Creating transformative gene-based medicines for serious diseases
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CRISPR Therapeutics Highlights

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

- **Achieving functional cures** 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

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**”
### Our Pipeline

#### Hemoglobinopathies
- **CTX001™**: β-thalassemia (Enrolling)
- **CTX001™**: Sickle cell disease (SCD) (Enrolling)

#### Immuno-oncology
- **CTX110™**: Anti-CD19 allogeneic CAR-T (Enrolling)
- **CTX120™**: Anti-BCMA allogeneic CAR-T (Enrolling)
- **CTX130™**: Anti-CD70 allogeneic CAR-T (Enrolling)

#### Regenerative medicine
- **Type I diabetes mellitus**: Enrolling (Collaboration)

#### In vivo approaches
- **Glycogen storage disease Ia (GSD Ia)**: Wholly-owned
- **Duchenne muscular dystrophy (DMD)**: License (Collaboration)
- **Myotonic dystrophy type 1 (DM1)**: License
- **Cystic fibrosis (CF)**: License

Additional undisclosed, early-stage programs subject to collaboration or license agreements with Vertex and Bayer.
Recent Collaborations to Combine Leading Capabilities

**Focus on co-developing and co-commercializing three gene-edited, donor-derived NK therapies:**

- CAR-NK program targeting CD70
- Combined NK and T cell program (NK+T) to harness the synergies of the innate and adaptive immune systems
- CAR-NK program optioned from Nkarta’s gene-edited pipeline

**Focus on advancing gene-edited therapies for familial amyotrophic lateral sclerosis (ALS) and Friedreich’s ataxia:**

- CRISPR leads Friedreich’s ataxia program, and performs gene-editing activities for both programs
- Capsida leads ALS program, and conducts capsid engineering and manufacturing for both programs
- CRISPR and Capsida each have the option to co-develop and co-commercialize the program that the other leads
Hemoglobinopathies – Devastating Blood Diseases

Sickle Cell Disease (SCD) and β-Thalassemia

Blood disorders caused by mutations in the β-globin gene

Significant worldwide burden

ANNUAL BIRTHS

300K
SCD

60K
β-thalassemia

High morbidity and mortality

Heavy burden of patient care

Anemia

Pain

Early death

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 transfusion-dependent β-thalassemia (TDT) and SCD, respectively.

#### Target enrollment

- **TDT**
  - 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.
- **SCD**
  - 45 patients aged 12-35 years with severe SCD and a history of ≥2 vaso-occlusive crises/year over the previous two years.

#### Primary endpoint

- **TDT**
  - Proportion of patients achieving sustained transfusion reduction of 50% for at least 6 months starting 3 months after CTX001 infusion.
- **SCD**
  - Proportion of patients with HbF ≥ 20%, sustained for at least 3 months starting 6 months after CTX001 infusion.

>45 patients with TDT and SCD dosed across both trials as of July 29, 2021.
# TDT: Patient Baseline and Treatment Characteristics

**Patients with ≥3-month follow-up (n=15)**

<table>
<thead>
<tr>
<th><strong>Patient baseline</strong></th>
<th>n</th>
<th><strong>Treatment characteristics</strong></th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Genotype</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β⁰ / β⁰</td>
<td>2</td>
<td>Drug product cell dose</td>
<td>6.5 (3.5-16.6)</td>
</tr>
<tr>
<td>β⁰ / IVS-I-110¹</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVS-I-110 / IVS-I-110¹</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β⁰ / βE</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β⁰ / β⁺</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β⁺ / β⁺</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female/Male</td>
<td>9/6</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age at consent</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years</td>
<td>23</td>
<td>Age at consent</td>
<td>23 (18-32)</td>
</tr>
<tr>
<td><strong>Pre-study pRBC transfusions²</strong></td>
<td></td>
<td></td>
<td>34 (20.5-61)</td>
</tr>
<tr>
<td>Units/year</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **Neutrophil engraftment³** | Median (range) |
| Study day⁴ | 29 (19-39) |

| **Platelet engraftment⁵** | Median (range) |
| Study day⁴ | 40 (29-56) |

| **Duration of follow-up** | Median (range) |
| Months                | 8.7 (4.0-26.2) |

Data as of March 30, 2021

(1) IVS-I-110 phenotype is severe and similar to β⁰;  
(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 ≥500 cells/µL on 3 consecutive days;  
(4) Study day 1 is the day of CTX001 infusion;  
(5) 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=15)**

Safety profile generally consistent with myeloablation and autologous stem cell transplant

