Creating transformative gene-based medicines for serious diseases

Corporate Overview | November 2020
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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, 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

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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

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>RESEARCH</th>
<th>IND-ENABLING</th>
<th>CLINICAL</th>
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<th>STATUS</th>
<th>PARTNER</th>
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<td><strong>Hemoglobinopathies</strong></td>
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<tr>
<td>CTX001™: β-thalassemia</td>
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<td>Enrolling</td>
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<td>CTX001™: Sickle cell disease (SCD)</td>
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<td>CTX110™: Anti-CD19 allogeneic CAR-T</td>
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<td>Type I diabetes mellitus</td>
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<td>Phi/II in 2021</td>
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<td>Collaboration</td>
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<td><strong>In vivo approaches</strong></td>
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<td>Glycogen storage disease Ia (GSD Ia)</td>
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<td>Duchenne muscular dystrophy (DMD)</td>
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<td>Myotonic dystrophy type 1 (DM1)</td>
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<td>Cystic fibrosis (CF)</td>
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<td></td>
<td>License</td>
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</tbody>
</table>

Additional undisclosed, early stage programs subject to collaboration or license agreements with Vertex and Bayer.
Hemoglobinopathies – Devastating Blood Diseases

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

- 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

**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 12 - 35 years of age with transfusion dependent thalassemia (TDT), including β0/β0 genotypes
- 45 patients between 12 - 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.
TDT Patient Baseline and Treatment Characteristics

<table>
<thead>
<tr>
<th>Patient baseline</th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td>$\beta_0 / \beta^+ (IVS-I-110)$</td>
<td>$\beta_0 / \beta^+ (IVS-II-745)$</td>
</tr>
<tr>
<td>Age at consent, years</td>
<td>19</td>
<td>26</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Pre-study pRBC transfusions(^1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Units/year</td>
<td>34</td>
<td>61</td>
</tr>
<tr>
<td>Transfusion episodes/year</td>
<td>16.5</td>
<td>15</td>
</tr>
</tbody>
</table>

| Treatment characteristics               |                                   |                                   |
| Cell dose, $CD34^+$ cells/kg           | $17.0 \times 10^6$               | $12.3 \times 10^6$               |
| Neutrophil engraftment\(^2\), Study day| 33                                | 36                                |
| Platelet engraftment\(^3\), Study day  | 37                                | 34                                |

Overall safety consistent with myeloablative conditioning and autologous transplant

- Each patient experienced 2 SAEs, none considered related to CTX001 by study investigators, all resolved:
  - Patient 1: Veno-occlusive liver disease attributed to busulfan conditioning and pneumonia in the presence of neutropenia
  - Patient 2: Pneumonia and upper respiratory tract infection

---

1 Annualized number during the 2 years before consenting to study participation
2 Defined as the first day of 3 measurements of absolute neutrophil count ≥500 cells/µL on 3 consecutive days
3 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

Data disclosed June 12, 2020

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TDT Patient 1: High Levels of HbF and Total Hb Achieved Rapidly and Sustained at 15 Months

Hemoglobin fractionation, Hb (g/dL)

<table>
<thead>
<tr>
<th>Monthly Levels</th>
<th>HbF</th>
<th>HbA</th>
<th>Hb, other[^1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>9.0</td>
<td>6.6</td>
<td>0.3</td>
</tr>
<tr>
<td>1</td>
<td>6.6</td>
<td>6.5</td>
<td>0.1</td>
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<tr>
<td>2</td>
<td>12.0</td>
<td>11.6</td>
<td>0.4</td>
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<tr>
<td>3</td>
<td>12.1</td>
<td>10.1</td>
<td>0.1</td>
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<tr>
<td>4</td>
<td>12.1</td>
<td>10.2</td>
<td>0.1</td>
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<tr>
<td>5</td>
<td>12.3</td>
<td>10.4</td>
<td>0.1</td>
</tr>
<tr>
<td>6</td>
<td>11.9</td>
<td>10.1</td>
<td>0.1</td>
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<tr>
<td>9</td>
<td>12.7</td>
<td>12.4</td>
<td>0.1</td>
</tr>
<tr>
<td>12</td>
<td>14.2</td>
<td>13.5</td>
<td>0.1</td>
</tr>
</tbody>
</table>

[^1]: Hb adducts and other variants

Data disclosed June 12, 2020

1. Circulating RBCs expressing fetal hemoglobin

Months post CTX001 infusion

- CTX001 infusion
- TDT Patient 1: High Levels of HbF and Total Hb Achieved Rapidly and Sustained at 15 Months

Peripheral F-cells[^2], %

- Months: 10.1, 3.9, 59.4, 83.4, 95.4, 97.4, 99.7, 99.8, 99.9, 100

Allelic editing in CD34+ bone marrow cells, %

- Months: 78.1, 76.1

[^1]: Hb adducts and other variants
[^2]: Circulating RBCs expressing fetal hemoglobin
TDT Patient 2: High Levels of HbF and Total Hb Achieved Rapidly and Sustained at 5 Months

Hemoglobin fractionation, Hb (g/dL)

