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): December 5, 2020

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**		**Not Applicable**
(Address of Principal Executive Offices)		**(Zip Code)**

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

Not Applicable
(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 (see General Instructions A.2. below):

☐ 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 December 5, 2020, CRISPR Therapeutics AG (the "Company") and its partner Vertex Pharmaceuticals Incorporated (together with its affiliates, "Vertex") issued a press release announcing new clinical data to be presented at the Plenary Scientific Session at the 62nd American Society of Hematology (ASH) Meeting and Exposition from two ongoing Phase 1/2 open-label clinical trials of CTX001™, an investigational CRISPR/Cas9 gene-editing therapy, in transfusion-dependent beta thalassemia, or TDT, and severe sickle cell disease, or SCD. A copy of the press release is attached hereto as Exhibit 99.1.

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

On December 6, 2020, new clinical data from two ongoing Phase 1/2 open-label clinical trials of CTX001 in TDT (CLIMB THAL-111) and severe SCD (CLIMB SCD-121) were presented during the Plenary Scientific Session at the ASH Meeting and Exposition by Dr. Haydar Frangoul, Medical Director of Pediatric Hematology and Oncology at Sarah Cannon Research Institute, HCA Healthcare's TriStar Centennial Medical Center. A copy of the slides used during the oral presentation is attached hereto as Exhibit 99.2 and is incorporated herein by reference.

In addition, on December 5, 2020, the Company and Vertex announced that 13 patients with TDT and six patients with SCD have been dosed with CTX001.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit Number	Description
99.1	Press release issued by CRISPR Therapeutics AG and Vertex Pharmaceuticals Incorporated, dated December 5, 2020
99.2	Presentation slides, dated December 6, 2020
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 hereunto duly authorized.

CRISPR THERAPEUTICS AG

Date: December 7, 2020

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

Exhibit 99.1

CRISPR Therapeutics and Vertex Present New Data for Investigational CRISPR/Cas9 Gene-Editing Therapy, CTX001™ at American Society of Hematology Annual Meeting and Exposition, Together With Publication in the New England Journal of Medicine

- Beta thalassemia: All seven patients were transfusion independent with 3 to 18 months of follow-up after CTX001 infusion -
- Sickle cell disease: All three patients were free of vaso-occlusive crises with 3 to 15 months of follow-up after CTX001 infusion -
- Nineteen patients have been dosed with CTX001 across both programs -
- *The New England Journal of Medicine* publishes CTX001 manuscript containing the first report of investigational use of CRISPR/Cas9-based gene editing to treat inherited diseases in humans -

ZUG, Switzerland and CAMBRIDGE, Mass. and BOSTON, December 5, 2020 – **CRISPR Therapeutics** (Nasdaq: CRSP) and **Vertex Pharmaceuticals Incorporated** (Nasdaq: VRTX) today announced new data on a total of 10 patients treated with the investigational CRISPR/Cas9-based gene-editing therapy, CTX001, that show a consistent and sustained response to treatment. All seven patients with transfusion-dependent beta thalassemia (TDT), including three who have either a severe or b0/b0 genotype, were transfusion independent at last follow-up and all three patients with sickle cell disease (SCD) were free of vaso-occlusive crises (VOCs) from CTX001 infusion through last follow-up. These data will be presented during the Scientific Plenary at the annual ASH Meeting and Exposition on December 6, 2020. A summary of the results from the CLIMB-111 and CLIMB-121 Phase 1/2 clinical studies is provided below.

The companies also announced that *The New England Journal of Medicine* (*NEJM*) has published an independently peer-reviewed article entitled “CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β Thalassemia.” The article includes detailed information on the first patient with TDT enrolled in CLIMB-111 and the first patient with severe SCD enrolled in CLIMB-121, at 18 and 15 months of follow-up, respectively.

CTX001 is being investigated in these two ongoing Phase 1/2 clinical trials as a potential one-time curative therapy for patients suffering from TDT and severe SCD.

“We are pleased with the data presented at ASH, which demonstrate potential benefit and durability among a larger population of patients with transfusion-dependent beta thalassemia and sickle cell disease,” said Samarth Kulkarni, Ph.D., Chief Executive Officer of CRISPR Therapeutics. “Additionally, the *NEJM* case study is the first peer-reviewed journal publication for our CRISPR/Cas9 gene therapy, CTX001. Together this is further validation of the potential of CTX001 to become a best-in-class therapy. We plan to continue the rapid advancement of our clinical trials to bring these much-needed therapies to patients.”

“These are the first published results from CRISPR/Cas9 therapy in people with a genetic disease and represent an important milestone in medicine and for our collaboration with CRISPR Therapeutics. Most importantly, these data represent a critical step in our effort to bring transformative and potentially curative therapies to patients,” said Reshma Kewalramani, M.D., Chief Executive Officer and President, Vertex. “With clinical proof-of-concept for both beta

thalassemia and sickle cell disease and 19 patients dosed, we look forward to continued efforts to bring our investigational treatment to patients living with TDT and SCD as quickly as we can."

"Our vision with this approach is to use the patient's own stem cells to provide a transformative treatment for these diseases, something almost unimaginable a few years ago," said Dr. Haydar Frangoul, M.D., Medical Director of Pediatric Hematology and Oncology at Sarah Cannon Research Institute, HCA Healthcare's TriStar Centennial Medical Center. "With these data in 10 patients, we can see the potential to fulfill this vision. With more data and longer duration of follow-up, we will hopefully confirm that we have a durable therapy that may transform the lives of many patients."

CLIMB-111 Trial in TDT: Updated Results
A total of 13 patients with TDT have been dosed with CTX001, including eight additional patients since the last update in June 2020.

The seven patients with TDT reported at ASH are patients who had reached at least three months of follow-up after CTX001 dosing and therefore could be assessed for initial safety and efficacy. All seven patients showed a similar pattern of response, with rapid and sustained increases in total hemoglobin, fetal hemoglobin and transfusion independence at last analysis.

All seven patients were transfusion independent with follow-up ranging from three to 18 months after CTX001 infusion, with normal to near normal total hemoglobin levels at last visit, including total hemoglobin from 9.7 to 14.1 g/dL and fetal hemoglobin from 40.9% to 97.7%.

Bone marrow allelic editing data collected from four patients with six months of follow-up and from one patient with 12 months of follow-up after CTX001 infusion demonstrated a durable effect.

