Delivering on the Promise of Targeted Protein Degradation

April 8, 2022
Forward-looking Statements and Intellectual Property

Forward-looking Statements

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Targeted Protein Degradation Has the Potential to Transform Treatment of Disease

TPD Has an Expansive Target Landscape
85% of proteins are currently undruggable or poorly drugged

TPD Offers a Powerful Modality
Benefits of genetic knockdown with a small molecule approach

C4T’s TORPEDO platform creates therapeutic candidates that have the potential to improve patient care

- Overcome Resistance
- Drug Undruggable Targets
- Improve Treatment Options


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Our TORPEDO Platform Efficiently Designs Potent Targeted Protein Degrader Medicines

<table>
<thead>
<tr>
<th>Elements</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Focus on Catalytic Efficiency</strong></td>
<td>Optimization of overall degradation process results in maximal efficacy</td>
</tr>
<tr>
<td><strong>Ability to Design, Analyze &amp; Predict Degrader Performance</strong></td>
<td>Rapid delivery of potent drug candidates through informed and efficient drug discovery</td>
</tr>
<tr>
<td><strong>Investment in Cereblon as E3 Ligase</strong></td>
<td>Cereblon is expressed in all tissues and cellular compartments, thereby providing the largest target selection opportunity</td>
</tr>
<tr>
<td><strong>Ability to Develop Both MonoDAC &amp; BiDAC Degraders</strong></td>
<td>Flexibility to address different targets with tailored approach</td>
</tr>
</tbody>
</table>
C4T is Well Positioned to Deliver on the Promise of Targeted Protein Degradation to Transform Patient Care

Leading in TPD Science
World-class medicinal chemistry coupled with fundamental enzymology approach

Validated Platform
TORPEDO platform enables efficient optimization of MonoDAC and BiDAC degraders

Oncology-Focused Clinical Pipeline
Transform patient care by targeting undrugged or poorly drugged targets

Strong Foundation to Support Growth
Capabilities across discovery and clinical coupled with experience in strategic partnerships and strong balance sheet

*Cash, cash equivalents, and marketable securities were $451.5M as of 12/31/21
Initial Programs Designed to Establish TORPEDO Platform for Validated Targets With Persistent Unmet Medical Need

Selective Target Criteria

• Strong rationale for a degrader approach
• Genetics are a clear driver of disease
• Clinically validated or de-risked targets
• Clear clinical development path
• Need for improved therapies to positively impact patient outcomes

Advancing High-Potential Programs through the Clinic

• CFT7455 – targeting IKZF1/3
• CFT8634 – targeting BRD9
• CFT1946 – targeting BRAF V600X
• CFT8919 – targeting EGFR L858R
Unlocking Potential of TPD Science by Developing the Next Wave of Oncology Programs

Leverage Experience to Tackle Higher-risk Novel Targets that Drive Value

- Difficult-to-drug targets not adequately addressable by existing modalities
- Potential to transform patient care
- Pursuing both MonoDAC and BiDAC degraders

C4T Has the Potential to Deliver:

- First-in-class molecules
- Therapies across oncology and other therapeutic areas driven by existing collaborations
- Degraders with high patient impact
### Robust Pipeline of Degrader Medicines Pursuing Meaningful Targets

<table>
<thead>
<tr>
<th>Program</th>
<th>Target</th>
<th>Indication</th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2/3</th>
<th>Next Milestone</th>
<th>Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFT7455</td>
<td>IKZF1/3</td>
<td>Multiple Myeloma &amp; Lymphoma</td>
<td>Enrolling</td>
<td></td>
<td></td>
<td></td>
<td>Recommended Phase 2 Dose</td>
<td>C4T</td>
</tr>
<tr>
<td>CFT8634</td>
<td>BRD9</td>
<td>Synovial Sarcoma &amp; SMARCB1-null Solid Tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initiate Phase 1 trial</td>
<td>C4T</td>
</tr>
<tr>
<td>CFT1946</td>
<td>BRAF V600X</td>
<td>Melanoma, CRC &amp; NSCLC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Submit IND application and initiate Phase 1 trial</td>
<td>C4T</td>
</tr>
<tr>
<td>CFT8919</td>
<td>EGFR L858R</td>
<td>NSCLC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Complete IND-enabling activities</td>
<td>C4T</td>
</tr>
</tbody>
</table>