<table>
<thead>
<tr>
<th>Months post CTX001 infusion</th>
<th>Baseline</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbF</td>
<td>10.1</td>
<td>8.9</td>
<td>9.8¹</td>
<td>11.5</td>
<td>12.9</td>
<td>12.5</td>
</tr>
<tr>
<td>HbA</td>
<td>0.0</td>
<td>0.1</td>
<td>5.1</td>
<td>9.5</td>
<td>12.5</td>
<td>12.2</td>
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<td>HbA2</td>
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<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
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<tr>
<td>Hb, other²</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Peripheral F-cells³, %</td>
<td>6.3</td>
<td>5.4</td>
<td>55.8</td>
<td>83.2</td>
<td>97.3</td>
<td>99.4</td>
</tr>
</tbody>
</table>

Data disclosed June 12, 2020

1 Total hemoglobin from local lab and hemoglobin fraction from central lab
2 Hb adducts and other variants
3 Circulating RBCs expressing fetal hemoglobin
Both TDT Patients Have Stopped pRBC Transfusions

Data disclosed June 12, 2020

1 In the 15 months after CTX001 infusion, phlebotomy for iron reduction occurred on Study Days 98, 147, 170, and 191. Iron chelation therapy received from Study Day 205 to Study Day 316.
SCD Patient Baseline and Treatment Characteristics

**Patient baseline**

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td>βS / βS</td>
</tr>
<tr>
<td>Age at consent, years</td>
<td>33</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
</tr>
<tr>
<td>Pre-study VOCs², VOCs/year</td>
<td>7</td>
</tr>
</tbody>
</table>

**Treatment characteristics**

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell dose, CD34+ cells/kg</td>
<td>$3.3 \times 10^6$</td>
</tr>
<tr>
<td>Neutrophil engraftment³, Study day</td>
<td>30</td>
</tr>
<tr>
<td>Platelet engraftment⁴, Study day</td>
<td>30</td>
</tr>
</tbody>
</table>

Overall safety consistent with myeloablative conditioning and autologous transplant

- 3 SAEs occurred, none considered related to CTX001 by study investigator, all resolved:
  - Sepsis in the presence of neutropenia
  - Cholelithiasis
  - Abdominal pain

Data disclosed June 12, 2020

1 Patient had received hydroxyurea treatment from 2016 to November 22, 2018 (Study Day −222)
2 Annualized rate during the 2 years before consenting to study participation
3 Defined as the first day of 3 measurements of absolute neutrophil count ≥500 cells/µL for 3 consecutive days with platelet count ≥50,000/µL without a platelet transfusion for 7 consecutive days
4 Defined as the first of 3 consecutive measurements on 3 separate days with platelet count ≥50,000/µL without a platelet transfusion for 7 consecutive days

© 2020 CRISPR Therapeutics
SCD: Robust, Pancellular HbF Expression Achieved Rapidly and Sustained at 9 Months

Hemoglobin fractionation, Hb (g/dL) and % of total Hb

<table>
<thead>
<tr>
<th>Months post CTX001 infusion</th>
<th>Baseline</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb, other</td>
<td>0.8%</td>
<td>8.9%</td>
<td>10.1%</td>
<td>11.3%</td>
<td>11.9%</td>
<td>11.3%</td>
<td>11.8%</td>
<td></td>
</tr>
<tr>
<td>HbA</td>
<td>21.3%</td>
<td>37.2%</td>
<td>46.6%</td>
<td>48.6%</td>
<td>47.3%</td>
<td>49.7%</td>
<td>50.6%</td>
<td></td>
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<tr>
<td>HbS</td>
<td>46.1%</td>
<td>25.9%</td>
<td>32.6%</td>
<td>41.2%</td>
<td>47.3%</td>
<td>47.3%</td>
<td>46.1%</td>
<td></td>
</tr>
<tr>
<td>HbF</td>
<td>74.1%</td>
<td>9.1%</td>
<td>8.3%</td>
<td>10.1%</td>
<td>11.3%</td>
<td>11.9%</td>
<td>11.8%</td>
<td></td>
</tr>
<tr>
<td>Peripheral F-cells^2, %</td>
<td>3.3%</td>
<td>4.3%</td>
<td>43.8%</td>
<td>70.2%</td>
<td>94.7%</td>
<td>99.9%</td>
<td>99.6%</td>
<td>99.7%</td>
</tr>
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</table>

Data disclosed June 12, 2020

1. Hb adducts and other variants
2. Circulating RBCs expressing fetal hemoglobin

Allelic editing in CD34+ bone marrow cells, %

© 2020 CRISPR Therapeutics
SCD: No VOCs Have Occurred Post-CTX001 Infusion

Prior to screening
2 years

On-study / pre-CTX001
6.5 months

Treatment period
9 months

Transfusions unrelated to SCD; post-transplant support

Transfusions related to SCD

VOCs

No VOCs in the 9 months of follow-up

Total Hb at last visit 11.8 g/dL

No pRBC transfusions have occurred since Study Day 19

Data disclosed June 12, 2020

1 Exchange transfusions per study protocol occurred during the on-study / pre-CTX001 period (not included here)
Before Patient Diagnosis

