Background

Nektar's polymer conjugate technology, an established platform, is used to develop NKTR-102, a novel polymer conjugate of topoisomerase I inhibitor TopoGel conjugated to a nontoxic polymer. The main significant potential benefits of NKTR-102 are:

1. The potential for improved efficacy of the drug, provided by a consistent exposure through dosing intervals due to the markedly reduced metabolic activity (TN 1/3 < 1 day compared to PLD 2 days) from the polymer.  The polymer also concentrates in tumor xenographs, indicating the potential of NKTR-102 to concentrate at the site of tumors with prominent vascular permeability (peripheral perfusion and capillary density) effect.

2. The potential for significantly reduced incidence in certain adverse events associated with the parent compound: topotecan, such as early, cholestatic derangements, likely due to the markedly reduced toxicity and delayed metabolite conversion of topotecan to SN38, leading to a smaller SN38 pool.  The metabolic instability of SN38 is a drug elimination, see less late toxicity for NKTR-102 due to the reduced SN38 pool which reduces the need to order starting doses for patients with renal impairment.

Clinical results from the Phase 1 demonstrated potential NKTR-102 anti-tumor activity in a variety of tumor types.

Study Design & Objectives

Original Study Design (33 previously treated with PLD, 37 PLD naïve)

NKTR-102 Phase 2 Study Design: Platinum Resistant Ovarian Cancer

Stage 1: 1:1, if a patient responds, the treatment regimen proceeds to the next stage.

Stage 2: Additional 15 patients enrolled

If ≤ 5 patients respond out of 35 patients (Stage 1 and Stage 2 combined), the drug has met the efficacy threshold.

NKTR-102 – Ovarian Cancer Study: Objectives

Primary Objective:

To determine the objective response rate (ORR) in patients with PROC who had prior PLD treated with NKTR-102 on one of two schedules: q14d and q21d

Secondary Objectives:

• To evaluate progression-free survival (PFS) with NKTR-102
• To evaluate overall survival (OS) with NKTR-102
• To characterize the safety profile of NKTR-102

Early stopping rules:

If ≥ 5 patients respond out of 35 patients (Stage 1 and Stage 2 combined), the drug has met the efficacy threshold.

Key Eligibility Criteria

Key Inclusion Criteria:

• Smartphone resistant ovarian cancer defined as:
  - Progression during platinum-based therapy OR
  - Progression within 6 months of receiving their last platinum-based therapy

Measurable disease as defined by RECIST version 1.0 at least 1.0 cm not previously irradiated or in resectable disease

Key Exclusion Criteria:

• Patients who have received any treatment with a capecitabine derivative (e.g., oxaliplatin, irinotecan, folinic acid; 30 days before study drug administration).

Study Demographics (Subpopulation Previously Treated with PLD)

<table>
<thead>
<tr>
<th>Population</th>
<th>N</th>
<th>Median Age</th>
<th>Median ECOG</th>
<th>Median Performance Status</th>
<th>Male</th>
<th>Female</th>
<th>Race</th>
<th>Ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>All PLD</td>
<td>60</td>
<td>69</td>
<td>1</td>
<td>75</td>
<td>7</td>
<td>93</td>
<td>76%</td>
<td>63%</td>
</tr>
<tr>
<td>N=35</td>
<td>16</td>
<td>69</td>
<td>1</td>
<td>75</td>
<td>7</td>
<td>93</td>
<td>76%</td>
<td>63%</td>
</tr>
<tr>
<td>N=17</td>
<td>20</td>
<td>69</td>
<td>1</td>
<td>75</td>
<td>7</td>
<td>93</td>
<td>76%</td>
<td>63%</td>
</tr>
</tbody>
</table>

Efficacy Results: Subpopulation Previously Treated with PLD

Objectives Response Rate by RECIST and GCIG

(Investigator Assessment)

Efficacy Results: Subpopulation Previously Treated with PLD

Progression-Free Survival

(All patients previously treated with PLD – dose groups pooled)

<table>
<thead>
<tr>
<th>Dose Group</th>
<th>OS Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>145 mg/m² q14d</td>
<td>5.4 (0.2 - 11.9)</td>
</tr>
<tr>
<td>145 mg/m² q21d</td>
<td>5.4 (0.2 - 11.9)</td>
</tr>
</tbody>
</table>

Overall Survival

(All patients previously treated with PLD – dose groups pooled)

<table>
<thead>
<tr>
<th>Dose Group</th>
<th>OS Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>145 mg/m² q14d</td>
<td>13.9 (0.2 - 18.9)</td>
</tr>
<tr>
<td>145 mg/m² q21d</td>
<td>13.9 (0.2 - 18.9)</td>
</tr>
</tbody>
</table>

Conclusions

• NKTR-102 is a new and novel approach to treating patients with platinum resistant/refractory ovarian cancer

• NKTR-102 has shown promising results in patients with platinum-resistant/refractory ovarian cancer who had prior PLD treatment.

Safety

Safety: Summary of Drug-Related Adverse Events

Table 1: Summary of Drug-Related Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>4 (11.1%)</td>
<td>14 (42.4%)</td>
<td>5 (14.7%)</td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>7 (21.2%)</td>
<td>12 (36.4%)</td>
<td>6 (17.6%)</td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6 (18.2%)</td>
<td>11 (33.3%)</td>
<td>4 (11.8%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7 (21.2%)</td>
<td>13 (39.4%)</td>
<td>3 (9.1%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

One patient in previous treatment and PLD died due to neutropenic sepsis and multi-organ failure leading to drug-related death.

Data as of May 9, 2011

This study is currently enrolling an additional 110 platinum-resistant/refractory ovarian cancer patients who have progressed after receiving PLD therapy to further evaluate single agent NKTR-102 in this population with a high degree of current medical need.

NKTR-102 is being evaluated in multiple cancer indications as a single and combination agent. Phase 3 planning is underway in ovarian and breast cancers.

NKTR-102 has been evaluated in a Phase 2 study in patients with platinum-resistant/refractory ovarian cancer. The updated results for the subpopulation who had also prior PLD are:

- Median progression-free survival (PFS) with NKTR-102 is 5.4 months (combined: q14d and q21d)
- Duration of confirmed response: 4.2 months/q14d, 4.4 months/q21d
- Overall survival (OS) rate with NKTR-102 is 13.9 months (combined: q14d and q21d)
- Phase 2 Study Results: Progression-Free Survival

NKTR-102 - Ovarian Cancer Study: Results

Phase 2 Study Results: Progression-Free Survival

(All patients previously treated with PLD – dose groups pooled)

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