UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 11, 2022

CRISPR THERAPEUTICS AG

(Exact name of Registrant as Specified in Its Charter)

Switzerland	**001-37923**	**Not Applicable**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
Baarerstrasse 14 **6300 Zug, Switzerland** **(Address of Principal Executive Offices)**		**Not Applicable** **(Zip Code)**

Registrant's Telephone Number, Including Area Code: 41 (0)41 561 32 77

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Shares, nominal value CHF 0.03	CRSP	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company
☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.
☐

Item 7.01 Regulation FD Disclosure.

On June 11, 2022, CRISPR Therapeutics AG (the "Company") and its partner Vertex Pharmaceuticals Incorporated (together with its affiliates, "Vertex") issued a press release announcing the presentation of new clinical data on exagamglogene autotemcel ("exa-cel"), formerly known as CTX001™, from CLIMB-111, CLIMB-121 and CLIMB-131 at the 2022 European Hematology Association (EHA) Congress ("EHA Congress"). A copy of the press release is attached hereto as Exhibit 99.1.

In addition, on June 11, 2022, the Company issued a press release announcing new clinical data from its ongoing Phase 1 COBALT™-LYM trial evaluating the safety and efficacy of CTX130™, its wholly-owned allogeneic CAR-T cell therapy targeting CD70 for the treatment of both solid tumors and certain hematologic malignancies. A copy of the press release is attached hereto as Exhibit 99.2.

The information in this Item 7.01 of Form 8-K, including the accompanying Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act"), or otherwise subject to the liability of such section, nor shall such information be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, regardless of the general incorporation language of such filing, except as shall be expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

Exagamglogene autotemcel (exa-cel), formerly known as CTX001

On June 11, 2022, Vertex and the Company announced presentation of new clinical data on exa-cel from the ongoing CLIMB-111, CLIMB-121, and CLIMB-131 clinical trials.

The data presented at the EHA Congress on June 11, 2022 are from 75 patients (44 with transfusion-dependent beta thalassemia ("TDT") and 31 with severe sickle cell disease ("SCD") with follow-up ranging from 1.2 to 37.2 months after exa-cel dosing.

Of the 44 patients with TDT, 26 had beta zero/beta zero or other beta-zero-like severe genotypes. Forty-two of 44 patients with TDT were transfusion-free with follow-up ranging from 1.2 to 37.2 months after exa-cel infusion. Two patients who were not yet transfusion-free had 75% and 89% reductions in transfusion volume. TDT patients had substantial mean increases in fetal hemoglobin ("HbF") and corresponding increases in mean total hemoglobin ("Hb") with mean total Hb levels increasing to >11 g/dL by Month 3 and maintained thereafter.

All 31 patients with severe SCD characterized by recurrent vaso-occlusive crises ("VOCs") (mean of 3.9 VOCs per year over the prior two years) were free of VOCs after exa-cel infusion through duration of follow-up, with follow-up ranging from 2.0 to 32.3 months. SCD patients had mean HbF (as a proportion of total Hb) of approximately 40% by Month 4 and maintained thereafter.

The safety was generally consistent with myeloablative conditioning with busulfan and autologous stem cell transplant. All patients engrafted neutrophils and platelets after exa-cel infusion. Among the 44 patients with TDT, two patients had serious adverse events ("SAEs") considered related to exa-cel. As previously reported, one patient had three SAEs considered related to exa-cel, hemophagocytic lymphohistiocytosis ("HLH"), acute respiratory distress syndrome and headache, and one SAE of idiopathic pneumonia syndrome that was considered related to both exa-cel and busulfan. All four SAEs occurred in the context of HLH and have resolved. One patient had SAEs of delayed neutrophil engraftment and thrombocytopenia, both of which were considered related to exa-cel and busulfan, and both SAEs have resolved. Among the 31 patients with SCD, there were no SAEs considered related to exa-cel.

CTX 130

On June 11, 2022 new clinical data from the Company's ongoing Phase 1 COBALT-LYM trial evaluating the safety and efficacy of CTX130 was presented during an oral presentation at the EHA Congress by Swaminathan P. Iyer, M.D., Professor, Lead of the T Cell Lymphoma Program, Department of Lymphoma/Myeloma, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center. Selected slides from the presentation are attached hereto as Exhibit 99.3 and are incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits:

Exhibit No.	Description
99.1	Press Release by Vertex Pharmaceuticals Incorporated and CRISPR Therapeutics AG, dated June 11, 2022
99.2	Press Release by CRISPR Therapeutics AG, dated June 11, 2022
99.3	Selected Slides from Presentation, dated June 11, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

CRISPR Therapeutics AG

Date: June 13, 2022

By: /s/ Samarth Kulkarni
Samarth Kulkarni, Ph.D.
Chief Executive Officer

Vertex and CRISPR Therapeutics Present New Data on More Patients With Longer Follow-Up Treated With exagamglogene autotemcel (exa-cel) at the 2022 European Hematology Association (EHA) Congress

- Data from 75 patients with transfusion-dependent beta thalassemia or severe sickle cell disease with follow-up of up to 37.2 months continue to demonstrate that exa-cel has the potential to be a one-time functional cure –

- Safety profile generally consistent with myeloablative conditioning and autologous stem cell transplant –

BOSTON and ZUG, Switzerland and CAMBRIDGE, Mass., June 11, 2022 -- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) and CRISPR Therapeutics (Nasdaq: CRSP) announce presentation of new data on exa-cel, formerly known as CTX001™, from CLIMB- 111, CLIMB-121 and CLIMB-131 highlighting the potentially transformative profile of this investigational therapy for people with transfusion-dependent beta thalassemia (TDT) or severe sickle cell disease (SCD) and provided additional program updates.

New Data for exa-cel from CLIMB Clinical Studies
The data presented at the European Hematology Association (EHA) Congress are from 75 patients (44 with TDT and 31 with SCD) with follow-up ranging from 1.2 to 37.2 months after exa-cel dosing.

Of the 44 patients with TDT, 26 had beta-zero/beta-zero or other beta-zero-like severe genotypes. Forty-two of 44 patients with TDT were transfusion-free with follow-up ranging from 1.2 to 37.2 months after exa-cel infusion. Two patients who were not yet transfusion- free had 75% and 89% reductions in transfusion volume. TDT patients had substantial mean increases in fetal hemoglobin (HbF) and corresponding increases in mean total hemoglobin (Hb) with mean total Hb levels increasing to >11 g/dL by Month 3 and maintained thereafter.

All 31 patients with severe SCD characterized by recurrent vaso-occlusive crises (VOCs) (mean of 3.9 VOCs per year over the prior two years) were free of VOCs after exa-cel infusion through duration of follow-up, with follow-up ranging from 2.0 to 32.3 months. SCD patients had mean HbF (as a proportion of total Hb) of approximately 40% by Month 4 and maintained thereafter.

The safety was generally consistent with myeloablative conditioning with busulfan and autologous stem cell transplant. All patients engrafted neutrophils and platelets after exa-cel infusion. Among the 44 patients with TDT, two patients had serious adverse events (SAEs) considered related to exa-cel. As previously reported, one patient had three SAEs considered related to exa-cel, hemophagocytic lymphohistiocytosis (HLH), acute respiratory distress syndrome and headache, and one SAE of idiopathic pneumonia syndrome that was considered related to both exa-cel and busulfan. All four SAEs occurred in the context of HLH and have resolved. One patient had SAEs of delayed neutrophil engraftment and thrombocytopenia, both of which were considered related to exa-cel and busulfan, and both

SAEs have resolved. Among the 31 patients with SCD, there were no SAEs considered related to exa-cel.