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Patients with non-serious AEs, n</th>
<th>Patients with SAEs, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related to plerixafor and/or G-CSF</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Related to busulfan only</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>Related to CTX001 only</td>
<td>1(^2)</td>
<td>1</td>
</tr>
<tr>
<td>Related to busulfan and CTX001</td>
<td>3(^3)</td>
<td>1</td>
</tr>
<tr>
<td>Not related to any study drug</td>
<td>15</td>
<td>9</td>
</tr>
</tbody>
</table>

- 3 patients experienced SAEs assessed as related or possibly related to busulfan only: venoocclusive liver disease (2 patients), febrile neutropenia (1 patient), colitis (1 patient), and pneumonia (1 patient); all have resolved
- 1 patient had 4 SAEs assessed by the investigator as related or possibly related to CTX001: headache, haemophagocytic lymphohistiocytosis (HLH), acute respiratory distress syndrome, and idiopathic pneumonia syndrome (latter also related to busulfan); all occurred in the context of HLH and have resolved
- In addition to the above, one patient with <3 months of follow-up experienced an SAE of cerebellar hemorrhage, assessed by the investigator to be life-threatening, related to busulfan-induced thrombocytopenia, and not related to CTX001; the SAE has since resolved

Data as of March 30, 2021

(1) Includes related, possibly related, and missing relationship 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 (all resolved)
TDT: Clinically Meaningful HbF and Total Hb Are Achieved Early and Maintained

Hemoglobin fractionation, Hb (g/dL)

<table>
<thead>
<tr>
<th>CTX001 infusion</th>
<th>Total Hb, Mean (range), g/dL</th>
<th>HbF, Mean (range), g/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>10.1 (7.2 - 13.7)</td>
<td>0.5 (0.0 - 1.9)</td>
</tr>
<tr>
<td>1</td>
<td>8.7 (4.6 - 13.2)</td>
<td>0.5 (0.1 - 1.8)</td>
</tr>
<tr>
<td>2</td>
<td>11.0 (6.6 - 16.2)</td>
<td>4.7 (1.9 - 9.9)</td>
</tr>
<tr>
<td>3</td>
<td>11.4 (8.5 - 17.6)</td>
<td>7.5 (4.0 - 10.4)</td>
</tr>
<tr>
<td>4</td>
<td>12.2 (9.7 - 17.2)</td>
<td>10.3 (6.1 - 13.4)</td>
</tr>
<tr>
<td>5</td>
<td>12.4 (10.0 - 16.9)</td>
<td>10.8 (7.4 - 13.2)</td>
</tr>
<tr>
<td>6</td>
<td>11.6 (8.9 - 13.7)</td>
<td>10.3 (6.9 - 13.0)</td>
</tr>
<tr>
<td>9</td>
<td>12.0 (9.9 - 13.5)</td>
<td>11.0 (9.1 - 12.9)</td>
</tr>
<tr>
<td>12</td>
<td>12.1 (11.1 - 12.9)</td>
<td>11.5 (9.1 - 12.6)</td>
</tr>
<tr>
<td>15</td>
<td>13.2 (12.1 - 14.2)</td>
<td>12.6 (11.7 - 13.5)</td>
</tr>
<tr>
<td>18</td>
<td>14.1 (13.3 - 14.1)</td>
<td>13.1 (12.5 - 14.1)</td>
</tr>
<tr>
<td>21</td>
<td>13.3 (12.5 - 14.1)</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>14.7 (13.3 - 14.7)</td>
<td></td>
</tr>
</tbody>
</table>

| Months after CTX001 infusion | n = 15 | 15 | 14 | 14 | 14 | 13 | 11 | 6 | 5 | 2 | 1 | 1 | 1 |

Data as of March 30, 2021

© 2021 CRISPR Therapeutics
IVS-1-110 phenotype is severe and similar to $\beta^0$

Data as of March 30, 2021

(1) IVS-1-110 phenotype is severe and similar to $\beta^0$
# SCD: Patient Baseline and Treatment Characteristics

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

<table>
<thead>
<tr>
<th>Patient baseline</th>
<th>n</th>
<th>Treatment characteristics</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td>β⁺ / β⁺</td>
<td>Drug product cell dose</td>
<td>3.3 (3.1-3.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CD34+ cells x 10⁶/kg</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>3/4</td>
<td>Neutrophil engraftment²</td>
<td>25 (17-33)</td>
</tr>
<tr>
<td>Female/Male</td>
<td></td>
<td>Study day³</td>
<td></td>
</tr>
<tr>
<td>Age at consent</td>
<td>22 (19-34)</td>
<td>Platelet engraftment⁴</td>
<td>33 (30-53)</td>
</tr>
<tr>
<td>Years</td>
<td></td>
<td>Study day³</td>
<td></td>
</tr>
<tr>
<td>Pre-study VOCs</td>
<td>5.5 (2.5-9.5)</td>
<td>Duration of follow-up Months</td>
<td>7.6 (4.9-22.4)</td>
</tr>
<tr>
<td>VOCs/year¹</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data as of March 15, 2021

