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


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MDNA11 is a Long-acting "Beta-enhanced Not-alpha" IL-2

**Distinctive Features of MDNA11**

- **Highly Selective Anti-tumor Effector Immune Cell Activation:**
  - “Beta-enhanced” IL-2 agonist promoting selective activation of CD8+ T and NK cells
  - “Not-alpha” binding with negligible to no expansion of Tregs
- **Improved Safety Profile Over High-dose rhIL-2:** No vascular leak syndrome or significant eosinophilia
- **Extended PK:** Albumin fusion prolongs half-life (given IV Q2W)
- **Tumor Accumulation:** Albumin promotes retention in tumor and tumor-draining lymph nodes

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**MDNA11**

- **IL-2 Component**
  - (G₄S)₃ linker
  - IL-2 component of MDNA11 is engineered to increase IL2Rβ affinity and eliminate IL2Rα binding

- **Human Albumin**
  - Fusion to human albumin extends half-life, overcoming need for frequent dosing and promotes MDNA11 accumulation in tumors
**ABILITY-1: First-in-Human Trial of MDNA11 in Advanced Solid Tumors**

(NCT05086692)

**MDNA11 Monotherapy Dose Escalation (IV Q2W)**
- Modified 3+3 design
- Intra-patient dose escalation & parallel backfill
- Identify monotherapy Recommended Dose for Expansion (RDE) @ 90 µg/kg

<table>
<thead>
<tr>
<th>Dose (µg/kg)</th>
<th>Indicates</th>
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<tbody>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>10</td>
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<tr>
<td>30</td>
<td></td>
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<tr>
<td>60*</td>
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<tr>
<td>90*</td>
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<tr>
<td>120*</td>
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</tbody>
</table>

* Step-up dosing (SUD)

**Monotherapy Dose Evaluation**
- Optimize Step-up dosing (SUD) schedule

**Monotherapy Dose Expansion (Phase 2)**
- Melanoma (2° CPI Resistance)
- Non-melanoma skin cancer (1°/2° CPI Resistance)
  - cSCC, BCC, MCC
- MSI-H/dMMR tumors (1°/2° CPI Resistance)

**MDNA11 (Q2W) + Pembrolizumab (Q6W) Dose Escalation**
- Select PD1/L1 refractory and CPI-naive indications
  - Identify combination RDE (cRDE) for MDNA11
  - Assess safety, tolerability and anti-tumor activity

**MDNA11 + Pembrolizumab Dose Expansion (Phase 2)**
- MDNA11(Q2W, cRDE) + Pembrolizumab (Q6W)
- Assess safety, tolerability and anti-tumor activity
### Baseline Patient and Tumor Characteristics

**Baseline characteristics (as of 22-Mar-2024)**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Escalation/Evaluation (N=30)</th>
<th>Expansion (N=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years: median (range)</strong></td>
<td>63 (27-78)</td>
<td>65.5 (49-85)</td>
</tr>
<tr>
<td><strong>Male, N (%)</strong></td>
<td>22 (73.3%)</td>
<td>4 (50%)</td>
</tr>
<tr>
<td><strong>Baseline ECOG = 0, N (%)</strong></td>
<td>19 (63.3%)</td>
<td>5 (62.5%)</td>
</tr>
<tr>
<td><strong>Baseline ECOG = 1, N (%)</strong></td>
<td>11 (36.6%)</td>
<td>3 (37.5%)</td>
</tr>
</tbody>
</table>

**Primary Tumor Type**

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Escalation/Evaluation (N=30)</th>
<th>Expansion (N=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma (16 Cutaneous, 1 Mucosal and 2 Acral)</td>
<td>16 (53.3 %)</td>
<td>3 (37.5%)</td>
</tr>
<tr>
<td>Non-small Cell Lung Cancer (NSCLC)</td>
<td>3 (10%)</td>
<td></td>
</tr>
<tr>
<td>Pancreatic Ductal Adenocarcinoma (PDAC)</td>
<td>3 (10%)</td>
<td></td>
</tr>
<tr>
<td>Renal Cell Carcinoma (Non-Clear Cell)</td>
<td>2 (6.6%)</td>
<td></td>
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<tr>
<td>Sarcoma (1 Pleiomorphic sarcoma and 1 Leiomyosarcoma)</td>
<td>2 (6.6%)</td>
<td></td>
</tr>
<tr>
<td>Ovarian Cancer</td>
<td>2 (6.6%)</td>
<td></td>
</tr>
<tr>
<td>Cutaneous Squamous Cell Carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal Cell Carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tonsillar Squamous Cell Carcinoma</td>
<td>1 (3.3%)</td>
<td>1 (12.5%)</td>
</tr>
<tr>
<td>Small Bowel Cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastro-esophageal/Gastric Adenocarcinoma</td>
<td>1 (3.3%)</td>
<td>1 (12.5%)</td>
</tr>
</tbody>
</table>

