



**CRISPR**  
THERAPEUTICS

The logo consists of the word "CRISPR" in a bold, black, sans-serif font, with "THERAPEUTICS" in a smaller, all-caps, black, sans-serif font below it. The text is white and set against a black rectangular background.



A photograph of a woman with a colorful patterned headscarf hugging a young girl from behind. The girl is smiling and holding a blue cloth to her mouth. The background is blurred, showing an indoor setting with a couch.

# Creating transformative gene-based medicines for serious diseases

Corporate Overview | April 2021

# Forward-Looking Statements



*The presentation and other related materials may contain a number of “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including statements regarding CRISPR Therapeutics’ expectations about any or all of the following: (i) the safety, efficacy and clinical progress of our various clinical programs; (ii) the status of clinical trials (including, without limitation, the expected timing of data releases, filing of clinical trial applications and INDs, any approvals thereof and the timing of commencement of clinical trials), development timelines and discussions with regulatory authorities related to product candidates under development by CRISPR Therapeutics and its collaborators; (iii) expectations regarding the data that is being presented; (iv) the number of patients that will be evaluated, the anticipated date by which enrollment will be completed and 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; (v) the intellectual property coverage and positions of CRISPR Therapeutics, its licensors and third parties as well as the status and potential outcome of proceedings involving any such intellectual property; (vi) the sufficiency of CRISPR Therapeutics’ cash resources; and (vii) 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, forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: the potential for initial and preliminary data from any clinical trial and initial data from a limited number of patients not to be indicative of final trial results; the potential that the outcomes for each of CRISPR Therapeutics’ planned clinical trials and studies may not be favorable; that one or more of CRISPR Therapeutics’ internal or external product candidate programs will not proceed as planned for technical, scientific or commercial reasons; that future competitive or other market factors may adversely affect the commercial potential for CRISPR Therapeutics’ product candidates; uncertainties inherent in the initiation and completion of preclinical studies for CRISPR Therapeutics’ product candidates; availability and timing of results from preclinical studies; whether results from a preclinical trial will be predictive of future results of the future trials; uncertainties about regulatory approvals to conduct trials or to market products; potential impacts due to the coronavirus pandemic; 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](http://www.sec.gov). Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. CRISPR Therapeutics disclaims any obligation or undertaking to update or revise any forward-looking statements contained in this presentation, other than to the extent required by law.*

*CRISPR THERAPEUTICS® standard character mark and design logo, CTX001™, CTX110™, CTX120™, and CTX130™ are trademarks and registered trademarks of CRISPR Therapeutics AG. All other trademarks and registered trademarks are the property of their respective owners.*

# CRISPR Therapeutics Highlights



Leading gene editing company focused on translating revolutionary CRISPR/Cas9 technology into transformative therapies



**Advancing CRISPR in the clinic** with CTX001™ in  $\beta$ -thalassemia and sickle cell disease



**Next-generation immuno-oncology platform** underlying wholly-owned, potentially best-in-class gene-edited allogeneic cell therapies CTX110™, CTX120™ and CTX130™



**Enabling regenerative medicine 2.0** with CRISPR/Cas9-edited allogeneic stem cells



**Advancing *in vivo* applications** based on in-licensed technologies, platform improvement and strategic partnerships

# The CRISPR/Cas9 Revolution

A **SPECIFIC**, **EFFICIENT** and **VERSATILE** tool for editing genes



**Disrupt**



**Delete**



**Correct or Insert**

*“If scientists can dream of a genetic manipulation,  
CRISPR can now make it happen”*

**Science**

# Our Pipeline



PROGRAM	RESEARCH	IND-ENABLING	CLINICAL	MARKETED	STATUS	PARTNER	STRUCTURE
Hemoglobinopathies							
CTX001™: β-thalassemia	<div><div></div><div></div><div></div><div></div></div>				Enrolling	VERTEX	Collaboration
CTX001™: Sickle cell disease (SCD)	<div><div></div><div></div><div></div><div></div></div>				Enrolling		Collaboration
Immuno-oncology							
CTX110™: Anti-CD19 allogeneic CAR-T	<div><div></div><div></div><div></div><div></div></div>				Enrolling		Wholly-owned
CTX120™: Anti-BCMA allogeneic CAR-T	<div><div></div><div></div><div></div><div></div></div>				Enrolling		Wholly-owned
CTX130™: Anti-CD70 allogeneic CAR-T	<div><div></div><div></div><div></div><div></div></div>				Enrolling		Wholly-owned
Regenerative medicine							
Type I diabetes mellitus	<div><div></div><div></div><div></div><div></div></div>				PhI/II in 2021	VIACYTE®	Collaboration
In vivo approaches							
Glycogen storage disease Ia (GSD Ia)	<div><div></div><div></div><div></div><div></div></div>					VERTEX	Wholly-owned
Duchenne muscular dystrophy (DMD)	<div><div></div><div></div><div></div><div></div></div>						License
Myotonic dystrophy type 1 (DM1)	<div><div></div><div></div><div></div><div></div></div>						Collaboration
Cystic fibrosis (CF)	<div><div></div><div></div><div></div><div></div></div>						License

Additional undisclosed, early stage programs subject to collaboration or license agreements with Vertex and Bayer



# Hemoglobinopathies – Devastating Blood Diseases

## Sickle Cell Disease (SCD) and $\beta$ -Thalassemia

Blood disorders caused by mutations  
in the  $\beta$ -globin gene



Sickled



Normal Cell



Thalassemic

Significant worldwide burden

ANNUAL BIRTHS

300K

SCD



60K

$\beta$ -thalassemia

High morbidity and mortality



Anemia

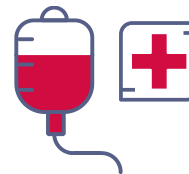


Pain



Early death

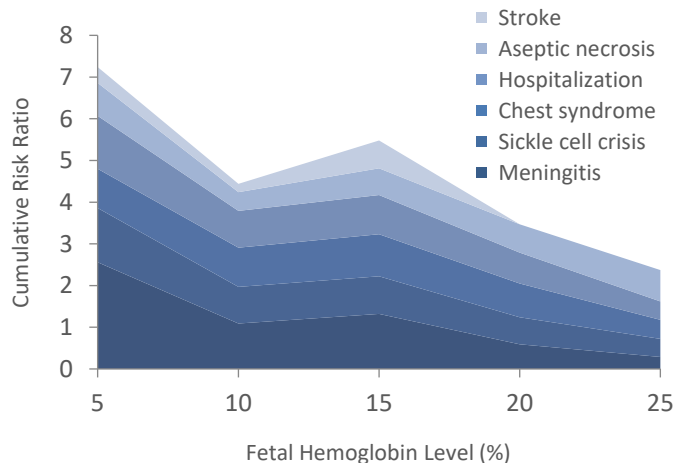
Heavy burden of patient care



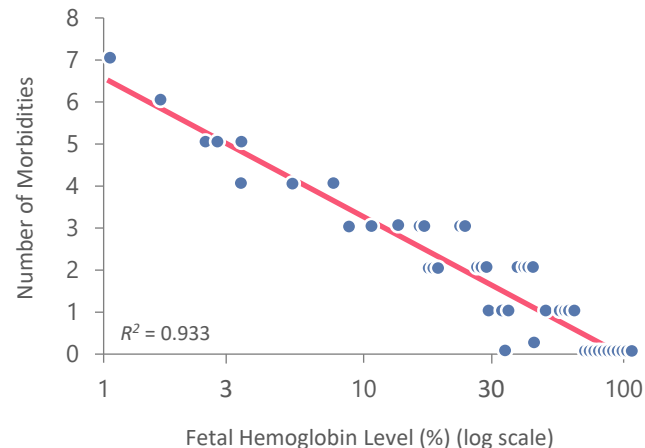
Frequent transfusions and hospitalizations