**Earlier-Stage Undisclosed Programs (includes RET)**

| | Various Cancers | 4 targets | |
|---|----------------|-----------||

**Undisclosed Collaboration Programs**

<table>
<thead>
<tr>
<th>Various Cancers</th>
<th>4 targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological Conditions</td>
<td>5 targets</td>
</tr>
<tr>
<td>Diseases of Aging, including Cancer</td>
<td>1 target through March 2023</td>
</tr>
</tbody>
</table>

Number of targets represents the total number of active or potentially active research programs remaining under the applicable collaboration.
CFT7455
Targeting IKZF1/3

Multiple Myeloma
& Lymphoma
IKZF1/3 are transcription factors required for cancer cell growth and survival in multiple myeloma (MM)

Approved IMiDs (lenalidomide, pomalidomide) are widely used in MM treatment and are IKZF1/3 degraders

Relapsed/refractory MM remains a high unmet medical need

Goal: Develop an IKZF1/3 Monofunctional Degradation Activating Compound (MonoDAC) with these properties:

- Class-leading catalytic activity to enable potent, rapid, and deep target degradation
- High binding affinity to overcome IMiD resistance
- Selective to reduce off-target liabilities
- Pharmacologic profile that enables sustained IKZF1/3 degradation

CFT7455: Potent Small Molecule IKZF1/3 Degrader with Enhanced Catalytic & Pharmacologic Properties
High Catalytic Activity of CFT7455 Improves Activity in H929 MM Cells Compared to Pomalidomide*

<table>
<thead>
<tr>
<th>Binding Affinity (FP)</th>
<th>Degradation Kinetics</th>
<th>MM Cell Viability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Concentration (nM)</strong></td>
<td><strong>% IKZF1 Remaining (2 hr)</strong></td>
<td><strong>% H929 Viability (96 hr)</strong></td>
</tr>
<tr>
<td>Fraction Bound</td>
<td>Pomalidomide</td>
<td>CC-220</td>
</tr>
<tr>
<td>0.0</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>10^1</td>
<td>10^2</td>
<td>10^3</td>
</tr>
<tr>
<td>0.0</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>10^4</td>
<td>10^2</td>
<td>10^0</td>
</tr>
<tr>
<td>0</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>125</td>
<td>100</td>
<td>75</td>
</tr>
</tbody>
</table>

**Key Takeaway:**
- Catalytic activity enhancement resulted in >1000-fold improvement in potency vs. Pomalidomide

*Pomalidomide is an approved IKZF1/3 degrader while CC-220, CC-92480 and CFT7455 are all investigational compounds. C4 Therapeutics data on file.
CFT7455 Demonstrates Superior Efficacy in NCI-H929 MM Xenograft Model

Key Takeaways:

- In comparison to CC-92480, CFT7455 achieves equivalent efficacy at 1/100th of the dose

CFT7455 vs. Comparators

CFT7455 Results in Durable Complete Regression

- In the NCI-H929 xenograft model, 100 µg/kg/day of CFT7455 resulted in durable tumor regressions
CFT7455 is Highly Efficacious in a Model of Systemic Multiple Myeloma

CFT7455 vs Comparators in a Model of Systemic MM

- **Vehicle (QD, PO)**
- **Pomalidomide (3000 µg/kg, QD)**
- **CC-92480 (1000 µg/kg, QD)**
- **CFT7455 (100 µg/kg, QD)**
- **CFT7455 (30 µg/kg, QD)**

*Mouse missing in CFT7455 100 µg/kg group due to changes unrelated to treatment or disease*
Single Dose PK/PD in H929 Xenografts Differentiates CFT7455 from CC-92480

