CRISPR Therapeutics Reports Positive Results from its Phase 1 CARBON Trial of CTX110™ in Relapsed or Refractory CD19+ B-cell malignancies

-58% overall response rate (ORR) and 38% complete response (CR) rate in large B-cell lymphoma (LBCL) with a single dose of CTX110 at Dose Level 2 (DL2) and above on an intent-to-treat (ITT) basis-

-Durable responses in LBCL achieved with six-month CR rate of 21% and longest response on-going at over 18 months after initial infusion-

-Response rates and durability are similar to approved autologous CD19 CAR-T therapies on an ITT basis-

-Positively differentiated safety profile; no Grade 3 or higher cytokine release syndrome (CRS) and low rates of infection and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)-

-Expanding CARBON into a potentially registrational trial in 1Q 2022-

-Management to host webcast and conference call today at 4:30 PM ET-

ZUG, Switzerland and CAMBRIDGE, Mass., October 12, 2021 -- CRISPR Therapeutics (Nasdaq: CRSP), a biopharmaceutical company focused on creating transformative gene-based medicines for serious diseases, today announced updated results from the Company's ongoing Phase 1 CARBON trial evaluating the safety and efficacy of CTX110™, its wholly-owned allogeneic CAR-T cell therapy targeting CD19+ B-cell malignancies.

"We are excited to share positive data from our CARBON trial, which show that CTX110 could offer patients with large B-cell lymphomas an immediately available 'off-the-shelf' therapy with efficacy similar to autologous CAR-T and a differentiated safety profile," said Samarth Kulkarni, Ph.D., Chief Executive Officer of CRISPR Therapeutics. "Furthermore, we have the potential to improve upon already observed efficacy with a consolidation dosing strategy. Based on these encouraging results, we are planning to expand CARBON into a potentially registrational trial in the first quarter of 2022."

CARBON Trial Overview

The Phase 1 CARBON trial is an open-label, multicenter clinical trial evaluating the safety and efficacy of CTX110 in adult patients with relapsed or refractory B-cell CD19+ malignancies who have received at least two prior lines of therapy. To date, enrollment has been focused on patients with the most aggressive disease presentations, including diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS), high-grade double- or triple-hit lymphomas, and transformed follicular lymphoma. The majority of patients had Stage IV lymphoma and were refractory to their last line of therapy before entering the trial. Nine patients received prior autologous stem cell transplant. Patients who received prior autologous CAR-T therapy were not eligible.

As of the August 26, 2021 data cutoff, 30 patients with large B-cell lymphoma (LBCL) had been enrolled, of which 26 patients had received CTX110 with at least 28 days of follow-up and are included in the analysis. Only one enrolled patient did not receive CTX110. Three patients at the time of the data cut had less than 28 days of follow-up and were not evaluable for this analysis.

Patients were infused with a single CTX110 infusion following three days of a standard lymphodepletion regimen consisting of fludarabine (30mg/m^2/day) and cyclophosphamide (500mg/m^2/day). Patients could be re-dosed with CTX110 following disease progression. The primary endpoints include safety as measured by the incidence of dose limiting toxicities (DLTs) and overall response rate (ORR). Key secondary endpoints include complete response (CR) rate, duration of response and overall survival.

Additional details may be found at clinicaltrials.gov, using identifier: NCT04035434.

Safety

CTX110 was well tolerated across all dose levels. The adverse events of interest for all evaluable patients are shown in the table below.

- There were no cases of Graft versus Host Disease (GvHD) and no infusion reactions to either lymphodepleting chemotherapy or CTX110.

- All cases of cytokine release syndrome (CRS) were Grade 1 or 2 per the American Society for Transplantation and Cellular Therapy (ASTCT) criteria and either required no specific intervention or resolved following standard CRS management. Neither the frequency nor severity of CRS has increased in patients who were re-dosed with CTX110.