# Our Approach – Upregulating Fetal Hemoglobin

## Symptoms in SCD and $\beta$ -Thalassemia Decrease as HbF Level Increases



Powars, et al. Blood 1984



Musallam, et al. Blood 2012

- **Naturally occurring genetic variants** cause a condition known as **hereditary persistence of fetal hemoglobin (HPFH)**, which **leads to reduced or no symptoms** in patients with SCD and  $\beta$ -thalassemia
- **Our gene editing strategy aims to mimic these variants in symptomatic patients**, an approach supported by well-understood genetics

# Pioneering CRISPR Trials



Design	Phase 1/2, international, multi-center, open-label, single arm studies to assess the safety and efficacy of CTX001 in patients with transfusion-dependent $\beta$ -thalassemia and (TDT) and SCD, respectively	
Target enrollment	45 patients aged 12 - 35 years with TDT, including $\beta^0 / \beta^0$ 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 - 35 years with severe SCD and a history of $\geq 2$ vaso-occlusive crises/year over the previous two years
Primary endpoint	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 $\geq 20\%$ , sustained for at least 3 months starting 6 months after CTX001 infusion

**Potential to expand into registrational trials**, as well as into additional age cohorts, if supported by safety and efficacy



# TDT: Patient Baseline and Treatment Characteristics

Patients with  $\geq 3$ -month follow-up (n=7)

## Patient baseline

	n
<b>Genotype</b>	$\beta^+ / \beta^+$
	$\beta^0 / \beta^+$ (not IVS-I-110)
	$\beta^0 / \beta^+$ (IVS-I-110) <sup>1</sup>
	$\beta^0 / \beta^0$
<b>Gender</b>	
Female/Male	5/2
<b>Median (range)</b>	
<b>Age at consent</b>	
Years	23 (19-26)
<b>Pre-study pRBC transfusions<sup>2</sup></b>	
Units/year	33.0 (23.5-61.0)
Transfusion episodes/year	15.0 (12.5-16.5)

## Treatment characteristics

	Median (range)
<b>Drug product cell dose</b>	
CD34+ cells x 10 <sup>6</sup> /kg	11.6 (4.5-16.6)
<b>Neutrophil engraftment<sup>3</sup></b>	
Study day <sup>4</sup>	32 (20-39)
<b>Platelet engraftment<sup>5</sup></b>	
Study day <sup>4</sup>	37 (29-52)
<b>Duration of follow-up</b>	
Months	8.9 (3.8-21.5)

Data disclosed December 5, 2020

(1) IVS-I-110 phenotype is severe and similar to  $\beta^0 / \beta^0$ ; (2) Annualized number during the 2 years before consenting to study participation; (3) Defined as the first day of 3 measurements of absolute neutrophil count  $\geq 500$  cells/ $\mu$ L on 3 consecutive days; (4) Study day defined as day after CTX001 infusion; (5) Defined as the first day of 3 consecutive measurements of platelet count  $\geq 20,000$ / $\mu$ L on 3 different days after CTX001 infusion, without a platelet transfusion in the past 7 days

# TDT: Summary of Adverse Events

Patients with  $\geq 3$ -month follow-up (n=7)

*AEs were generally consistent with myeloablation and autologous stem cell transplant*

	Patients with non-serious AEs, n	Patients with SAEs, n
Relationship <sup>1</sup>		
Related to plerixafor and/or G-CSF	6	0
Related to busulfan only	7	2
Related to CTX001 only	1 <sup>2</sup>	1
Related to busulfan and CTX001	3 <sup>3</sup>	1
Not related to any study drug	7	4

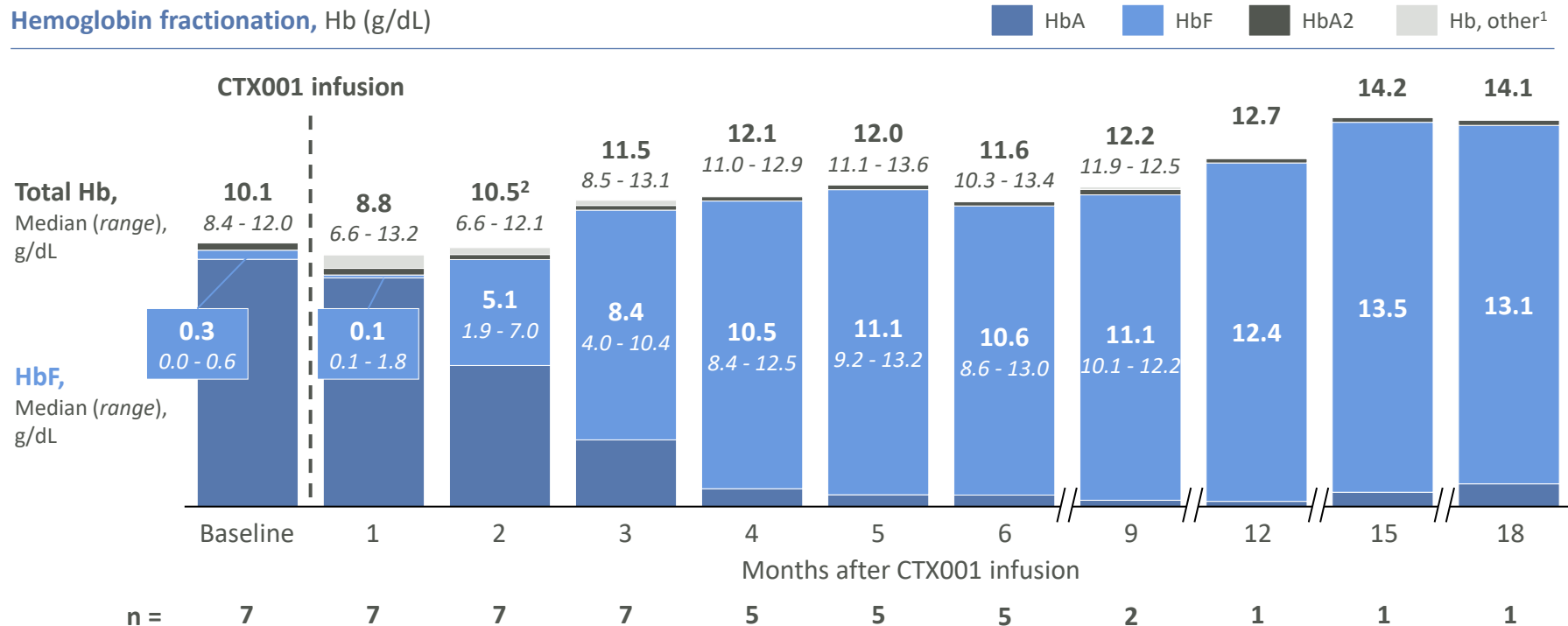
- 4 of 7 patients experienced at least one post-infusion SAE
- Majority of AEs occurred within first 60 days after CTX001 infusion
- 2 patients experienced a combined total of 5 SAEs related or possibly related to busulfan only: venoocclusive liver disease (in both patients), febrile neutropenia (2 events 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

