CRISPR THERAPEUTICS

Creating transformative gene-based medicines for serious diseases

Corporate Overview | March 2020

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 timing of 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) 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; (iv) 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; (v) the sufficiency of CRISPR Therapeutics' cash resources; and (vi) 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 not to be indicative of final trial results; the risk that the initial data from a limited number of patients (as is the case with CTX001 at this time) may not be indicative of results from the full planned study population; 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; 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, and in any other subsequent filings made by CRISPR Therapeutics with the U.S. Securities and Exchange Commission, which are available on the SEC's website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. CRISPR Therapeutics disclaims any obligation or undertaking to update or revise any forward-looking statements contained in this presentation, other than to the extent required by law.

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 β-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

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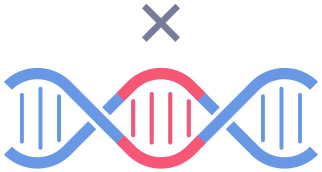
A **SPECIFIC**, **EFFICIENT** and **VERSATILE** tool for editing genes



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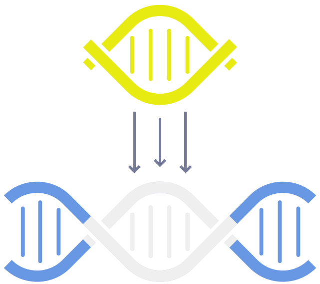

Correct or Insert

"If scientists can dream of a genetic manipulation,
CRISPR can now make it happen"

Science

Our Pipeline

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

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

VERTEX BAYER

Hemoglobinopathies – Devastating Blood Diseases

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Sickle Cell Disease (SCD) and β-Thalassemia

Blood disorders caused by mutations in the β-globin gene

Sickled | Normal Cell | Thalassemic

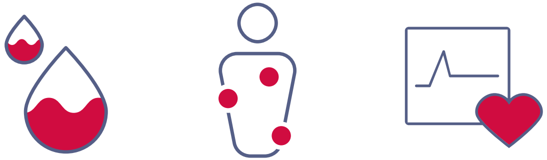
Significant worldwide burden

ANNUAL BIRTHS

300K SCD

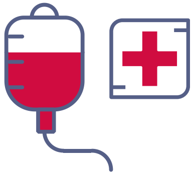
60K β-thalassemia

High morbidity and mortality



Anemia | Pain | Early death

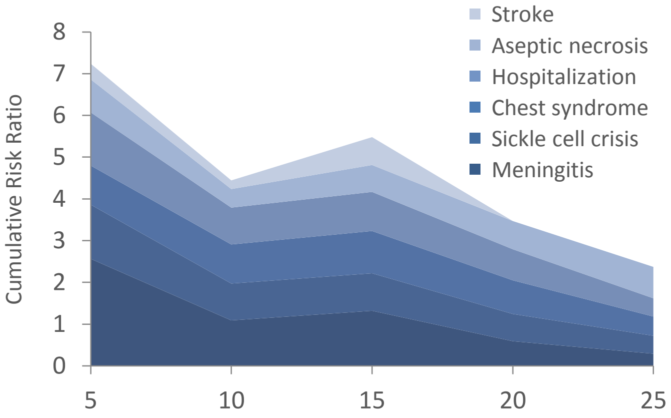
Heavy burden of patient care



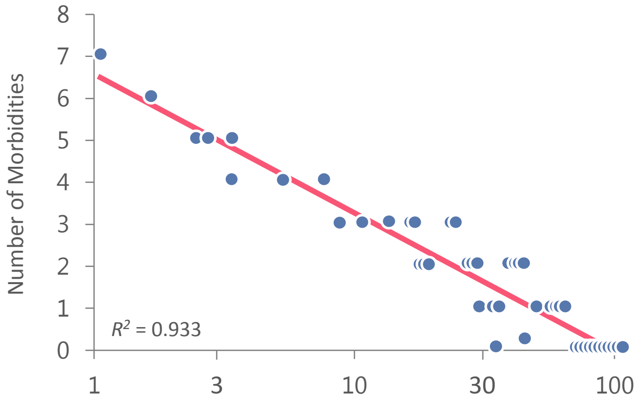
Frequent transfusions and hospitalizations