Additional details were presented during the EHA media briefing and can be found in the published abstract and presentation.

Late-breaking abstract #LB2367 entitled “Efficacy and Safety of a Single Dose of CTX001 For Transfusion-Dependent Beta-Thalassemia and Severe Sickle Cell Disease,” will be an oral presentation on Sunday, June 12 at 09:45-11:15 CEST.

“These robust data from 75 patients, of which 33 have one year or more of follow-up after exa-cel infusion, further demonstrate the potential of this investigational therapy as a one- time functional cure for patients with transfusion-dependent beta thalassemia or severe sickle cell disease,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex.

“By reactivating a naturally occurring developmental process, exa-cel restores fetal hemoglobin production and thereby can ameliorate the course of these diseases,” said Haydar Frangoul, M.D., Medical Director of Pediatric Hematology and Oncology at Sarah Cannon Research Institute, HCA Healthcare’s The Children’s Hospital at TriStar Centennial Medical Center. “The remarkable results based on this approach give me great optimism and confidence in the potential of this treatment for patients.”

“I have seen first-hand the impact that this investigational therapy has had on patients in these clinical trials and continue to be impressed by the totality of the data,” said Franco Locatelli, M.D., Ph.D., Professor of Pediatrics at the Sapienza University of Rome, Director of the Department of Pediatric Hematology and Oncology at Bambino Gesù Children’s Hospital. “Given the urgency for highly effective and curative therapies for patients with hemoglobinopathies, I am excited to be part of the team working towards the goal of addressing this unmet need.”

Exa-cel Study Updates
Following ongoing discussions with regulators, the clinical trial protocols for CLIMB-111 and CLIMB-121 were amended to incorporate feedback on the primary endpoints for regulatory submission. Specifically, the primary endpoint in CLIMB-111 for TDT has been amended from proportion of subjects achieving transfusion reduction after exa-cel infusion to proportion of subjects maintaining weighted average Hb ≥9 g/dL without red blood cell (RBC) transfusions for at least 12 consecutive months after exa-cel infusion.

The primary endpoint in CLIMB-121 for SCD has been updated from proportion of subjects with HbF ≥20% after exa-cel infusion, to proportion of subjects who have not experienced any severe VOCs for at least 12 consecutive months after exa-cel infusion.

Both clinical trials are now in Phase 3 and are fully enrolled. All patients will have the opportunity to join CLIMB-131, a long-term follow-up study, after completing participation in the initial studies.

Additional Pediatric Studies
In line with the company's strategy of developing therapies for patients of all ages, two additional Phase 3 studies of exa-cel have begun. Earlier this year, the Independent Data Monitoring Committee (DMC) met to review the data in adults and adolescents and endorsed expanding into younger pediatric patients. CLIMB-141 and CLIMB-151 are Phase 3 open- label trials designed to assess the safety and efficacy of a single dose of exa-cel in patients ages 2 to 11 years with TDT or SCD, respectively. The trials are now open for enrollment and currently enrolling patients ages 5 to 11 years and will plan to extend to patients 2 to less than 5 years of age at a later date. Each trial will enroll approximately 12 patients. Patients will be followed for approximately two years after infusion. Each patient will be asked to participate in CLIMB-131, a long-term follow-up trial.

Vertex also presented three additional abstracts on the burden of disease in sickle cell disease and beta thalassemia at the EHA Congress.

1. Abstract #P1704 entitled "Projected Lifetime Economic Burden of Severe Sickle Cell Disease in the United States," presented via poster on Friday, June 10 at 16:30- 17:45 CEST.
2. Abstract #P1703 entitled "Economic Burden of Transfusion-Dependent Beta- Thalassemia in the United States," presented via poster on Friday, June 10 at 16:30- 17:45 CEST.
3. Abstract #P1482 entitled "Patients With Severe Sickle Cell Disease on Standard-of- Care Treatment Are Very Unlikely to Become VOC-Free for One Year: A Cohort Study of Medicaid Enrollees," presented via poster on Friday, June 10 at 16:30-17:45 CEST.

About exagamglogene autotemcel (exa-cel)
Exa-cel, formerly known as CTX001, is an investigational, autologous, *ex vivo* CRISPR/Cas9 gene-edited therapy that is being evaluated for patients with TDT or SCD characterized by recurrent VOCs, in which a patient's own hematopoietic stem cells are edited to produce high levels of fetal hemoglobin (HbF; hemoglobin F) in red blood cells. HbF is the form of the oxygen-carrying hemoglobin that is naturally present during fetal development, which then switches to the adult form of hemoglobin after birth. The elevation of HbF by exa-cel has the potential to alleviate transfusion requirements for patients with TDT and reduce painful and debilitating sickle crises for patients with SCD. Earlier results from these ongoing trials were published in *The New England Journal of Medicine* in January of 2021.

Based on progress in this program to date, exa-cel has been granted Regenerative Medicine Advanced Therapy (RMAT), Fast Track, Orphan Drug, and Rare Pediatric Disease designations from the U.S. Food and Drug Administration (FDA) for both TDT and SCD. Exa-cel has also been granted Orphan Drug Designation from the European Commission, as well as Priority Medicines (PRIME) designation from the European Medicines Agency (EMA), for both TDT and SCD.

Among gene-editing approaches being evaluated for TDT and SCD, exa-cel is the furthest advanced in clinical development.

About CLIMB-111 and CLIMB-121
The ongoing Phase 1/2/3 open-label trials, CLIMB-111 and CLIMB-121, are designed to assess the safety and efficacy of a single dose of exa-cel in patients ages 12 to 35 years with TDT or with SCD, characterized by recurrent VOCs, respectively. The trials are now closed for enrollment. Patients will be followed for approximately two years after exa-cel infusion. Each patient will be asked to participate in CLIMB-131, a long-term follow-up trial.

About CLIMB-131
This is a long-term, open-label trial to evaluate the safety and efficacy of exa-cel in patients who received exa-cel in CLIMB-111, CLIMB-121, CLIMB-141 or CLIMB-151. The trial is designed to follow participants for up to 15 years after exa-cel infusion.

About CLIMB-141 and CLIMB-151
The ongoing Phase 3 open-label trials, CLIMB-141 and CLIMB-151, are designed to assess the safety and efficacy of a single dose of exa-cel in patients ages 2 to 11 years with TDT or with SCD, characterized by recurrent VOCs, respectively. The trials are now open for enrollment and currently enrolling patients ages 5 to 11 years of age and will plan to extend to patients 2 to less than 5 years of age at a later date. Each trial will enroll approximately 12 patients. Patients will be followed for approximately two years after infusion. Each patient will be asked to participate in CLIMB-131, a long-term follow-up trial.

About the Gene-Editing Process in These Trials
Patients who enroll in these trials will have their own hematopoietic stem and progenitor cells collected from peripheral blood. The patient's cells will be edited using the CRISPR/Cas9 technology. The edited cells, exa-cel, will then be infused back into the patient as part of an autologous hematopoietic stem cell transplant (HSCT), a process which involves a patient being treated with myeloablative busulfan conditioning. Patients undergoing HSCT may also encounter side effects (ranging from mild to severe) that are unrelated to the administration of exa-cel. Patients will initially be monitored to determine when the edited cells begin to produce mature blood cells, a process known as engraftment. After engraftment, patients will continue to be monitored to track the impact of exa-cel on multiple measures of disease and for safety.

About the Vertex-CRISPR Collaboration
Vertex and CRISPR Therapeutics entered into a strategic research collaboration in 2015 focused on the use of CRISPR/Cas9 to discover and develop potential new treatments aimed at the underlying genetic causes of human disease. Exa-cel represents the first potential treatment to emerge from the joint research program. Under an amended collaboration agreement, Vertex now leads global development, manufacturing and commercialization of exa-cel and splits program costs and profits worldwide 60/40 with CRISPR Therapeutics.

