Pre-Clinical Evaluation of a Camsrciadmin Analog MNPR-202 in Diffuse Large B Cell Lymphoma (DLBCL)

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**Background**

**MNPR-202: Promising DNA Damaging Response Drug Candidate**

The standard R-CHOP treatment for DLBCL has a high relapse risk because dose intensity cannot be maintained due to Doxorubicin (Dox) cardiotoxicity. Camsrciadmin, a novel analog of Dox engineered to reduce cardiotoxicity, has shown no signs of irreversible heart damage across two Phase 1 trials (one ongoing) and a Phase 2 trial.

**Cardiotoxic Lifetime-Dose Limitation**

- Calcium disruption via C13-OH doxorubicin
- Redox cycling at the CS quinone
- Inhibition of topoisomerase II

**Present Study Shows Similar Potency in Blood Cancers**

Viability of DLBCL Cell Lines

**MNPR-202: Previous in vitro Study in Solid Tumors**

In vitro IC50s of Doxorubicin and MNPR-202 (µM)

<table>
<thead>
<tr>
<th>Cell Line</th>
<th>Cell Type</th>
<th>Dox (µM)</th>
<th>MNPR-202 (µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RD</td>
<td>Non-small cell</td>
<td>0.438</td>
<td>0.468</td>
</tr>
<tr>
<td>SW-221</td>
<td>Non-small cell</td>
<td>4.315</td>
<td>4.589</td>
</tr>
<tr>
<td>SW-620</td>
<td>Non-small cell</td>
<td>0.751</td>
<td>0.540</td>
</tr>
<tr>
<td>T47D</td>
<td>Breast ductal</td>
<td>10.978</td>
<td>8.262</td>
</tr>
<tr>
<td>MESS-DA4</td>
<td>Uterine fibrosarcoma</td>
<td>0.550</td>
<td>0.676</td>
</tr>
<tr>
<td>MESS-DA5</td>
<td>Uterine fibrosarcoma</td>
<td>0.781</td>
<td>0.668</td>
</tr>
</tbody>
</table>

**MNPR-202: Induces Increased Apoptosis**

Apoptosis Assay by Flow Cytometry

- MNPR-202 demonstrates increased apoptosis in lymphoma cells compared to doxorubicin.

**Support for Camsrciadmin’s Toxicity Profile**

- No irreversible drug-related clinical cardiotoxicity observed to date in any trial.
- In a prior Phase 2 trial, patients were dosed for up to 16-20 cycles at a dose level of 265 mg/m². The current dose level in the ongoing Phase 3b trial is at 520 mg/m² and continues to escalate.

**MNPR-202 Affects DNA Damage Response (DDR)**

Elevated DNA Damage and Cell Death Response

- MNPR-202 demonstrates increased DNA damage in lymphoma cells compared to doxorubicin.

**Citations & Acknowledgments:**

- MNPR-202 Affects DNA Damage Response (DDR)
- Elevated DNA Damage and Cell Death Response
- MNPR-202 vs Dox: Unique Immune Activation Profile
- MNPR-202 Induces Increased Apoptosis
- MNPR-202 vs Dox: Differential Gene Expression Analysis
- Conclusions
- Future Directions