Our Approach – Upregulating Fetal Hemoglobin

Symptoms in SCD and β-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 β-thalassemia
- **Our gene editing strategy aims to mimic these variants in symptomatic patients,** an approach supported by well-understood genetics

Pioneering CRISPR Trials

	CLIMB THAL-111	CLIMB SCD-121
Design	**Phase 1/2, international, multi-center, open-label, single arm studies to assess the safety and efficacy of CTX001 in patients with β-thalassemia and SCD, respectively**	
Target enrollment	45 patients between 18 - 35 years of age with transfusion dependent thalassemia (TDT), including β0/β0 genotypes	45 patients between 18 - 35 years of age with severe SCD and a history of ≥2 vaso-occlusive crises/year over the previous two years
Primary endpoint	Proportion of patients achieving sustained transfusion reduction 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

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

First Patient Successfully Treated in CLIMB THAL-111

Patient baseline

Genotype	**β^0/IVS-I-110**
Gender	**F**
Age at consent, *years*	**19**
Pre-study pRBC transfusions, *episodes/year*[2]	**16.5**

Treatment characteristics

- Successful engraftment[1]
  - Neutrophil engraftment at study day 33
  - Platelet engraftment at study day 37
- Initial safety profile consistent with myeloablative busulfan conditioning and autologous HSCT
- 2 SAEs occurred, neither considered related to CTX001 by study investigator, both resolved:
  - Veno-occlusive liver disease attributed to busulfan conditioning
  - Pneumonia in the presence of neutropenia

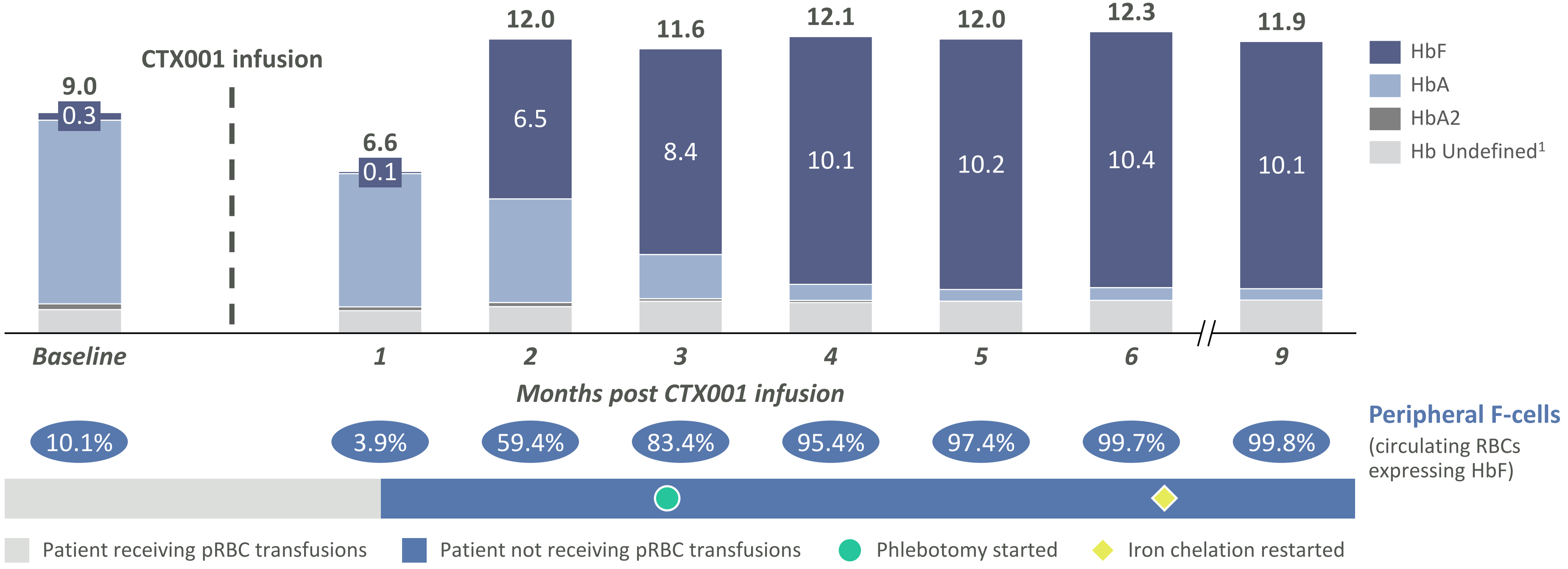
Data disclosed November 19, 2019

1 Neutrophil engraftment defined as absolute neutrophil count ≥500 cells/µL for three consecutive days, and platelet engraftment defined as unsupported platelet count ≥ 20,000/µL