Data disclosed December 5, 2020

(1) Includes related and possibly related AEs; (2) 1 patient experienced a non-serious AE of anaemia possibly related to CTX001 (resolved); (3) 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

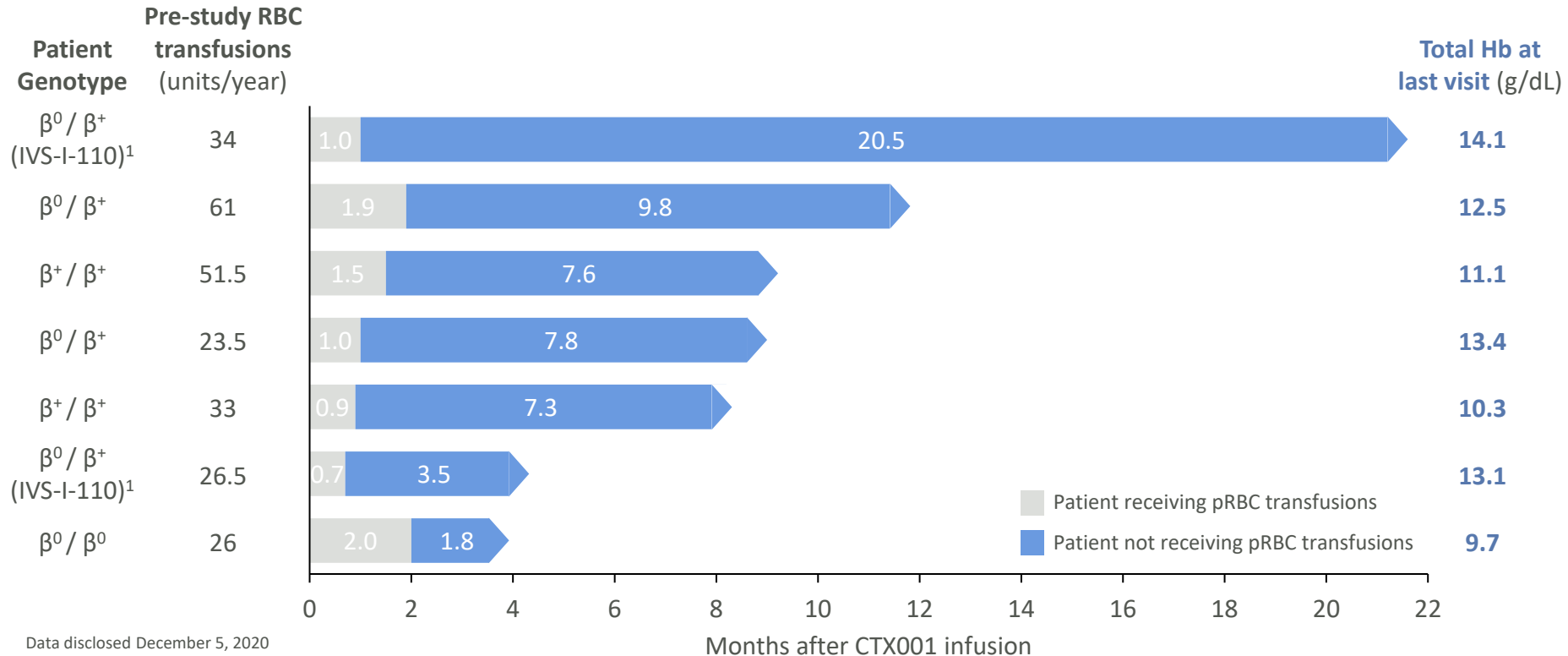
Hemoglobin fractionation, Hb (g/dL)



Data disclosed December 5, 2020

(1) Hb adducts and other variants; (2) With respect to Patient 2, Total Hb from local laboratory and Hb fraction from central laboratory

# TDT: Duration of Transfusion Independence After CTX001



Data disclosed December 5, 2020

(1) IVS-I-110 phenotype is severe and similar to  $\beta^0 / \beta^0$

# SCD: Patient Baseline and Treatment Characteristics

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

## *Patient baseline*

	n
<b>Genotype</b> $\beta^s / \beta^s$	<b>3</b>
<b>Gender</b> Female/Male	<b>2/1</b>
	Median (range)
<b>Age at consent</b> Years	<b>22 (22-33)</b>
<b>Pre-study VOCs</b> VOCs/year <sup>1</sup>	<b>7 (4.0-7.5)</b>

## *Treatment characteristics*

	Median (range)
<b>Drug product cell dose<sup>2</sup></b> CD34+ cells x 10 <sup>6</sup> /kg	<b>3.8 (3.1-3.9)</b>
<b>Neutrophil engraftment<sup>3</sup></b> Study day <sup>4</sup>	<b>22 (17-30)</b>
<b>Platelet engraftment<sup>5</sup></b> Study day <sup>4</sup>	<b>30 (30-33)</b>
<b>Duration of follow-up</b> Months	<b>7.8 (3.8-16.6)</b>

Data disclosed December 5, 2020

(1) Annualized rate during the 2 years before consenting to study participation; (2) Across multiple drug product lots per patient; (3) Defined as the first day of 3 measurements of absolute neutrophil count ≥500 cells/μL on 3 consecutive days; (4) Study day defined as day after CTX001 infusion; (5) 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  $\geq 3$ -month follow-up (n=3)

*AEs were generally consistent with myeloablation and autologous stem cell transplant*

	Patients with non-serious AEs, n	Patients with SAEs, n
Relationship <sup>1</sup>		
Related to plerixafor only	3	1
Related to busulfan only	3	1
Related to CTX001 only	0	0
Related to busulfan and CTX001	2 <sup>2</sup>	0
Not related to any study drug	3	2

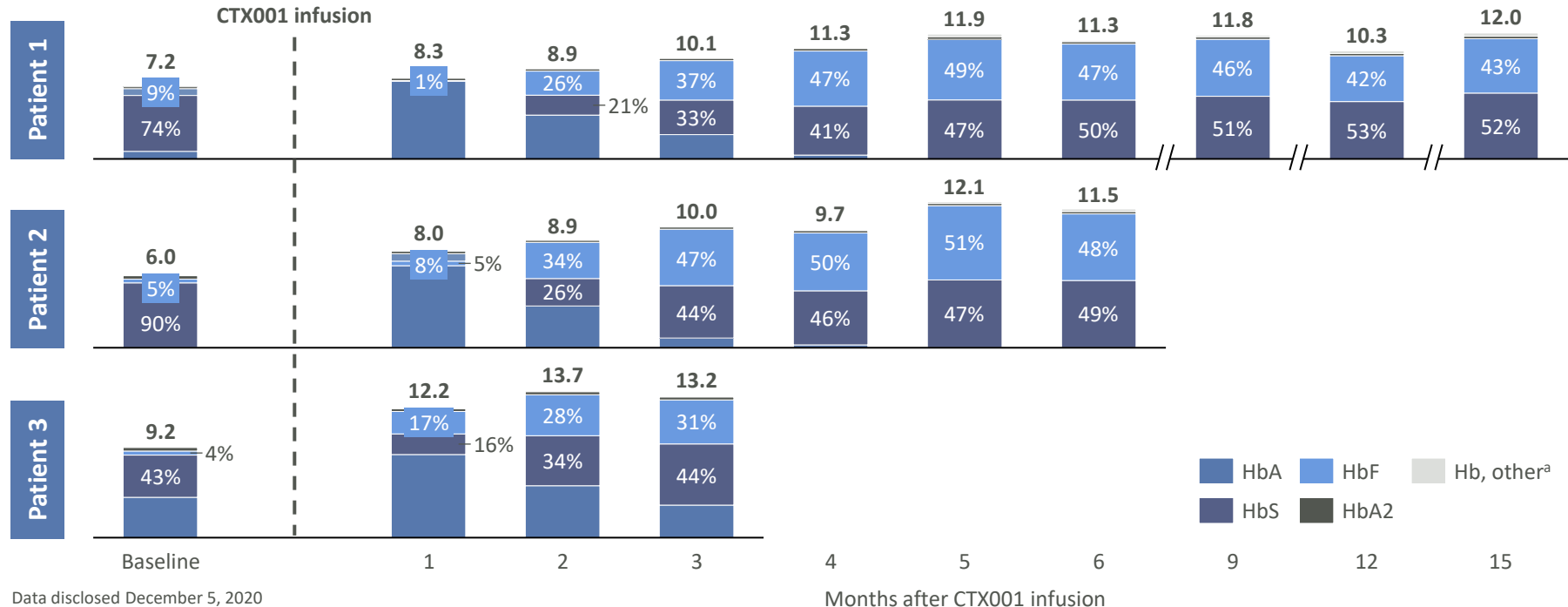
- 1 of 3 patients experienced at least one post-infusion SAE
- Majority of AEs occurred within first 60 days after CTX001 infusion
- 1 patient experienced SAEs related to plerixafor: chest pain, neck pain, headache, and abdominal pain; all resolved
- Post-CTX001, only 1 patient experienced SAEs: sepsis (related to busulfan), cholelithiasis, and abdominal pain (both unrelated to any study drug); all resolved
- There were no SAEs related to CTX001

