### RESULTS

**ABSTRACT**

Necuparanib ("necu") inhibits multiple heparin-binding growth factors, chemokines, and adhesion molecules in preclinical studies. In a Phase 1 trial, safety, pharmacokinetics (PK) and pharmacodynamics (PD) of necuparanib (1-5 mg/kg) were evaluated in patients with metastatic pancreatic cancer. The Phase 2 trial was amended to include nab-P after 2 necu + gem cohorts were completed. The maximum tolerated dose was determined (which was 5 mg/kg). The protocol was amended to include nab-P and gemcitabine (gem) in patients (pts) with metastatic pancreatic cancer. Necuparanib (“necu”) inhibits multiple heparin-binding growth factors, chemokines, and adhesion molecules in preclinical studies. In a Phase 1 trial, safety, pharmacokinetics (PK) and pharmacodynamics (PD) of necuparanib (1-5 mg/kg) were evaluated in patients with metastatic pancreatic cancer. The Phase 2 trial was amended to include nab-P after 2 necu + gem cohorts were completed. The maximum tolerated dose was determined (which was 5 mg/kg). The protocol was amended to include nab-P and gemcitabine (gem) in patients (pts) with metastatic pancreatic cancer.

### BACKGROUND

Reports of antitumor activity have been generated in clinical trials using necuparanib (necu) alone or in combination with nab-Paclitaxel (Abraxane®) and 1000 mg/m^2 gemcitabine (gem) on Days 1, 8, 15 of each 28-day cycle. The rationale behind developing necuparanib was to exploit its unique mechanism of action, with promising biomarker results in preclinical and clinical studies. The potential of necuparanib is recognized, but it has not been fully investigated in clinical trials,

### METHODS

**METHODS**

Necuparanib was given on an evaluable day to patients who had ≥1 scan on treatment; 9 (56%) achieved RECIST partial response. Among evaluable patients (n=16), 12 (75%) had ≥1 dose; 8 (50%) achieved RECIST partial response; 6 (37.5%) had ≥1 scan on treatment; and 7 (43.7%) achieved RECIST partial response. The maximum tolerated dose was determined (which was 5 mg/kg). The protocol was amended to include nab-P and gemcitabine (gem) in patients (pts) with metastatic pancreatic cancer. The rationale behind developing necuparanib was to exploit its unique mechanism of action, with promising biomarker results in preclinical and clinical studies.

### RESULTS

- **Baseline Characteristics (Dose Cohort Progression)**
  - *Mean age*: 63 yrs (range: 36-85)
  - *Sex*: 8 M, 8 F
  - *Race*: White: 56 (90%), Black/African American: 10 (16%)

- **Safety, Pharmacokinetics, Pharmacodynamics, and Antitumor Activity of Necuparanib Combined with nab-Paclitaxel and Gemcitabine in Patients with Metastatic Pancreatic Cancer: Updated Phase 1 Results**

- **Pharmacokinetics/Pharmacodynamics**
  - Measurable levels of necuparanib were seen starting at the 2 mg/kg dose level. Release of heparin-binding proteins (e.g., fibrinogen, von Willebrand factor, fibronectin, fibulin-1) was observed starting at 2 mg/kg.

- **Hematological Toxicities**
  - Neutropenia: 3 (50%)
  - Anemia: 5 (63)

- **Pharmacokinetics**
  - *PK samples*: ongoing and the data represented here should be considered preliminary.

- **PK data**: shown for necuparanib in patients with metastatic pancreatic cancer. The rationale behind developing necuparanib was to exploit its unique mechanism of action, with promising biomarker results in preclinical and clinical studies.

### CONCLUSIONS

- **Phase 3 data**: 23% PR; 50.3% DCR; 8.5 months OS; 12 months PFS; 46 weeks OS; 3, 3-month, 1-year survival rates: 52% (95% CI 43-61)
- **Phase 1/2 data**: 48% PR; 68% DCR; 12.2 months OS; 21 months PFS; 46 weeks OS; 3, 3-month, 1-year survival rates: 72% (95% CI 61-81)

### REFERENCES