About Vertex
Vertex is a global biotechnology company that invests in scientific innovation to create

transformative medicines for people with serious diseases. The company has multiple approved medicines that treat the underlying cause of cystic fibrosis (CF) — a rare, life- threatening genetic disease — and has several ongoing clinical and research programs in CF. Beyond CF, Vertex has a robust pipeline of investigational small molecule, cell and genetic therapies in other serious diseases where it has deep insight into causal human biology, including sickle cell disease, beta thalassemia, APOL1-mediated kidney disease, pain, type 1 diabetes, alpha-1 antitrypsin deficiency and Duchenne muscular dystrophy.

Founded in 1989 in Cambridge, Mass., Vertex's global headquarters is now located in Boston's Innovation District and its international headquarters is in London. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including 12 consecutive years on Science magazine's Top Employers list and one of the 2021 Seramount (formerly Working Mother Media) 100 Best Companies. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on Facebook, Twitter, LinkedIn, YouTube and Instagram.

(VRTX-GEN)

Vertex Special Note Regarding Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, (i) statements by Dr. Carmen Bozic, Dr. Haydar Frangoul, and Dr. Franco Locatelli in this press release, (ii) our plans and expectations to present clinical data from the ongoing exa-cel clinical trials during the EHA Congress, (iii) the progress of the ongoing exa-cel clinical trials, including expectations regarding the abstracts that will be made available on the virtual platform including anticipated projections and estimates related to the various economic impacts of SCD and TDT, (iv) the potential benefits, efficacy, and safety of exa-cel, including the potentially transformative nature of the therapy and the potential of the treatment for patients, (v) our plans and expectations for our clinical trials and pipeline products, and (vi) the status of our clinical trials of our product candidates under development by us and our collaborators, including activities at the clinical trial sites, patient enrollment, and expectations regarding clinical trial follow-up. While Vertex believes the forward-looking statements contained in this press release are accurate, these forward-looking statements represent the company's beliefs only as of the date of this press release and there are a number of risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that data from a limited number of patients may not be indicative of final clinical trial results, that data from the company's development programs, including its programs with its collaborators, may not support registration or further development of its compounds due to safety and/or efficacy, or other reasons, that internal or external factors could delay, divert, or change our plans and objectives with respect to our research and development programs, that future competitive or other market factors may adversely affect the commercial potential for exa-cel, and other risks listed under the heading “Risk Factors” in Vertex's most recent annual report and subsequent quarterly reports filed with the Securities and Exchange Commission (SEC) and available through the

company's website at www.vrtx.com and on the SEC's website at www.sec.gov. You should not place undue reliance on these statements or the scientific data presented. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

(CRSP-GEN)

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 collaborations 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 Therapeutics 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, as well as statements made by Dr. Carmen Bozic, Dr. Haydar Frangoul, and Dr. Franco Locatelli in this press release, as well as statements regarding CRISPR Therapeutics' expectations about any or all of the following: i) the safety, efficacy and clinical progress of the ongoing exa- cel clinical trials, including expectations regarding the abstracts that will be made available on the virtual platform and our plans and expectations to present and the clinical data that are being presented during the EHA Congress, as well as the potentially transformative nature of exa-cel and the potential of the treatment for patients; and (ii) the therapeutic value, development, and commercial potential of CRISPR/Cas9 gene editing technologies and 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, existing and prospective investors are cautioned that forward-looking statements are inherently uncertain, are neither promises nor guarantees and not to place undue reliance on such statements, which speak only as of the date they are made. 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 (as is the case with exa-cel at this time) not to be indicative of final or future trial results; the potential that the exa-cel clinical trial results may not be favorable or may not support registration or further development; that future competitive or other market factors may adversely affect the commercial potential for exa-cel; CRISPR Therapeutics may not realize the potential benefits of its collaboration with Vertex; potential impacts due to the coronavirus pandemic, such as to the timing and progress of clinical trials; uncertainties regarding the intellectual property protection for CRISPR Therapeutics' technology and intellectual property belonging to third parties; 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. 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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CRISPR Therapeutics Presents Positive Results from its Phase 1 COBALT™-LYM Trial of CTX130™ in Relapsed or Refractory T Cell Malignancies at the 2022 European Hematology Association (EHA) Congress

-70% overall response rate (ORR) and 30% complete response (CR) rate in peripheral T-cell lymphoma (PTCL) and cutaneous T cell lymphoma (CTCL) at Dose Level 3 (DL3) and above; clinical benefit for 90% of patients-

-Well tolerated safety profile across all dose levels with no DLTs observed-

ZUG, Switzerland and CAMBRIDGE, Mass., June 11, 2022 -- CRISPR Therapeutics (Nasdaq: CRSP), a biopharmaceutical company focused on creating transformative gene-based medicines for serious diseases, today presented positive results from the Company's ongoing Phase 1 COBALT™-LYM trial evaluating the safety and efficacy of CTX130™, its wholly-owned allogeneic CAR-T cell therapy targeting CD70 for the treatment of both solid tumors and certain hematologic malignancies.

"We are very pleased with the preliminary results from our COBALT-LYM trial, which showed efficacy and safety that suggest that CTX130, the first allogeneic CAR-T directed against the novel target CD70, can produce deep responses in patients with relapsed or refractory T cell lymphomas," said Samarth Kulkarni, Ph.D., Chief Executive Officer of CRISPR Therapeutics. "Additionally, we may be able to further optimize the profile by continuing our consolidation dosing strategy. These data reinforce our belief that engineered cell therapies are the future in our fight against cancer and we are well-positioned to be leaders in this field."

"While overall survival in a subset of patients with T cell lymphoma has improved with front-line combination chemotherapy, relapsed or refractory patients continue to have very limited treatment options," said Swaminathan P. Iyer, M.D., Professor, Lead of the T Cell Lymphoma Program, Department of Lymphoma/Myeloma, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center. "The data from the CTX130 trial demonstrate the potential of cell therapies as a new treatment modality for these patients. I am particularly encouraged by the response rates and safety data, which suggest that treatment with CTX130 could elicit clinically meaningful responses, including complete responses, in patients with difficult-to-treat T cell lymphomas."

COBALT-LYM Trial Overview

The Phase 1 COBALT-LYM trial is an open-label, multicenter clinical trial evaluating the safety and efficacy of CTX130 in adult patients with relapsed or refractory T or B cell malignancies. Dose escalation of CTX130 was performed in adult patients with relapsed or refractory T cell lymphoma, with at least 10% expression of CD70. Patients who received prior treatment with any CD70 targeting agents were not eligible.

Patients received three days of lymphodepleting chemotherapy, consisting of fludarabine at 30 mg/m2/day and cyclophosphamide at 500 mg/m2/day, followed by a single CTX130 infusion. Patients completed screening in as few as five days, and the median time from enrollment to the start of lymphodepleting chemotherapy was only three days. This timeline was possible because there is no need for leukapheresis or bridging chemotherapy, and CTX130 is available at the site before a patient is enrolled. Additionally, patients who showed clinical benefit from the first CTX130 infusion could be re-dosed following disease progression.

As of the April 26, 2022, data cutoff, 19 patients with T cell malignancies had been enrolled, of which 18 patients had received CTX130 with at least 28 days of follow-up and are included in the analysis. Prior to enrollment, all patients were heavily pre-treated, with a median of four systemic therapies. Additionally, all patients were refractory to their last line of therapy. Eight patients had peripheral T-cell lymphoma (PTCL) and 10 patients had cutaneous T-cell lymphoma (CTCL).