- The only case of Grade 3 or higher immune effector cell-associated neurotoxicity syndrome (ICANS) was in the patient with concurrent HHV-6 encephalitis who was previously disclosed. There have been no cases of ICANS in any other patients treated at Dose Level (DL3) through Dose Level (DL4).

- Only two patients experienced Grade 3 or higher infections: the previously discussed patient with HHV-6 encephalitis, and one patient who developed pseudomonal sepsis that resolved in four days.

Adverse events of interest N (%)

	DL1 (N=3)		DL2 (N=3)		DL3 (N=6)		DL3.5 (N=6)		DL4 (N=8)		DL2+ (N=23)	
	Gr 1-2	Gr 3+	Gr 1-2	Gr 3+	Gr 1-2	Gr 3+	Gr 1-2	Gr 3+	Gr 1-2	Gr 3+	Gr 1-2	Gr 3+
CRS	1 (33)	-	2 (67)	-	2 (33)	-	3 (50)	-	6 (75)	-	13 (57)	-
ICANS	-	-	1 (33)	-	-	-	-	-	-	1 (13)	1 (4)	1 (4)
GvHD	-	-	-	-	-	-	-	-	-	-	-	-
Infusion reactions	-	-	-	-	-	-	-	-	-	-	-	-
Infections[1]	-	1 (33)	-	-	1 (17)	1 (17)	1 (17)	-	1 (13)	1 (13)	3 (13)	2 (9)

CRS and ICANS graded per ASTCT criteria; other adverse events graded per CTCAE; (1) All infections (bacterial, fungal, and viral) included

The emerging safety profile of CTX110 is positively differentiated from autologous CAR-T therapies that show high frequencies of severe CRS and ICANS, and from other allogeneic CAR-T therapies that require more toxic lymphodepletion regimens and can result in prolonged immunosuppression and increased risk of serious infections.

Clinical Activity

Data are shown below for the 26 patients that received CTX110 and had at least 28 days of follow-up. The ORR and CR rates for patients treated at DL2 and above are shown both on an intent-to-treat (ITT) and modified ITT (mITT) basis. ITT includes all enrolled patients (n=24 at DL2 and above) whereas mITT includes only those patients who received an infusion of CTX110 (n=23 at DL2 and above). Dose-dependent responses and durable complete responses were seen with CTX110. Disease assessment was performed by investigator review according to the 2014 Lugano response criteria.

Cell dose (CAR+ T cells)	DL1 $30x10^6$ *N=3*	DL2 $100x10^6$ *N=3*	DL3 $300x10^6$ *N=6*	DL3.5 $450x10^6$ *N=6*	DL4 $600x10^6$ *N=8*	DL2+ mITT *N=23*	DL2+ ITT *N=24*
Overall response rate (ORR), N (%)	0 (0%)	1 (33%)	3 (50%)	4 (67%)	6 (75%)	14 (61%)	14 (58%)
Complete response (CR) rate, N (%)	0 (0%)	1 (33%)	2 (33%)	3 (50%)	3 (38%)	9 (39%)	9 (38%)

- A single dose of CTX110 at DL2 and above resulted in a 58% ORR and 38% CR rate on an ITT basis.
- Responses were seen in a variety of patients, including patients who had refractory disease, bulky disease, or who had progressed after prior autologous stem cell transplant.
- The data demonstrate the potential for CTX110 to produce durable remissions, as evidenced by a 21% six-month CR rate (4 of the 9 patients who achieved CR at Day 28, remained in CR at 6 months; 5 patients had not reached their 6-month evaluation point), which is in the range of durable remissions observed with approved autologous CAR-T therapies on an ITT basis.
- The data provide a strong rationale that consolidation dosing can improve on an already competitive profile for CTX110.

Based on this safety and efficacy profile, the Company plans to expand into a potential registrational trial that incorporates consolidation dosing in Q1 2022. In parallel, the Company continues to advance the rest of its immuno-oncology portfolio and scale its manufacturing capabilities in its new state-of-the-art manufacturing facility in Framingham, Massachusetts.