Data disclosed December 5, 2020

(1) Includes related and possibly related AEs; (2) 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

Hemoglobin fractionation, Hb (g/dL)

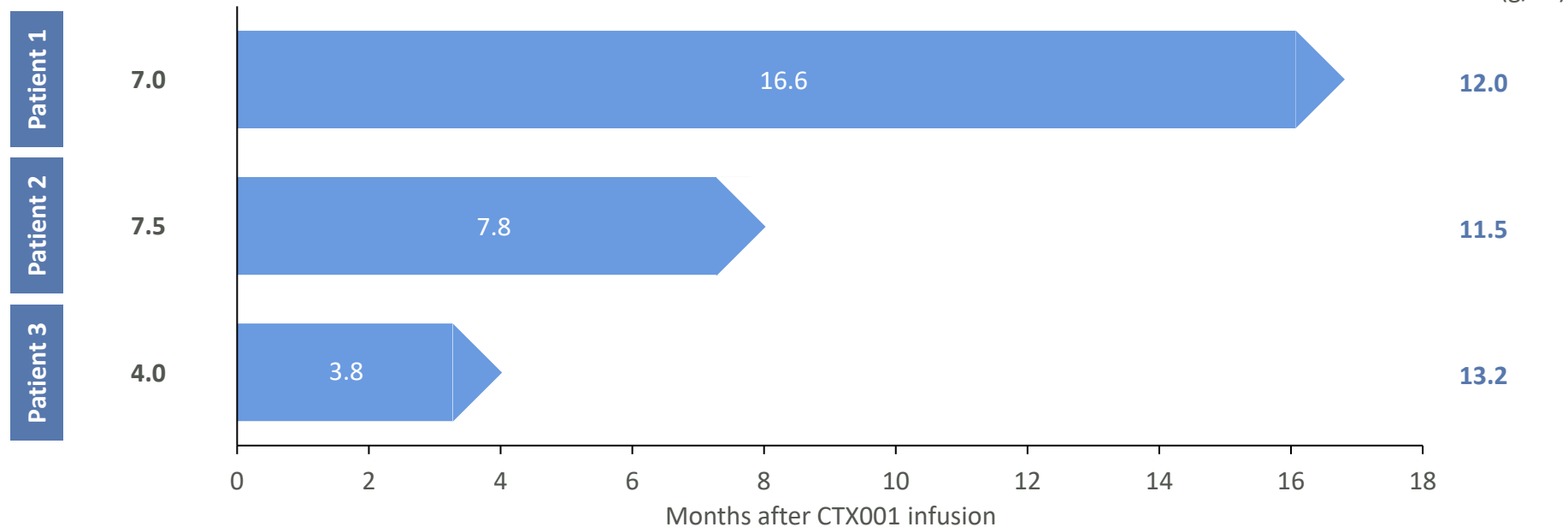


Data disclosed December 5, 2020  
(1) Hb adducts and other variants

# SCD: Duration VOC-Free After CTX001

## Pre-study VOC burden

Average number per year  
over the previous 2 years



**All patients have detectable haptoglobin and improved LDH, indicating no evidence of hemolysis**

Data disclosed December 5, 2020

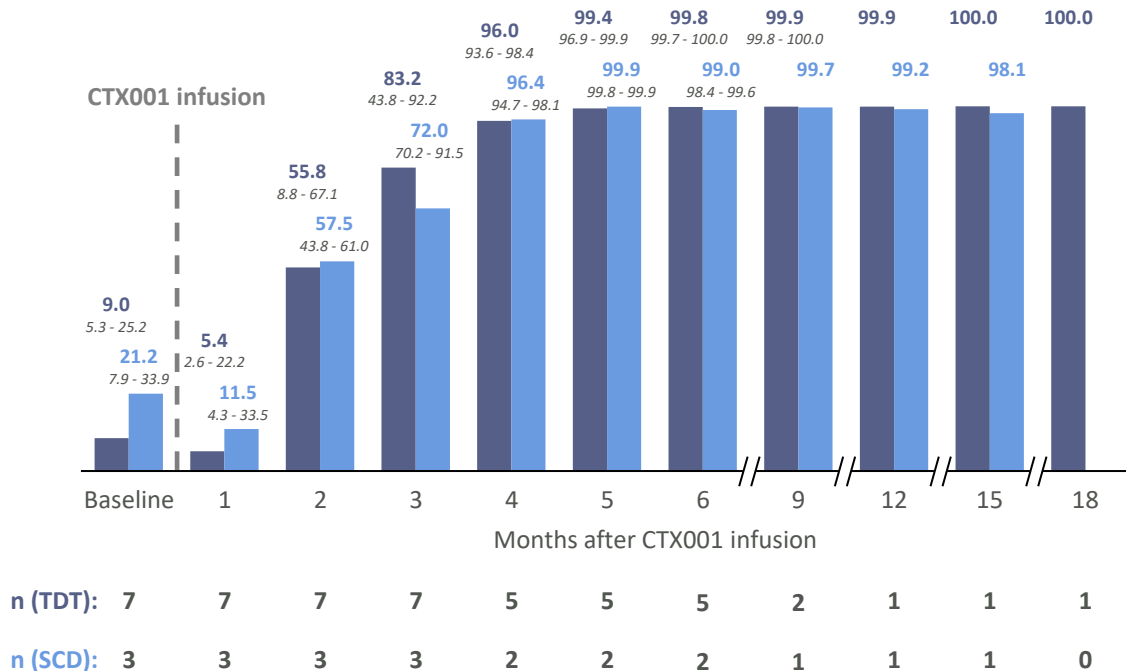


# Pancellular HbF Expression and Durable Editing



## Pancellular expression of HbF maintained

Median % peripheral F-cells (*range*), % circulating RBCs expressing HbF



Data disclosed December 5, 2020

(1) Bone marrow editing assessments performed starting at 6 months, 12 months, and 24 months of follow-up