The primary endpoints include safety as measured by the incidence of dose limiting toxicities (DLTs) and overall response rate (ORR). Key secondary endpoints include progression free survival (PFS) and overall survival (OS).

Safety
CTX130 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); no dose limiting toxicities (DLTs); and no instances of tumor lysis syndrome (TLS).
- All cases of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) 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 CTX130.
- There was a sudden death in one patient with William's syndrome in the context of a lung infection, deemed unrelated to CTX130. There were no treatment related deaths in the trial. Overall, CTX130 has an emerging safety profile that is well tolerated.

Adverse Events of Interest

	DL1 $3x10^7$ N=4		**DL2 $1x10^8$ N=4**		**DL3 $3x10^8$ N=5**		**DL4 $9x10^8$ N=5**		**DL≥3 N=10**	
	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 (25)	-	1 (25)	-	4 (80)	-	4 (80)	-	8 (80)	-
ICANS	-	-	-	-	3 (60)	-	-	-	3 (30)	-
GvHD	-	-	-	-	-	-	-	-	-	-
Infections	2 (50)	1 (25)	-	1 (25)	2 (40)	1 (20)	1 (20)	1 (20)	3 (30)	2 (20)

**All events listed in table are treatment-emergent adverse events*

Clinical Activity

Deep responses were seen with CTX130 in a significant fraction of patients at DL3 and above. Data are shown below for the 18 patients who received CTX130 and had at least 28 days of follow-up. Disease assessment was performed by investigator review according to the 2014 Lugano Response Criteria for PTCL or the International Society for Cutaneous Lymphoma Response Criteria (Olsen criteria) for CTCL, as appropriate.

Best overall response, N (%)

Cell dose (CAR+ T cells)	**DL1 $3x10^7$ N=4**	**DL2 $1x10^8$ N=4**	**DL3 $3x10^8$ N=5**	**DL4 $9x10^8$ N=5**	**DL≥3 N=10**
Overall Response Rate (ORR)	2 (50)	0	3 (60)	4 (80)	**7 (70)**
CR	1 (25)	0	2 (40)*	1 (20)	**3 (30)**
PR	1 (25)	0	1 (20)	3 (60)	**4 (40)**
Disease Control Rate (DCR = CR + PR + SD)	3 (75)	1 (25)	5 (100)	4 (80)	**9 (90)**

	PTCL		**CTCL**	
	DL≥3 N=5	**Total N=8**	**DL≥3 N=5**	**Total N=10**
ORR	4 (80)	5 (63)	3 (60)	4 (40)
CR	2 (40)	3 (38)	1 (20)	1 (10)
PR	2 (40)	2 (25)	2 (40)	3 (30)
DCR	4 (80)	5 (63)	5 (100)	8 (80)

**One patient in DL3 who initially achieved a PR was re-infused at DL4 following a change to SD and achieved a CR at DL4.*

- Patients were heavily pre-treated with a median of four systemic therapies prior to enrollment in the study. None of the 18 patients had achieved a complete response (CR) in their previous line of therapy.
- Median CD70 expression among the patients was 90%. Responses were observed across all levels of CD70 expression.
- Clinically meaningful responses were observed with CTX130 with a higher percentage of patients responding at higher dose levels. At DL3 and above, ORR was 70% with 30% of patients achieving a CR. In addition, 90% of patients at DL3+ had clinical benefit defined as a stable disease or better response. These responses were largely consistent in both PTCL and CTCL with ORRs of 80% and 60%, respectively, at DL3+.
- Broad activity and deep responses were seen in all disease compartments including lymph nodes, skin and blood in patients with CTCL following treatment with CTX130.

These preliminary data demonstrate that CTX130 has the potential to provide meaningful clinical benefit with a well-tolerated safety profile. Given the inherent difficulties and potential risks of manufacturing a CAR-T therapy from a patient's own diseased T cells, allogeneic cellular therapy approaches for T cell lymphoma have greater potential to address the unmet need in this patient population.

CTX130 is currently being investigated in two ongoing Phase 1 clinical trials for the treatment of various subtypes of lymphoma (COBALT-LYM) or relapsed or refractory renal cell carcinoma (COBALT-RCC),

respectively. Additional details on COBALT-LYM may be found at clinicaltrials.gov, using identifier: NCT04502446. In parallel, the Company continues to advance the rest of its immuno-oncology portfolio.

The Company plans to recap this data during the CRISPR Therapeutics Innovation Day, an event focused on early research and development, on June 21, 2022, at 2:00 pm ET.

Innovation Day Webcast

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 replay of the webcast will be archived on the Company's website for 30 days following the presentation. Please contact crisprtx@argotpartners.com for any questions regarding the event.

About CTX130

CTX130, a wholly-owned program of CRISPR Therapeutics, is a healthy donor-derived gene-edited allogeneic CAR-T investigational therapy targeting cluster of differentiation 70, or CD70, an antigen expressed on various solid tumors and hematologic malignancies. CTX130 is being developed for the treatment of both solid tumors, such as renal cell carcinoma, and T-cell and B-cell hematologic malignancies. CTX130 is being investigated in two ongoing independent Phase 1, single-arm, multi-center, open-label clinical trials that are designed to assess the safety and efficacy of several dose levels of CTX130 for the treatment of relapsed or refractory renal cell carcinoma and various subtypes of lymphoma, respectively. CTX130 for the treatment of T-cell lymphoma has received Orphan Drug Designation from the FDA.

About COBALT-LYM

The ongoing Phase 1 single-arm, multi-center, open label clinical trial, COBALT-LYM, is designed to assess the safety and efficacy of several dose levels of CTX130 for the treatment of relapsed or refractory T- or B-cell malignancies.

About COBALT-RCC

The ongoing Phase 1 single-arm, multi-center, open label clinical trial, COBALT-RCC, is designed to assess the safety and efficacy of several dose levels of CTX130 for the treatment of relapsed or refractory Renal Cell Carcinoma.

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. Samarth Kulkarni and Dr. Swaminathan P. Iyer in this press release, as well as statements 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 CTX130 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 ongoing COBALT-LYM 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 inherently uncertain, are neither promises nor guarantees and not to place undue reliance on such statements, which speak only as of the date they are made. 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 (as is the case with CTX130 at this time) not to be indicative of final or future trial results; the potential that clinical trial results may not be favorable or may not support registration or further development; 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. 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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THE COBALT-LYM STUDY OF CTX130: A PHASE 1 DOSE ESCALATION STUDY OF CD70-TARGETED ALLOGENEIC CRISPR-CAS9–ENGINEERED CAR T CELLS IN PATIENTS WITH RELAPSED/REFRACTORY (R/R) T-CELL MALIGNANCIES

Swaminathan P. Iyer[1], R. Alejandro Sica[2], P. Joy Ho[3], Boyu Hu[4], Jasmine Zain[5], Anca Prica[6], Wen-Kai Weng[7], Youn H. Kim[8], Michael S. Khodadoust[9], M. Lia Palomba[10], Francine M. Foss[11], Kimberly Tipton[12], Erika L. Cullingford[12], Qiuling He[12], Anjali Sharma[12], Steven M. Horwitz[10]

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Presented at the European Hematology Association Annual Meeting. 11 June 2022

Disclosures

- The COBALT™ – LYM study of CTX130™ is sponsored by CRISPR Therapeutics
- Dr. Swaminathan P. Iyer is a Professor, Lead of the T Cell Lymphoma Program, Department of Lymphoma/Myeloma, Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center
- Dr. Iyer receives research support from CRISPR Therapeutics, Merck, Seagen, Rhizen, Acrotech, Legend, Innate Pharma, Astra Zeneca, Dren Bio, Yingli, and Secura Bio; participates in scientific advisory boards for Seagen, Yingli, and Secura Bio; and participates in Biocure's and Targeted Oncology's speaker bureaus as a speaker