CFT7455 and CC-92480* Tumor and Plasma Concentrations

- CC-92480 (1000 μg/kg, Tumor)
- CFT7455 (100 μg/kg, Tumor)
- CC-92480 (1000 μg/kg, Plasma)
- CFT7455 (100 μg/kg, Plasma)

CC-92480 is not detectable after 4 hours

CFT7455 DC80 (total)

Degradation Kinetics for CFT7455, CC-92480 and Pomalidomide

- Pomalidomide (3000 μg/kg)
- CC-92480 (1000 μg/kg)
- CFT7455 (100 μg/kg)

Percent of IKZF3 Remaining/Normalized to GAPDH in NCI-H929 Tumors

Marketed IKZF1/3 Degraders Leave Room for Improvement for Multiple Myeloma Patients

IMiDs are suboptimal degraders, yet remain a **backbone therapy** for MM

Median time to first relapse occurs **3 – 4 years** after diagnosis

R/R MM patients **not adequately addressed by currently available therapies**

Significant toxicity from **chronic dexamethasone use**

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Unmet Need Remains High for Non-Hodgkin’s Lymphoma Patients

Non-Hodgkin’s Lymphoma (NHL)

IKZF1/3 are key drivers of malignancy in NHLs

Approved IMiDs have limited activity in NHLs

Peripheral T-Cell Lymphoma is 4% of NHL, Median Overall Survival 2 years

Mantle Cell Leukemia is 7% of NHL, Median Overall Survival 4–5 years

82K cases/year in the U.S.¹


CFT7455 Phase 1/2 Trial Design

Phase 1 Dose Escalation

Cohort A:
Monotherapy
R/R Multiple Myeloma & Non-Hodgkin’s Lymphoma
N=5
Status: Complete

Cohort B1:
R/R Multiple Myeloma Monotherapy
N =~15
Status: Enrolling

Cohort B2:
R/R Multiple Myeloma Combination with Dexamethasone
N =~15

Cohort B3:
R/R Multiple Myeloma Combo w/ Dexamethasone
N =~30

Cohort C:
Non-Hodgkin’s Lymphoma Monotherapy
N =~15
Status: Enrolling

Phase 2 Expansion

R/R Multiple Myeloma Monotherapy
N =~30

Mantle Cell Lymphoma
N =~20

Peripheral T-Cell Lymphoma
N =~20

Cohorts B1 & C Enrolling Patients to Determine Recommended Phase 2 Dose

1. 28-day cycle / dose limiting toxicity (DLT) window
2. Combination therapy cohorts will open once the selected CFT7455 dose level has been cleared for safety

Note: 6-12 patient food effect enrichment cohort also included during escalation, not pictured in the schema
### Cohort A Enrolled Heavily Pre-Treated and Highly Refractory MM Patients

<table>
<thead>
<tr>
<th>N (%) of patients unless stated</th>
<th>N=5</th>
<th>N (%) of patients unless stated</th>
<th>N=5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, median (range)</td>
<td>63 (51,73)</td>
<td>Number of lines of prior therapy, median (range)</td>
<td>5 (4–14)</td>
</tr>
<tr>
<td>Sex, male</td>
<td>3 (60)</td>
<td>Prior stem cell transplantation</td>
<td>3 (60)</td>
</tr>
<tr>
<td>Time since initial diagnosis, median (range), years</td>
<td>11 (4,21)</td>
<td>IMiD agent refractory</td>
<td>5 (100)</td>
</tr>
<tr>
<td>ECOG PS</td>
<td></td>
<td>POM</td>
<td>5 (100)</td>
</tr>
<tr>
<td>0</td>
<td>2 (40)</td>
<td>LEN</td>
<td>5 (100)</td>
</tr>
<tr>
<td>1</td>
<td>2 (40)</td>
<td>PI refractory</td>
<td>4 (80)</td>
</tr>
<tr>
<td>2</td>
<td>1 (20)</td>
<td>BORT</td>
<td>5 (100)</td>
</tr>
<tr>
<td>R-ISS stage at screening, n (%)</td>
<td></td>
<td>CFZ</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Stage I</td>
<td>1 (20)</td>
<td>Prior anti-CD38 antibody</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Stage II</td>
<td>1 (20)</td>
<td>Prior CAR-T</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Stage III</td>
<td>2 (40)</td>
<td>Prior ADC</td>
<td>1 (20)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (20)</td>
<td>Prior bispecific antibody</td>
<td>1 (20)</td>
</tr>
<tr>
<td>Presence of extramedullary plasmacytoma</td>
<td>3 (60)</td>
<td>Triple-class refractory (≥1 IMiD, ≥1 PI, and ≥1 anti-CD38 antibody)</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Assessable serum free light chain</td>
<td>5 (100)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Observed Steady State Exposures Suggest CFT7455 50 µg QD Achieves Efficacious Exposures

