Top-Line Results from the Phase 1 CARBON Trial of CTX110™

October 21, 2020
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We Have Made Tremendous Progress Over the Past 5 Years

- **Built the leading CRISPR company:** 4 programs in the clinic; >300 employees; >$1B cash balance

- **Demonstrated, for the first time, the power of CRISPR gene editing in rare diseases:** initial data with CTX001™ supportive of a potential functional cure for sickle cell disease and beta thalassemia

- **Advanced three gene-edited allogeneic CAR-T programs into the clinic** across four trials

- **In parallel, expanded into regenerative medicine and progressed our in vivo efforts**

- **Created a sustainable innovation engine with pre-eminent capabilities**

- **And today, we show the promise and potential of CRISPR-edited cell therapies in the fight against cancer**
Allogeneic CAR-T Therapy Has Transformative Potential

Before Patient Diagnosis

Autologous: patient derived

After Patient Diagnosis

WEEK 1

WEEK 2

WEEK 3

- 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

Specificity, efficiency, and versatility of CRISPR gene editing facilitates consistent, multiplex editing to produce allogeneic cell therapies and enhance immune cell performance

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CTX110: Differentiated CRISPR-Edited Allogeneic CAR-T Design

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

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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

ICF

Median time from enrollment to start of LD: 2 days

CTX110 infusion

Screening

Lymphodepletion (LD)

Follow up

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

NCT04035434
CARBON: Patient Flow

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

- At each completed dose level, two lots of CTX110 manufactured from different healthy donors were used.

- Given antitumor activity observed, additional patients enrolled at DL3 and DL4 added.

Data as of September 28, 2020

- DL1: 3
- DL2: 3
- DL3: 3 + DL3: 1
- DL4: 1

- 600x10^6 CAR+ T cells
- 300x10^6 CAR+ T cells
- 100x10^6 CAR+ T cells
- 30x10^6 CAR+ T cells

Enrolled: 12 patients
Treated: 12 patients
CARBON: Baseline Patient Characteristics

| Cell dose (CAR⁺ T cells) | DL1 30x10⁶  
|                          | N=3 | DL2 100x10⁶  
|                          | N=3 | DL3 300x10⁶  
|                          | N=4 | DL4 600x10⁶  
|                          | 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) |
| Lymphoma subtypes         |      |      |      |      |
| Diffuse large B-cell lymphoma (DLBCL)¹ | 3 (100) | 3 (100) | 4 (100) | 1 (100) |
| Follicular lymphoma       | 0    | 0    | 0    | 0    |
| Current disease stage (per Lugano 2014)² |      |      |      |      |
| Stage III                 | 1 (33.3) | 1 (33.3) | 2 (50) | 0    |
| Stage IV                  | 2 (66.7) | 2 (66.7) | 1 (25) | 1 (100) |
| Prior treatments          |      |      |      |      |
| 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 criteria¹ by independent central assessment**

| Cell dose (CAR+ T cells) | DL1 30x10⁶  
N=3   | DL2 100x10⁶  
N=3   | DL3 300x10⁶  
N=4   | DL4 600x10⁶  
N=1   |
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<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>
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</tbody>
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First efficacy assessment occurs at M1 visit

Dose-Dependent Reduction in Tumor Size with CTX110

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

-660%

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

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Acceptable Safety Profile with CTX110 at DL3 and Below

<table>
<thead>
<tr>
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<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
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<tr>
<td>Graft-versus-Host Disease (GvHD)</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<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>
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<tr>
<td>ICANS(^{1,3})</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>
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</tbody>
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(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

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)

Data as of September 28, 2020
Patient Treated at DL4 (600x10^6 CAR^+ T cells)

- **Patient characteristics:** 72-year-old male with relapsed transformed follicular lymphoma following five prior lines of therapy, including autologous stem cell transplant

- **Efficacy:** Complete response on Day 25 post infusion of CTX110

- **Safety:**
  - 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
Emerging Pharmacokinetic Profile of CTX110

For patients in DL2 through DL4:

- **CAR-T cells detected at multiple time points in all patients**
- **Redistribution phase** observed from Day 1 to Day 3, followed by expansion
- **Consistent peak expansion** of CTX110 in the peripheral blood **seen around 1-2 weeks post infusion**
- **CTX110 detected out as late as 180 days** after administration
CTX110 Case Study: Stable Disease with Remaining Tumor Negative for CD19