2 Annualized rate during the two years prior to consenting for the study

First TDT Patient Treated is Transfusion Free with Sustained HbF > 10 g/dL

Hemoglobin fractionation over time pre and post CTX001 infusion, Hemoglobin (g/dL)



Data disclosed November 19, 2019

1 Hb adducts and other variants

First Patient Successfully Treated in CLIMB SCD-121

CLIMB SCD-121 | CRISPR THERAPEUTICS

Patient baseline

Genotype	**β^S/β^S**
Gender	**F**
Age at consent, *years*	**33**
Pre-study VOCs, *VOCs/year*[2]	**7**

Treatment characteristics

- Successful engraftment[1]
  - Neutrophil engraftment at study day 30
  - Platelet engraftment at study day 30
- Initial safety profile consistent with myeloablative busulfan conditioning and autologous HSCT
- 3 SAEs occurred, none considered related to CTX001 by study investigator, all resolved:
  - Sepsis in the presence of neutropenia
  - Cholelithiasis
  - Abdominal pain

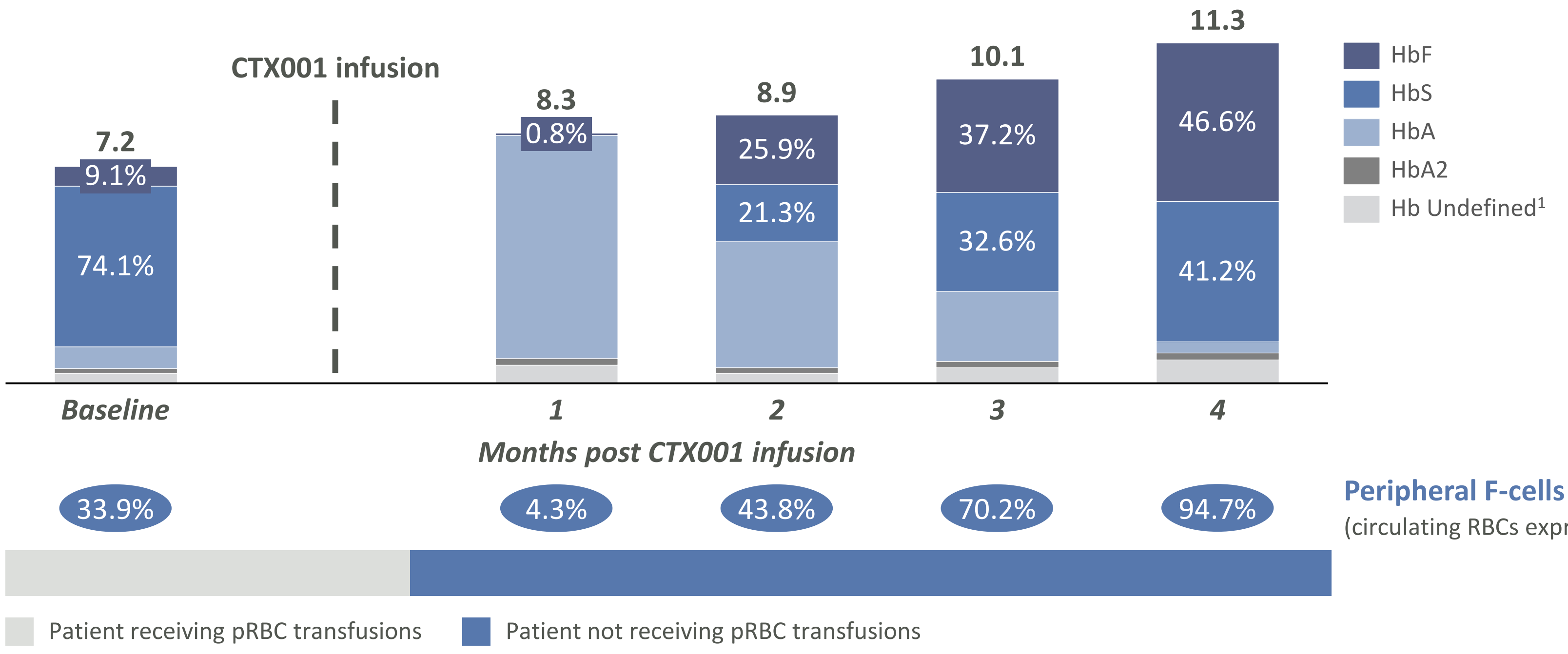
Data disclosed November 19, 2019

