Introduction:

- DSP107 is a bi-functional, trimeric, fusion protein composed of sequences from the extracellular domains of SIRPαs and 4-1BB.
- The SIRPα arm targets CD47 overexpressed on tumor cells, blocking the “don’t eat me” checkpoint and triggering tumor cell phagocytosis. The trimeric 4-1BB arm, once cross-presented and immobilized by SIRPα binding to CD47, interacts with 4-1BB expressed on activated immune cells, mainly T- and NK cells in the tumor microenvironment, and stimulates their proliferation and activation. Thus, DSP107 triggers both an innate and an adaptive immune response.

Methods:

- Adult patients with advanced solid tumors (N=23) were treated in escalating dose cohorts with intravenous DSP107 (0.01 - 10 mg/kg QW) during 3-week treatment cycles.
- Patients were treated in single patient cohorts (dose levels 0.01, 0.03 and 0.1 mg/kg) followed by a standard 3 + 3 design at doses 0.1, 1, 3 and 10 mg/kg.
- Primary study objective: To determine the safety, tolerability and pharmacokinetic (PK) parameters. When possible, paired biopsies were collected at screening and after 6 weeks (cycle 2).
- Here we report data from the completed DSP107 monotherapy dose escalation portion of study NCT04440735.

Results:

Table 1: Patient Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 23 (cohorts 1 – 7)</td>
</tr>
<tr>
<td>Sex</td>
<td>10 (43%) 9; 13 (57%) c</td>
</tr>
<tr>
<td>Age</td>
<td>Median 63 (Range 29-78)</td>
</tr>
<tr>
<td>Previous lines of therapy</td>
<td>Median 3 (Range 2-8)</td>
</tr>
<tr>
<td>PD1/PD-L1 experienced</td>
<td>11 (48%)</td>
</tr>
</tbody>
</table>

Conclusions:

- DSP107 is a novel, CD47 and 4-1BB targeting fusion protein with a differentiated safety, binding and pharmacodynamic profile compared to other CD47 and 4-1BB targeting agents.
- DSP107 showed excellent safety profile with full receptor occupancy and no binding to RBCs.
- Treatment with DSP107 induced increased tumor necrosis and infiltration of T and NK cells at the tumor and tumor margin.
- Fifty percent of the DSP107 treated patients showed stable disease.

Table 2: DSP107 Related AEs

<table>
<thead>
<tr>
<th>Treatment-related AEs in 2 Patients</th>
<th>Total No. of Patients N=23 (Cohorts 1-7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any 16 (70)</td>
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<tr>
<td></td>
<td>Dose 4 (17)</td>
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<tr>
<td></td>
<td>Fatigue 4 (17)</td>
</tr>
<tr>
<td></td>
<td>Constipation 2 (9)</td>
</tr>
<tr>
<td></td>
<td>Nausea 3 (13)</td>
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<tr>
<td></td>
<td>IRR 1 (9)</td>
</tr>
</tbody>
</table>

*RRs Grade 1-2 in severity. Easily abrogated (except 10-004 and 11-012 who withdrew consent) in subsequent infusions by reduced rate of infusion and concomitant IV fluids.

Pharmacokinetics and Target Engagement:

- Greater than dose-proportional exposure at 3 and 10 mg/kg.
- Duration of exposure, t1/2, and AUC increased with dose reaching Cmax ~100 – 500 times higher than the EC50 concentration at 3 and 10 mg/kg, respectively.
- Exposure levels above the EC50 at doses ≥ 0.3 mg/kg.
- Dose dependent target engagement with 100% receptor occupancy on circulating immune cells.
- No binding to RBCs at any dose level.
- DSP107 increased tumor necrosis and triggered T and NK-cell infiltration into tumor microenvironment.

Response:

- Best response of Stable Disease observed in 11/22 patients with treatment duration up to 26 weeks.

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#301: Phase 1 dose escalation study of DSP107, a first-in-class CD47 and 4-1BB targeting multifunctional immune-recruitment protein, in patients with advanced solid tumors

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![Image](image-url)