Preliminary Safety, PK/PD, and Antitumor Activity of XmAb18087, an SSTR2 x CD3 Bispecific Antibody, in Patients With Advanced Neuroendocrine Tumors

Bassel El-Rayes,1 Shubham Pant,2 Victor Villalobos,3 Andrew Handtfer,4 Warren A Chou5 Bhavana Konda5 Matthew Reilly6 Ali Benson7 George Fisher7 Jason Starr7 Jonathan Brosborg8 Daniel Ahu8 Kimberly Perez,3 Nitya Raj1 Jennifer Eads8 Timothy J. Hobday9 Ying Ding9 Andrew Hendifar10 Victor Villalobos11

BACKGROUND

• SSTR2 is highly overexpressed in neuroendocrine tumors (NET).
• XmAb18087 (Ademun), a humandized, anti-SSTR2 anti-CD3 bispecific antibody, directs T-cell mediated cytotoxicity to SSTR2+ tumor cells.
• Duet 1 is an ongoing, Phase 1, first-in-human study of XmAb18087 in patients with NET and GIST.

We here report preliminary data for NET cohorts, based on a 26 August 2020 data cut.

STUDY OBJECTIVES

• To determine the safety and tolerability profile of XmAb18087 in patients with advanced, well-differentiated NET, pancreaticNET, gastrointestinal (GI), lung, and undetermined origin.
• To identify the maximum tolerated dose (MTD) and/or recommended dose and regimen.
• To characterize pharmacokinetics (PK) and immunogenicity.
• To assess preliminary antitumor activity using RECIST 1.1 based on objective response rate, duration of response, and progression-free survival (PFS).
• To assess biomarkers of cytokine release syndrome (CRS).
• To characterize immune response in peripheral blood based on changes in lymphocyte subsets and markers of T-cell activation and exhaustion.

METHODS

• Study design – 3+3 dose escalation design with cohort expansion (n = 20) at MTD.
• XmAb18087 is administered as a 2-hour intravenous infusion on Days 1, 8, 15, and 22 of each 28-day cycle.
• Dosing includes a priming dose on Cycle 1, Day 1, followed by a higher, repeated dose on subsequent dosing days.
• Patients receive prophylaxis for CRS and nausea and vomiting at least through Cycle 1.
• Imaging is performed at screening and at the end of every third cycle of treatment for response assessment.
• Samples are collected for evaluation of PK and pharmacodynamics in peripheral blood (T-cell activation and proliferation, cytokines) at multiple time points throughout treatment.

RESULTS

• In 22 evaluable NET patients, including 2/6 expansion cohort patients, stable disease in 43% of patients across dose levels
• Disease control rate of 43%, with a disease control rate of 56% in the 1.0 µg/kg dose level.
• CRS was restricted to Grades 1 and 2 and limited to the first 2 doses.

Cytokine Release Syndrome by XmAb18087 Dose Level

| Dose Level (µg/kg) | % of Patients with CRS
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td>0.3</td>
<td>0</td>
</tr>
<tr>
<td>1.0</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>2.0</td>
<td>0</td>
</tr>
</tbody>
</table>

PK was dose proportional at priming and repeated doses. Median half-life was 34 hours (~4 days).

CONCLUSIONS

• Preliminary data from this ongoing, Phase 1 study in patients with low- and intermediate-grade NET indicate XmAb18087.
• Was generally well tolerated at the expansion dose (0.3–1.0 µg/kg).
• DLT – nausea and vomiting
• CRS limited to Grades 1 and 2
• Demonstrated dose proportional PK with a half-life that supports weekly dosing.
• Induced acute and sustained T-cell activation in peripheral blood.
• Was associated with stable disease in 43% of patients across dose levels.
• Completion of enrollment in the expansion cohort and longer follow-up are required to evaluate PFS and the clinical utility of XmAb18087 in this patient population.

ACKNOWLEDGEMENTS

Many thanks for support in the conduct of this research to the patients, their families, and caregivers, and the XmAb18087-01 investigational study teams.