BACKGROUND

- Bromodomain-containing protein-9 (BRD9) interactions in the non-receptor SRC/SRC-like complex and its essential role in the activation of a number of processes is a promising therapeutic target.

- CFT8634 is an orally bioavailable selective bifunctional degradation activating compound (BiDAC™) of BRD9.

- CFT8634 was developed using CellCarta's TORPEDO® platform.

- Mechanism of Action (Figure 1):
  - CFT8634 induced nuclear complex formation with BRD9 and carnitine O ligase I (step 1).
  - BRD9 is ubiquitinated and subsequently released for degradation in the proteasome (steps 2-4).

- CFT8634 leads to robust and dose-dependent degradation of BRD9 in vitro and in vivo models of SMARCB1 perturbed cancer, which translates to significant and dose-dependent anti-tumor activity in patient derived xenograft models (Figure 2).

PRE-CLINICAL DATA: IN VIVO IN PATIENT-DERIVED XENOGRAFTS (PDX)

- CFT8634 selectively degrades BRD9 in PDX models of SMARCB1-deficient tumors, which translates to significant and dose-dependent anti-tumor activity in patient derived xenograft models (Figure 2).

PHASE 1/2 STUDY DESIGN

- Key Eligibility Criteria:
  - Age ≥18 years.
  - Histologically confirmed locally advanced or metastatic solid tumor with no prior approved targeted therapy.
  - Baseline measures:
    - ECOG PS 0-1.
    - At least one measurable lesion.
    - Adequate organ function.

PHASE 1 STUDY ENDPOINTS

- Primary endpoint:
  - Assessment of safety and tolerability.

- Secondary endpoints:
  - Assessment of antitumor activity.

SAFETY DATA

- Incidence of AEs, SAEs, and Grade 3 AEs were consistent across all cohorts.

RESULTS

Table 4: Overview of AEs across cohorts

<table>
<thead>
<tr>
<th>AE Category</th>
<th>N (%) of patients unless stated</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAEs</td>
<td>3 (9.4)</td>
</tr>
<tr>
<td>Grade 3 AEs</td>
<td>1 (3.1)</td>
</tr>
</tbody>
</table>

Table 5: TEAEs occurring in ≥10% or of interest

<table>
<thead>
<tr>
<th>TEAE</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>N (%) of patients unless stated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>7 (21.9)</td>
<td>4 (12.5)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>11 (34.4)</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>1 (3.1)</td>
<td>2 (6.3)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>3 (9.4)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>4 (12.5)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>4 (12.5)</td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td>1 (3.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (3.1)</td>
</tr>
</tbody>
</table>

Table 6: TEAEs reported, including those reported at least once:

- Table 6 reports all TEAEs occurring in ≥10% or of interest.

- TEAEs with a high level of exposure were monitored in the order of their occurrence.

- TEAEs with a high level of exposure were monitored in the order of their occurrence.

- TEAEs with a high level of exposure were monitored in the order of their occurrence.

- TEAEs with a high level of exposure were monitored in the order of their occurrence.

- TEAEs with a high level of exposure were monitored in the order of their occurrence.

- TEAEs with a high level of exposure were monitored in the order of their occurrence.

- TEAEs with a high level of exposure were monitored in the order of their occurrence.

- TEAEs with a high level of exposure were monitored in the order of their occurrence.

PHARMACOKINETICS

- Pharmacokinetics of CFT8634:
  - CFT8634 demonstrated a dose proportional peak concentration and AUC across escalating dose levels.
  - CFT8634 was well tolerated across dose levels at tumor sites after 15 days of treatment.
  - CFT8634 has shown preliminary evidence of anti-tumor activity in patients with synovial sarcoma and SMARCB1-null tumors.

CONCLUSIONS

- The Phase 1 dose escalation study is currently ongoing and an RP2D has not yet been identified.