The safety data from all seven patients were generally consistent with an autologous stem cell transplant and myeloablative conditioning. There were four serious adverse events (SAEs) considered related or possibly related to CTX001 reported in one patient: headache, hemophagocytic lymphohistiocytosis (HLH), acute respiratory distress syndrome and idiopathic pneumonia syndrome. All four SAEs occurred in the context of HLH and have resolved. The majority of non-serious adverse events were considered mild to moderate.

CLIMB-121 Trial in Severe SCD: Updated Results
A total of six patients with SCD have been dosed with CTX001, including four additional patients since the last update in June 2020.

The three patients reported at ASH are patients who had reached at least three months of follow-up after CTX001 dosing and therefore could be assessed for initial safety and efficacy. All three patients showed a similar pattern of response, with rapid and sustained increases in total hemoglobin and fetal hemoglobin, as well as elimination of VOCs through last analysis.

All three patients remained VOC-free with follow-up ranging from three to 15 months after CTX001 infusion and had hemoglobin levels in the normal to near normal range at last visit,

including total hemoglobin from 11.5 to 13.2 g/dL and fetal hemoglobin levels from 31.3% to 48.0%.

Bone marrow allelic editing data collected from one patient with six months of follow-up and from one patient with 12 months of follow-up after CTX001 infusion demonstrated a durable effect.

The safety data from all three patients were generally consistent with an autologous stem cell transplant and myeloablative conditioning. There were no SAEs considered related to CTX001, and the majority of non-serious adverse events were considered mild to moderate.

About CTX001
CTX001 is an investigational, autologous, *ex vivo* CRISPR/Cas9 gene-edited therapy that is being evaluated for patients suffering from TDT or severe SCD, in which a patient's hematopoietic stem cells are edited to produce high levels of fetal hemoglobin (HbF; hemoglobin F) in red blood cells. HbF is a form of the oxygen-carrying hemoglobin that is naturally present at birth, which then switches to the adult form of hemoglobin. The elevation of HbF by CTX001 has the potential to alleviate transfusion requirements for patients with TDT and reduce painful and debilitating sickle crises for patients with SCD.

Based on progress in this program to date, CTX001 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. CTX001 has also been granted Orphan Drug Designation from the European Commission for both TDT and SCD, as well as Priority Medicines (PRIME) designation from the European Medicines Agency (EMA) for SCD.

CTX001 is being developed under a co-development and co-commercialization agreement between CRISPR Therapeutics and Vertex. Among gene-editing approaches being investigated/evaluated for TDT and SCD, CTX001 is the furthest advanced in clinical development.

About CLIMB-111
The ongoing Phase 1/2 open-label trial, CLIMB-Thal-111, is designed to assess the safety and efficacy of a single dose of CTX001 in patients ages 12 to 35 with TDT. The trial will enroll up to 45 patients and follow patients for approximately two years after infusion. Each patient will be asked to participate in a long-term follow-up trial.

About CLIMB-121
The ongoing Phase 1/2 open-label trial, CLIMB-SCD-121, is designed to assess the safety and efficacy of a single dose of CTX001 in patients ages 12 to 35 with severe SCD. The trial will enroll up to 45 patients and follow patients for approximately two years after infusion. Each patient will be asked to participate in 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, CTX001, will then be infused back into the patient as part of a stem cell transplant, a process which involves, among other things, a patient being treated with myeloablative busulfan conditioning. Patients undergoing stem cell transplants may also encounter side effects (ranging from mild to severe) that are unrelated to the administration of CTX001. 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 CTX001 on multiple measures of disease and for safety.

About the CRISPR-Vertex Collaboration
CRISPR Therapeutics and Vertex 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. CTX001 represents the first potential treatment to emerge from the joint research program. CRISPR Therapeutics and Vertex will jointly develop and commercialize CTX001 and equally share all research and development costs and profits worldwide.

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, including statements made by Dr. Kulkarni, Dr. Kewalramani and Dr. Frangoul 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 CRISPR Therapeutics’ various clinical programs including CTX001; (ii) the status of clinical trials (including, without limitation, the expected timing of data releases) related to product candidates under development by CRISPR Therapeutics and its collaborators, including expectations regarding the data that are being presented in this press release, at the annual ASH Meeting and Exposition, and in the NEJM article; (iii) the expected benefits of CRISPR Therapeutics’ collaborations; and (iv) 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. 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: that preliminary data from any clinical trial and initial data from a limited number of patients (as is the case with CTX001 at this time) may not be indicative of final or future trial results; that CTX001 clinical trial results may not be favorable or may not support registration or further development; potential impacts due to the coronavirus pandemic, such as to the timing and progress of clinical trials; that future competitive or other market factors may adversely affect the commercial potential for CTX001; uncertainties regarding the intellectual property protection for CRISPR Therapeutics' technology; 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.

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 medicines in other serious diseases where it has deep insight into causal human biology, including pain, alpha-1 antitrypsin deficiency and APOL1-mediated kidney diseases. In addition, Vertex has a rapidly expanding pipeline of genetic and cell therapies for diseases such as sickle cell disease, beta thalassemia, Duchenne muscular dystrophy and type 1 diabetes mellitus.

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 11 consecutive years on Science magazine's Top Employers list and a best place to work for LGBTQ equality by the Human Rights Campaign. 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.

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, including, without limitation, statements made by Dr. Samarth Kulkarni, Dr. Reshma Kewalramani and Dr. Haydar Frangoul in this press release and statements regarding the expectations and plans to present data at the annual ASH Meeting and Exposition, the development, including expected timeline for development, updated data on patients treated to

date and new data on additional patients, and the potential benefits and curative therapy of CTX001, our plans and expectations for our clinical trials and clinical trial sites, including statements regarding patient enrollment, and the status of our clinical trials of our product candidates under development by us and our collaborators, including activities at the clinical trial sites and potential outcomes. 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, efficacy, or other reasons, that the COVID-19 pandemic may impact the status or progress of our clinical trials and clinical trial sites and the clinical trials and clinical trial sites of our collaborators, including patient enrollment, 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 at www.sec.gov and available through the company's website at www.vrtx.com. 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.

