

⁹⁰Y-~~h~~PAM4 Program

- **Reactive with 85% of pancreatic cancers**
- **Orphan drug status for pancreatic cancer**
- **Phase I dose escalation study completed**



Our solid tumor therapeutic, humanized PAM4 antibody, reacts with about 85% of pancreatic cancers and has shown a high specificity for pancreatic cancer and minimal activity with normal tissue, including normal pancreas. The yttrium-90-labeled antibody has received orphan drug status from the FDA for the treatment of pancreatic cancer. We have completed our Phase I single dose escalation clinical trials, which have shown early evidence of efficacy in patients who have failed prior therapy.

⁹⁰Y-*h*PAM4 Current Phase Ib Study

- **First-line therapy in patients with inoperable pancreatic cancer**
- **Fractionated Y-90-*h*PAM4 combined with Gemzar**
 - Y-90 *h*PAM4 weekly x 3
 - Gemzar weekly x 4
- **Patients treated at dose level 1**
 - 6.5 mCi/m² ⁹⁰Y-*h*PAM4
 - 200 mg/m² Gemzar



Our current study is a Phase Ib, open-label, dose exploration of ⁹⁰Y-*h*PAM4 administered as fractionated multi-dose radioimmunotherapy in combination with radiosensitizing doses of gemcitabine as front line therapy for patients with Stage III unresectable locally advanced or Stage IV metastatic pancreatic cancer. Patients first undergo pre-treatment targeting and dosimetry imaging via uptake of the *h*PAM4 antibody labeled with Indium111. Once successful tumor targeting and radiation limits have been established, the patients receives three fractionated doses of y90-*h*PAM4, administered over three weeks. Additionally, each patient is given a non-cytotoxic dose of gemcitabine following each administration of *h*PAM4, which we believe with potentiate the radiation effects of the y90 on the cancer cells. Therapy cycles have been repeated up to a total of 3 cycles in some patients.

⁹⁰Y-~~h~~PAM4 Current Phase Ib Study

- **First patient**
 - Large pancreatic tail mass
 - Multiple liver metastases
 - Excellent response
 - Retreated twice
- **Second patient**
 - Pancreatic tail mass
 - Portacaval lymph node & liver metastases
 - Excellent response
 - Retreated once



The first patient to receive treatment had a large pancreatic tail mass with multiple liver metastases. The therapy was well tolerated, and the patient has completed a 3rd treatment cycle. The second patient, who had a pancreatic tail mass, portacaval lymph node metastases, and a large metastatic liver mass, also tolerated the initial treatment very well, and has completed her second treatment cycle. After treatments, both patients had significant improvements in their performance status and quality of life, which are presently being maintained.

⁹⁰Y-~~h~~PAM4 Early Phase 1b Results

First patient's imaging response to 1st cycle

Lesion	CT (cm)		PET (SUV)	
	Baseline	4 wk post-therapy	Baseline	4 wk post-therapy
PA Tail (1°)	4.5	4.3	9.2	4.2
Liver #1	1.9	1.9	4.1	background
Liver #2	1.7	1.6	3.7	background
Liver #3	1.9	1.2	3.2	background

At our recent R&D Day event, we presented some of the early results obtained from the first treated patient. As you can see, after the first cycle of therapy, there were modest but significant decreases in tumor size at 4 weeks post therapy. When we look at the PET scan data, we see the dramatic changes that have occurred in tumor metabolic activity. The SUV, as a measure of metabolism within the specific lesion, has decreased within the primary mass by more than half, and the three largest liver metastases are now indistinguishable from the surrounding tissues, indicating a state of relative metabolic inactivity. Similar dramatic results were also observed in a second patient.