Selinexor (KPT-330) is a covalent, slowly reversible, oral selective inhibitor of nuclear XPO1. XPO1 is the sole nuclear exporter of the major tumor suppressor proteins (TSP).

**Trial Objectives**

- **Primary:** Determine the pharmacokinetic effects of high & low fat food and formulation of selinexor administered twice weekly.
- **Secondary:**
  - Safety and tolerability of oral selinexor.
  - Cancer response in sarcoma patients (REPOST-i, v1.1 clinical). Stabilized or progressive disease at baseline.
  - Stable disease as measured by time to progression (duration of stable disease as TTP).

**Study Design**

- Phase I: 18, open-label, randomized, four-week, four-period, study conducted at 2 sites in US and Canada; patients who have metastatic, locally advanced, unresectable or locally recurrent sarcoma.
  - Eligibility criteria: 12 patients will be enrolled in each group. PK Group (Arm A) 1-2 vs. 3-4 vs. Non-PK Group (Arm B) 1-2 vs. 3-4. Patients are treated as early clinical benefit arm in Arm A 1-2.

**Study Methods**

- **Randomization:** Patients are randomized in a 2:1 ratio to receive either 30 mg/m² or 20 mg/m² selinexor every 4 weeks with 8 doses of selinexor.

**Study Population**

- **Mean age (range):** 53 years (18-80)
- **Male:** 9
- **Fasting blood glucose:** 4.7 (2.7-6.78) mmol/L
- **ECOG performance status:** 0/1

**Pharmacokinetics Analysis**

<table>
<thead>
<tr>
<th>Dose (mg/m²)</th>
<th>AUC max (ng*h/mL)</th>
<th>Cmax (ng/mL)</th>
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<tbody>
<tr>
<td>30</td>
<td>3197</td>
<td>120</td>
</tr>
<tr>
<td>20</td>
<td>2020</td>
<td>80</td>
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**Characteristics N=21**

<table>
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<tr>
<th>Characteristic</th>
<th>N</th>
<th>Mean age (range)</th>
<th>Male:Female</th>
<th>Mean weight (kg)</th>
<th>Mean body mass index</th>
<th>Cmax (ng/mL)</th>
<th>Cmax (ng*h/mL)</th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>21</td>
<td>53 years (18-80)</td>
<td>9:12</td>
<td>80.2</td>
<td>25.2</td>
<td>120</td>
<td>3197</td>
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<tr>
<td>Cmax (ng/mL)</td>
<td>13</td>
<td>9</td>
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**Subgroups of Leukosarcoma N**

<table>
<thead>
<tr>
<th>Leukosarcoma N</th>
<th>Leukosarcoma 6</th>
<th>Leukosarcoma 4</th>
<th>Sarcoid sarcoma 4</th>
<th>Sarcoma 3</th>
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<tr>
<td>N</td>
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<td>5</td>
<td>2</td>
<td>2</td>
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</table>

**Clinical Activity**

- **Best Responses in Patients with Leukosarcoma N**
  - **N** SD PD NE
  - 21 11 0 10

- **Best Responses in Patients by Subgroup on 13-May-2014**
  - **N** SD PD NE
  - 52% 38% 10%

**Conclusions**

- Selinexor is generally well tolerated with dose limiting and nausea.
- Selinexor is well tolerated in both fasted and fed states. Independent of food of course.
- Food did not have a high impact.
- Single agent oral selinexor demonstrated clinical stable disease in liposarcoma and leiomyosarcoma.
- The median duration of response had not been reached as of the last interim analysis.

- **Safety and tolerability of oral selinexor.**

- **Cancer response in sarcoma patients (REPOST-i, v1.1 clinical).**