(VRTX-GEN)

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Exhibit 99.2

Safety and Efficacy of CTX001™ in Patients With Transfusion-Dependent β-Thalassemia or Sickle Cell Disease: Early Results From the CLIMB THAL-111 and CLIMB SCD-121 Studies of Autologous CRISPR-CAS9-Modified CD34+ Hematopoietic Stem and Progenitor Cells

Haydar Frangoul, Yael Bobruff, Maria Domenica Cappellini, Selim Corbacioglu, Christine Marie Fernandez, Josu de la Fuente, Stephan Grupp, Rupert Handgretinger, Tony W. Ho, Suzan Imren, Antonis Kattamis, Julie Lekstrom-Himes, Franco Locatelli, Yimeng Lu, Markus Mapara, Sarah Mulcahey, Mariane de Montalembert, Damiano Rondelli, Niraj Shanbhag, Sujit Sheth, Sandeep Soni, Martin H. Steinberg, Michael Weinstein, John Wu, Donna Wall

62nd Annual American Society of Hematology Meeting
December 6, 2020

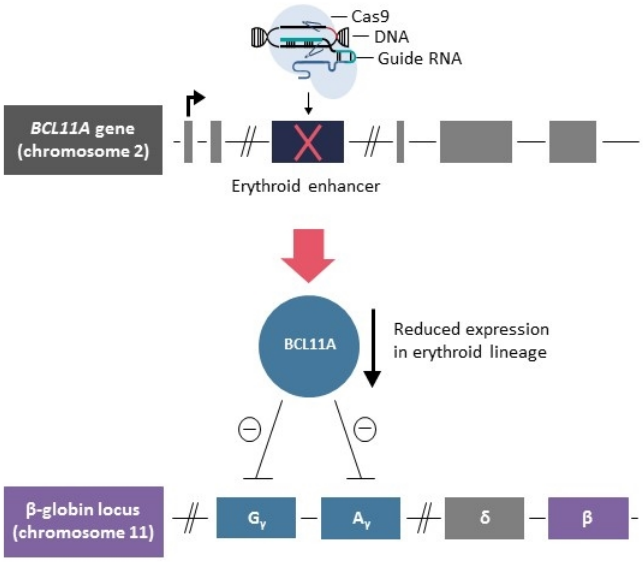
Studies in Patients With Transfusion-dependent β-Thalassemia (TDT) and Sickle Cell Disease (SCD) Are Ongoing

	CLIMB THAL-111	CLIMB SCD-121
Design	Phase 1 / 2, international, multicenter, open-label, single-arm study (NCT03655678)	Phase 1 / 2, international, multicenter, open-label, single-arm study (NCT03745287)
Target enrollment	45 patients aged 12 to 35 years with TDT, including β^0 / β^0 genotypes, defined as a history of at least 100 mL/kg/year or 10 units/year of pRBC transfusions in the previous 2 years	45 patients aged 12 to 35 years with severe SCD and a history of ≥2 vaso-occlusive crises per year over the previous 2 years
Primary endpoints	Proportion of patients achieving sustained transfusion reduction of 50% for at least 6 months starting 3 months after CTX001 infusion	Proportion of patients with HbF ≥20% sustained for at least 3 months starting 6 months after CTX001 infusion

Here, we present safety and efficacy results from the first 10 patients infused with CTX001

HbF: fetal hemoglobin; pRBC: packed red blood cell; SCD: sickle cell disease; TDT: transfusion-dependent β-thalassemia.

CRISPR-Cas9-Mediated Editing of *BCL11A* Increases HbF Levels[1]

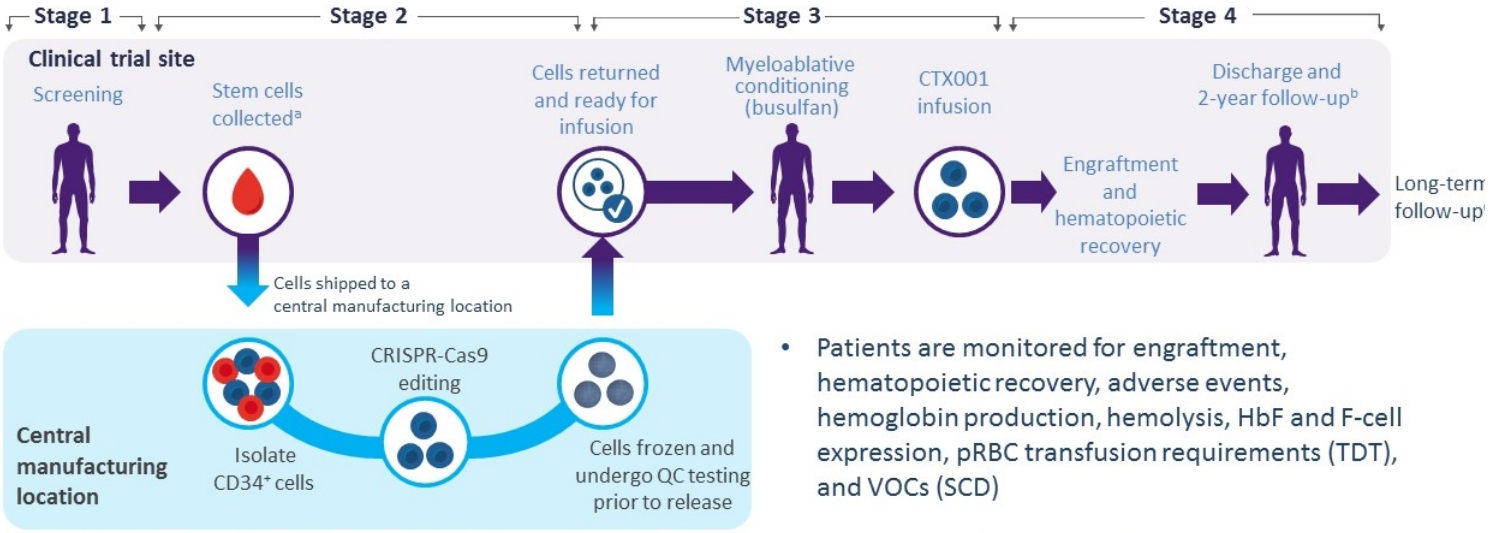


- Naturally occurring genetic polymorphisms in *BCL11A* are associated with elevated HbF and decreased severity of TDT and SCD[2-4]
- BCL11A suppresses expression of HbF
- Editing of *BCL11A* results in reactivation of γ-globin expression and formation of HbF ($\alpha 2\gamma 2$) in mouse models
- CTX001 is produced using ex vivo editing of the erythroid enhancer region of *BCL11A* in $CD34^+$ HSPCs and reduces erythroid-specific expression of BCL11A
- Infusion of CTX001 leads to an increase in HbF levels in erythroid cells in vivo

HbF: fetal hemoglobin; HSPCs: hematopoietic stem progenitor cells; SCD: sickle cell disease; TDT: transfusion-dependent β-thalassemia.