Key Takeaways:

- The 50 µg dose achieved exposures which were active (and superior to pomalidomide) in pre-clinical models
- CFT7455 was rapidly absorbed, with a plasma half-life of approximately two days
- Accumulation of drug was observed up to four-fold by day 15 (360 hours)

* Patient 4 received 50 µg for 8 days followed by 25 µg for 13 days followed by the regular 7-day rest period in Cycle 1, subsequent cycles continued at 25 µg 21 days on and 7 days off in a 28-day cycle. Data not available for Patient 5.
Deep and Sustained Degradation of IKZF1/3 Observed in Cycle 1 of Single Agent CFT7455

Key Takeaways:
- IKZF3 degradation was deeper in human PBMCs at 50 and 25 μg/day than was projected based on observed pre-clinical IKZF3 degradation of ~70% at equivalent exposures.

Data not available for Patient 1 and Patient 3 due to compromised sample integrity.

PBMC: peripheral blood mononuclear cells.
Meaningful Decreases in dFLC Achieved with Single Agent CFT7455 at Lower Exposure and Dose Than Seen with Another Investigational IKZF1/3 Degrader

Key Takeaways:

- Meaningful reduction in differences in serum free light chain (at nadir) was observed at achieved steady state exposures
- Reductions in dFLC were observed in the 3 patients for whom data is available (all dosed at 50 μg) for plotting*
- Decreases in dFLC were observed at lower exposures in comparison to other clinical stage IKZF1/3 degraders
  - CFT7455: 50 μg resulted in active exposures with reduction (>40%) in dFLC in 3 patients
  - CC-92480: 100 μg (starting dose) + dexamethasone resulted in no reduction in dFLC

* Patient 4 had an increase in dFLC of 56%, however it is not plotted as exposure data is not available; Patient 5 sample was not obtained

dFLC, difference between involved FLC and uninvolved FLC

\[
dFLC = \frac{[\text{Abnormal light chain}]_{\text{baseline}} - [\text{Normal light chain}]_{\text{baseline}} - [\text{Abnormal light chain}]_{\text{nadir}} + [\text{Normal light chain}]_{\text{nadir}}}{[\text{Abnormal light chain}]_{\text{baseline}} - [\text{Normal light chain}]_{\text{baseline}}} \times 100
\]

1 From CC-92480 PD Poster at ASCO 2020 (Abstract 8531)
### Efficacy Assessment of Single Agent CFT7455

#### Key Takeaways:

- Across the five patients treated, a best response of SD was observed. Three patients achieved SD and two patients had a best response of PD.

- Patient 2 achieved a decrease in dFLC of 78%. This patient did not achieve PR due to the presence of measurable radiographically stable plasmacytomas.