Conference Call and Webcast

To access the conference call, please dial +1 (866) 952-8559 (domestic) or +1 (785) 424-1743 (international) and reference the conference ID “CRISPR.”

A live webcast of the event will be available on the "Events & Presentations" page in the Investors section of the Company's website at https://crisprtx.gcs-web.com/events. A webcast replay will be available on the CRISPR Therapeutics website after the event and will be archived for 14 days.

About CTX110

CTX110, a wholly owned program of CRISPR Therapeutics, is a healthy donor-derived gene-edited allogeneic CAR-T investigational therapy targeting Cluster of Differentiation 19, or CD19. CTX110 is being investigated in the ongoing CARBON trial.

About CARBON

The ongoing Phase 1 single-arm, multi-center, open label clinical trial, CARBON, is designed to assess the safety and efficacy of several dose levels of CTX110 for the treatment of relapsed or refractory B-cell malignancies.

About CRISPR Therapeutics

CRISPR Therapeutics is a leading gene editing company focused on developing transformative gene-based medicines for serious diseases using its proprietary CRISPR/Cas9 platform. CRISPR/Cas9 is a revolutionary gene editing technology that allows for precise, directed changes to genomic DNA. CRISPR Therapeutics has established a portfolio of therapeutic programs across a broad range of disease areas including hemoglobinopathies, oncology, regenerative medicine and rare diseases. To accelerate and expand its efforts, CRISPR Therapeutics has established strategic partnerships with leading companies including Bayer, Vertex Pharmaceuticals and ViaCyte, Inc. CRISPR Therapeutics AG is headquartered in Zug, Switzerland, with its wholly-owned U.S. subsidiary, CRISPR Therapeutics, Inc., and R&D operations based in Cambridge, Massachusetts, and business offices in San Francisco, California and London, United Kingdom. For more information, please visit www.crisprtx.com.

CRISPR Forward-Looking Statement

This press release may contain a number of "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including statements made by Dr. Kulkarni in this press release, as well as regarding CRISPR Therapeutics' expectations about any or all of the following: (i) the safety, efficacy and clinical progress of our various clinical programs including our CTX110 program; (ii) the status of clinical trials (including, without limitation, activities at clinical trial sites) and expectations regarding the data that is being presented from our CARBON clinical trial; (iii) the data that will be generated by ongoing and planned clinical trials, and the ability to use that data for the design and initiation of further clinical trials; and (iv) the therapeutic value, development, and commercial potential of CRISPR/Cas9 gene editing technologies and therapies, including as compared to other therapies. Without limiting the foregoing, the words "believes," "anticipates," "plans," "expects" and similar expressions are intended to identify forward-looking statements. You are cautioned that forward-looking statements are inherently uncertain. Although CRISPR Therapeutics believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: the potential for initial and preliminary data from any clinical trial and initial data from a limited number of patients not to be indicative of final trial results; the potential

that clinical trial results may not be favorable; potential impacts due to the coronavirus pandemic, such as the timing and progress of clinical trials; that future competitive or other market factors may adversely affect the commercial potential for CRISPR Therapeutics' product candidates; uncertainties regarding the intellectual property protection for CRISPR Therapeutics' technology and intellectual property belonging to third parties, and the outcome of proceedings (such as an interference, an opposition or a similar proceeding) involving all or any portion of such intellectual property; and those risks and uncertainties described under the heading "Risk Factors" in CRISPR Therapeutics' most recent annual report on Form 10-K, quarterly report on Form 10-Q and in any other subsequent filings made by CRISPR Therapeutics with the U.S. Securities and Exchange Commission, which are available on the SEC's website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. CRISPR Therapeutics disclaims any obligation or undertaking to update or revise any forward-looking statements contained in this press release, other than to the extent required by law.

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