Background

Ephrin receptor A2 (EphA2) is expressed in cancer and stroma cells in a wide range of solid tumors. MM-310 is an EphA2-targeting liposomal form of a docetaxel prodrug. Preclinical investigation revealed a high correlation between EphA2 expression on cancer cells and MM-310 uptake. In vivo studies in multiple xenograft models demonstrated superior antitumor activity compared with standard of care agents and toxicity analysis in rodents and non-rat animal models revealed a favorable toxicity profile. The overexpression of EphA2 in a wide range of tumors, the high tumor specificity of MM-310 through the enhanced permeability and retention effect, and the EphA2 targeting support the investigation of MM-310 for potential clinical utility.

MM-310: An EphA2-Targeting Liposomal Form of a Docetaxel Prodrug

**EphA2 Targeting Antibody**
- 15 scfv per liposome
- High prevalence in tumors
- Limited accessibility in healthy organs
- Expressed in tumor and stromal cells

**Docetaxel Prodrug**
- Approximately 30,000 per Ls
- Broad spectrum activity
- Improved stabilization and release

**Lipid Matrix**
- Provides encapsulation and stability

High Tumor Specificity
- EphA2 targeting
- Enhanced permeability and retention (EPR) effect

Wide Therapeutic Window
- Slow prodrug release
- Conversion to docetaxel

EphA2 Prevalence

EphA2 is an attractive target due to its high prevalence in a wide range of solid tumors and its expression in both cancer cells and stromal components of tumors, such as tumor associated blood vessels.

<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>Cancer Cells %</th>
<th>Tumor-associated Blood Vessels %</th>
<th>EphA2 Overall Score %</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC (n=19)</td>
<td>95%</td>
<td>79%</td>
<td>95%</td>
</tr>
<tr>
<td>G/GEJE (n=20)</td>
<td>90%</td>
<td>85%</td>
<td>100%</td>
</tr>
<tr>
<td>SCCHN (n=18)</td>
<td>83%</td>
<td>42%</td>
<td>100%</td>
</tr>
<tr>
<td>Ovarian (n=18)</td>
<td>85%</td>
<td>95%</td>
<td>95%</td>
</tr>
<tr>
<td>PDAC (n=19)</td>
<td>79%</td>
<td>56%</td>
<td>89%</td>
</tr>
<tr>
<td>NSCLC (n=37)</td>
<td>45%</td>
<td>65%</td>
<td>76%</td>
</tr>
<tr>
<td>Prostate (n=45)</td>
<td>46%</td>
<td>62%</td>
<td>72%</td>
</tr>
<tr>
<td>TNBC (n=78)</td>
<td>8%</td>
<td>44%</td>
<td>49%</td>
</tr>
</tbody>
</table>

EphA2 prevalence using 50% cutoff of positive cancer cells or 2 positive high power fields of view in the case of tumor associated blood vessels. EphA2 overall score reflects patients that show EphA2 positivity in any of the two compartments.

Preclinical Activity

MM-310 preclinical activity was tested in a set of patient-derived (PDO) and cell-derived (CDX) models covering 5 indications. Tumor-bearing animals were treated with weekly doses of MM-310 at 59 mg/kg (at around 50% preclinical MTD).

Key Eligibility Criteria

**INCLUSION**
- One of the following cancers:
  - Urothelial carcinoma (UC)
  - Gastric/ gastroesophageal junction/ esophageal carcinoma (G/GEJE)
  - Squamous cell carcinoma of the head and neck (SCCHN)
  - Ovarian cancer
  - Pancreatic ductal adenocarcinoma (PDAC)
  - Prostate adenocarcinoma (PAC)
  - Non-small cell lung cancer (NSCLC)
  - Small cell lung cancer (SCLC)
  - Triple negative breast cancer (TNBC)
  - Endometrial carcinoma
  - Soft tissue sarcoma subtypes except GIST, desmoid tumors and pleomorphic rhabdomyosarcoma
  - ≥ 18 years of age
  - ECOG performance status 0 or 1
  - Adequate hematologic parameters, hepatic and renal function
  - Adequate coagulation function (PT, APTT, and INR) within normal limits
  - Availability of a cancerous lesion amenable to biopsy and willingness to undergo biopsy

**EXCLUSION**
- Prior treatment with docetaxel within 6 months of study enrollment
- Treatment with systemic antiangiogenic
- Received prior treatment known to have anti-VEGF/VEGFR activity within 5 half-lives of study enrollment
- Any evidence of hematemesis, melena, hematochezia, severe hemoptysis, or gross hematuria
- Any hereditary bleeding disorders
- Peripheral neuropathy
- Known CNS metastasis

Study Design

**Preclinical Toxicity**

MM-310 demonstrated an improved hematologic toxicity profile in rats when compared with docetaxel.

**Study Objectives**

**PRIMARY**
- Determine the maximum tolerated dose (MTD) and describe the dose-limiting toxicities (DLT) of MM-310 administered once every 3 weeks, in patients with metastatic solid tumors

**SECONDARY**
- Determine the pharmacokinetic parameters
- Characterize the adverse event profile
- Determine the immunogenicity parameters
- Describe any objective response based on RECIST v1.1 or other disease-relevant criteria
- Assess disease control rate (RECIST response of SD, PR and CR for > 3 months)
- Assess progression-free survival (PFS) based on RECIST v1.1 or other disease-relevant criteria

**EXPLORATORY**
- Assess correlation of safety, efficacy, pharmacokinetics, pharmacodynamics, with EphA2 expression and other predictive biomarkers

Acknowledgments

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A PASSION FOR OUTTHINKING CANCER