1. Figure modified from Canver MC, Orkin SH. *Blood*. 2016;127:2536-2545; 2. Murray N, et al. *Br J Haematol*. 1988;69:89-92; 3. Conley CL, et al. *Blood*. 1963;21:261-281; 4. Bank A. *Blood*. 2006;107:435-443.

CTX001 Infusion Process



- Patients are monitored for engraftment, hematopoietic recovery, adverse events, hemoglobin production, hemolysis, HbF and F-cell expression, pRBC transfusion requirements (TDT), and VOCs (SCD)

F-cell: HbF-containing cell; HbF: fetal hemoglobin; pRBC: packed red blood cell; SCD: sickle cell disease; TDT: transfusion-dependent β-thalassemia; QC: quality control; VOCs: vaso-occlusive crises.
[a]Patients enrolled in CLIMB THAL-111 received a combination of plerixafor and filgrastim for mobilization, while patients enrolled in CLIMB SCD-121 received plerixafor only. Back-up cells kept at site as a safety measure; [b]Patients will be followed for 24 months after CTX001 infusion with physical exams, laboratory and imaging assessments, and adverse-event evaluations; [c]All patients who receive CTX001 will be followed for 15 years in a long-term follow-up study (NCT04208529) after completion or withdrawal from CLIMB THAL-111 or CLIMB SCD-121.

TDT: Patient Baseline and Treatment Characteristics

Patients with ≥3-month follow-up (n=7)

Patient characteristics		
Genotype, n	**β^+ / β^+**	**2**
	β^0 / β^+ (not IVS-I-110)	**2**
	β^0 / β^+ (IVS-I-110)[a]	**2**
	β^0 / β^0	**1**
Gender, Female/Male, n		**5/2**
Age at consent, years Median (range)		**23** (19 – 26)
Pre-study pRBC transfusions[b]		
Units/year, median (range)		**33.0** (23.5–61.0)
Transfusions episodes/year, median (range)		**15.0** (12.5–16.5)

Treatment characteristics	Median (range)
Drug product cell dose, $CD34^+$ cells × 10^6/kg	**11.6** (4.5 – 16.6)
Neutrophil engraftment,[c] Study Day[d]	**32** (20 – 39)
Platelet engraftment,[e] Study Day[d]	**37** (29 – 52)
Duration of follow-up, Months	**8.9** (3.8 – 21.5)

pRBC: packed red blood cell; TDT: transfusion-dependent β-thalassemia.

[a]IVS-I-110 phenotype is severe and similar to β^0 / β^0; [b]Annualized number during the 2 years before consenting to study participation; [c]Defined as the first day of 3 measurements of absolute neutrophil count ≥500 cells/μL on 3 consecutive days; [d]Study day defined as day after CTX001 infusion; [e]Defined as the first day of 3 consecutive measurements of platelet count ≥20,000/μL on 3 different days after CTX001 infusion, without a platelet transfusion in the past 7 days.

TDT: Summary of Adverse Events

Patients with ≥3-month follow-up (n=7)

AEs were generally consistent with myeloablation and autologous stem cell transplant

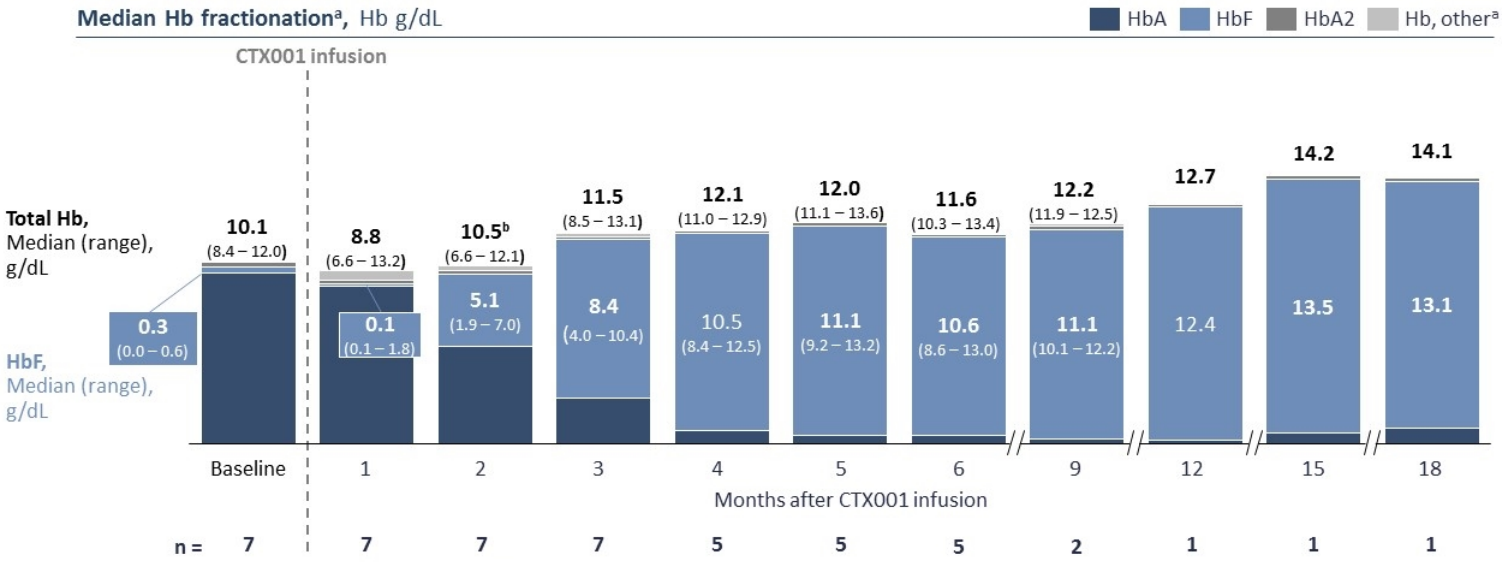
Months of follow-up, median (range)	8.9 (3.8–21.5)	
	Patients with non-serious AEs, n	**Patients with SAEs, n**
Relationship[a]		
Related to plerixafor and/or G-CSF	6	0
Related to busulfan only	7	2
Related to CTX001 only	1[b]	1
Related to busulfan and CTX001	3[c]	1
Not related to any study drug	7	4

- Majority of AEs occurred within first 60 days after CTX001 infusion
- 2 patients experienced a combined total of 5 SAEs related or possibly related to busulfan only: venoocclusive liver disease (in both patients), febrile neutropenia (2 events in 1 patient), and colitis; all resolved
- One patient experienced 4 SAEs related or possibly related to CTX001: headache, haemophagocytic lymphohistiocytosis (HLH), acute respiratory distress syndrome, and idiopathic pneumonia syndrome (latter also related to busulfan). All SAEs occurred in the context of HLH and have resolved.
- No CTX001-related SAEs were reported in the other patients

AEs: adverse events; G-CSF: granulocyte colony-stimulating factor; SAEs: serious adverse events.