1 Neutrophil engraftment defined as absolute neutrophil count ≥500 cells/µL for three consecutive days, and platelet engraftment defined as unsupported platelet count ≥ 50,000/µL

2 Annualized rate during the two years prior to consenting for the study

First SCD Patient Treated had 46.6% HbF at 4 Months after CTX001 Infusion

Hemoglobin fractionation over time pre and post CTX001 infusion, % of total g/dL hemoglobin



Patient has had no reported VOCs since CTX001 infusion

Peripheral F-cells
(circulating RBCs expressing HbF)

Data disclosed November 19, 2019

1 Hb adducts and other variants

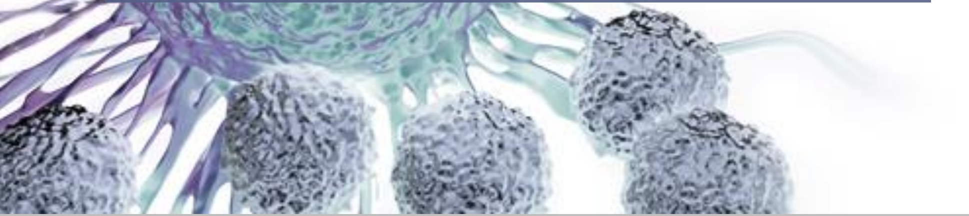
CRISPR Enables the Next Generation of I/O Cell Therapy

ALLOGENEIC CAR-T

- Off-the-shelf
- More potent starting material
- More consistent product
- Broader access
- Flexible dosing (e.g., re-dosing)

SOLID TUMOR EFFICACY

- Avoid exhaustion
- Modulate suppressive TMEs
- Target tumors with greater selectivity
- Sense and respond via genetic circuits
- Recruit endogenous immunity