- **Autologous: patient derived**

After Patient Diagnosis

- **WEEK 1**: Apheresis
- **WEEK 2**: Manufacture
- **WEEK 3**: Single 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**

Allogeneic CAR-T Therapy Has Transformative Potential
Multiplex CRISPR gene editing in one step designed to:

- **Improve persistence in the allo setting** via β2M 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™ and CTX130™ 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

---

Cyclophosphamide (500 mg/m²) and Fludarabine (30 mg/m²) for 3 days

Median time from enrollment to start of LD: **2 days**

**Screening**

**Lymphodepletion (LD)**

**CTX110 infusion**

**Follow up**

---

**ICF**

NCT04035434
### CARBON: Patient Flow and Baseline Characteristics

**As of the data cutoff date:**

- **Enrolled:** 12 patients
- **Treated:** 12 patients
- **At least 28 days of follow-up (included in data cut):** 11 patients

### CARBON: Patient Flow and Baseline Characteristics

#### Cell dose (CAR+ T cells)

<table>
<thead>
<tr>
<th></th>
<th>DL1 30x10^6 (N=3)</th>
<th>DL2 100x10^6 (N=3)</th>
<th>DL3 300x10^6 (N=4)</th>
<th>DL4 600x10^6 (N=1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>52 (50-61)</td>
<td>64 (58-74)</td>
<td>64.5 (62-74)</td>
<td>72</td>
</tr>
<tr>
<td>Male</td>
<td>2 (66.7)</td>
<td>2 (66.7)</td>
<td>1 (25)</td>
<td>1 (100)</td>
</tr>
</tbody>
</table>

#### Lymphoma subtypes

- **Diffuse large B-cell lymphoma (DLBCL):**
  - DL1: 3 (100)
  - DL2: 3 (100)
  - DL3: 4 (100)
  - DL4: 1 (100)
- **Follicular lymphoma:**
  - DL1: 0
  - DL2: 0
  - DL3: 0
  - DL4: 0

#### Current disease stage (per Lugano 2014)

- **Stage III**
  - DL1: 1 (33.3)
  - DL2: 1 (33.3)
  - DL3: 2 (50)
  - DL4: 0
- **Stage IV**
  - DL1: 2 (66.7)
  - DL2: 2 (66.7)
  - DL3: 1 (25)
  - DL4: 1 (100)

#### Prior treatments

- **Median number (range):**
  - DL1: 2.0 (2-8)
  - DL2: 3.0 (2-3)
  - DL3: 2.0 (2-4)
  - DL4: 5
- **Hematopoietic stem cell transplant:**
  - DL1: 0
  - DL2: 0
  - DL3: 3 (75)
  - DL4: 1 (100)
- **Refractory to last therapy:**
  - DL1: 3 (100)
  - DL2: 3 (100)
  - DL3: 0
  - DL4: 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\(^1\) by independent central assessment

| Cell dose (CAR+ T cells) | DL1 \(30 \times 10^6\)  
N=3 | DL2 \(100 \times 10^6\)  
N=3 | DL3 \(300 \times 10^6\)  
N=4 | DL4 \(600 \times 10^6\)  
N=1 |
<table>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response rate (ORR), N (%)</td>
<td>0 (0%)</td>
<td>1 (33%)</td>
<td>2 (50%)</td>
<td>1 (100%)</td>
</tr>
<tr>
<td>Complete response (CR) rate, N (%)</td>
<td>0 (0%)</td>
<td>1 (33%)</td>
<td>2 (50%)</td>
<td>1 (100%)</td>
</tr>
</tbody>
</table>

- 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

First efficacy assessment occurs at M1 visit;  (1) Cheson, *et al.* *J Clin Oncol.* (2014)
**Best tumor size reduction per 2014 Lugano criteria by independent central assessment**

- **CR**: Complete Response
- **SD**: Stable Disease
- **PD**: Progressive Disease

Data as of September 28, 2020

*Patient subsequently failed autologous CAR-T*
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 (%)

<table>
<thead>
<tr>
<th>N=10</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graft-versus-Host Disease (GvHD)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cytokine Release Syndrome (CRS)(^1,2)</td>
<td>1 (10%)</td>
<td>2 (20%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ICANS(^3)</td>
<td>0</td>
<td>1 (10%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Infections</td>
<td>0</td>
<td>0</td>
<td>1 (10%)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

### Safety for patient treated at DL4 (600x10\(^6\) CAR\(^+\) 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

For patients in DL1 through DL3 (N=10):
- No GvHD despite all patients with ≤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)

---

(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

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Data as of September 28, 2020
## Our I/O Strategy and Allogeneic CAR-T Pipeline

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

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
- Plan to initiate trials in 2021
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
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
  - 33 Patents of broad scope granted, including the patent involved in the first interference
  - 2 Patent applications of broad scope allowed
  - 25+ Additional patent applications moving forward in parallel with both broad and narrow claims
  - 2nd Interference entering priority phase 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
  - 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

As of September 2020

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Building a Great Company

EXPERIENCED Management Team

END-TO-END CAPABILITIES With >300 Employees

COLLABORATIVE & ENTREPRENEURIAL Culture

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