A Phase 1 Study of ALX148, a CD47 Blocker, in Combination with Standard Anti Cancer Antibodies and Chemotherapy Regimens in Patients with Advanced Malignancy

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Background

ALX148 is a high affinity CD47 blocker fusion protein with an inactive human Fc domain. ALX148 is intended as a chemotherapy-sensitizing agent with an antineoplastic effect.

Methods

AT148001 Study Design

1. Part 1 (Dose escalation) — Thirty-six patients enrolled with advanced solid tumor or hematologic malignancy, including 18 patients with advanced hematologic malignancy.

2. Part 2 (Combination) — Patients with advanced solid tumors were enrolled in ALX148 (10 mg/kg QW) + pembrolizumab (200 mg Q2W) cohorts. The combination cohort was expanded to a total of 20 patients.

Results

Patient Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ALX148 Monotherapy</th>
<th>Pembrolizumab Monotherapy</th>
<th>ALX148 + Pembrolizumab</th>
<th>Pembrolizumab + Trastuzumab</th>
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</thead>
<tbody>
<tr>
<td>% Change in Baseline Measureable Lesions</td>
<td>-80</td>
<td>20</td>
<td>60</td>
<td>80</td>
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<tr>
<td>ORR</td>
<td>5% (95% CI 0.1, 24.9)</td>
<td>17.9 months (95% CI 13.6; 19.1)</td>
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Safety

Adverse Events (AEs) — ALX148 treated patients experienced grade 3 or greater clinical adverse events (AEs) and treatment-related adverse events (TRAEs) comparable to those observed with ALX148 treatment alone. No TRAEs of ALX148 were reported in combination with pembrolizumab or pembrolizumab + trastuzumab.

Response

ALX148 Monotherapy — CAPEO (1 PR, 9 SD, 10 PD) was observed across all dosing cohorts.

Combination Treatment — ALX148 + pembrolizumab showed clinical activity, with 1 PR, 9 SD, 10 PD observed in combination with pembrolizumab. ALX148 + pembrolizumab + trastuzumab showed comparable clinical activity with 1 PR, 9 SD, 10 PD in combination with pembrolizumab + trastuzumab.

Conclusions

ALX148 is well-tolerated and has the potential to improve outcomes for patients with advanced solid tumors and hematologic malignancies. ALX148 in combination with pembrolizumab and ALX148 + pembrolizumab + trastuzumab is being further evaluated in a Phase 2 study.