#### Table: First Actual Dose (µg) and Extramedullary Disease

<table>
<thead>
<tr>
<th>First Actual Dose (µg)</th>
<th>Extramedullary Disease</th>
<th>% Change at Nadir in dFLC*</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>No</td>
<td>48.2 ▼</td>
</tr>
<tr>
<td>50</td>
<td>Multiple Plasmacytomas</td>
<td>78.1 ▼</td>
</tr>
<tr>
<td>50*</td>
<td>Lytic Bone Lesions</td>
<td>41.0 ▼</td>
</tr>
<tr>
<td>50*</td>
<td>No</td>
<td>▲ 56.3</td>
</tr>
<tr>
<td>25</td>
<td>Plasmacytomas and Bone Lesions</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*Patients were dose reduced from 50 µg to 25 µg.

Each bar represents one patient in the study. Right arrow cap indicates continued on study.

dFLC, difference between iFLC and uninvolved FLC; SCR, Stringent Complete Response; CR, Complete Response; VGPR, Very Good Partial Response; PR, Partial Response; SD, Stable Disease; PD, Progressive Disease; NE, Non-evaluable; ND, Not done.
Patient 2 Vignette: Encouraging CFT7455 Single Agent Activity in Heavily Pre-treated, High-risk MM Patient

- 60-year-old female enrolled 2 June 2021 into Cohort A
- Diagnosed with MM (IgG κ) Jan 2017
- Heavily pretreated

Per IMWG response criteria, patient achieved Stable Disease:
- Best response of 78.1% decrease in difference between light chains at nadir
- Best response of 26.5% percent radiographic reduction of plasmacytomas, from baseline

<table>
<thead>
<tr>
<th>Line</th>
<th>Therapy</th>
<th>Best Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Velcade+Dex</td>
<td>CR</td>
</tr>
<tr>
<td>1</td>
<td>Revlimid Velcade Dex/ Rev+Dex</td>
<td>CR</td>
</tr>
<tr>
<td>1</td>
<td>Melphalan</td>
<td>PD</td>
</tr>
<tr>
<td>1</td>
<td>RVD consolidation</td>
<td>VGPR</td>
</tr>
<tr>
<td>1</td>
<td>Autologous stem cell transplant (ASCT)</td>
<td>Stringent CR</td>
</tr>
<tr>
<td>2</td>
<td>Carfilzomib Dex</td>
<td>SD</td>
</tr>
<tr>
<td>3</td>
<td>Carfilzomib Pom Dex</td>
<td>SD</td>
</tr>
<tr>
<td>4</td>
<td>Dara +KPD</td>
<td>PD</td>
</tr>
<tr>
<td>5</td>
<td>GPRC5D Bispecific Antibody</td>
<td>PR</td>
</tr>
</tbody>
</table>

CR, complete response; Dara, daratumumab; Dex, dexamethasone; dFLC, difference between involved minus uninvolved serum free light chains; EMD, extramedullary disease; IKZF1/3, Ikaros family zinc finger proteins 1 and 3; IMWG, International Myeloma Working Group; KPD, carfilzomib–pomalidomide–dexamethasone; MM, multiple myeloma; PD, progressive disease; Pom, pomalidomide; PR, partial response; Rev, Revlimid; RVD, Revlimid-velcade-dexamethasone; SD, stable disease; VGPR, very good partial response.
### Summary of Adverse Events

<table>
<thead>
<tr>
<th>Blood and lymphatic system disorders</th>
<th>Grade 1 (N=5)</th>
<th>Grade 2 (N=5)</th>
<th>Grade 3 (N=5)</th>
<th>Grade 4 (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>0</td>
<td>0</td>
<td>1 (20)</td>
<td>3 (60)</td>
</tr>
<tr>
<td>Thrombocytopenia*</td>
<td>1 (20)</td>
<td>1 (20)</td>
<td>1 (20)</td>
<td>0</td>
</tr>
<tr>
<td>Anemia</td>
<td>0</td>
<td>0</td>
<td>1 (20)</td>
<td>0</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>0</td>
<td>0</td>
<td>1 (20)</td>
<td>0</td>
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</table>