## Durable BCL11A editing in the bone marrow

Patients with ≥6 months of follow-up<sup>1</sup>

	Total follow-up, months	Allelic editing in CD34 <sup>+</sup> bone marrow cells, %	
		6-month visit	12-month visit
1	21.5	78.1	76.1
2	11.7	41.8	
3	9.1	72.6	
4	8.9	76.6	
5	8.2	88.1	
1	16.6	81.4	80.4
2	7.8	87.3	

# Allogeneic CAR-T Therapy Has Transformative Potential

## Before Patient Diagnosis

### Autologous: patient derived

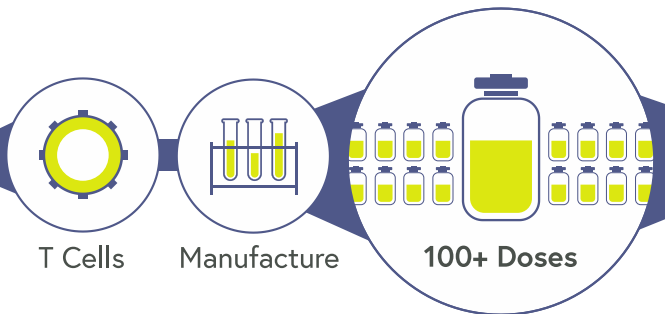


PATIENT

### Allogeneic: healthy-donor derived



HEALTHY DONOR



T Cells

Manufacture

100+ Doses

## After Patient Diagnosis

WEEK 1



WEEK 2



Manufacture

WEEK 3



Single Treatment

Apheresis



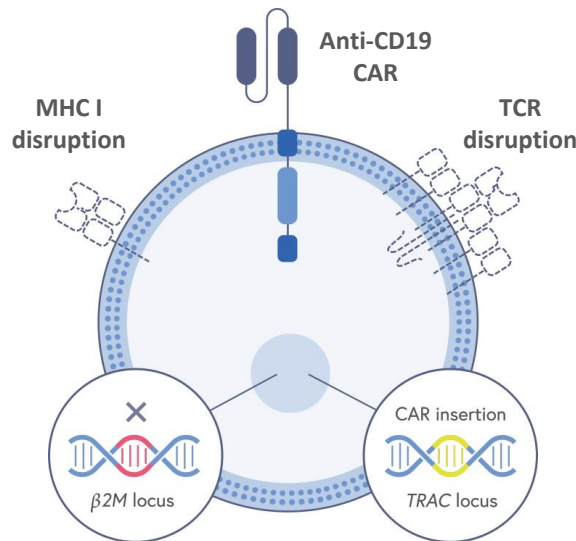
Treatment

- **Off-the-shelf:** Immediate treatment without risk of manufacturing failure, saving patients valuable time in which their disease could progress
- **Flexible dosing** (e.g., re-dosing)
- **A more consistent product**
- **Scalable manufacturing and simpler logistics**
- **Broader accessibility**

# CTX110: Differentiated CRISPR-Edited Allogeneic CAR-T Design

Multiplex CRISPR gene editing in one step designed to:

- **Improve persistence in the allo setting** via  $\beta$ 2M knock-out to eliminate MHC I expression
- **Avoid need** for more toxic lymphodepletion regimens



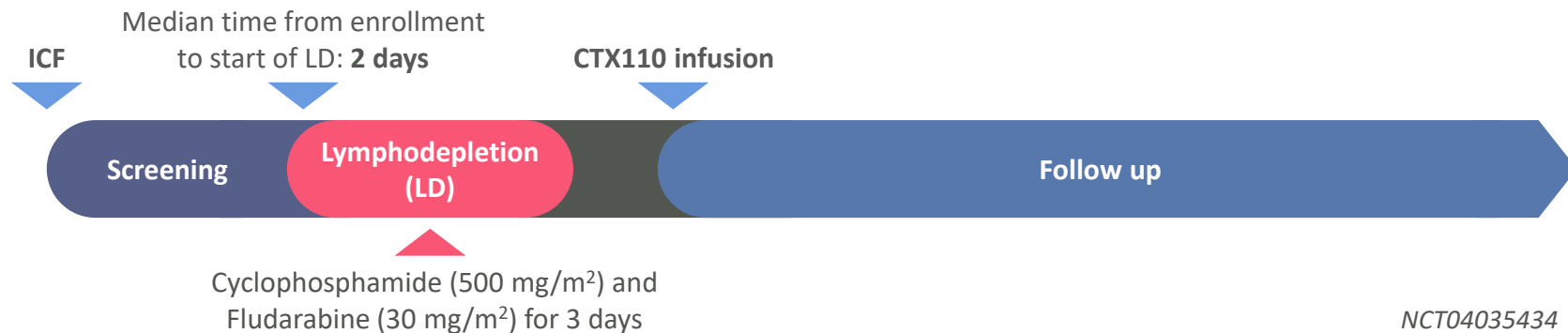
- **Prevent GvHD** via TCR disruption
- **Improve consistency and safety by precise insertion** of CAR construct into *TRAC* locus without using lentivirus or retrovirus

*CTX120<sup>TM</sup> and CTX130<sup>TM</sup> utilize the **same CRISPR-edited allogeneic T cell design**, but with different CAR targets, as well as additional editing in the case of CTX130*

# CARBON: Trial Design

## CARBON: Single-arm study evaluating the safety and efficacy of CTX110

Allogeneic CAR-T enables simplified trial design: short screening timeframe, no apheresis, no bridging chemotherapy, and on-site availability of CAR-T cell product



### Key eligibility criteria

- Age ≥18 years
- Relapsed/refractory non-Hodgkin lymphoma, as evidenced by 2+ lines of prior therapy
- ECOG performance status 0 or 1
- Adequate renal, liver, cardiac, and pulmonary organ function
- No prior allogeneic SCT or treatment with CAR-T therapy

### Primary endpoints

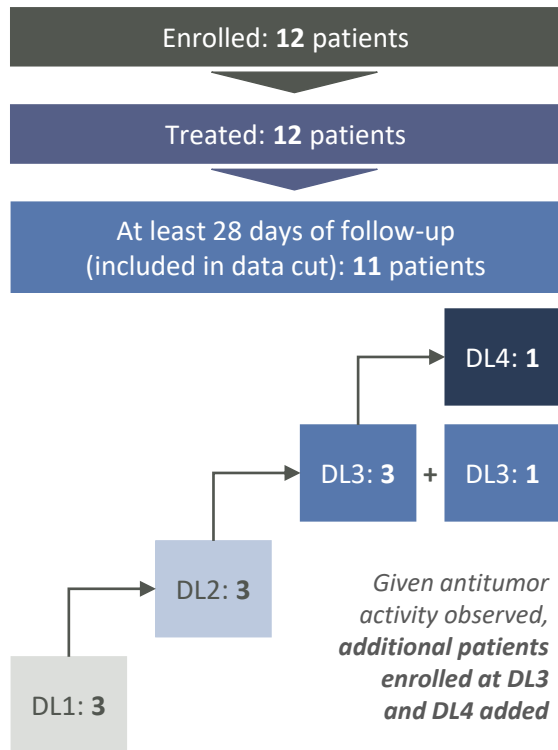
- Incidence of adverse events, defined as DLTs
- ORR