**Prior Systemic Therapies**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Escalation/Evaluation (N=30)</th>
<th>Expansion (N=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior Lines of Therapy: 1-2</td>
<td>22 (73.3%)</td>
<td>6 (75%)</td>
</tr>
<tr>
<td>Prior Lines of Therapy: 3-4</td>
<td>8 (26.6%)</td>
<td>2 (23%)</td>
</tr>
<tr>
<td>Immunotherapy</td>
<td>22 (73.3%)</td>
<td>8 (100%)</td>
</tr>
<tr>
<td>Targeted Therapy</td>
<td>5 (16.6%)</td>
<td>1 (12.5%)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>15 (50 %)</td>
<td>2 (25%)</td>
</tr>
</tbody>
</table>
MDNA11 Demonstrates Favorable Safety Profile Across All Doses

Most Common Treatment Related Adverse Events (TRAEs in ≥10% of Patients)

- No dose limiting toxicity (DLT)
- No grade 4 or 5 TRAE
- 95% of TRAEs were grade 1-2; majority resolved within 48 hours
- Grade 3 LFT elevations were asymptomatic and transient; resolved prior to next scheduled dose

IRR: Infusion Related Reaction
Sustained Immune Effector Cell Expansion with Repeat Dosing

**MDNA11 @ 90 µg/kg (Q2W)**

N=8, patients received two priming doses (Q2W) prior to 90 µg/kg target dose. Data for target dose are shown. Measurements on Day 1, 15 and 29 are prior to dose administration. Baseline is prior to any MDNA11 exposure.

**Virtually No Expansion of Regulatory T cells**
Potent Effector Immune Cell Profile at MDNA11 RDE (90 µg/kg)

**CD8/Treg Ratio**
- 30 µg/kg: 2.9x (n=4)
- 60 µg/kg: 3.1x (n=5)
- 90 µg/kg: 7.0x (n=8)
- 120 µg/kg: 4.4x (n=4)

**CD25+ CD8+ T Cells**
- 30 µg/kg: 2.1x (n=4)
- 60 µg/kg: 2.0x (n=5)
- 90 µg/kg: 4.2x (n=8)
- 120 µg/kg: 1.7x (n=4)

**OX40+ CD8+ T Cells**
- 30 µg/kg: 2.9x (n=4)
- 60 µg/kg: 5.3x (n=5)
- 90 µg/kg: 8.5x (n=8)
- 120 µg/kg: 1.5x (n=4)

**OX40+ Tregs**
- 30 µg/kg: 3.5x (n=4)
- 60 µg/kg: 3.3x (n=5)
- 90 µg/kg: 9.1x (n=8)
- 120 µg/kg: 6.7x (n=4)

**Superior expansion and activation of CD8+ T cells at RDE**
**OX40 positivity stimulates CD8+ T cells while impairing Tregs**
Single Agent Efficacy of MDNA11 (≥60μg/kg) in Phase 2 Eligible Patients

Response Rate (4PR): 28.6% | Clinical Benefit Rate (4PR + 3SD > 24 weeks): 50%

**Melanoma**
- 60 μg/kg: 6 patients with partial response
- 90 μg/kg: 10 patients with partial response
- 120 μg/kg: 8 patients with partial response

**PDAC**
- 60 μg/kg: 1 patient with stable disease
- 90 μg/kg: 1 patient with stable disease
- 120 μg/kg: 1 patient with stable disease

**Acral Melanoma**
- 60 μg/kg: 1 patient with stable disease
- 90 μg/kg: 1 patient with stable disease
- 120 μg/kg: 1 patient with stable disease

**Small Bowel Ca**
- 60 μg/kg: 1 patient with stable disease
- 90 μg/kg: 1 patient with stable disease
- 120 μg/kg: 1 patient with stable disease

**Melanoma**
- 90 μg/kg: 1 patient with iUPD

**Partial Response**
- Following MDNA11 resumption all baseline lesions resolved and treatment was discontinued

**Stable Disease**
- Vacation: Rx Break
- Radiotherapy of new lesion
- MDNA11 paused.

**Progressive Disease**
- MDNA11 paused.

**Unconfirmed progressive disease**
- Target lesion reduced by >30%
- Non-target lesion stable
- New lymph node lesion (unconfirmed) at week 16

Efficacy evaluable patients: Cut-off date: 22-Mar-2024
Phase 2 Eligible Patients: 4 Partial Responses and 100% Reduction of Target Lesions in One Pancreatic Patient and One Melanoma Patient

2 of 4 evaluable dose expansion Patients (90 µg/kg) have had a PR
MDNA11 Achieves Objective Response in Anti-PD-1 Resistant MSI-H

### Pancreatic Ductal Adenocarcinoma (MSI-H)

**PR**

- 100% resolution of all target lesions (60 µg/kg)