**Investigations**

<table>
<thead>
<tr>
<th>Aspartate aminotransferase increased</th>
<th>Grade 1 (N=5)</th>
<th>Grade 2 (N=5)</th>
<th>Grade 3 (N=5)</th>
<th>Grade 4 (N=5)</th>
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</thead>
<tbody>
<tr>
<td>2 (40)</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<table>
<thead>
<tr>
<th>Alanine aminotransferase increased</th>
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<th>Grade 2 (N=5)</th>
<th>Grade 3 (N=5)</th>
<th>Grade 4 (N=5)</th>
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</thead>
<tbody>
<tr>
<td>1 (20)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</table>

**Gastrointestinal disorders**

<table>
<thead>
<tr>
<th>Diarrhea</th>
<th>Grade 1 (N=5)</th>
<th>Grade 2 (N=5)</th>
<th>Grade 3 (N=5)</th>
<th>Grade 4 (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (20)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**General disorders and administration site conditions**

<table>
<thead>
<tr>
<th>Fatigue</th>
<th>Grade 1 (N=5)</th>
<th>Grade 2 (N=5)</th>
<th>Grade 3 (N=5)</th>
<th>Grade 4 (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (20)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pyrexia</th>
<th>Grade 1 (N=5)</th>
<th>Grade 2 (N=5)</th>
<th>Grade 3 (N=5)</th>
<th>Grade 4 (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (20)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Infections and infestations**

<table>
<thead>
<tr>
<th>Rhinitis</th>
<th>Grade 1 (N=5)</th>
<th>Grade 2 (N=5)</th>
<th>Grade 3 (N=5)</th>
<th>Grade 4 (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (20)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Upper respiratory tract infection</th>
<th>Grade 1 (N=5)</th>
<th>Grade 2 (N=5)</th>
<th>Grade 3 (N=5)</th>
<th>Grade 4 (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (20)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Nervous system disorders**

<table>
<thead>
<tr>
<th>Balance disorder</th>
<th>Grade 1 (N=5)</th>
<th>Grade 2 (N=5)</th>
<th>Grade 3 (N=5)</th>
<th>Grade 4 (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (20)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Headache</th>
<th>Grade 1 (N=5)</th>
<th>Grade 2 (N=5)</th>
<th>Grade 3 (N=5)</th>
<th>Grade 4 (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (20)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Renal and urinary disorders**

<table>
<thead>
<tr>
<th>Nephrolithiasis</th>
<th>Grade 1 (N=5)</th>
<th>Grade 2 (N=5)</th>
<th>Grade 3 (N=5)</th>
<th>Grade 4 (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1 (20)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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No Serious Adverse Events

*Thrombocytopenia includes the preferred term thrombocytopenia and platelet decreased*
On-target Neutropenia Seen Across Patients; Most Severe at Day 21

Key Takeaways:

- Neutropenia tended to worsen following day 15 and recovery was incomplete during the 7 day drug holiday

- The mechanism is considered due to on-target effects of degrading IKZF1 resulting in the downstream decrease in PU.1 causing transient neutrophil maturation arrest.

- Two DLTs were observed at the 50 µg per day dose, both consistent with on-target activity:
  - Grade 4 neutropenia lasting more than 5 days
  - A delay (more than 7 days) in initiating treatment in Cycle 2, in the setting of persistent Grade 3 neutropenia

Neutrophil Change Over Time

- Patient 4 received 50 µg for 8 days, followed by 25 µg
- Patient 5 received 25 µg dose

DLT, dose-limiting toxicity

Alternative CFT7455 Dosing Schedule Expected to Increase Therapeutic Index

**Key Takeaways:**

- There is insufficient time for neutrophil recovery during the 21 day on, 7 day off schedule.
- A 14 day on, 14 day off schedule may limit neutropenia by permitting neutrophil maturation and recovery while effecting tumor apoptosis day 1-14 and limiting tumor recovery during break.
CFT8634
Targeting BRD9

Synovial Sarcoma & SMARCB1-null Solid Tumors
Synovial Sarcoma Remains an Unmet Medical Need Due to its Undruggable Target

Synovial Sarcoma

900 cases/year in the U.S.

