PRIME™ IL-15 (RPTR-147): Preliminary clinical results and biomarker analysis from a first-in-human Phase 1 study of IL-15 loaded peripherally-derived autologous T cell therapy in solid tumor patients

Erika P. Hamilton1, Sarah Nikiforov2, Philip D. Bardwell4, Christine M. McInnis5, Jeffrey Zhang6, George Blumenschein, Jr.6, Mihalta Cristea7, Keren Osmanski8, Anthony Shields8, Marylne Motta8, Sanela Bilic9, Oliver Schoenborn-Kellenberger9, James A. Rakas8, Shaw P. Carey9, Elena Goretti9, Karsten Sauv9, Tim Harris1, Tap Maniar1, Becker Hewes1, Thomas Andresen1, Jonathan B. Fitzgerald4†, Harriett Kluger1 1Sarah Cannon Research Institute, 2Cancer and Vaccine Institute, 3Cancer Immunotherapy, 4R+D Anderson Cancer Center, 5City of Hope, 6Mount Sinai Medical Center, 7Karmanos Cancer Institute, 8Yale Cancer Center

**RESULTS**

**Table 1** Patient Population and Safety Profile

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Number of Patients</th>
<th>Safety Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendixal Carcinoma</td>
<td>1</td>
<td>20 SAEs</td>
</tr>
<tr>
<td>Melanoma</td>
<td>6</td>
<td>20 SAEs</td>
</tr>
<tr>
<td>Bladder</td>
<td>4</td>
<td>20 SAEs</td>
</tr>
<tr>
<td>Renal Cell Carcinoma</td>
<td>2</td>
<td>20 SAEs</td>
</tr>
<tr>
<td>RCC</td>
<td>2</td>
<td>20 SAEs</td>
</tr>
<tr>
<td>Head and Neck Cancer</td>
<td>2</td>
<td>20 SAEs</td>
</tr>
<tr>
<td>Lung</td>
<td>2</td>
<td>20 SAEs</td>
</tr>
<tr>
<td>Immunotherapy</td>
<td>1</td>
<td>20 SAEs</td>
</tr>
</tbody>
</table>

**Study Design:** A phase 1, dose-escalation, multi-center study was initiated in patients with relapsed/refractory or advanced solid tumors. Patients were administered PRIME IL-15 as a monotherapy or in combination with anti-PD1 checkpoint inhibitors. The study was designed to escalate doses in an accelerated manner, with 6 patients per cohort and 4 dose levels: 20 Million (cells/m²) IL-15Fc was not detected. The highest dose tested did not result in any dose-limiting toxicities.

**Flow Cytometry:** Non-significant increase of NK & CD8+ T Cells in Circulation at 360M cells/m²

Dose level 1 is in millions of cells/m² Arrow indicates continued on study

**Expression of targeted TAAs in tumor biopsies was confirmed by RNASeq and IHC:**

**Figure 5:** PRIME T Cells Armed with Immuno-modulators

**Figure 6:** Product Specific Clones Show Persistence in Blood and Tumor

**CONCLUSIONS**

- PRIME IL-15 T cell therapy (RPTR-147) has a favorable safety profile.
- Dose Escalation is proceeding.
- Preliminary evidence of clinical activity.
- 10 of 17 late-stage tumor patients experienced stable disease.
- In 4 patients, stable disease lasted longer than 6 months.
- Pharmacodynamic changes in immune system and tumor microenvironment were consistent with MDA.
- Increase in tumor infiltrating CD8 and CD4 T cells observed post infusion.
- Evidence of persisting product-specific T cell clones in blood and tumor (analysis of antigen specificity ongoing).
- Dosing biomarker analysis will inform future clinical strategies to optimize PRIME IL-15 immunotherapy.
- Determine product reactivity towards individual antigens and assess for epitope spreading.
- Proprietary antigen decoding technologies will be applied to track epitope-specific CD8 and CD4-clonotypes in products, periphery and tumors.
- Deeper understanding of the effects of PRIME IL-15 T cell therapy on the tumor microenvironment.

**Figure 7:** Majority of Evaluable Matched Biopsies Demonstrate an Increase in CD8 & GMT T Cell Tumor Infiltrates

**Figure 8:** Expression of targeted TAAs in tumor biopsies was confirmed by RNASeq and IHC.