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Overview

- **PTCL and CTCL are complex diseases with significant unmet need and limited approved systemic therapies.** Few therapies effectively treat all disease compartments (lymph nodes, skin, blood) or achieve meaningful CR rates. For patients with R/R PTCL and transformed CTCL, median OS is 1-2.5 and <5 years, respectively[1-5]
- **CTX130™ is a first-in-class, CD70-targeting allogeneic CAR T therapy that represents the first potential cell therapy for TCL patients.** Allogeneic cellular therapy approaches for TCL have greater potential to meet the unmet need in this patient population given the patients' own T cells are not suitable for autologous manufacturing[6]
- **CD70** is a ligand for CD27 with transient expression on activated lymphocytes and is **highly expressed in many TCLs**[7-10]
- **Preliminary data from dose escalation of CTX130 shows promising efficacy,** including a 70% ORR and a 30% CR rate at DL≥3 (≥3x10^8 cells), with an acceptable safety profile

CAR, chimeric antigen receptor; CR, complete response; CTCL, cutaneous T cell lymphoma; ORR, overall response rate; OS, overall survival; PTCL, peripheral T cell lymphoma; R/R, relapsed/refractory; TCL, T cell lymphoma.

References: 1. Fleischer LC, et al. *J Hematol Oncol.* 2019;12:141. 2. Toki H, et al. *Jpn J Clin Oncol.* 1986;16:41-48.3. Lansigan F, et al. *Acta Hematol.* 2020;143:40-50. 4. Scarisbrick JJ, et al. *J Clin Oncol.* 2015;33:3766-3733. 5. Lansigan F, et al. *Clin Lymphoma Myeloma Leuk.* 2020;20:744-748. 6. Alcantara M, et al. Leukemia. 2018; 32, 2307–2315. 7. Wajant H. *Expert Opin Ther Targets.* 2016;20:959-973. 8. Hintzen RQ, et al. *Int Immunol.* 1994;6:477-480. 9. Lens SM, et al. *Immunology.* 1997;90:38-45. 10. Marques-Piubelli M, et al. *Histopathology.* 2022 Apr 26. doi: 10.1111/his.14670. Online ahead of print.

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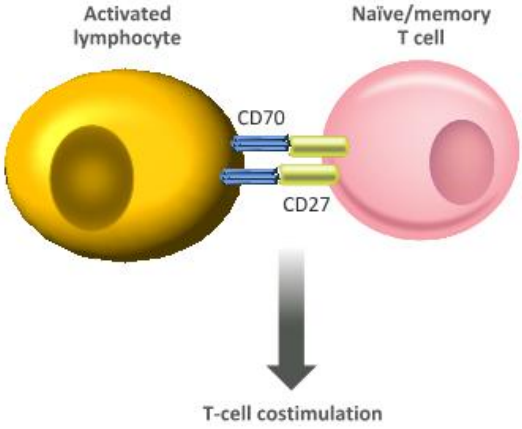
Role of CD70 in Immune Response and Cancer

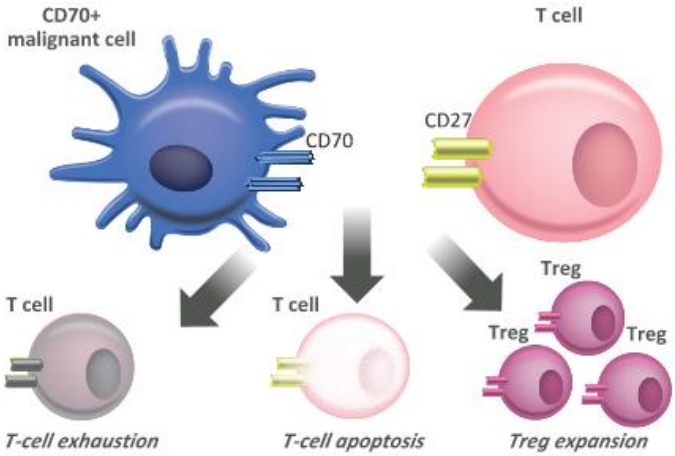
Physiological role of CD70[1]

- Transient CD70 expression on activated lymphocytes
- Controls naïve and memory T-cell activation via interaction with CD27



Role of CD70 in cancer[1]

- Increased CD70 expression has been **detected in certain cancers, including 85% of TCL samples** with a median surface expression of 40%[2]
- Possible immunosuppressive role due to T-cell exhaustion, apoptosis, or Treg expansion



TCL, T cell lymphoma; Treg, regulatory T cell.

References: 1. Wajant H. *Expert Opin Ther Targets*. 2016;20:959-973. 2. Marques-Piubelli M, et al. *Histopathology*. 2022 Apr 26. doi: 10.1111/his.14670. Online ahead of print.

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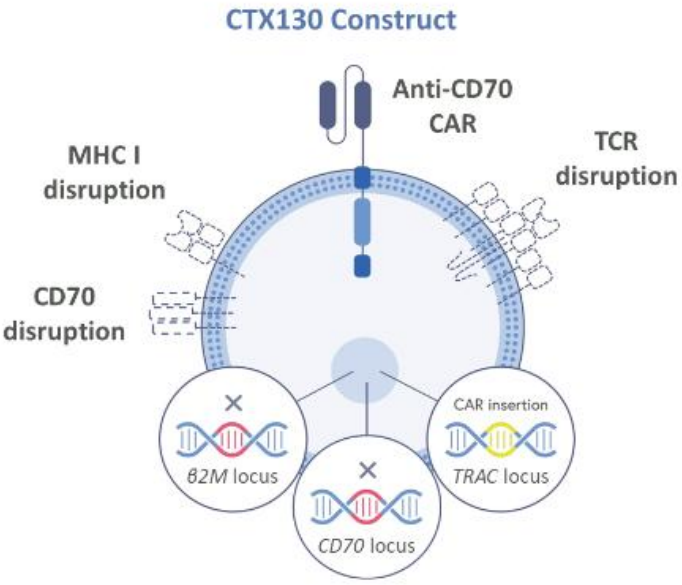
CTX130

- **Autologous approaches continue to be challenging** due to the poor function of donor T cells, potential for fratricide, and risk of infusing transduced malignant CAR T cells into patients
- **CTX130 is an investigational allogeneic, CRISPR/Cas9 gene-edited, anti-CD70 CAR T cell therapy** with TRAC, β2M, and CD70 disruptions
  - An **anti-CD70 CAR cassette is site-specifically inserted into the TRAC locus** by homology-directed repair
- **CTX130 is manufactured from T cells collected from a healthy donor,** which are then selected and edited before expansion and cryopreservation for **off-the-shelf availability**



β2M, β2-microglobulin; CAR, chimeric antigen receptor; MHC, major histocompatibility complex; TCR, T-cell receptor; TRAC, T-cell receptor alpha constant.

Reference: Dequeant M-L, et al. CD70 knockout: A novel approach to augment CAR-T cell function. Poster presented at American Association for Cancer Research 2021. April 10-15 and May 17-21, 2021.