**Patient characteristics**
- 62-year-old male with transformed follicular lymphoma
- Relapsed following two prior lines of therapy
- Treated with CTX110 at DL3 (300x10^6 CAR⁺ T cells)

**Safety and efficacy**
- No fever, CRS, or ICANS
- Visible reduction in lymph nodes on physical exam
- SD at day 28 with 59% reduction in tumor size, but remaining sites of disease were FDG avid
- Pre-treatment tumor biopsy showed positive staining for CD19 by IHC, whereas Day 41 post-CTX110 tumor biopsy did not, indicative of CD19-negative disease

IHC: Immunohistochemistry; FDG: Fluorodeoxyglucose
CTX110 Case Study: Complete Response Following Eradication of a Large Tumor Mass

**Patient characteristics**

- 62-year-old female diagnosed with DLBCL
- Relapsed following two prior lines of therapy, including autologous SCT
- Treated with CTX110 at DL3 (300x10^6 CAR^+ T cells)

**Safety and efficacy**

- CR at Day 28 with no tumor visible
- Deauville 5 to Deauville 1 for FDG uptake
- No fever, CRS, or ICANS
- CR ongoing at 3+ months
Initial CTX110 Data Supports Our Approach

- Early evidence of dose response
- Complete responses achieved in 4 patients (both DLBCL and tFL)
- Data in line with early autologous CAR-T trials

- Dose-dependent antitumor activity

- Acceptable safety profile at DL3 and below
  - No CRS or ICANS above Grade 2 at DL3 and below; no GvHD at any dose level
  - Responses achieved without the use of more toxic lymphodepletion agents, consistent with CTX110 being engineered for immune evasion

- Initial experience demonstrates versatility of allogeneic CAR-T
  - All enrolled patients treated rapidly – no need for bridging chemotherapy or risk of manufacturing failure
  - Responses seen across multiple product lots manufactured from different donors
  - Validates our CRISPR-edited allogeneic CAR-T approach
Planned Next Steps for CTX110 and Our CRISPR-Edited CAR-T Pipeline

- **“Full steam ahead” on CTX110**
  - Proceed into expansion cohort following selection of optimal dose
  - Re-dosing now included as an option in all cohorts
    - One patient (SD following initial treatment with CTX110 at DL3) re-dosed at DL3

- **Continue rapid progress on CTX120 and CTX130**
  - Dosing ongoing in trial of CTX120 in multiple myeloma
  - Dosing ongoing in trials of CTX130 in renal cell carcinoma and in T and B cell lymphomas
  - Initial data for both programs expected in 2021

- **Building on the pipeline**: announcement of additional programs planned in 2021
## Our I/O Strategy and Pipeline

### Validate allogeneic platform with proven targets
- **CTX110**
  - Anti-CD19 allogeneic CAR-T
  - Status: Enrolling
- **CTX120**
  - Anti-BCMA allogeneic CAR-T
  - Status: Enrolling

### Expand from hematologic cancers into solid tumors
- **CTX130 in lymphomas**
  - Anti-CD70 allogeneic CAR-T
  - Status: Enrolling
- **CTX130 in RCC**
  - Anti-CD70 allogeneic CAR-T
  - Status: Enrolling

### Unlock the full potential of I/O cell therapy with CRISPR
- Anti-CD33 allogeneic CAR-T
- Anti-PTK7 allogeneic CAR-T
- Additional undisclosed programs
  - Status: Incorporating additional editing, novel targeting, etc.

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Thank You to Patients and Their Families

Thank you to patients and their families, investigators, and site staff

**CTX110 sites**

**United States**
- University of Kansas Medical Center  Westwood, KS
- Oregon Health and Science University  Portland, OR
- Sarah Cannon Research Institute  Nashville, TN
- University of Chicago  Chicago, IL
- Mayo Clinic  Jacksonville, FL
- Texas Transplant Institute  San Antonio, TX

**Europe**
- University Medical Center Hamburg-Eppendorf  Hamburg, Germany

**Australia**
- Peter MacCallum Cancer Centre  Melbourne
- Royal Prince Alfred Hospital  Sydney

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