Results from Monotherapy Dose Escalation of MDNA11, a Long-acting IL-2 Superkine, in a Phase 1/2 Trial Show Evidence of Single-agent Activity in Advanced Solid Tumors

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MDNA11 is a Long-acting “Beta-Enhanced-not-Alpha” IL-2

- Highly Selective anti-tumor Effector Immune Cell Activation:
  - "Beta-enhanced" IL-2 binding with negligible binding to naïve T cells
  - "Not-alpha" binding with negligible binding to expansion of naïve T cells
- Improved Safety Profile Over High-dose rIL-2: No vascular leak syndrome or significant endothilgie
- Extended PK: Albumin fusion prolongs half-life (given qIV GW)
- Tumor Accumulation: Albumin promotes retention in tumor and tumor-draining lymph nodes

**Safety Profile from Dose Escalation/Evaluation**

<table>
<thead>
<tr>
<th>Most Common Treatment-Related Adverse Events</th>
<th>(TRAEs in ≥10% of Patients)</th>
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<tbody>
<tr>
<td>Grade 1-2</td>
<td>Grade 3</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>No dose limiting toxicity (DLT)</td>
</tr>
<tr>
<td>Nausea</td>
<td>No grade 4 or 5 TRAE</td>
</tr>
<tr>
<td>Fatigue</td>
<td>95% of TRAEs were grade 1-2; majority resolved within 48 hours</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Grade 3 LFT elevations were asymptomatic and transient; resolved prior to next scheduled dose</td>
</tr>
</tbody>
</table>

**Monotherapy Dose Escalation/Expansion (IV Q2W)**

- Modified 3+3 design
- Intra-patient dose escalation & parallel b&cIl
- Identify monotherapy recommended dose for Expansion (R0) 80 µg/kg
- No grade 4 or 5 TRAE
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**Select PD1/L1 refractory and CPI Resistant**

- Melanoma (2’ CPI Resistant)
- Non-melanoma skin cancer (MCC, BCC, MEL, 2’ CPI Resistant)
- PDAC
- Small Bowel Cancer

- Melanoma: CD4+ (15S, 1M, 2M), CD8+ (1S, 2M), PD-L1+ (1S, 2M)
- No grade 4 or 5 TRAE

- Primary Tumor Type
  - N (%)
  - Non-melanoma skin cancer (MCC, BCC, MEL, 2’ CPI Resistant)
  - PDAC
  - Small Bowel Cancer
  - Overan Cancer
  - Cancer: Small Squamous Cell Carcinoma
  - Basal Cell Carcinoma
  - Small Bowel Cancer
  - Gastric-epithelial/Gastric Adenocarcinoma

- Prior Anti-Cancer Systemic Therapies
  - N (%)
  - CBR: 2/6 (33.3%)
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- Prior Line of Therapy: 3-4
  - 2/6 (33.3%)
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- ImmunoTherapy
  - 2/6 (33.3%)
  - 2/6 (33.3%)
  - 2/6 (33.3%)

- Targeted Therapy
  - 2/6 (33.3%)

- Chemotherapy
  - 2/6 (33.3%)

- CBR: 2/6 (33.3%)
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**Conclusions**

- MDNA11 was well-tolerated with no DLTs observed at all dose levels up to 120 µg/kg IV qIV GW
- MDNA11 shows robust increase in CD8+ T and NK cells with activation markers peaking at 90 µg/kg
- Dose of 90 µg/kg selected as monotherapy RDE
- Compelling evidence of single-agent anti-tumor activity in checkpoint inhibitor refractory disease including tumor types not normally responsive to IL-2 immunotherapies

**Potent Effect Immune Profile at Monotherapy RDE (90 µg/kg)**

- N=5 patients showed good tumor response
- 5+/6+ PDAC: 2/5 (40%), 1/5 (20%)
- 5/6+ NSCLC: 2/5 (40%), 1/5 (20%)
- 5/6+ Melanoma: 2/5 (40%), 1/5 (20%)
- 5/6+ Lung Adeno Ca: 2/5 (40%), 1/5 (20%)
- 5/6+ Small bowel cancer: 2/5 (40%), 1/5 (20%)
- 5/6+ Melanoma: 2/5 (40%), 1/5 (20%)
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- No grade 4 or 5 TRAE
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**Single Agent Efficacy of MDNA11 (≥ 60µg/kg) in Phase 2 Eligible Patients**

- 5/5 PDAC: Whipple procedure + Adjuvant FOLFOX6X
- 3/3+ NSCLC: Pembrolizumab (PB) (primary resistance)

**Preliminary Clinical Efficacy**

- Time to progression (TPG): 24 weeks
- Duration of response (DOR): 24 weeks
- MDNA11: 28 weeks
- Pembrolizumab: 12 weeks
- CBR: 28% (6/21)
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**Conclusions**

- MDNA11 Monotherapy: Duration of Treatment & Response

- Sustained Dose Monotherapy was well-tolerated
- MDNA11: No grade 4 or 5 TRAE
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