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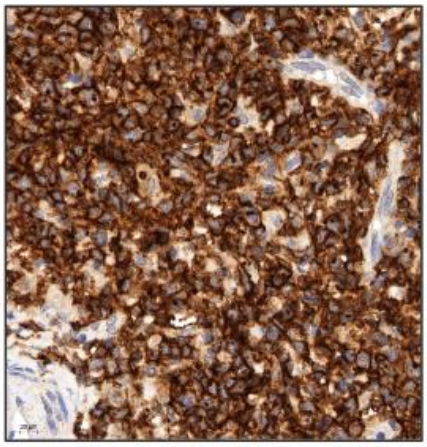
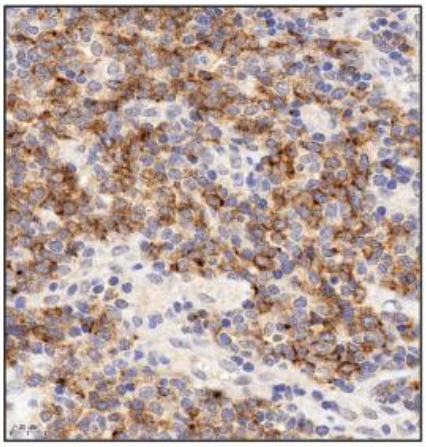
CTX130 – Preclinical Data

CD70 surface expression on clinical samples of TCL as measured by immunohistochemistry

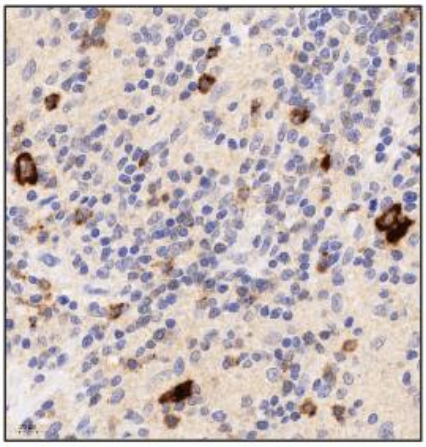
High



Moderate



Low



Reference: Karnik S, et al.. Poster presented at American Association for Cancer Research 2020.

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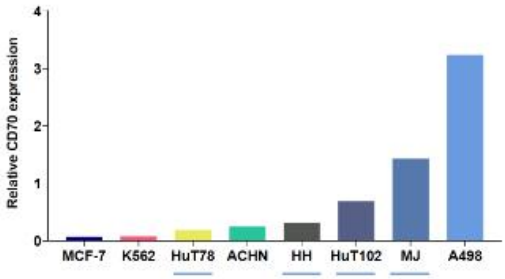
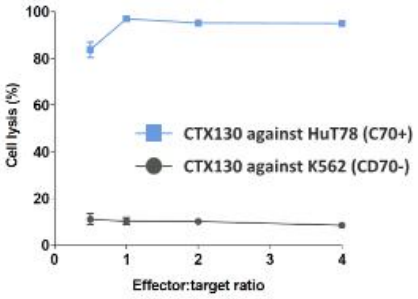
CTX130 – Preclinical Data

CD70 expression by flow cytometry in TCL and RCC cancer cell lines



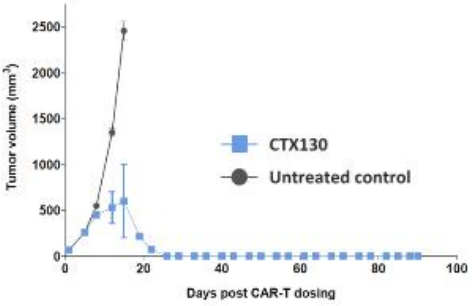
Consistent with the IHC data, TCL cell lines HuT78, HH, HuT102 and MJ (blue lines) show a range of CD70 expression from low/medium to high. RCC cell lines A498 and ACHN show high and low expression, respectively. MCF-7 and K562 are CD70-negative cell lines shown as negative controls

In vitro cytotoxicity against CD70+ but not CD70- cell lines



CTX130 was co-cultured with HuT78 or K562 cells for 24 hours at a range of T-cell:tumor cell ratios. CTX130 showed high cytotoxicity against CD70-expressing cells, even the low expressing HuT78 cell line, but not against CD70-negative cells (K562)

In vivo efficacy against an established HuT78 xenograft tumor model of Sézary Syndrome



3x10^6 HuT78 cells were injected subcutaneously into the right flank of NSG mice. When mean tumor size reached an average size of ~66 mm^3, mice were either left untreated or injected intravenously with 8.6x10^6 CTX130 cells per mouse (N=5 per group)

IHC, immunohistochemistry; RCC, renal cell carcinoma; TCL, T-cell lymphoma

Reference: Karnik S, et al.. Poster presented at American Association for Cancer Research 2020.

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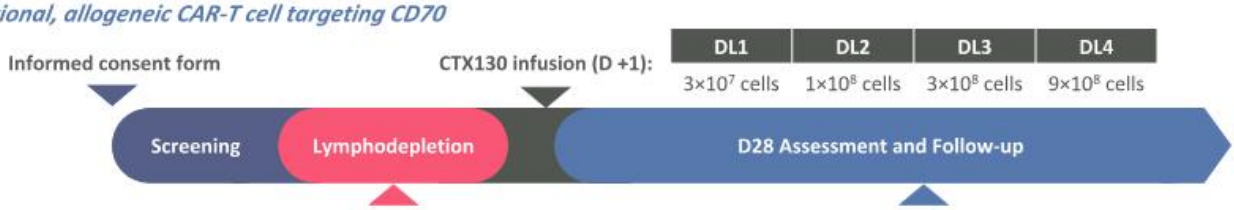
COBALT-LYM (NCT04502446) Clinical Trial Design

Phase 1, open-label, multicenter, international, single-arm study (NCT04502446) evaluating the safety and efficacy of CTX130, an investigational, allogeneic CAR-T cell targeting CD70



Flu 30mg/m² + Cy 500mg/m² for 3 days (D −5, −4, −3)

2nd course of CTX130 can be administered with LD after:

1. Loss of CR within the first 2 years after initial infusion
2. PR, SD, or PD with clinical benefit as determined by the investigator

Key inclusion criteria

- Age ≥18 years
- Confirmed diagnosis of a **CD70+ (≥10% of cells)** T-cell malignancy
- ECOG performance status of 0–1
- Adequate renal, liver, cardiac, and pulmonary organ function
- **Platelets >25,000/mm³** and **absolute neutrophil count >500/mm³**

Key exclusion criteria

- Prior allogeneic SCT
- Prior treatment with any anti-CD70 agents
- History of certain CNS, cardiac, or pulmonary conditions

Primary endpoint

- Part A (Dose Escalation): Incidence of adverse events
- Part B (Cohort Expansion): Objective response rate*

Secondary endpoints

- Progression-free survival
- Overall survival

*As assessed by Lugano response criteria for PTCL, International Society for Cutaneous Lymphoma Response Criteria for CTCL.
CNS, central nervous system; CR, complete response; CTCL, cutaneous T cell lymphoma; D: day; LD, lymphodepletion; PD, progressive disease; PR, partial response; PTCL, peripheral, T cell lymphoma; SCT, stem cell transplant; SD, stable disease.

