product candidates, CB-010, is being evaluated in an ongoing Phase 1 clinical trial in patients with relapsed or refractory B cell non-Hodgkin lymphoma and we look forward to initial clinical data in 2022."

The studies in the *Molecular Cell* paper were part of a collaboration between Caribou and the laboratory of Martin Jinek, Ph.D., at the University of Zurich, Switzerland. Dr. Jinek is a co-founder of Caribou and a leader in the field of CRISPR.

The *Molecular Cell* paper describes studies comparing the editing activity and specificity of Cas9 programmed with either chRDNA or all-RNA guides at multiple independent genomic sites in human primary T cells. The data demonstrate that chRDNA guides enable highly specific Cas9-mediated editing, with little to no perturbation of on-target efficiency, while the all-RNA guides give rise to multiple unintended off-target editing events across the genome. The study also demonstrates that the number and location of DNA nucleotides in a chRDNA design can be tuned for each intended target site to allow for the maximal level of discrimination between on- and off-target sites. Structural analysis of target-bound Cas9-chRDNA complexes revealed that chRDNAs result in an altered geometry of the chRDNA and target DNA interface, and this alteration is accompanied by structural rearrangements of the Cas9 protein. These changes disfavor off-target DNA binding and modulate Cas9 cleavage activity to inhibit editing at off-target sites. The publication can be accessed [here](#).

(Donohoue, Pacesa, et al., September 2, 2021, *Molecular Cell* 81(17), 3637-3649.)

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 the chRDNA technology to carry out high efficiency multiple edits, including multiplex gene insertions, to develop CRISPR-edited therapies.

About Caribou Biosciences, Inc.

Caribou is a clinical-stage CRISPR genome-editing biopharmaceutical company dedicated to transforming the lives of patients with devastating diseases by applying the company's proprietary chRDNA technology toward the development of next-generation, genome-edited cell therapies. The company is developing a pipeline of genome-edited, off-the-shelf CAR-T and CAR-NK cell therapies for the treatment of both hematologic malignancies and solid tumors against cell surface targets for which autologous CAR-T cell therapeutics have previously demonstrated clinical proof of concept, as well as additional emerging targets.

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 regarding Caribou's expectations with respect to the higher specificity of genomic edits using its chRDNA technology and the timing and availability of clinical trial data. Management believes that these forward-looking statements are reasonable as and when made. However, no assurance can be given that the specificity of genomic edits in actual practice will match the results of published data or that clinical trial data will be available on the timing indicated, or at all. 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 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 final prospectus filed on July 23, 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.

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

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Caribou Biosciences, Inc.

Media Contact:

Greg Kelley

Ogilvy

gregory.kelley@ogilvy.com

617-461-4023

Caribou Biosciences, Inc.

Investor Relations Contact:

Elizabeth Wolffe, Ph.D., and Sylvia Wheeler

Wheelhouse LSA

lwolffe@wheelhouseslsa.com

swheeler@wheelhouseslsa.com