Sources: NIH SEER Database 2020, Primary Literature Consensus

10% of all soft tissue sarcomas are Synovial Sarcoma

All synovial sarcoma tumors harbor the SS18-SSX fusion gene resulting in BRD9 dependency

Current treatments have very limited benefit for advanced and metastatic patients
BRD9 Dependency in Synovial Sarcoma

**Degrader Rationale**

Protein degrader approach effectively targets BRD9 and does not require the binding site to be specifically at the physiologically active domain.

**Advantages of BRD9 Degradation**

- Specifically degrades BRD9 and spares BRD4 and BRD7, avoiding potential off-target toxicities
- Oncogenicity of BRD9 depends on sub-domains not addressed by traditional inhibitors
Robust Responses of CFT8634 Seen in Preclinical Synovial Sarcoma Models

**Dose Response Activity**

**Yamato Xenograft Model**

<table>
<thead>
<tr>
<th>Tumor Volume (mm$^3$)</th>
<th>Days of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle</td>
<td>0</td>
</tr>
<tr>
<td>CFT8634, 3 mg/kg (PO QD)</td>
<td>7</td>
</tr>
<tr>
<td>CFT8634, 12 mg/kg (PO QD)</td>
<td>14</td>
</tr>
<tr>
<td>CFT8634, 20 mg/kg (PO BID)</td>
<td>21</td>
</tr>
<tr>
<td>CFT8634, 50 mg/kg (PO QD)</td>
<td>28</td>
</tr>
</tbody>
</table>

Source: C4T data on file

**Dose Response Activity**

**Patient Derived Xenograft Model**

<table>
<thead>
<tr>
<th>Tumor Volume (mm$^3$) Mean ±SEM</th>
<th>Days of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle</td>
<td>0</td>
</tr>
<tr>
<td>CFT8634, 50 mg/kg (QD)</td>
<td>4</td>
</tr>
<tr>
<td>CFT8634, 25 mg/kg (BID)</td>
<td>7</td>
</tr>
<tr>
<td>CFT8634, 16.6 mg/kg (TID)</td>
<td>11</td>
</tr>
</tbody>
</table>

Source: C4T data on file
CFT8634 First-in-Human Trial Design

**CFT8634 First-in-Human Trial Design**

**Phase 1 Dose Escalation**

- **Cohort A:** CFT8634 Monotherapy Synovial Sarcoma and SMARCB1-null Solid Tumors  
  N = ~20

- **CFT8634 MTD/RP2D**

**Phase 2 Expansion**

- **Cohort B:** CFT8634 Monotherapy Synovial Sarcoma  
  N = ~30

- **Cohort C:** CFT8634 Monotherapy SMARCB1-null Solid Tumors  
  N = ~20

**Orphan Drug Designation Granted; Phase 1/2 Trial Initiation Expected in 1H 2022**

MTD = Maximum Tolerated Dose; RP2D = Recommended Phase 2 Dose
CFT1946
Targeting BRAF V600X

Melanoma, Colorectal & NSCLC
Multiple Tumors are Driven by BRAF Mutations; Current Treatments Often Lead to Resistance

**BRAF Mutations Occur in ~15% of Cancers**

- >70K annual incidence across Melanoma, Non-Small Cell Lung Cancer (NSCLC), Colorectal Cancer (CRC) and other malignancies
- ~70 – 90% of BRAF mutations are V600X

**Approved BRAF inhibitors cause paradoxical RAF activation, which may result in diminished efficacy**

**Resistance to 3 approved BRAF inhibitors emerges through multiple paths, resulting in a median PFS of <15 months**

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>BRAF Mutation Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC</td>
<td>1–2%</td>
</tr>
<tr>
<td>late-stage melanoma</td>
<td>50%</td>
</tr>
<tr>
<td>CRC</td>
<td>10–20%</td>
</tr>
<tr>
<td>Papillary thyroid</td>
<td>50%</td>
</tr>
<tr>
<td>Langerhans cell histiocytosis</td>
<td>50%</td>
</tr>
<tr>
<td>Hairy cell leukemia</td>
<td>100%</td>
</tr>
</tbody>
</table>

