**Background:** (Colors in text refer to Figure 1)

- Proliferating Cell Nuclear Antigen (PCNA) is essential for DNA replication and repair and is shown to have cytostatic roles in regulation of cellular signaling, metabolism and immune responses
- **APIM**: a PCNA binding motif with high binding strength (affinity) only during cellular stress is found mainly in proteins involved in cellular stress defense mechanisms.
- Cancer and anti-cancer treatments cause cellular stress
- **ATX-101** blocks protein - PCNA interactions in stressed cells (indicated by \( \Phi \) in Figure 1)
- **ATX-101** inhibits cellular stress responses

**Methods:** Phase 1 study

Study ATX101-01: Open label, safety & tolerability study using a common 3+3 design

- Three active sites in Australia
- Patients with solid tumors
- ATX101 infused weekly over 6 weeks
- Prim. objective: Safety and tolerability (DLT)

Study ATX101-02: Long-Term Follow-Up for patients not progressing after 6 weeks treatment in study -01: continue with same weekly regimen

- 22 patients treated; safety/PK cut-off on 31 Oct 2020 (n=21):
  - Median age 57 [31-73]; 48% female; solid tumors (see Figure 3)
  - Heavily pretreated: median of 3.8 prior systemic treatments [1-9]
  - 95% of patients with progressive disease at study entry
  - 76% of patients refractory to the most recent treatment
  - Standard anti-tumor treatment has been exhausted

**Results:**

- **ATX-101 has a favorable safety profile**
  - Mild to moderate infusion related reactions, observed in 71% of patients, are not dose dependent
  - The short half-life in plasma confirms in vivo data demonstrating a quick uptake of ATX-101 by cells of all organs

**Long disease stabilization** in progressive tumors has been observed at all doses levels and may be attributed to ATX-101 activity

1. Scientia Clinical Research and Prince of Wales Clinical School, Randwick, Australia
2. Flinders University, Woodville, Australia
3. Therapim Pty Ltd, Southport, Australia
4. Department of Clinical and Molecular Medicine, Faculty of Medicine and Health Sciences, NTNU, Trondheim, Norway
5. Linear Clinical Research and School of Medicine, University of Western Australia

**Correspondence:** Jens-Peter Marschner (jpmarschner@apimtherapeutics.com)

**Results:**

**Number of patients with at least one treatment related adverse event:**

<table>
<thead>
<tr>
<th>Severity (CTCAE)</th>
<th>ATX-101 (n=22)</th>
<th>Placebo (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 4</td>
<td>2 (9%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>5 (23%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>10 (45%)</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Grade 1</td>
<td>7 (32%)</td>
<td>10 (83%)</td>
</tr>
</tbody>
</table>

**Preferred Term**

<table>
<thead>
<tr>
<th>ATX-101 (n=22)</th>
<th>Placebo (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>4 (18%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7 (32%)</td>
</tr>
<tr>
<td>DVT</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Mucositis</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Chills</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**Tolerated Dose**

- 30 mg/m² (n=3)
- 45 mg/m² (n=4)
- 60 mg/m² (n=4)
- 90 mg/m² (n=4)
- 120 mg/m² (n=4)

**Maximum Tolerated Dose (MTD)**

- 60 mg/m²

**Phase 2 Dose (RP2D)**

- 45 mg/m²

**Methods for Pharmacokinetics**

- Efficacy
- Biomarkers

**Results from first 6 weeks of treatment:**

- median PFS: > 4.2 months [2.1-13.4]
- 60 mg/m² dose level showed a higher PK and MTD
- Phase 1/2 study has demonstrated a PK/MTD relationship

**Dose dependent exposure**

- Different infusion times (115-345 min) affected PK profile (\( c_{\text{max}} \))
- Short half-life
- No signs of accumulation or changes in elimination

**Future Directions for Research:**

- A phase 1b/2a study with ATX-101 plus platinum based therapy in ovarian carcinoma is ready to start (NCT04814875)
- An IST with ATX-101 monotherapy in sarcoma will be supported

**Authors:** Charlotte Rose Lemech1, Ganessan Kichenadasse2, Jens-Peter Marschner3, Kostas Alevizopoulos3, Marit Otterlei1,3,4, Michael Millward5