Fibroblast growth factors (FGFs) and their receptors (FGFRs) are a family of 22 human FGFs and 4 FGFRs (Gemo, 2014). There are three basic classes of FGFRs based on receptor structure: type I, type II, and type III, which correspond to FGFR1, FGFR2, and FGFR3 and FGFR4, respectively. A couple of these receptors appear to be tissue specific. FPA144 is a fully human IgG1 monoclonal antibody that selectively targets FGFR2b. It is a DCC (drug conjugated cell) enhancing, FGFR2b selective monotherapy agent that blocks receptor activation and blocks downstream signaling. Previous studies have shown that FPA144 is well tolerated, with an overall safety profile differing from small molecule kinase inhibitors. The interpretation of any potential difference in clearance between gastric cancer and other cancer types is preliminary and subject to change.

**Background**
- FGFRs and their receptors are implicated in a variety of human diseases, including cancer. They are overexpressed in numerous malignancies.
- Inhibitors of FGFRs have demonstrated antitumor activity in preclinical models.
- FPA144 is a fully human monoclonal antibody that selectively targets FGFR2b.

**Clinical Trial Design**
- A Phase 1 trial was conducted with two parts: Part 1A and Part 1B.
- Part 1A was an open-label, dose escalation study with a 3+3 design to determine the maximum tolerated dose (MTD).
- Part 1B was an open-label, dose expansion study.
- Approximately 28 patients enrolled and dosed with FPA144 as of October 29, 2015.

**Study Results – Safety Summary**
- The overall safety profile of FPA144 appears different from small molecule kinase inhibitors.
- No on-study deaths were observed.
- No on-study adverse events (AEs) assessed as Grade 5 were reported.
- No treatment-related deaths reported.
- The treatment-related AEs reported were mainly rash, fatigue, and hypophosphatemia.
- No treatment-related increases leading to treatment discontinuation.
- All reported treatment-related AEs were consistent with the expected adverse events of monoclonal antibodies.

**Study Results – Preliminary Radiographic Responses in FGFR2b-selected Gastric Cancer Patients in Part 1B**
- FPA144: A therapeutic antibody for treating patients with gastric cancers bearing FGFR2b overexpression (605-1006).
- The patient currently continues on therapy.

**Study Results – Pharmacokinetic Profile of FPA144**
- PK characteristics support once every other week or less frequent dosing.
- PK profile is typical of monoclonal antibodies with a short distribution phase and a long elimination phase.
- Exposure increased slightly more than dose proportionally from 0.3 mg/kg to 1 mg/kg and approximately dose proportionally from 1 mg/kg to 15 mg/kg.

**Conclusions**
- FPA144 is a well-tolerated agent in doses up to 15 mg/kg in patients with advanced solid tumors.
- No DLTs in the dose-escalation (MTD not reached).
- No on-study deaths were observed.
- No treatment-related deaths were reported.
- The treatment-related AEs reported were mainly rash, fatigue, and hypophosphatemia.
- No treatment-related increases leading to treatment discontinuation.
- Treatment-related AEs were consistent with the expected adverse events of monoclonal antibodies.

**References**