Utilizing a Degrader Approach to Overcome Limitations of BRAF Inhibition

Advantages of BRAF V600E Degradation

- Specifically target mutant BRAF over wildtype BRAF
- Prevent mutant BRAF incorporation into RAF dimers
- Avoid paradoxical activation and associated failure of therapy due to resistance mechanisms dependent on BRAF inhibitor mediated paradoxical activation
- Effect deeper elimination of mutant BRAF signaling and create more durable response
CFT1946 Shows Superior Efficacy Compared to Approved BRAF Inhibitor and Is Well Tolerated

CFT1946 Shows More Durable Efficacy Than Encorafenib

CFT1946 is Well Tolerated

IND Submission and Phase 1 Initiation Expected in 2H 2022

Source: C4T data on file
CFT8919
Targeting EGFR L858R

EGFR L858R
+ NSCLC
EGFR L858R Driven NSCLC Is Common and Inadequately Treated by EGFR Inhibitors

Non-Small Cell Lung Cancer (NSCLC)

195K US patients diagnosed in 2020

10 – 15% of NSCLC patients have mutant EGFR (mEGFR) in the U.S. population

40% of NSCLC patients have mEGFR in the Asian population

30 – 40% of mEGFR NSCLC patients will develop brain metastases

L858R activating mutation

25–45% mEGFR NSCLC

Osimertinib 1st line median PFS

- 14.4 months (L858R)
- 21.4 months (Exon 19 del)

Sources:
CFT8919 is a Potent, Oral, Allosteric, Mutant-selective Degrader of EGFR L858R

- CFT8919 exploits **allosteric binding site**, close to L858R activating mutation
- Allosteric binding site avoids known resistance-causing mutations in **orthosteric binding site**
- Allosteric binders do not require covalent binding through C797S and do not compete with osimertinib binding

Allosteric Binding Avoids Resistance Mutations and Wild-type Activity
CFT8919 is active in Ba/F3 models expressing secondary mutations resistant to approved EGFR inhibitors.

Viability of Ba/F3 cells expressing the indicated EGFR variant

Ba/F3 cell growth inhibition potency

Source: Keystone 2021, C4T data on file
CFT8919 Induces Tumor Regression in Mouse Models Resistant to First and Third-Generation EGFR Inhibitors

1\textsuperscript{st}-Generation EGFR Inhibitor (EGFRi) Resistant H1975 (L858R-T790M) Xenograft

3\textsuperscript{rd}-Generation EGFRi Resistant Ba/F3 (L858R-T790M-C797S) Allograft

Complete IND-Enabling Activities by Year-End 2022

Source: Keystone 2021, C4T data on file
## Advancing Multiple Oncology Programs to Patients

<table>
<thead>
<tr>
<th>Drug Code</th>
<th>Disease</th>
<th>Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFT7455 (IKZF1/3)</td>
<td>✓ Present Cohort A Phase 1 data at AACR ✓ Present new pre-clinical data at AACR</td>
<td></td>
</tr>
<tr>
<td>CFT8634 (BRD9)</td>
<td>✓ Orphan Drug Designation ✓ Present pre-clinical data at AACR ❑ Initiate Phase 1 trial in 1H</td>
<td></td>
</tr>
<tr>
<td>CFT1946 (BRAF V600X)</td>
<td>✓ Present pre-clinical data at AACR ❑ Submit IND application in 2H ❑ Initiate Phase 1 trial in 2H</td>
<td></td>
</tr>
<tr>
<td>CFT8919 (EGFR L858R)</td>
<td>❑ Complete IND-enabling activities</td>
<td></td>
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