### Key secondary endpoints

- DoR, PFS, and OS

# CARBON: Patient Flow and Baseline Characteristics

*As of the data cutoff date:*



**N (%) (unless otherwise noted)**

Cell dose (CAR <sup>+</sup> T cells)	DL1 30x10 <sup>6</sup> N=3	DL2 100x10 <sup>6</sup> N=3	DL3 300x10 <sup>6</sup> N=4	DL4 600x10 <sup>6</sup> N=1
Median age, years (range)	52 (50-61)	64 (58-74)	64.5 (62-74)	72
Male	2 (66.7)	2 (66.7)	1 (25)	1 (100)
<b>Lymphoma subtypes</b>				
Diffuse large B-cell lymphoma (DLBCL) <sup>1</sup>	3 (100)	3 (100)	4 (100)	1 (100)
Follicular lymphoma	0	0	0	0
<b>Current disease stage (per Lugano 2014)<sup>2</sup></b>				
Stage III	1 (33.3)	1 (33.3)	2 (50)	0
Stage IV	2 (66.7)	2 (66.7)	1 (25)	1 (100)
<b>Prior treatments</b>				
Median number (range)	2.0 (2-8)	3.0 (2-3)	2.0 (2-4)	5
Hematopoietic stem cell transplant	0	0	3 (75)	1 (100)
Refractory to last therapy	3 (100)	3 (100)	0	0

(1) Including high grade lymphoma (e.g., triple hit), transformed follicular lymphoma (tFL), Richter's Transformation;

(2) One patient with Stage II disease treated at DL3

Data as of September 28, 2020

# Dose-Dependent Responses Observed with CTX110

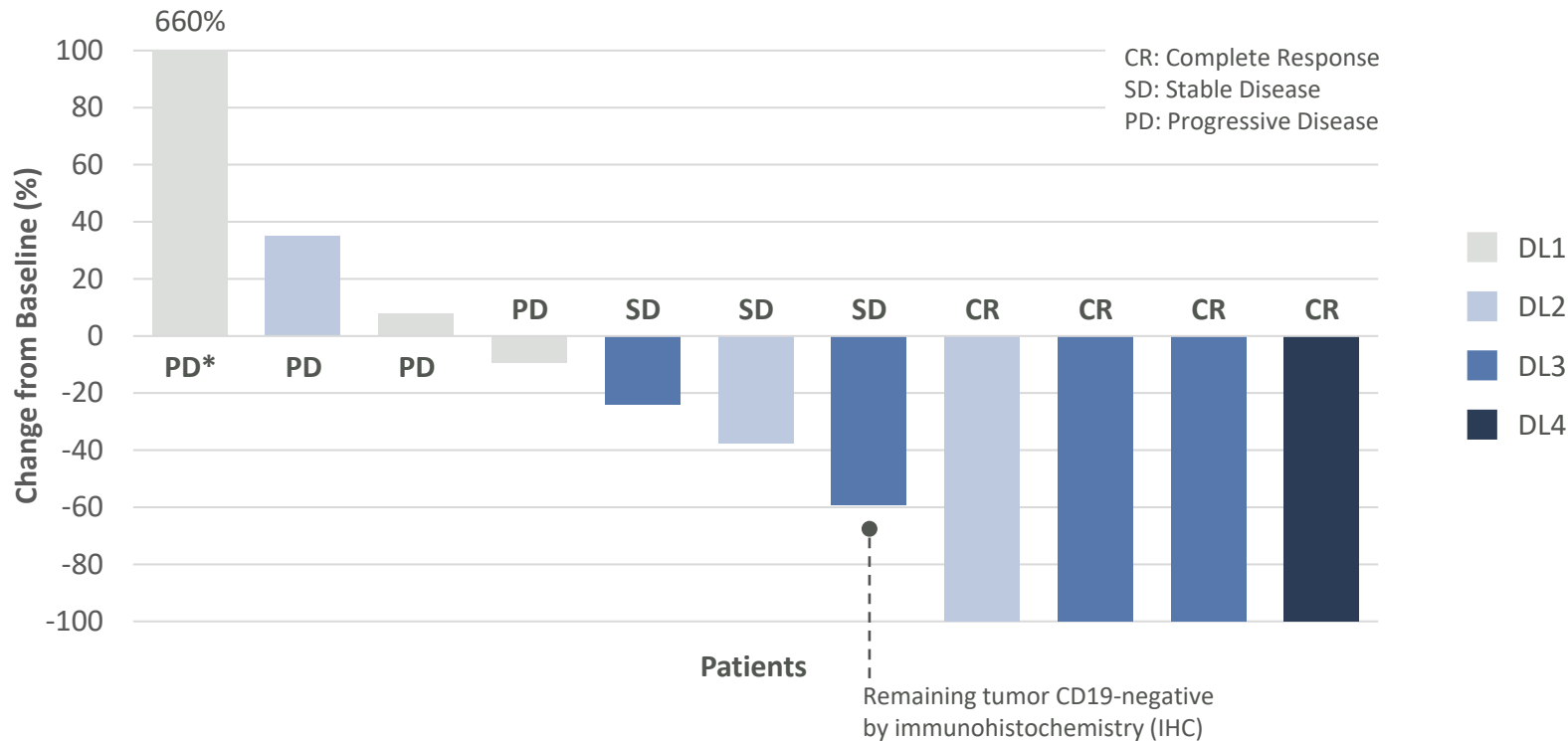
Best response per 2014 Lugano criteria<sup>1</sup> by independent central assessment

Cell dose (CAR+ T cells)	DL1 30x10 <sup>6</sup> N=3	DL2 100x10 <sup>6</sup> N=3	DL3 300x10 <sup>6</sup> N=4	DL4 600x10 <sup>6</sup> N=1
Overall response rate (ORR), N (%)	0 (0%)	1 (33%)	2 (50%)	1 (100%)
Complete response (CR) rate, N (%)	0 (0%)	1 (33%)	2 (50%)	1 (100%)

- Early evidence of **dose response, with complete responses achieved in 4 patients**
- **Responses achieved without the use of more toxic lymphodepletion agents**, consistent with engineering of CTX110 for immune evasion
- **CAR-T cells detected at multiple time points in all patients** in DL2-4, with **consistent peak expansion** of CTX110 in the peripheral blood seen around 1-2 weeks post infusion and CTX110 detected out **as late as 180 days** after administration