- 55 Y/M PDAC:
  - Whipple procedure + Adjuvant FOLFIRINOX
  - 1L: Gemcitabine + nab-Paclitaxel
  - 2L: Pembrolizumab (PD; primary resistance)

- PR at week 16 of MDNA11 treatment

- A new lymph node (LN) lesion developed during treatment break (vacation; week 55-62)

- 100% regression of all baseline lesions (week 66) prior to radiotherapy

- New LN lesion (18 mm) treated with radiotherapy (week 67-73); MDNA11 resumed at week 73

- LN lesion reduced to < 10 mm; **MDNA11 treatment ended at week 90 with 100% regression of baseline target and non-target lesions originally in the liver**

### Small Bowel Cancer (MSI-H)

**PR**

- 85 Y/F small bowel cancer:
  - Treated with pembrolizumab (confirmed progression; secondary resistance)

- PR at week 20 (90 µg/kg)

- Week 20 scan on MDNA11 showed 37% reduction in target lesions

- Continuing on MDNA11
MDNA11 Achieves Objective Response in Anti-PD-1 Resistant Melanoma

**Cutaneous Melanoma**

| PR  | 100% resolution of target lesion (90 µg/kg) |

- 63 Y/F cutaneous melanoma patient:
  - Progressed on prior line of dual checkpoint inhibitors (Nivolumab + Ipilimumab)
  - PR at week 12 with target lesion reduced by 70%
  - Deepening of response with 100% reduction of target lesion (week 28, 36) and decreasing non-target lesions
  - Continuing on MDNA11

- 56 Y/F cutaneous melanoma:
  - Treated with nivolumab (& rechallenge) (confirmed PD; secondary resistance)
  - Developed a new lesion at week 8 and 18.75% increase in target lesion (pseudo-progression)
  - iPR at week 12 confirmatory scan: marked reduction in target lesion (31.25% from baseline) and new lesion remained stable.
  - New lymph node lesion at week 16; all baseline lesions and previous new lesion (week 8) were stable or decreased
  - Continuing on MDNA11
Conclusions

**RDE**
- Dose of 90 µg/kg selected as monotherapy RDE

**SAFETY**
- MDNA11 is well-tolerated with no DLTs observed at all dose levels up to 120 µg/kg IV Q2W

**PHARMACODYNAMICS**
- MDNA11 shows robust increase in CD8⁺ T and NK cells with activation markers peaking at 90 µg/kg

**EFFICACY**
- Compelling evidence of single-agent anti-tumor activity in checkpoint inhibitor refractory disease including tumor types not normally responsive to other IL-2 immunotherapies
  - 4 Partial Responses (1 PDAC, 1 small bowel cancer, and 2 cutaneous melanoma)
  - 3 Durable Stable Disease of 24 – 82 weeks in melanoma (2 cutaneous, 1 acral)
- **Single Agent Response Rate of 28.6% and Clinical Benefit Rate of 50% in Phase 2 Eligible Patients (MDNA11 ≥60 µg/kg) who all have failed checkpoint inhibitor therapies**

**ENROLLMENT**
- Monotherapy dose expansion and combination dose escalation with pembrolizumab are continuing to enroll
Acknowledgements

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➢ The investigators and all clinical and support trial staff at each of the study sites for their investment of time and effort into the trial

➢ The ABILITY-1 Trial is funded and sponsored by Medicenna Therapeutics
Appendix
MDNA11 Monotherapy: Duration of Treatment & Response

- **Time on Treatment (Weeks):** 0, 4, 8, 12, 16, 20, 24, 28, 32, 40, 50, 60, 70, 80, 90
- **Dose (μg/kg):** 3, 10, 30, 60, 90, 120

**Efficacy Evaluable Patients**
- **Cut-off date:** 22-Mar-2024
- **Target lesion reduced by >30%**
  - Non-target lesion stable
  - New lymph node lesion (unconfirmed) at week 16

**Response Categories:****
- Partial Response
- Stable Disease
- iUPD*
- Progressive Disease

**Legend:**
- Continuing MDNA11
- Following MDNA11 resumption all baseline lesions resolved and treatment was discontinued

**Notes:**
- Following MDNA11 resumption all baseline lesions resolved and treatment was discontinued.
- Vacation: Rx Break
- Radiotherapy of new lesion

*Unconfirmed disease progression

**Cancers Studied:**
- Melanoma
- Sarcoma
- PDAC
- RCC
- GE Junction
- Tonsil SCC
- Lung Adeno Ca
- NSCLC
- Melanoma
- NSCLC
- Melanoma
- Acral Melanoma
- RCC
- Melanoma
- Melanoma
- Melanoma
- Melanoma
- Acral Melanoma
- NSCLC
- Melanoma
- Small Bowel Ca
- Melanoma
- Acral Melanoma
- cSCC

**Monotherapy Expansion (Ph 2)**

**Efficacy evaluable patients**