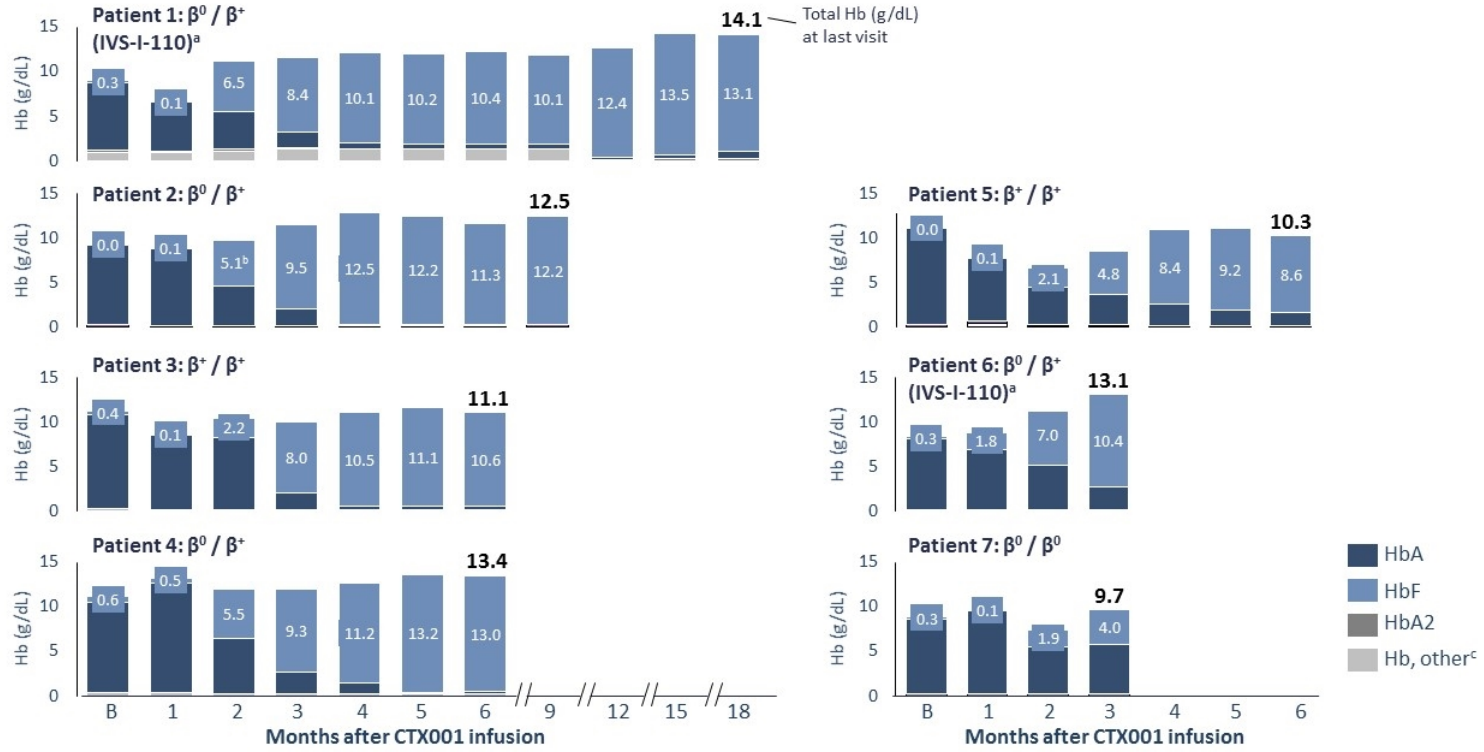
[a]Includes related and possibly related AEs. [b]1 patient experienced a non-serious AE of anaemia possibly related to CTX001 (resolved). [c]3 patients experienced non-serious AEs related or possibly related to busulfan and CTX001: petechiae, pyrexia, epistaxis, lymphocyte count decreased, neutrophil count decreased, WBC count decreased, and platelet count decreased.

TDT: Clinically Meaningful HbF and Total Hb Are Achieved Early and Maintained



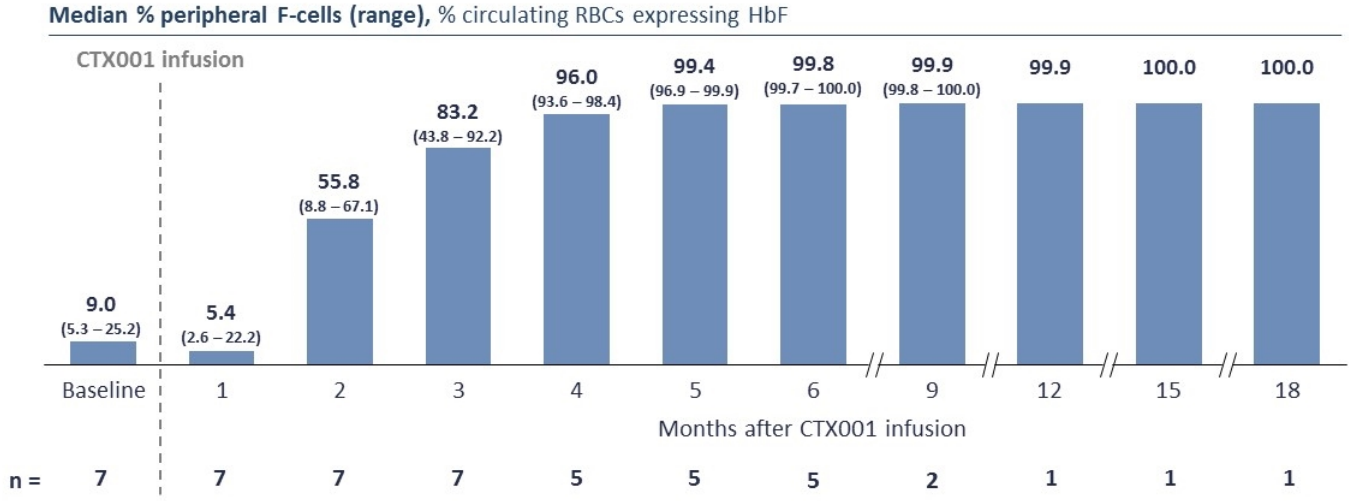
Hb: hemoglobin; HbA: adult hemoglobin; HbF: fetal hemoglobin; TDT: transfusion-dependent β-thalassemia.
[a]Hb adducts and other variants. [b] With respect to Patient 2, Total Hb from local laboratory and Hb fraction from central laboratory.