Allogeneic CAR-T Therapy Has Transformative Potential

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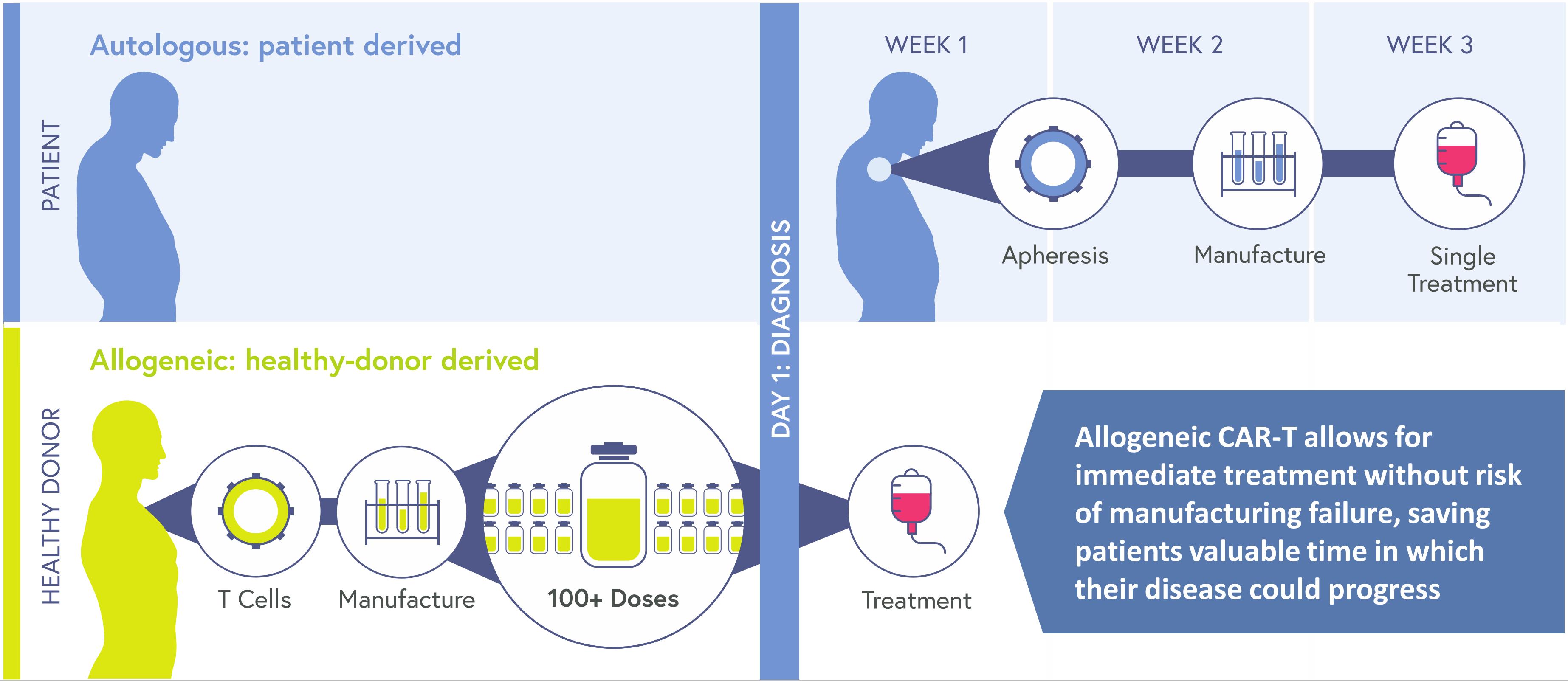
Before Patient Diagnosis

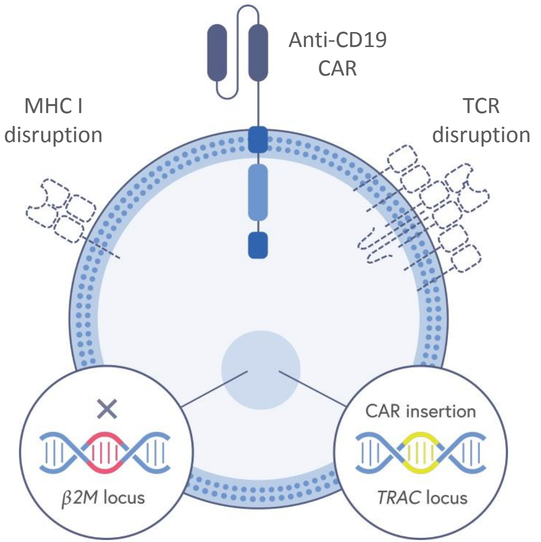
After Patient Diagnosis



CRISPR-Edited Allogeneic T Cell Design

Initial Allogeneic CAR-T Candidate – CTX110

- **Improve persistence in the allo setting** with β2M knock-out to eliminate MHC I expression

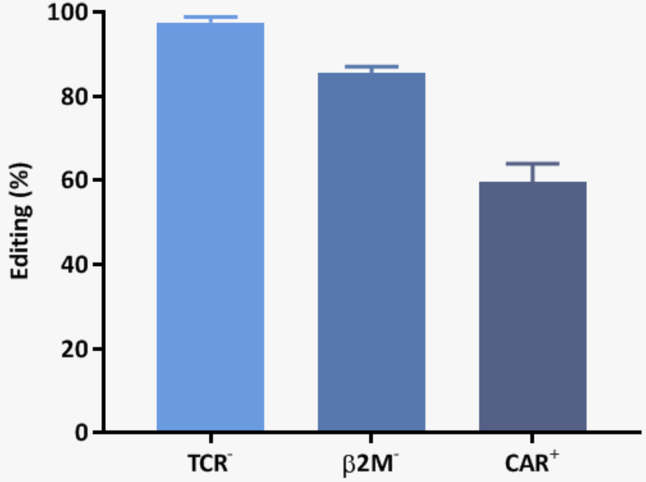


- **Prevent GvHD** via TCR disruption
- **Improve safety and potency by precise insertion** of CAR construct into *TRAC* locus