(1) Annualized rate 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) Study day 1 is the day of CTX001 infusion;  
(4) 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=7)

**Safety profile generally consistent with myeloablation and autologous stem cell transplant**

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<td>2</td>
</tr>
<tr>
<td>Related to busulfan only</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Related to CTX001 only</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Related to busulfan and CTX001</td>
<td>3&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0</td>
</tr>
<tr>
<td>Not related to any study drug</td>
<td>7</td>
<td>6</td>
</tr>
</tbody>
</table>

Data as of March 15, 2021

1. Includes related, possibly related, and missing relationship AEs;
2. 3 patients experienced non-serious AEs related or possibly related to busulfan and CTX001: dermatitis, lymphopenia, and CD4 lymphocytes decreased

- Post-CTX001 infusion, 1 patient experienced an SAE related to busulfan of sepsis, which resolved
- No SAEs related to CTX001 were reported
SCD: Clinically Meaningful HbF and Total Hb Are Achieved Early and Maintained

Hemoglobin fractionation, Hb (g/dL)

<table>
<thead>
<tr>
<th>months after CTX001 infusion</th>
<th>HbF</th>
<th>HbS</th>
<th>HbA</th>
<th>HbA2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4.0%</td>
<td>0.0%</td>
<td>57.7%</td>
<td>38.3%</td>
</tr>
<tr>
<td>1</td>
<td>11.2</td>
<td>9.5</td>
<td>5.7 - 9.7</td>
<td>4.0%</td>
</tr>
<tr>
<td>2</td>
<td>12.1</td>
<td>11.2</td>
<td>8.9 - 13.7</td>
<td>37.4%</td>
</tr>
<tr>
<td>3</td>
<td>12.5</td>
<td>13.2</td>
<td>10.0 - 15.4</td>
<td>12.1</td>
</tr>
<tr>
<td>4</td>
<td>11.3</td>
<td>13.5</td>
<td>7.7 - 9.7</td>
<td>9.5</td>
</tr>
</tbody>
</table>

Data as of March 15, 2021

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SCD: Duration VOC-Free After CTX001

Pre-study VOC burden
Average number per year over the previous 2 years

<table>
<thead>
<tr>
<th>Patient</th>
<th>Pre-study VOC</th>
<th>Total Hb at last visit (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.0</td>
<td>12.0</td>
</tr>
<tr>
<td>2</td>
<td>7.5</td>
<td>11.0</td>
</tr>
<tr>
<td>3</td>
<td>4.0</td>
<td>13.7</td>
</tr>
<tr>
<td>4</td>
<td>2.5</td>
<td>15.9</td>
</tr>
<tr>
<td>5</td>
<td>5.5</td>
<td>15.2</td>
</tr>
<tr>
<td>6</td>
<td>9.5</td>
<td>15.7</td>
</tr>
<tr>
<td>7</td>
<td>4.0</td>
<td>12.5</td>
</tr>
</tbody>
</table>

Improvements in markers of hemolysis (serum lactate dehydrogenase and haptoglobin) observed; haptoglobin detectable by Month 6 in all 4 patients with Month 6 values

Data as of March 15, 2021
Pancellular HbF Expression and Durable Editing

Pancellular expression of HbF maintained
Mean % peripheral F-cells (range), % circulating RBCs expressing HbF

Data as of March 30, 2021 for TDT and March 15, 2021 for SCD
(1) Bone marrow editing assessments performed starting at 6 months, 12 months, and 24 months of follow-up
Allogeneic CAR-T Therapy Has Transformative Potential

**Before Patient Diagnosis**

- **Autologous: patient derived**

**After Patient Diagnosis**

- **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**

**WEEK 1**
- Apheresis

**WEEK 2**
- Manufacture

**WEEK 3**
- Single Treatment

**T Cells**
- Manufacture
- 100+ Doses

**Healthy Donor**

**Patient**

© 2021 CRISPR Therapeutics
 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*
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

Primary endpoints

- Incidence of adverse events, defined as DLTs
- ORR

Key secondary endpoints

- CR rate, DoR, and OS

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
- On-site availability of CAR-T cell product

Median time from enrollment to start of LD: 2 days

CTX110 infusion

Option for 2nd CTX110 infusion with LD following disease progression

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

NCT04035434
CARBON: Patient Flow

As of the data cutoff date:

- **Enrolled:** 30 patients
- **Treated:** 29 patients
- **≥28 days of follow-up (included in data cut):** 26 patients

Modified ITT (mITT) nearly identical to ITT: just one patient enrolled but not treated

- **At DL2 and above:**
  - mITT: 23 patients infused
  - ITT: 24 patients enrolled

Data as of August 26, 2021

(1) Includes patients in the process of being treated as of the cutoff date
## CARBON: Baseline Patient Characteristics

CARBON only enrolled patients with aggressive LBCL

- **High burden of disease** with significant baseline tumor volume
- Both relapsed and refractory patients, including primary refractory patients that had no prior response to any anti-cancer therapy
- **History of rapidly progressive disease** – 31% of patients had progressed through 2+ lines of therapy and received CTX110 within 9 months of their first lymphoma treatment

### 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=6</th>
<th>DL3.5 450x10^6 N=6</th>
<th>DL4 600x10^6 N=8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median age, years (range)</td>
<td>52 (50-61)</td>
<td>64 (58-74)</td>
<td>69 (62-74)</td>
<td>67.5 (25-74)</td>
<td>65.5 (55-75)</td>
</tr>
<tr>
<td>Female</td>
<td>1 (33)</td>
<td>1 (33)</td>
<td>4 (67)</td>
<td>2 (33)</td>
<td>2 (25)</td>
</tr>
<tr>
<td><strong>Lymphoma subtypes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large B-cell lymphoma (LBCL)</td>
<td>3 (100)</td>
<td>3 (100)</td>
<td>6 (100)</td>
<td>6 (100)</td>
<td>8 (100)</td>
</tr>
<tr>
<td><strong>Current disease stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IV</td>
<td>2 (67)</td>
<td>2 (67)</td>
<td>2 (33)</td>
<td>5 (83)</td>
<td>4 (50)</td>
</tr>
<tr>
<td><strong>Prior treatments</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median number (range)</td>
<td>2 (2-8)</td>
<td>3 (2-3)</td>
<td>2 (2-4)</td>
<td>2.5 (2-10)</td>
<td>3 (2-10)</td>
</tr>
<tr>
<td>Hematopoietic stem cell transplant</td>
<td>0</td>
<td>0</td>
<td>3 (50)</td>
<td>4 (67)</td>
<td>2 (25)</td>
</tr>
<tr>
<td>Refractory to last therapy</td>
<td>3 (100)</td>
<td>3 (100)</td>
<td>2 (33)</td>
<td>1 (17)</td>
<td>5 (63)</td>
</tr>
</tbody>
</table>

(1) Including DLBCL NOS, high grade lymphoma (e.g., triple hit), transformed follicular lymphoma (tFL); (2) Per Lugano 2014

Data as of August 26, 2021
## Dose-Dependent Responses with CTX110

### D28 response following first CTX110 dose per 2014 Lugano criteria

| Cell dose (CAR+ T cells) | DL1 30x10^6  
N=3 | DL2 100x10^6  
N=3 | DL3 300x10^6  
N=6 | DL3.5 450x10^6  
N=6 | DL4 600x10^6  
N=8 |
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response rate (ORR), N (%)</td>
<td>0 (0%)</td>
<td>1 (33%)</td>
<td>3 (50%)</td>
<td>4 (67%)</td>
<td>6 (75%)</td>
</tr>
<tr>
<td>Complete response (CR) rate, N (%)</td>
<td>0 (0%)</td>
<td>1 (33%)</td>
<td>2 (33%)</td>
<td>3 (50%)</td>
<td>3 (38%)</td>
</tr>
</tbody>
</table>

### DL2+ mITT  
N=23 | DL2+ ITT  
N=24

|              | DL2+ mITT  
N=23 | DL2+ ITT  
N=24 |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response rate (ORR), N (%)</td>
<td>14 (61%)</td>
<td>14 (58%)</td>
</tr>
<tr>
<td>Complete response (CR) rate, N (%)</td>
<td>9 (39%)</td>
<td>9 (38%)</td>
</tr>
</tbody>
</table>

Durable Responses Observed with CTX110

Durable responses have been observed with CTX110, with all patients in complete response at 6 months remaining clinically well without receiving any systemic anticancer therapy other than CTX110.

1. Patient had a localized tumor recurrence that was excised and is clinically well having received no additional anticancer therapy.
2. Unaudited data as of Oct. 7 after the data cut.

Imaging per protocol occurs at M1, M3, and M6; CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease.

(1) Death due to disease progression
(2) Other death

Dose level of re-dose indicated if different from initial dose level.