# Dose-Dependent Reduction in Tumor Size with CTX110

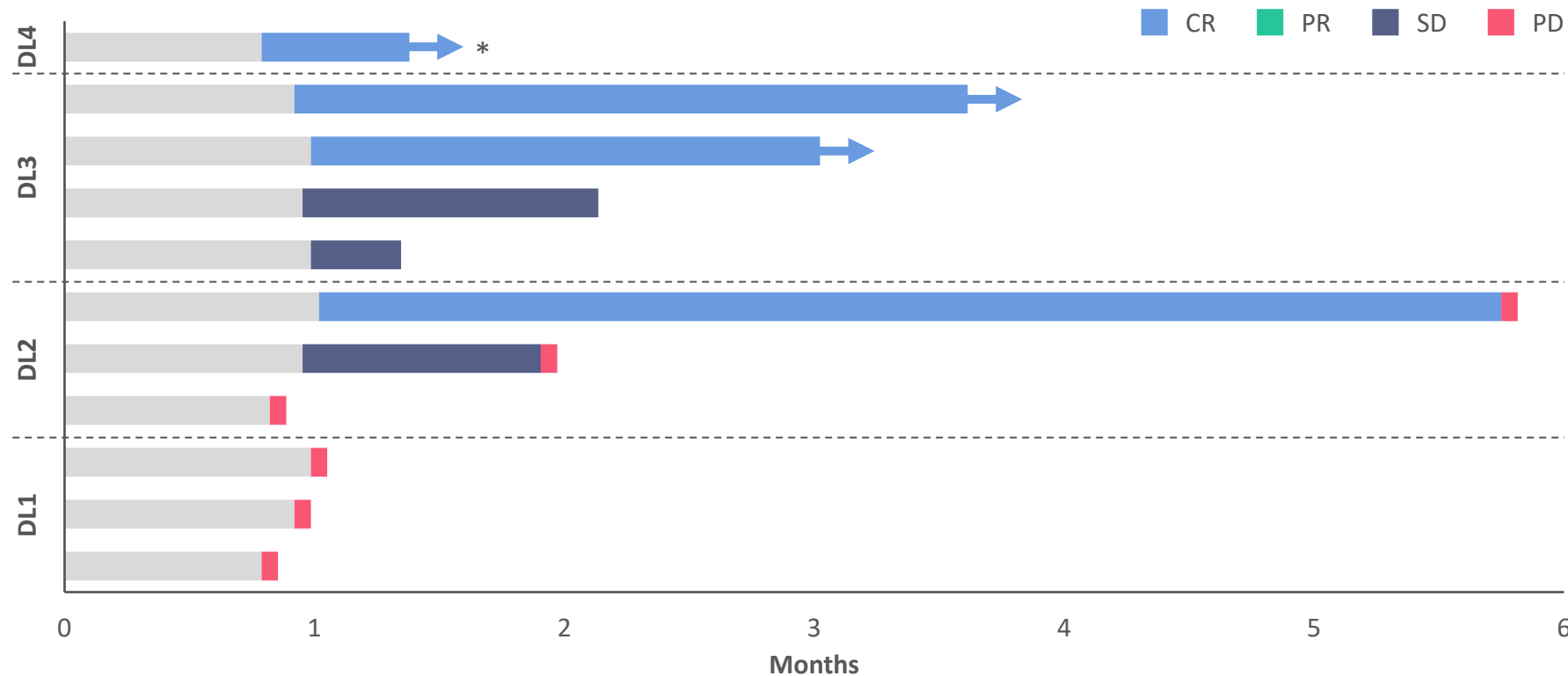
## Best tumor size reduction per 2014 Lugano criteria by independent central assessment



\* Patient subsequently failed autologous CAR-T

Data as of September 28, 2020

# Complete Responses with CTX110 Showed Durability at Month 3 and Beyond



Imaging per protocol occurs at M1, M3, and M6; \* Patient died while in CR at Day 52 post CTX110 infusion following data cutoff

Data as of September 28, 2020



# Acceptable Safety Profile with CTX110 at DL3 and Below

## Treatment-emergent adverse events (AEs) of special interest in DL1-3, N (%)

N=10	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Graft-versus-Host Disease (GvHD)	0	0	0	0	0
Cytokine Release Syndrome (CRS) <sup>1,2</sup>	1 (10%)	2 (20%)	0	0	0
ICANS <sup>1,3</sup>	0	1 (10%)	0	0	0
Infections	0	0	1 (10%)	0	0

### For patients in DL1 through DL3 (N=10):

- **No GvHD** despite all patients with  $\leq 3/12$  HLA match to CTX110 donors
- **No CRS or ICANS above Grade 2**
- **No infusion reactions**
- **4 serious adverse events (SAEs) following CTX110 infusion not related to disease progression among 3 treated patients:** ICANS (n=1), CRS (n=1), periorbital cellulitis (n=1), febrile neutropenia (n=1)

### Safety for patient treated at DL4 (600x10<sup>6</sup> CAR<sup>+</sup> T cells):

- Patient had received five prior lines of therapy, including autologous stem cell transplant
- Experienced Grade 2 CRS at Day 5 that resolved
- Admitted with febrile neutropenia at Day 26 and developed confusion and memory loss starting at Day 28, with further deterioration ultimately requiring intubation for airway protection
- Initially treated for ICANS and later found to have reactivation of HHV-6 and HHV-6 encephalitis
- Despite treatments, patient remained obtunded and died on Day 52 after family requested withdrawal of care

(1) Per ASTCT criteria; other AEs graded per CTCAE; (2) Includes two separate episodes of CRS (1 G1, 1 G2) in single patient; worst grade reported;

(3) Immune effector Cell-Associated Neurotoxicity Syndrome

# Our I/O Strategy and Allogeneic CAR-T Pipeline



	PROGRAM	RESEARCH	IND-ENABLING	CLINICAL	MARKETED	STATUS
<b>Validate</b> <i>allogeneic platform with proven targets</i>	<b>CTX110</b> (anti-CD19) <i>B-cell malignancies</i>					<i>Enrolling</i>
	<b>CTX120</b> (anti-BCMA) <i>Multiple myeloma</i>					<i>Enrolling</i>
<b>Expand</b> <i>from hematologic cancers into solid tumors</i>	<b>CTX130</b> (anti-CD70) <i>T- and B-cell lymphomas</i>					<i>Enrolling</i>
	<b>CTX130</b> (anti-CD70) <i>Renal cell carcinoma</i>					<i>Enrolling</i>
<b>Unlock</b> <i>the full potential of I/O cell therapy with CRISPR</i>	Anti-CD33 allogeneic CAR-T					<i>Incorporating additional editing, novel targeting, etc.</i>
	Anti-PTK7 allogeneic CAR-T					
	Additional undisclosed programs					

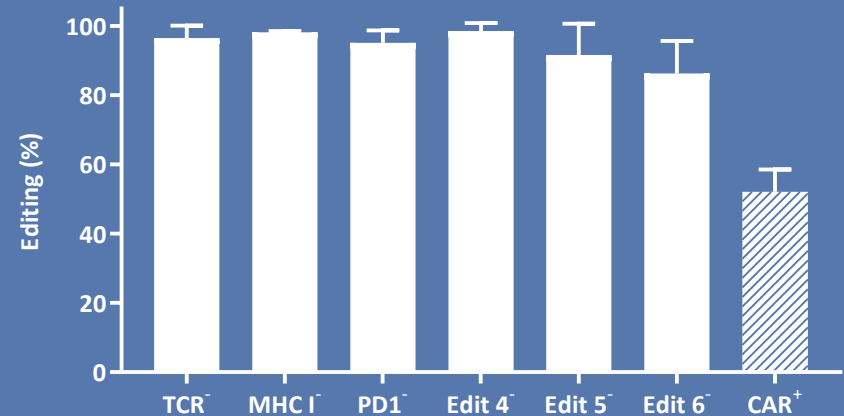
# CRISPR Enables the Next Generation of I/O Cell Therapy



## CRISPR gene editing facilitates consistent, multiplex editing to:

- Produce allogeneic cell therapies
- Enhance immune cell performance
- Speed the discovery and generation of novel therapeutic candidates