Multiplex editing in one step

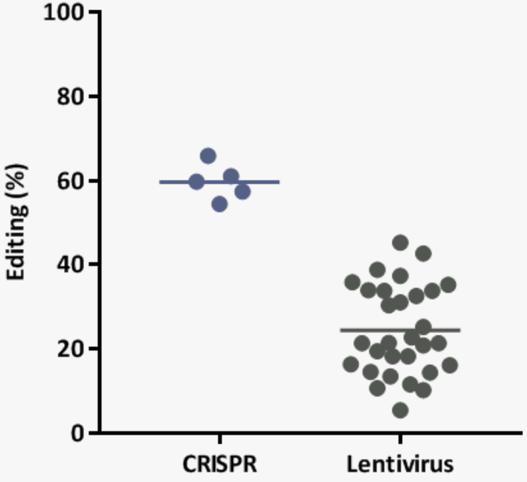
CRISPR Editing Allows for a More Consistent Product

Precise and Efficient Editing to Produce CTX110



Consistently high editing across **5 different donors**
>50% of cells have all three desired edits

Greater Consistency than Viral Approaches



54-66% CAR+ range with CRISPR
vs. **6-45%** for lentiviral CAR-T[1]

1. Maude, *et al*. NEJM 2014

Initial Allogeneic CAR-T Trials for CTX110 and CTX120

CRSP-ONC-001 and CRSP-ONC-002: Single-arm trials to assess the safety and efficacy of CTX110 and CTX120, respectively

Patients and Sites

- CTX110 – Subjects with relapsed or refractory (r/r) B-cell malignancies, starting with adult patients with r/r non-Hodgkin lymphoma
- CTX120 – Subjects with r/r multiple myeloma
- Conducted at sites with CAR-T or cell therapy experience

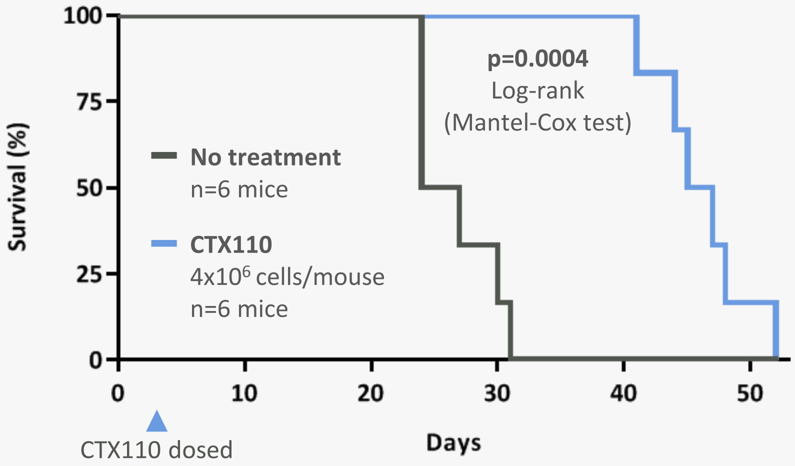
Trial Design and Dosing

- Dose escalation followed by dose expansion cohort
- Allogeneic CAR-T enables simplified trial design with short screening timeframe, no apheresis, no bridging chemo, and on-site availability of CAR-T cell product
- Lymphodepleting chemotherapy regimen administered before CAR-T infusion

