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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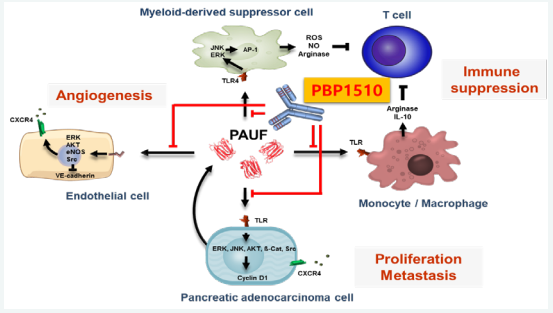
BACKGROUND

- **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

Figure 1. Mechanism of action 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

Table 1. Summary of *in vivo* mouse studies

Mouse model (BALB/c nude mice)	Implanted material	Treatments Compared
SC CDX	BxPC-3-Luc (PC cell line) 1×10^6 cells	Intravenous (IV) 10mg/kg twice a week for 5 weeks • Control (human IgG) • PBP1510
SC PDX	PAUF-positive PC patient samples	IV 10 mg/kg twice a week for 4 weeks • Control (human IgG) • PBP1510
Orthotopic PDX		
SC PDX	PAUF-negative PC patient samples	IV 50 mg/kg single dose • Gemcitabine

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

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.

Figure 2. Results from the SC CDX study (n=3). A) Tumour volume throughout the study B) Comparison of tumour volume on Day 0 vs. Day 38

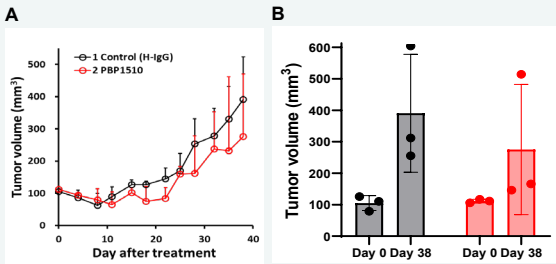


Figure 3. Representative results from SC PDX study. A) Visual representation B) Tumour volume throughout the study C) Tumour weights at endpoint. * or **=significant results; NS=non-significant

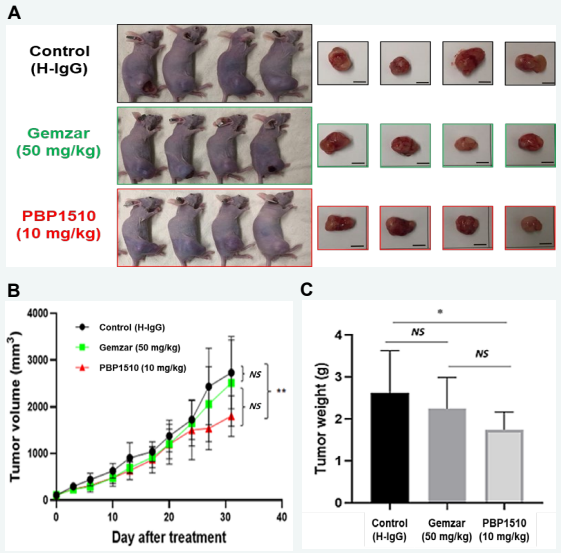
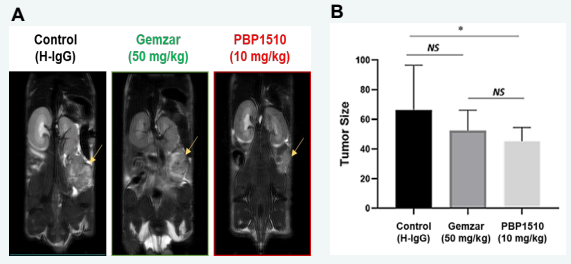


Figure 4. Representative results from Orthotopic PDX study. A) MRI B) Tumour size. *=significant results; NS=non-significant



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

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.

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