TDT: Early, Sustained Increases in Total Hb & HbF Across Genotypes



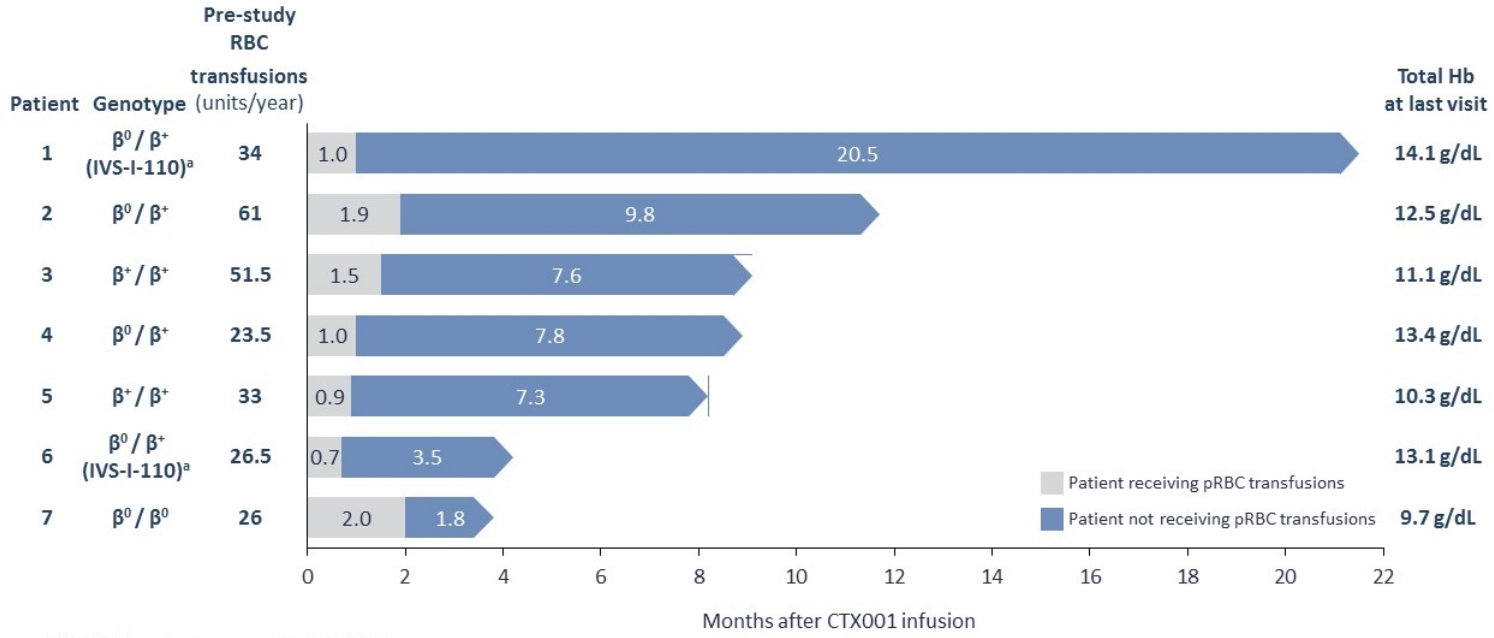
B: Baseline, Hb: hemoglobin; HbA: adult hemoglobin; HbF: fetal hemoglobin; TDT: transfusion-dependent β-thalassemia. [a]Total Hb from local laboratory and Hb fraction from central laboratory.
[a]IVS-I-110 phenotype is severe and similar to β⁰ / β⁰ [c]Hb adducts and other variants

TDT: Pancellular Expression of HbF Is Maintained



F-cells: HbF-containing cells; HbF: fetal hemoglobin; RBCs: red blood cells; TDT: transfusion-dependent β-thalassemia.

TDT: Duration of Transfusion Independence After CTX001



[a]IVS-I-110 phenotype is severe and similar to β^0 / β^0.
Hb: hemoglobin; pRBC: packed red blood cell; RBC: red blood cell; TDT: transfusion-dependent β-thalassemia.

SCD: Patient Baseline and Treatment Characteristics

Patients with ≥3-month follow-up (n=3)

Patient characteristics		
Genotypes, n	β^S / β^S	**3**
Gender, Female/Male, n		**2/1**
Age at consent, years Median (range)		**22** (22 – 33)
Pre-study VOCs VOCs/year[a], Median (range)		**7** (4.0 – 7.5)

Treatment characteristics	Median (range)
Drug product cell dose,[b] $CD34^+$ cells × 10^6/kg	**3.8** (3.1 – 3.9)
Neutrophil engraftment,[c] Study Day[d]	**22** (17 – 30)
Platelet engraftment,[e] Study Day[d]	**30** (30 – 33)
Duration of follow-up, Months	**7.8** (3.8 – 16.6)

SCD: sickle cell disease; VOCs: vaso-occlusive crises.

[a]Annualized rate during the 2 years before consenting to study participation; [b]Across multiple drug product lots per patient; [c]Defined as the first day of 3 measurements of absolute neutrophil count ≥500 cells/µL on 3 consecutive days; [d]Study day defined as day after CTX001 infusion [e]Defined as the first day of 3 consecutive measurements of platelet count ≥50,000/µL on 3 different days after CTX001 infusion, without a platelet transfusion in the past 7 days.

SCD: Summary of Adverse Events

Patients with ≥3-month follow-up (n=3)

AEs were generally consistent with myeloablation and autologous stem cell transplant

Months of follow-up, *median (range)*	7.8 (3.8 – 16.6)	
	Patients with non-serious AEs, n	**Patients with SAEs, n**
Relationship[a]		
Related to plerixafor only	3	1
Related to busulfan only	3	1
Related to CTX001 only	0	0
Related to busulfan and CTX001	2[b]	0
Not related to any study drug	3	2