CTX110/CTX120 – Novel Approach Against Validated Targets

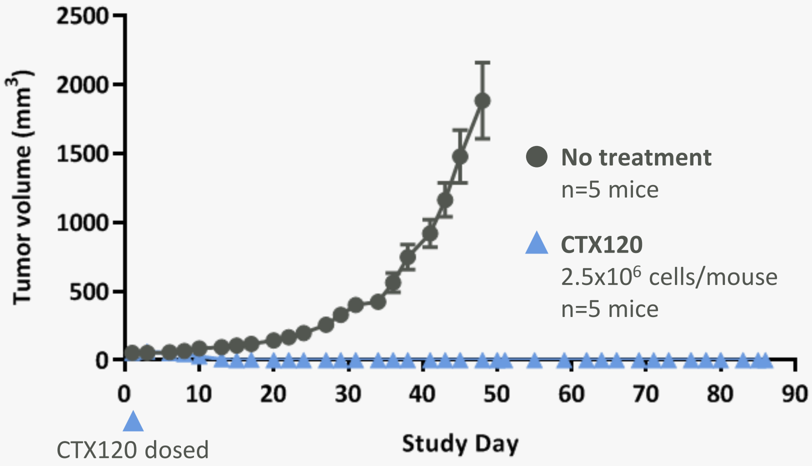
CTX110 – Anti-CD19 Allogeneic CAR-T

Prolonged survival in disseminated Nalm6 B-ALL xenograft tumor model



CTX120 – Anti-BCMA Allogeneic CAR-T

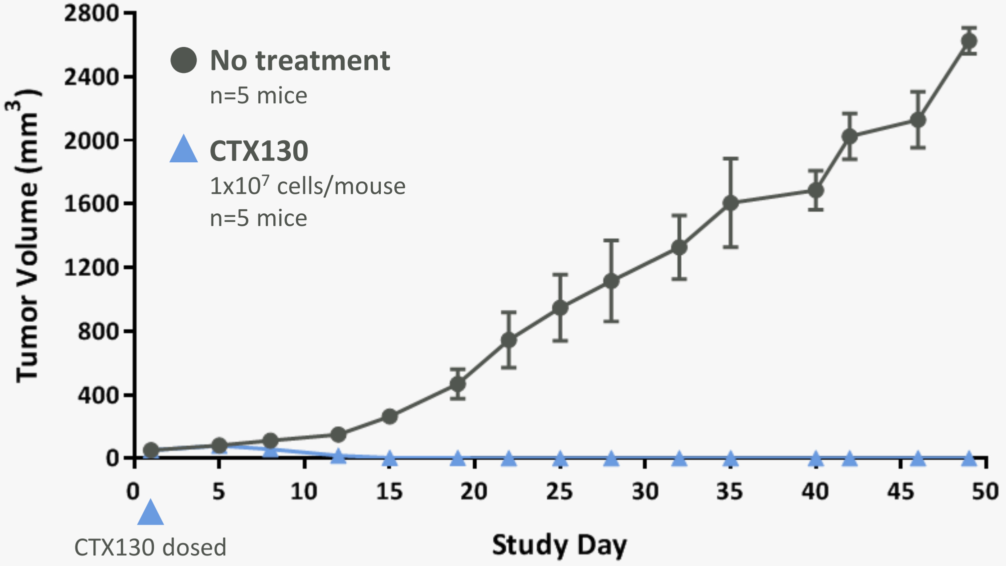
Subcutaneous RPMI-8226 multiple myeloma model completely eliminated



Strong anti-tumor activity observed with healthy donor-derived CAR-T cells – potential for better outcomes than autologous CAR-T given poor health of patient T cells

CTX130 – Anti-CD70 Program as a Bridge to Solid Tumors

Subcutaneous A498 Renal Cell Carcinoma Model Completely Eliminated



CTX130

- Anti-CD70 allogeneic CAR-T
- Additional editing beyond TCR and β2M knock-outs
- For both heme and solid tumors

Strong rationale for targeting CD70 for solid tumors

- Initial focus on clear cell renal cell carcinoma – immune-infiltrated disease and >80% CD70-positive
- Minimal CD70 expression on healthy tissues[1]

