FPA144: A Therapeutic Monoclonal Antibody with Enhanced Antibody-Dependent Cell Killing for the Treatment of Fibroblast Growth Factor Receptor 2b Overexpressing Cancers
I have the following financial relationships to disclose:
Stockholder in: Five Prime Therapeutics
Employee of: Five Prime Therapeutics

- and -

I will discuss the following off label use and/or investigational use in my presentation:
*Phase 1 Clinical Development of FPA144*
FPA144 - A Humanized Monoclonal Antibody to FGFR2 Isoform b for Gastric Cancer

Engineered for enhanced antibody-dependent cell-mediated cytotoxicity (ADCC) to increase natural killer (NK) cell recruitment

FPA144: antibody specific to FGFR2b splice variant

Blocks Ligand Binding

FGF7

FGF10

FGF22
FGFR Biology

FGFR tyrosine kinase inhibitors indiscriminately block FGFRs

“Classical” FGFs

KGF Sub-family

Blocked by FPA144

Hormonal FFGs

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Both FGFR2 Amplification and FGFR2b Overexpression in Gastric Cancer Are Associated with Poor Prognosis

- FGFR2 gene amplification and FGFR2b protein overexpression are associated with lower survival in gastric cancer patients
- Most commonly found in patients with diffuse, poorly differentiated gastric cancer

Data are for all disease stages, including early
FPA144 Monotherapy is Effective in Preclinical Models

OCUM-2M Gastric Cancer Xenograft

Cells courtesy of M. Yashiro, Osaka City University Graduate School of Medicine
FPA144 Treatment Recruits NK cells and Enhances ADCC in a Xenograft Model with Low FGFR2b Expression

- FPA144 treatment leads to:
  - Recruitment of NK and subsequent T cell infiltration into the tumors
  - Upregulation of PD-L1
  - Regression of tumor growth
  - Enhanced ADCC may be critical for activity in tumors with low and moderate expression of FGFR2b

Poster: Powers, J  Monday 8 am 4/18/2016 Abstract # 1407
FPA144 Phase 1 Study Is Enrolling Selected Gastric Cancer Patients

**PART 1**
Dose Escalation

**PART 1A:** Dose escalation in solid tumors

**PART 1B:** Selected/Unselected Gastric Cancer

**PART 2**
Selected Gastric Patients

**Study Objectives**

- **Safety**
- **Objective**
  - response rate
  - and duration

**Initiated November 2015**

**PART 2A:** IHC 3+ FISH+ (n=30)

**PART 2B:** IHC < 3+
Patient Selection Strategy for Part 1B and Part 2 of Study

- IHC provides information about heterogeneity that FISH does not
- IHC will be the primary assay used to identify FPA144 eligible patients

**FGFR2b Overexpression**

**IHC**

Positive – 3+ membrane staining in ≥10% of tumor
FPR2-D – proprietary anti-FGFR2b antibody
Distinguishes FGFR2b and 2c
Commercial antibodies less specific

**FGFR2 Amplification**

**FISH**

Positive - FGFR2 probe: centromere probe
≥2 in 50 nuclei
Commercially available probes
Validated by LabCorp
Study Results – Part 1A and Part 1B

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>No. of Patients</th>
<th>Tumor Types</th>
<th>Mean Exposure (weeks)*</th>
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<tr>
<td>0.3</td>
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<td>Breast, Colon, Neuroendocrine</td>
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<td>1</td>
<td>4</td>
<td>Colon, Lung, Gallbladder, Submandibular</td>
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<tr>
<td>3</td>
<td>3</td>
<td>Bladder, Colon, Gastric</td>
<td>13.6</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>2 Colon, Gastric</td>
<td>3.5</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td>Colon, Gastric, Peritoneal</td>
<td>4.2</td>
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<tr>
<td>15</td>
<td>3</td>
<td>Bile Duct, Esophageal, Pancreatic</td>
<td>4.2</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>12 Tumor Types</td>
<td>10.6</td>
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</table>

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
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<th>Tumor Types</th>
<th>Mean Exposure (weeks)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>8</td>
<td>All Gastric</td>
<td>4.4</td>
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</table>

* 2 of 6 patients in the 10 mg/kg cohort did not meet the criteria for FGFR2b overexpression (IHC-)
As of the data cut off of 10/29/15
As of the data cut-off of October 29th, 2015:

• No dose-limiting toxicities in the dose escalation portion of the study
• Maximally tolerated dose not reached
• No on-study deaths
• 4 serious adverse events (SAEs) (across 2 subjects) reported, but none were treatment-related
• No treatment related hyperphosphatemia
Study Results – Radiographic Response and Decreased FDG PET Uptake in a Subject with Urothelial Bladder Cancer (UBC)

• Some evidence for a role of FGFs/FGFRs in bladder cancer
• Patient dosed with FPA144 at 3 mg/kg every two weeks and continues on study as of April 1, 2016 (day 353)
• Patient has moderate overexpression of FGFR2b without FGFR2 amplification

![Screening (Day -5)](image1)

![Cycle 8 Day 15 (Day 213)](image2)

![FGFR2b Staining](image3)
Study Results – Preliminary Radiographic Responses in FGFR2b-selected Gastric Cancer Patients in Part 1B

Tumor Responses in Selected Part 1B Patients Treated with FPA144

Days Post 1st FPA144 Dose

% Change Sum of Longest Diameters (SLD)

0 20 40 60 80 100 120 140

-40 -30 -20 -10 0

Tumor responses were assessed with the use of RECIST 1.1
Data as of 1/15/2016
Additional data to be presented at ASCO

Partial Response in Patient Treated with 6 mg/kg FPA144

Screening (Day -14)

Cycle 4 Day 1 (Day 83)
Summary

- FPA144 is an FGFR2b-specific antibody that FivePrime glycoengineered for enhanced ADCC (Abstract #1407)
  - Leads to recruitment of Natural Killer (NK) and T cells into the tumor and inhibition of tumor growth in vivo
  - Drives both innate and adaptive immune responses
- In ongoing Phase 1 testing FPA144 has been well tolerated with no dose limiting toxicities and no hyperphosphatemia
  - Patient enrollment in selected gastric cancer patients continues at 15 mg/kg, the highest dose tested
- There has been one confirmed partial response in a urothelial bladder cancer patient treated with 3 mg/kg FPA144. This patient has moderate FGFR2b expression
- Of 6 selected gastric cancer patients treated in part 1B as of January 15, 2016, there were 2 partial responses (1 confirmed), 3 stable diseases and 1 progressive disease
Acknowledgements

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• The FivePrime FPA144 team
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