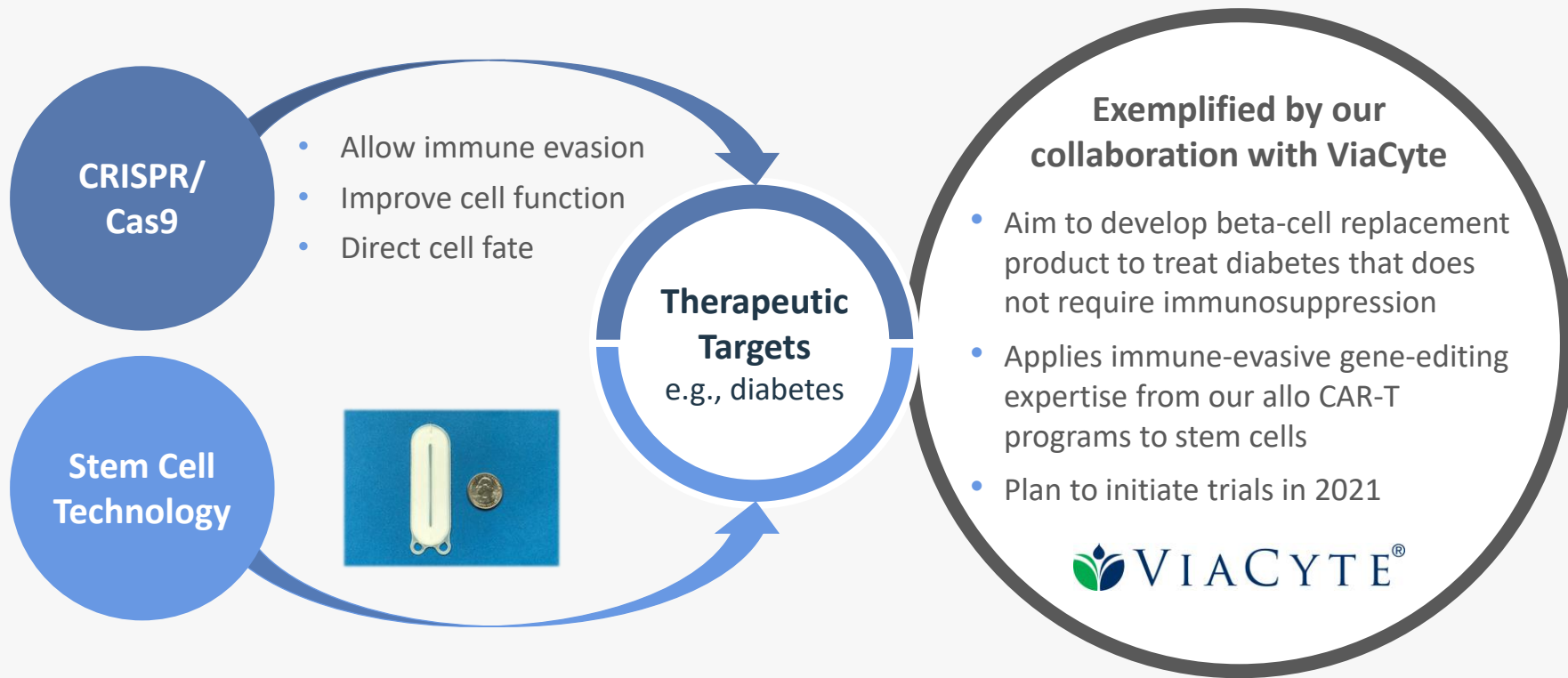
Multiplexed, single-shot 6x knock-out plus CAR insertion performed at high efficiency



*6x-edited CAR-T cells show no viability decrease, no cytokine-independent growth and robust target-specific cytotoxicity*

# CRISPR Enables Regenerative Medicine 2.0

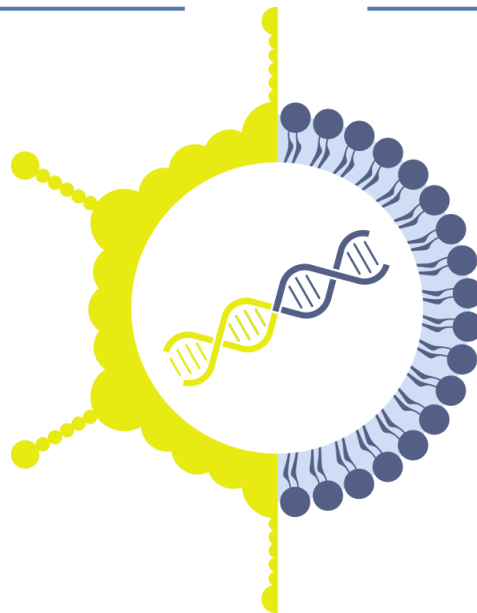
## CRISPR/Cas9 Technology Opens Broader Applications for Regenerative Medicine



# Unlocking *In Vivo* Applications of CRISPR/Cas9

## AAV Vectors for Neuromuscular Indications

- **Adeno-associated virus (AAV)** to deliver Cas9 and gRNA to muscle, the nervous system and other tissues
- Collaboration with StrideBio to improve tissue specificity and reduce immunogenicity
- Programs include DMD and DM1 in collaboration with Vertex, as well as other early research programs



## LNPs for Liver Indications

- **Lipid nanoparticles (LNPs)** containing mRNA encoding Cas9 and gRNA for delivery to the liver
- Lipid technology from MIT and mRNA technology from CureVac
- Programs include GSD Ia and other early research programs

Enabling collaborations



# Optimizing the CRISPR/Cas9 Platform

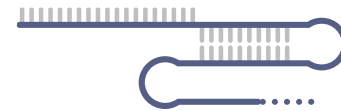
## Nuclease Engineering

Enhance CRISPR/Cas9 system through protein engineering



## Guide RNA Optimization

Identify optimal guide RNA formats and sequences for therapeutic editing



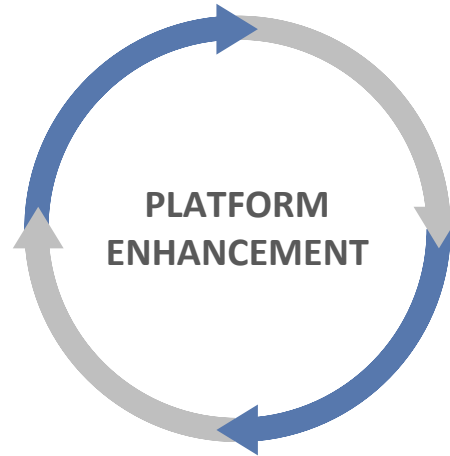
## Advanced Editing

Improve efficiency of gene correction and multiplexing



## Synthetic Biology

Engineer improved cellular therapeutics



# Strong U.S. and Global Foundational IP Position



## United States

**Charpentier / UC Berkeley / U. Vienna granted patents of broad scope; multiple applications progressing**

35

Patents of broad scope granted, including the patent involved in the 1<sup>st</sup> interference

25+

Additional patent applications moving forward in parallel with both broad and narrow claims, including 2 patent applications of broad scope allowed

2<sup>nd</sup>

Interference with Broad Institute in priority phase to determine who was first to invent CRISPR/Cas9 gene editing in eukaryotic cells; separate interference declared with Toolgen on same subject matter



## Europe and Global

**Charpentier / UC Berkeley / U. Vienna granted foundational patents, including use in eukaryotes**

3

Patents of broad scope granted in the EU

31

Patents of broad scope granted in the UK, Germany, Japan, China, Singapore, Hong Kong, Ukraine, Israel, Australia, New Zealand, Mexico, South Africa and elsewhere

~80

Jurisdictions worldwide in which applications with both broad and narrow claims are advancing

# Building a Great Company



**EXPERIENCED**  
*Management Team*

**END-TO-END  
CAPABILITIES**  
*With >400 Employees*

**COLLABORATIVE &  
ENTREPRENEURIAL**  
*Culture*