Data as of August 26, 2021.
CTX110 Was Well Tolerated Across All Dose Levels

### Adverse events of interest N (%)

<table>
<thead>
<tr>
<th></th>
<th>DL1 (N=3)</th>
<th>DL2 (N=3)</th>
<th>DL3 (N=6)</th>
<th>DL3.5 (N=6)</th>
<th>DL4 (N=8)</th>
<th>DL2+ (N=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gr 1-2</td>
<td>Gr 3+</td>
<td>Gr 1-2</td>
<td>Gr 3+</td>
<td>Gr 1-2</td>
<td>Gr 3+</td>
</tr>
<tr>
<td><strong>CRS</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>1 (33)</td>
<td>-</td>
<td>2 (67)</td>
<td>-</td>
<td>2 (33)</td>
<td>-</td>
</tr>
<tr>
<td><strong>ICANS</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
<td>-</td>
<td>-</td>
<td>1 (33)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>GvHD</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Infusion reactions</strong></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Infections</strong>&lt;sup&gt;3&lt;/sup&gt;</td>
<td>-</td>
<td>1 (33)</td>
<td>-</td>
<td>-</td>
<td>1 (17)</td>
<td>1 (17)</td>
</tr>
</tbody>
</table>

- **No CRS and only one case of ICANS above Grade 2**<sup>4</sup>
- **No GvHD or infusion reactions**
- **Low rate of infections, with only 2 Grade 3+ events: HHV-6<sup>4</sup> and pseudomonal sepsis that resolved in 4 days**
- **Includes events following re-dosing**

**One treatment-emergent death without disease progression:** ICANS/HHV-6 encephalitis<sup>4</sup>

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CRS and ICANS graded per ASTCT criteria; other adverse events graded per CTCAE; (1) Cytokine Release Syndrome; (2) Immune Effector Cell-associated Neurotoxicity Syndrome; (3) All infections (bacterial, fungal, and viral) included; (4) As disclosed in October 2020

Data as of August 26, 2021
Strong Rationale for Consolidation Dose of CTX110

CTX110 shows a dose response, with better responses achieved with higher “effector:target” ratios

Consolidation has potential to create 2nd round of antitumor activity with favorable “E:T” ratio to increase deep and durable responses

(1) CAR+ T cells (millions) divided by baseline sum of perpendicular diameters (mm²)

Data as of August 26, 2021
Conclusions and Next Steps for CTX110

CTX110 is a potentially best-in-class allogeneic cell therapy in r/r LBCL with a profile that can compete with approved autologous CAR-T therapies

- **Initial response rates in line** with approved autologous CAR-T therapies
- **Ability to achieve** long-lasting complete remissions
- **Positively differentiated safety profile**
- **Potential to improve profile further with consolidation dosing**
- **Expand CARBON into a potentially registrational trial** in Q1 2022
- **Broaden into outpatient and community settings**
- **Further scale manufacturing in our state-of-the-art facility**
- **Continue to innovate** by advancing additional gene-edited allogeneic CAR-T programs to the clinic, including novel edits for increased potency
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></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTX110 (anti-CD19)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Enrolling</td>
</tr>
<tr>
<td><em>B-cell malignancies</em></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>CTX120 (anti-BCMA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Enrolling</td>
</tr>
<tr>
<td><em>Multiple myeloma</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Expand</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTX130 (anti-CD70)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Enrolling</td>
</tr>
<tr>
<td><em>T- and B-cell lymphomas</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTX130 (anti-CD70)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Enrolling</td>
</tr>
<tr>
<td><em>Renal cell carcinoma</em></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Unlock</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-CD33 allogeneic CAR-T</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Incorporating additional editing, novel targeting, etc.</td>
</tr>
<tr>
<td>Anti-PTK7 allogeneic CAR-T</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional undisclosed programs</td>
<td></td>
<td></td>
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</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

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

CRISPR/Cas9

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

Therapeutic Targets e.g., diabetes

Stem Cell Technology

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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
- mRNA technology from CureVac
- Programs include GSD Ia and other early research programs

---

Enabling collaborations

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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

PLATFORM ENHANCEMENT
Strong U.S. and Global Foundational IP Position

**United States**

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

- 40 Patents of broad scope granted, including the patent involved in the 1st interference
- Additional patent applications moving forward in parallel with both broad and narrow claims, including 4 patent applications of broad scope allowed
- 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

As of Q2 2021
Building a Great Company

EXPERIENCED
Management Team

END-TO-END CAPABILITIES
With >400 Employees

COLLABORATIVE & ENTREPRENEURIAL Culture

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