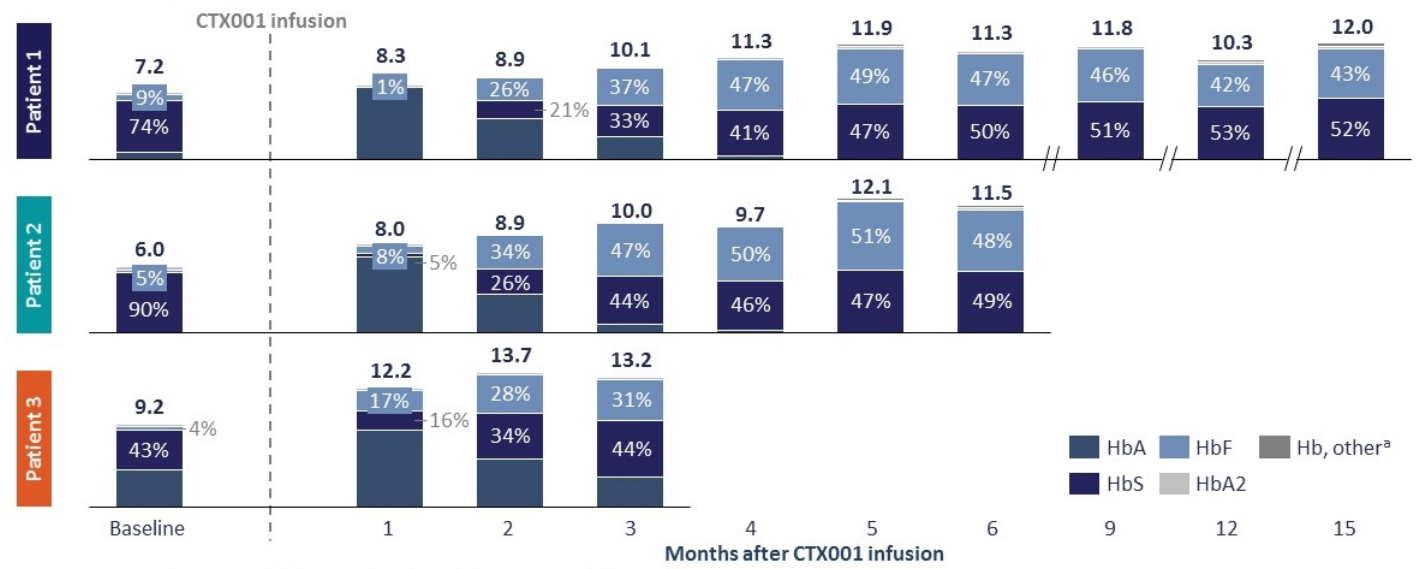
- Majority of AEs occurred within first 60 days after CTX001 infusion
- 1 patient experienced SAEs related to plerixafor: chest pain, neck pain, headache, and abdominal pain; all resolved
- Post-CTX001, only 1 patient experienced SAEs: sepsis (related to busulfan), cholelithiasis, and abdominal pain (both unrelated to any study drug); all resolved
- There were no SAEs related to CTX001

AEs: adverse events; SAEs: serious adverse events.

[a]Includes related and possibly related AEs. [b]2 patients experienced non-serious AEs related or possibly related to busulfan and CTX001: lymphopenia and dermatitis.

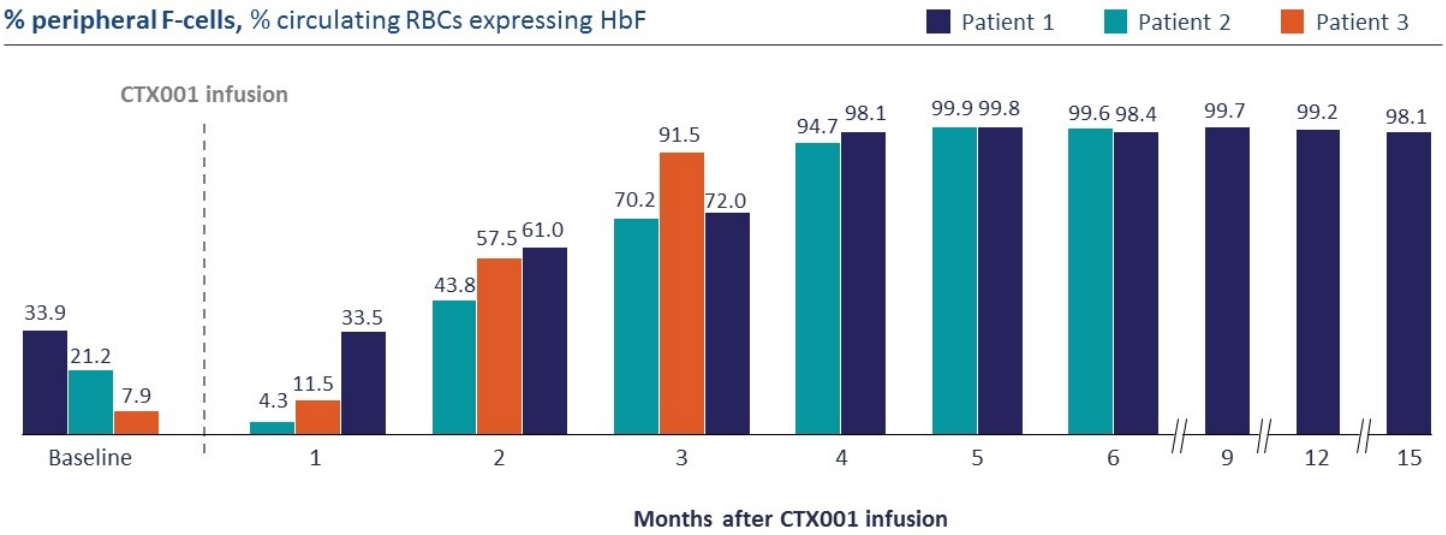
SCD: Clinically Meaningful HbF and Total Hb Are Achieved Early and Maintained

