MGD013: First Bispecific Checkpoint Molecule in Clinic

- Humanized, proprietary PD-1 x LAG-3 DART® molecule
- Hinge-stabilized human IgG4
- Benchmarks favorably against leading monoclonal antibodies (mAbs)

Function/MoA: Reactivation of exhausted T cells
Indications: Multiple solid tumors and hematological malignancies

Rationale for Dual Targeting of PD-1 and LAG-3

- Tumors activate immune inhibitory pathways
- PD-1 & LAG-3 receptors overexpressed on "exhausted" T-cells
- Animal tumor models demonstrate synergy of anti-PD-1 + anti-LAG-3 mAbs
- Combination clinical trials of anti-PD-1 and anti-LAG3 are ongoing

Overlap of PD-1 and LAG-3 Expressing TIL Detection in NSCLC and TNB Cancers

Validation Study Performed by MG

<table>
<thead>
<tr>
<th>Expression of Checkpoint(s) Across All TMAa</th>
<th>Overlapping Expressionb</th>
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</thead>
<tbody>
<tr>
<td>Tumor MicroArray (TMA) Spot Count for Particular Indication</td>
<td>LAG-3 Total</td>
</tr>
<tr>
<td>Lung Squamous Cell Carcinoma</td>
<td>18/36</td>
</tr>
<tr>
<td>Lung Adenocarcinoma</td>
<td>19/33</td>
</tr>
<tr>
<td>Triple Negative Breast Cancer</td>
<td>16/29</td>
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*Spot Counts indicate the number of TMA positive for LAG-3, PD-1, or LAG-3 + PD-1 expression divided by the total TMAs

Rationale

- MGD013 can enhance T-cell activation in a synergistic fashion beyond that observed with the anti-PD-1 and anti-LAG-3 mAbs alone or the combination of the single agents
- Bispecific approach to target these checkpoint proteins with a single molecule may confer additional benefits beyond that realized with the individual mAb combination and represents a rationale for dual checkpoint blockade
- MGD013 may offer clinical opportunities to checkpoint naive patients as well as to checkpoint experienced patients who have progressed on prior therapy with PD-1/PD-L1 inhibitors

Key Study Objectives

- Characterize safety, tolerability, DLT, maximum tolerated dose (MTD) or maximum administered dose (MAD) of MGD013 when administered IV every two weeks to patients with relapsed/refractory unresectable or metastatic neoplasms
- Characterize pharmacokinetics (PK) and immunogenicity of MGD013
- Investigate preliminary anti-tumor activity of MGD013 using both conventional RECIST 1.1 and immune-related response criteria (irRC)

Exploratory Objectives

- Explore relationships between PK, pharmacodynamics, patient safety, and anti-PD-1 and anti-LAG-3 activity
- Investigate immune-regulatory activity of MGD013 in vivo, including various measures of T-cell activation in peripheral blood and/or tumor biopsy specimens
- Determine relationships between PD-1, PD-L1, LAG-3, and MHC-II expression in tumor cells and immune cell infiltration within biopsy specimens (including CD4+ and CD8+ T-cells) and antitumor activity

Study Design

- Multi-center, Phase 1, open-label, study with single-patient escalation followed by 3+3 design dose escalation and cohort expansion
- MGD013 administered at escalating doses by intravenous infusion every 2 weeks in 8-week cycles
- MTD: Dose at which <33% of patients experience a drug-related DLT during the first 28 days of Cycle 1. If no DLT defined, highest dose level will be designated as MAD
- Patient management according to immune response principles and may receive up to 12 cycles

Entry Criteria

- Dose escalation: histologically proven, locally advanced unresectable or metastatic solid tumors of any histology with no approved therapy.
- Disease-specific criteria to be applied in Cohort Expansion
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Life expectancy ≥12 weeks
- Measurable disease per RECIST 1.1
- Previous immune checkpoint inhibitor toxicities resolved to ≤ Grade 1/baseline
- Acceptable laboratory parameters
- Must have a formalin-fixed, paraffin embedded tumor specimen

Key Inclusion Criteria

- Symptomatic central nervous system metastases
- History of known or suspected autoimmune disease with specific exceptions
- Treatment with any systemic anti-neoplastic therapy, or investigational therapy within 4 weeks; radiation therapy or corticosteroid treatment within 2 weeks
- Clinically significant cardiovascular, pulmonary, or gastrointestinal disease