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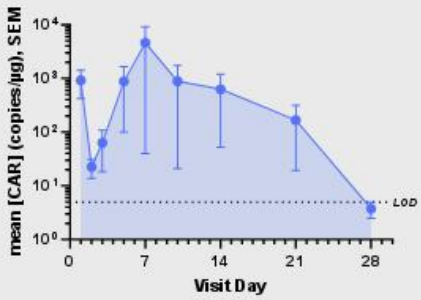
Patient Demographics and Pharmacokinetics

Data cutoff date: 26 April 2022

Patient characteristics, *All Dose Levels n = 18*	
Age, median years (range)	65 (39 – 78)
ECOG PS at screening, n (%)	
0	8 (44)
1	10 (56)
Prior lines of therapy, median n (range)	4 (1 – 8)
TCL subtype, n (%)	
PTCL	8 (44)
AITL	3 (17)
ALCL	1 (6)
ATLL	3 (17)
PTCL - NOS	1 (6)
CTCL (MF, SS, tMF)	10 (56)
Skin involvement, n (%)	12 (67)
Blood involvement, n (%)	6 (33)
Bone marrow involvement, n (%)	4 (22)
CD70 expression level, median % (range)	90 (20 – 100)
Second CTX130 infusion received, n (%)	5 (28)

Pharmacokinetics, *All Dose Levels n = 18*	
Peak expansion concentration (C_{max})*†, geometric mean copies/µg (range)	80.9 (<4.9 – 61,349.8)
Time to peak expansion (T_{max})†, median days (range)	8.5 (5 – 14)

Peak expansion concentration (C_{max})*† at DL4, n=5[1]



* For summary statistics of C_{max} values below the limit of detection (LOD) were imputed as half the LOD and values below the limit of quantification (LOQ) were imputed as (LOQ+LOD)/2. † From Screening to D28 post infusion.
[1] Includes first infusions only

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Safety

Data cutoff date: 26 April 2022

Adverse Events of Interest, N (%)

	DL1 $3x10^7$ N=4		DL2 $1x10^8$ N=4		DL3 $3x10^8$ N=5		DL4 $9x10^8$ N=5		DL≥3 N=10	
	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 (25)	-	1 (25)	-	4 (80)	-	4 (80)	-	**8 (80)**	**-**
ICANS	-	-	-	-	3 (60)	-	-	-	**3 (30)**	**-**
GvHD	-	-	-	-	-	-	-	-	**-**	**-**
Infections	2 (50)	1 (25)	-	1 (25)	2 (40)	1 (20)	1 (20)	1 (20)	**3 (30)**	**2 (20)**

All events listed in table are treatment-emergent adverse events.
CRS, cytokine release syndrome; DLT, dose-limiting toxicity; EBV, Epstein-Barr virus; Gr, grade; GvHD, graft versus host disease; HLH, hemophagocytic lymphohistiocytosis; ICANS, immune effector cell associated neurotoxicity syndrome; LDC, lymphodepleting chemotherapy; SAE, serious adverse events; TLS, tumor lysis syndrome.

- Acceptable safety profile across all DLs: no DLTs or instances of TLS with LDC or CTX130
- Treatment-emergent (TE) SAEs occurred in 10/18 (56%) patients and included Gr ≥3 infections (n=4, 22%), Gr 1-2 tumor hemorrhage, Gr ≥3 syncope, Gr ≥3 presyncope, Gr ≥3 HLH, Gr ≥3 drug eruption, and Gr 1-2 ligament sprain (n=1 each, 6%). With exception of one Gr 3 infection, all other TE SAEs were not found to be related to CTX130.
- There was a sudden death in 1 patient with William's syndrome in the context of a lung infection, deemed unrelated to CTX130
- Three cancers were diagnosed in patients with CTCL post treatment: 1 patient had EBV-associated lymphoma which resolved and a squamous cell carcinoma, 1 patient had invasive ductal breast carcinoma which was resected and cured. These were deemed unrelated to CTX130

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Efficacy

Data cutoff date: 26 April 2022

Best overall response, n (%)

Cell dose (CAR+ T cells)	DL1 $3x10^7$ N=4	DL2 $1x10^8$ N=4	DL3 $3x10^8$ N=5	DL4 $9x10^8$ N=5	DL≥3 N=10
Overall Response Rate (ORR)	2 (50)	0	3 (60)	4 (80)	**7 (70)**
CR	1 (25)	0	2 (40)*	1 (20)	**3 (30)**
PR	1 (25)	0	1 (20)	3 (60)	**4 (40)**
Disease Control Rate (DCR = CR + PR + SD)	3 (75)	1 (25)	5 (100)	4 (80)	**9 (90)**

	PTCL		CTCL	
	DL≥3 N=5	Total N=8	DL≥3 N=5	Total N=10
ORR	4 (80)	5 (63)	3 (60)	4 (40)
CR	2 (40)	3 (38)	1 (20)	1 (10)
PR	2 (40)	2 (25)	2 (40)	3 (30)
DCR	4 (80)	5 (63)	5 (100)	8 (80)

*1 patient in DL3 who initially achieved a PR was re-infused at DL4 following a change to SD and achieved a CR at DL4.
CAR, chimeric antigen receptor; CR, complete response; CTCL, cutaneous T cell lymphoma; DCR, disease control rate; DL, dose level; ORR, overall response rate; PR, partial response; PTCL, peripheral T cell lymphoma; SD, stable disease.

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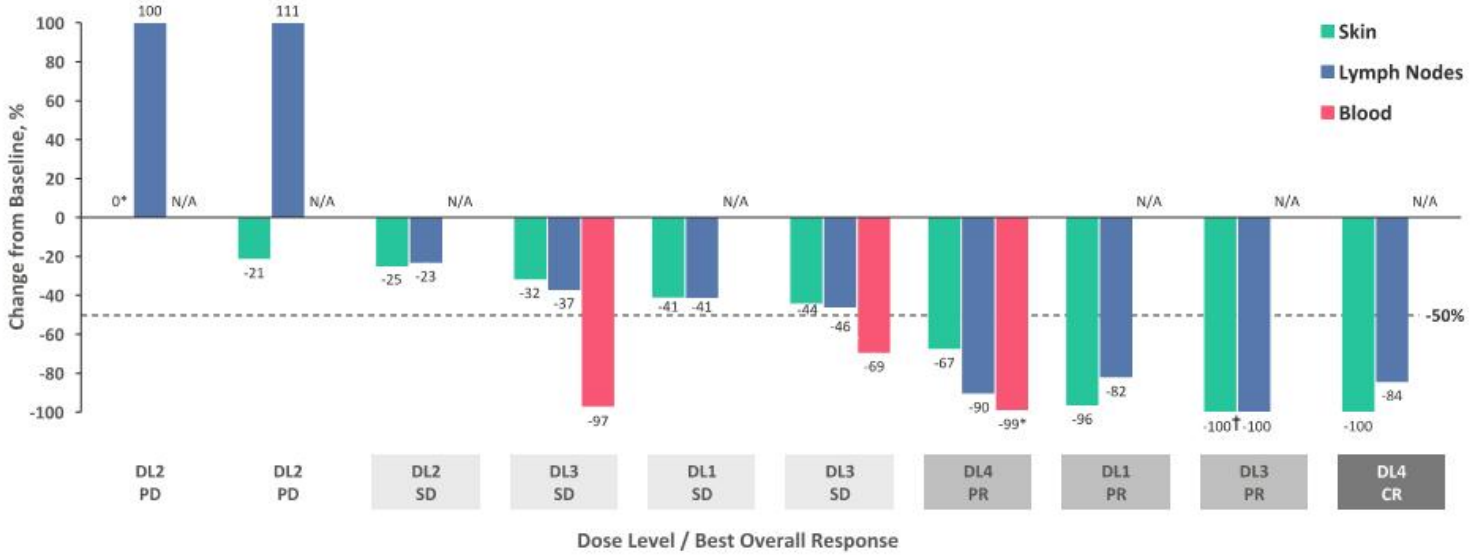
CTCL Responses Observed Across All Compartments



*Day 7 assessment; †Initially unconfirmed CR, later confirmed to be PR by mSWAT and biopsy.
CR, complete response; CTCL, cutaneous T cell lymphoma; DL, dose level; PR, partial response; SD, stable disease.

