TARGETING PANCREATIC ADENOCARCINOMA UPREGULATED FACTOR (PAUF) TO TREAT PANCREATIC CANCER (PC): IN VIVO EFFICACY AND SAFETY OF PBP1510, A FIRST IN CLASS MONOCLONAL ANTIBODY (mAb)

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Abstract 216

BACKGROUND

• Pancreatic cancer (PC) is an aggressive disease characterized by overall therapeutic resistance and rapid disease progression.

• Pancreatic Adenocarcinoma Upregulated Factor (PAUF), a gene overexpressed in PC plays a major role in tumour progression and metastases via various pathways (Figure 1).

• PBP1510 (INN: Ulenistamab), a first in class, recombinantly expressed humanized immunoglobulin G1 (IgG1) kappa isotype mAb, specifically binds to and neutralises PAUF.

• Objectives: To establish preclinical efficacy and safety of PBP1510.

METHODS

Efficacy

Following in vivo studies were conducted in mice (Table 1) to assess tumour size and tumour size inhibition (TGI):
• Subcutaneous (SC) cell-derived xenograft (CDX) study
• SC patient-derived xenograft (PDX) study
• Orthotopic PDX studies

RESULTS

Efficacy

• Superior anti-tumour efficacy of PBP1510 treatment, compared to IgG control, was observed in all the three mouse models, particularly in PAUF-positive cancer models.

• The SC PDX model derived from PAUF negative sample did not respond to PBP1510, indicating specificity of treatment.

Safety

A 4-week repeated dose study was conducted in mice for toxicity, toxicokinetic and immunogenicity analysis:
• 370 CD-1 mice divided into 4 dosing groups (highest dose administered: 40 mg/kg)
• Blood sampling at predefined timepoints

Figure 1. Mechanism of action of PBP1510

Safety

• Dose proportional response
• No observed effect level (NOEL) concluded as 40 mg/kg
• Absence of anti-drug antibodies in all animals
• No notable systemic or local toxicity up to 40 mg/kg

Table 1. Summary of in vivo mouse studies

<table>
<thead>
<tr>
<th>Mouse model (BALB/c nude mice)</th>
<th>Implanted material</th>
<th>Treatments Compared</th>
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<tbody>
<tr>
<td>SC CDX</td>
<td>BxPC-3-Luc (PC cell line) 1×10⁶ cells</td>
<td>Intravenous (IV) 10 mg/kg twice a week for 5 weeks</td>
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<td></td>
<td></td>
<td>• Control (human IgG)</td>
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<td>• PBP1510</td>
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<tr>
<td>SC PDX</td>
<td>PAUF-positive PC patient samples</td>
<td>IV 10 mg/kg twice a week for 4 weeks</td>
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<td></td>
<td></td>
<td>• Control (human IgG)</td>
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<tr>
<td></td>
<td></td>
<td>• PBP1510</td>
</tr>
<tr>
<td>Orthotopic PDX</td>
<td>PAUF-negative PC patient samples</td>
<td>IV 50 mg/kg single dose</td>
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<td>• Gemcitabine</td>
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</tbody>
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Figure 2. Results from the SC CDX study (n=3). A) Tumour volume throughout the study B) Comparison of tumour volumes on Day 0 vs. Day 38

Figure 3. Representative results from SC PDX study. A) Visual representation B) Tumour volume throughout the study C) Tumour weights at endpoint. * or **=significant results; NS=non-significant

Figure 4. Representative results from Orthotopic PDX study. A) MRI B) Tumour size. *=significant results; NS=non-significant

CONCLUSION

• Data presented here, along with other pre-clinical data, support further clinical development of PBP1510 as a novel anti-cancer agent to treat PAUF-positive PC.

• PBP1510 granted Orphan Drug Designation by EMA, US FDA and Korea MFDS

• First in human Phase 1/2a study (PAUF-I) to start in first quarter of 2022.

REFERENCES


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