Hb fractionation[a], Hb g/dL



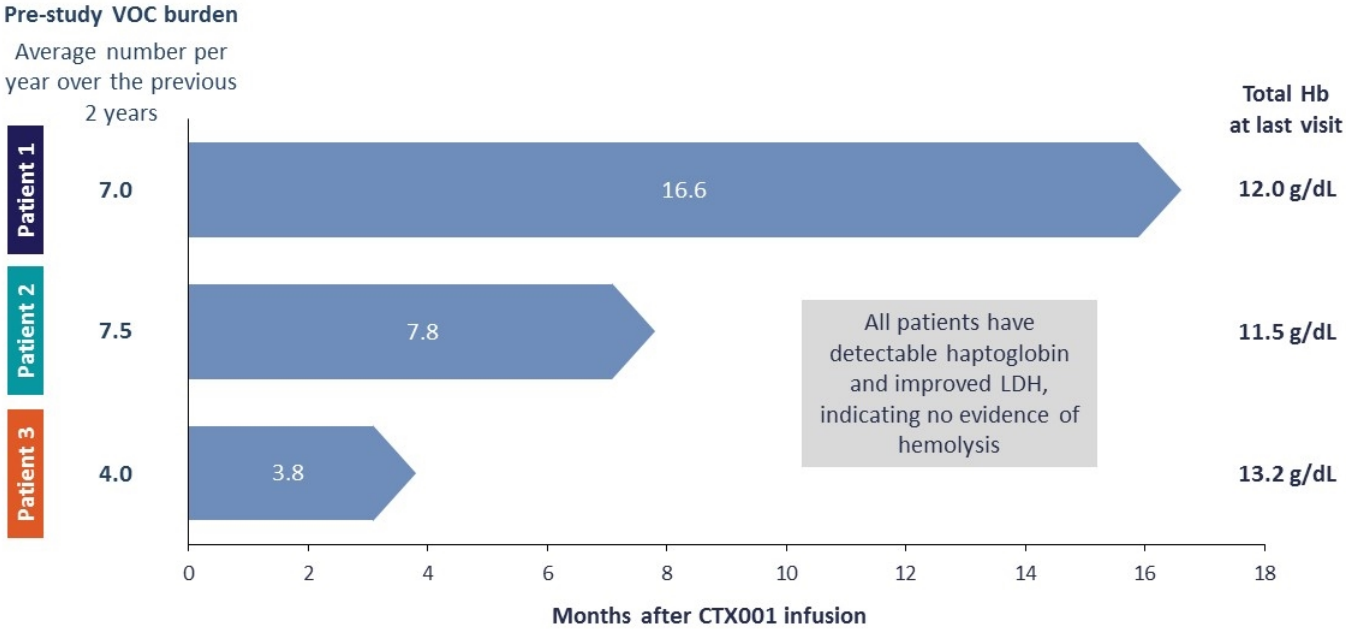
Hb: hemoglobin; HbA: adult hemoglobin; HbF: fetal hemoglobin; HbS: sickle hemoglobin; SCD: sickle cell disease.
[a]Hb adducts and other variants.

SCD: Pancellular HbF Expression is Maintained



F-cells: HbF-containing cells; HbF: fetal hemoglobin; RBCs: red blood cells; SCD: sickle cell disease.

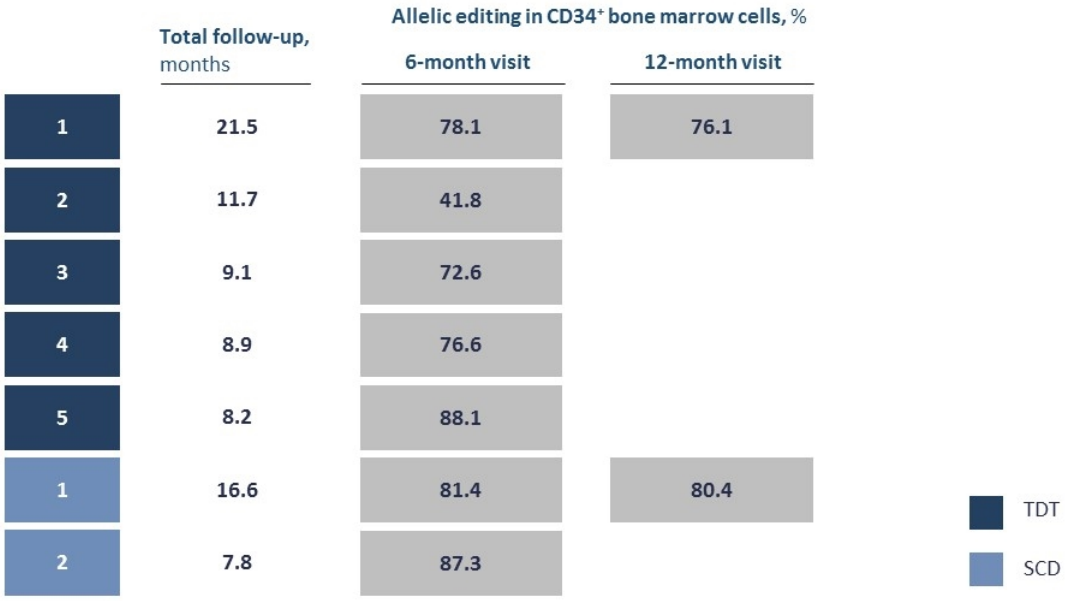
SCD: Duration VOC-free After CTX001



SCD: sickle cell disease; VOCs: vaso-occlusive crises.

Durable *BCL11A* Editing Observed in Bone Marrow CD34⁺ Cells

Patients with ≥6-month follow-up (n=5 TDT patients, n=2 SCD patients)[a]



SCD: sickle cell disease; TDT: transfusion-dependent β-thalassemia.

[a]Bone marrow editing assessments performed starting at 6 months, 12 months, and 24 months of follow-up.

Conclusions

The first 10 patients treated with CTX001 have been followed for 3.8 to 21.5 months and have stopped transfusions (TDT) and are VOC-free (SCD)

- Overall safety profile is generally consistent with myeloablative conditioning and autologous bone marrow transplant
- Clinically meaningful HbF and total hemoglobin levels are observed early and maintained across all 10 patients
- Clinical proof-of-concept for CTX001 has now been demonstrated for both TDT and SCD
- These data demonstrate that CTX001 is a potential functional cure for the treatment of TDT and SCD

HbF: fetal hemoglobin; SCD: sickle cell disease; TDT: transfusion-dependent β-thalassemia; VOCs: vaso-occlusive crises.

Thank You to Study Participants and Their Families

CLIMB THAL-111 and CLIMB SCD-121 sites

Both

- Lucille Packard Children's Hospital of Stanford University, Palo Alto
- Columbia University Medical Center, New York
- The Children's Hospital at TriStar Centennial Medical Center / Sarah Cannon Center for Blood Cancers, Nashville
- The Hospital for Sick Children, Toronto
- Regensburg University Hospital, Clinic and Polyclinic for Paediatric and Adolescent Medicine, Paediatric Haemotology, Oncology and Stem Cell Transplantation
- Dipartimento di Onco-Ematologia e Terapia Cellulare e Genica Ospedale Pediatrico Bambino Gesù – IRCCS, Rome
- Imperial College Healthcare, London

SCD-121

- University of Illinois at Chicago Hospitals and Health Systems
- Children's Hospital of Philadelphia
- St. Jude Children's Research Hospital, Memphis
- Methodist Children's Hospital / Texas Transplant Institute, San Antonio
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THAL-111

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