1. Adam, *et al*. Br J Cancer 2006

Rapid Generation of Novel Candidates Using CRISPR

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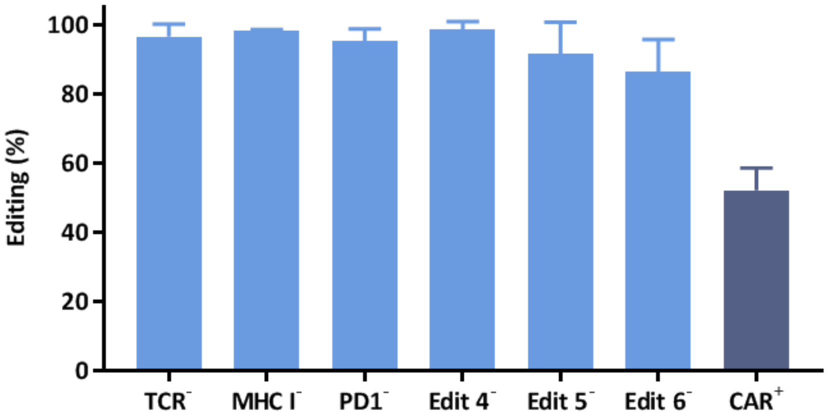
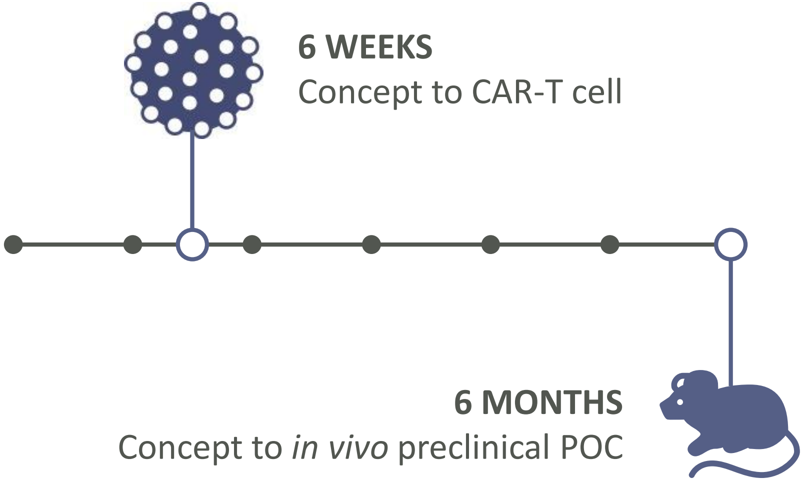
Multiplex Editing

Single-shot sextuple knock-out plus CAR insertion performed at high efficiency



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

Speed of Discovery



CRISPR Enables Regenerative Medicine 2.0

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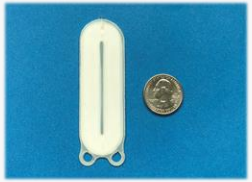
CRISPR/Cas9 Technology Opens Broader Applications for Regenerative Medicine

CRISPR/ Cas9

- Allow immune evasion
- Improve cell function
- Direct cell fate

Stem Cell Technology



Therapeutic Targets
e.g., diabetes

Exemplified by our collaboration with ViaCyte

- Aim to develop beta-cell replacement product to treat diabetes that does not require immunosuppression
- Applies immune-evasive gene-editing expertise from our allo CAR-T programs to stem cells

VIACYTE®

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

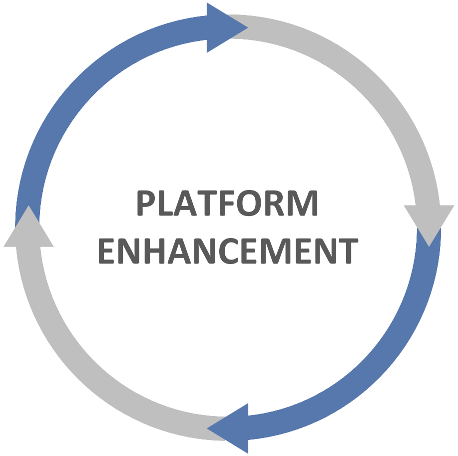
Optimizing the CRISPR/Cas9 Platform

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

- **23** Patents of broad scope granted, including the patent involved in the first interference
- **4** Patent applications of broad scope allowed
- **>45** Additional patent applications moving forward in parallel with both broad and narrow claims
- **2nd** Interference declared June 2019 to determine who was first to invent CRISPR/Cas9 gene editing in eukaryotic cells

Europe and Global

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

- **3** Patents of broad scope granted in the EU
- **23** 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

As of February 2020

Building a Great Company

CRISPR THERAPEUTICS

EXPERIENCED
Management Team

END-TO-END CAPABILITIES
With >300 Employees

COLLABORATIVE & ENTREPRENEURIAL
Culture