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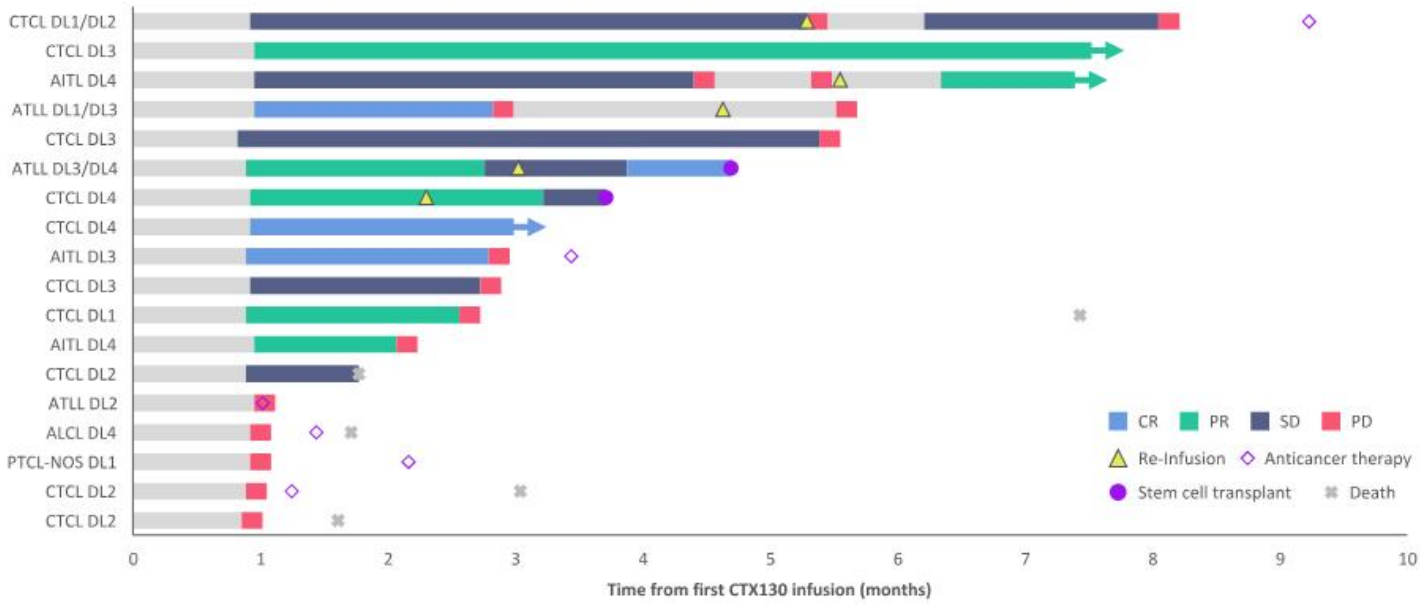
Efficacy (continued)



AITL, angioimmunoblastic T cell lymphoma; ALCL, anaplastic large cell lymphoma; ATLL, adult T-cell leukemia/lymphoma; CR, complete response; CTCL, cutaneous T cell lymphoma; DL, dose level; PD, progressive disease; PR, partial response; PTCL-NOS, peripheral T cell lymphoma not otherwise specified; SD, stable disease

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Case Study

Complete Response with Single-Infusion of CTX130

Subject Overview

Patient profile

- 47-year-old male with stage IVA2 transformed mycosis fungoides (tMF)
- 5 prior lines of therapy
- Refractory after last treatment with brentuximab vedotin
- CD70+ expression: 100% at baseline

Efficacy

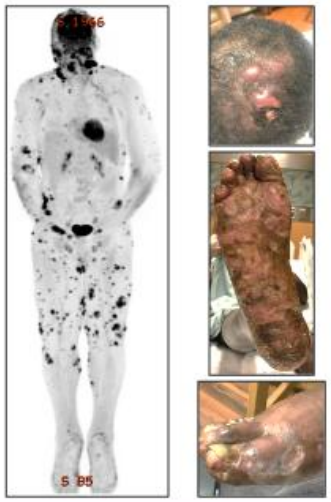
- CR at D28 after a single infusion of $9x10^8$ CAR+ T cells
- Remains in CR at Month 3

Safety

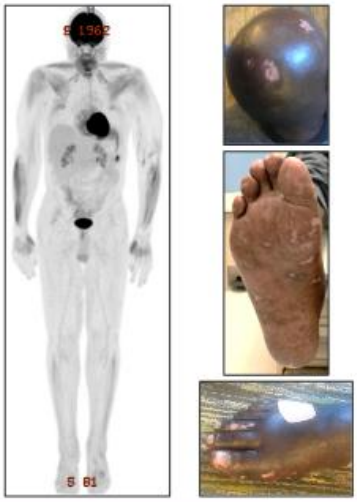
- Gr 3 anemia (D3) & Gr 3 neutropenia (D4)
- All other AEs were Gr 1

Response

Pre-Treatment | mSWAT = 84.74



Post-CTX130 (D18 skin, D28 PET) | mSWAT = 0



AE, adverse event; CAR, chimeric antigen receptor; CR, complete response; D, day; DL, dose level; Gr, grade; mSWAT; modified severity weight assessment tool.

Presented at the European Hematology Association Annual Meeting. 11 June 2022

Case Study

Complete Response at D28 After Re-Infusion

Subject Overview

Patient profile

- 54-year-old female with stage IV ATLL, with skin involvement
- 2 prior lines of therapy
- Refractory after last treatment with IFNα-b, zidovudine
- CD70+ expression: 100% (skin), 1% (lymph nodes) at baseline

Efficacy

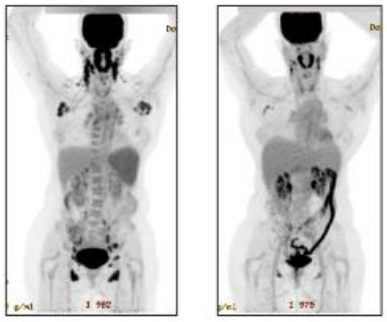
- PR at D28 after 1st infusion of $3x10^8$ CAR+ T cells and SD at Month 3
- CR at D28 after 2nd infusion with $9x10^8$ CAR+ T cells

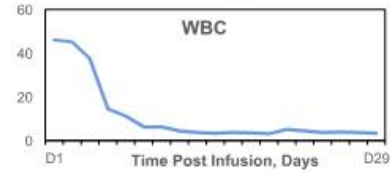
Safety

- Gr 4 neutropenia (D8 post 1st infusion, D5 post 2nd infusion)
- All other AEs Gr 1-2

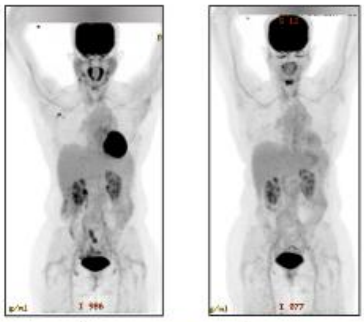
Response

1st Infusion (DL3) | D28 Assessment





2nd Infusion (DL4) | D28 Assessment



	Bone marrow	Skin
Before 1st infusion	25% ATLL with aberrant CD25+	mSWAT = 3.6
After 2nd infusion	1.3% aberrant cells, 0.1% of total	mSWAT = 0

AE, adverse event; ATLL, adult T-cell leukemia/lymphoma; CAR, chimeric antigen receptor; CR, complete response; D, day; DL, dose level; Gr, grade; IFN, interferon; mSWAT; modified severity weight assessment tool; PR, partial response; SD, stable disease.

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COBALT-LYM (NCT04502446) Study Sites

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