Antitumor Activity and Safety of FPA144, an ADCC-enhanced, FGFR2b Isoform-Selective Monoclonal Antibody, in Patients with FGFR2b+ Gastric Cancer and Advanced Solid Tumors

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I have no conflicts to disclose.

- and -

I will discuss the following off label use and/or investigational use in my presentation:

Phase 1 Clinical Development of FPA144
FGFR2 Dysregulation is Linked to Shorter Survival in Gastric Cancer Patients*

* Data are for all disease stages, including early stage
FPA144 – An ADCC Enhanced Monoclonal Antibody Against FGFR2b

Engineered for enhanced antibody-dependent cell-mediated cytotoxicity (ADCC)
FPA144 Reprograms the Tumor Microenvironment in a Syngeneic Mouse Model Resulting in NK and T Cell Recruitment
FPA144 Phase 1 Study is Currently Enrolling FGFR2b+ Patients in Defined Cohorts

PART 1
Dose Escalation

PART 1A: Dose Escalation* in Solid Tumors

0.3mg/kg-15mg/kg q 2w
N=19 (3 GC)

PART 1B: Gastric Cancer

3mg/kg – 10 mg/kg q 2w
Unselected (6 FGFR2b+)
N=8

PART 2
Selected Patients

RD: 15 mg/kg q2w

- IHC High Gastric (N=3)
- IHC Moderate Gastric
- IHC Low Gastric
- IHC Negative Gastric
- IHC Positive Non Gastric

Study Objectives

- Safety
- PK
- Objective response rate and duration
- Baseline and on-treatment biopsies to evaluate changes in the tumor microenvironment

* 6 dose cohorts ranging from 0.3 to 15 mg/kg

Initiated
November 2015
FPA144 Patient Selection with a Proprietary Diagnostic Antibody Can Distinguish FGFR2b from FGFR2c

IHC High Staining With Proprietary Diagnostic Antibody (FPR2-D)

- IHC High is defined as 3+ membrane staining in ≥10% of tumor cells
- Commercial antibodies are less specific than FPR2-D antibody
- IHC provides information about tumor heterogeneity that FISH does not
- ~ 5% of gastric cancers have been shown to be IHC High
## Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All Gastric Population*</th>
<th>FGFR2b+ Gastric Population*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FPA144 (N=24)</td>
<td>FPA144 (N=9)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (yrs) (min, max)</td>
<td>57.5 (39, 77)</td>
<td>54.0 (39, 67)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16 (66.7)</td>
<td>6 (66.7)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>5 (20.8)</td>
<td>1 (11.1)</td>
</tr>
<tr>
<td>Asian</td>
<td>19 (79.2)</td>
<td>8 (88.9)</td>
</tr>
<tr>
<td><strong>ECOG</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>8 (33.3)</td>
<td>2 (22.2)</td>
</tr>
<tr>
<td>1</td>
<td>16 (66.7)</td>
<td>7 (77.8)</td>
</tr>
<tr>
<td><strong>Prior Therapies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (N) (min, max)</td>
<td>3 (1, 6)</td>
<td>2 (1, 6)</td>
</tr>
</tbody>
</table>

* Includes subjects enrolled as of the cut-off date of April 1, 2016
Safety Summary

- No DLTs: MTD was not reached
- No treatment-related SAEs: 17 unrelated SAEs across 9 subjects
- No AEs of hyperphosphatemia or retinal toxicity
- One transient treatment-related Grade 3 AE of decreased neutrophil count
- No discontinuations due to treatment-related AEs

### Most Common Treatment-related Adverse Events (Incidence 5%)*

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>All Part 1 and 2 Patients (Combined) N=40</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 1/2 N (%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9 (22.5)</td>
</tr>
<tr>
<td>Nausea</td>
<td>8 (20.0)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5 (12.5)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>Dry Eye</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>Keratitis</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>Lacrimation Increased</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>3 (7.5)</td>
</tr>
</tbody>
</table>

* Treatment relatedness is based on an assessment of possible or probable attribution to study drug by the investigator. Data cut-off of April 1, 2016. The full safety population includes all patients receiving any portion of at least one dose of FPA144 in Parts 1 and 2 combined (N=40). This consists of patients with gastric cancer and other solid tumor types.
Initial Monotherapy Antitumor Activity of FPA144 in FGFR2b+ Gastric Patients in Multiple Dosing Cohorts

Line of Therapy

- 15 mg/kg
  - 3L
  - 2L
  - 5L
  - 4L
  - 10 mg/kg
  - 3L
  - 3L
  - 6 mg/kg
  - 7L
  - 3 mg/kg
  - 3L

Dosing Cohort

Days Post 1st FPA144 Dose

- PR
- SD

On-going
40/male
AGC, diffuse type (signet ring cell)
2013.7 Total gastrectomy
2014.4 multiple metastases
6 lines of chemotherapy including DXP, FOLFOX, FOLFIRI, oral 5-FU
2015.9 ~ 2016.2 FPA144 (PR)

FGFR2/CEP10 ratio by FISH 16: 1
FGFR2 IHC 3+ (80% of tumor cells)
Initial Monotherapy Antitumor Activity of FPA144 in FGFR2b+ Gastric Patients in Multiple Dosing Cohorts

* Tumor responses were assessed with the use of RECIST. Data cutoff: April 1, 2016

Days Post 1st FPA144 Dose

% Change Sum of Longest Diameters (SLD)

-80.0 -60.0 -40.0 -20.0 0.0 20.0 40.0 60.0 80.0 100.0

0 20 40 60 80 100 120 140 160 180

FPA144 Dose

- 15 mg/kg (Part 2 dose)
- 10 mg/kg
- 6 mg/kg
- 3 mg/kg

Legend:
- SD
- PR
- On-going
### Summary of Initial Monotherapy Antitumor Activity of FPA144 in FGFR2b+ Gastric Patients

<table>
<thead>
<tr>
<th>Outcome</th>
<th>FPA144 Treated (N=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR * (95% CI)</td>
<td>33% (7%, 70%)</td>
</tr>
<tr>
<td>Best Objective Response (%)</td>
<td></td>
</tr>
<tr>
<td>Complete Response</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Partial Response</td>
<td>3* (33%)</td>
</tr>
<tr>
<td>Stable Disease</td>
<td>4 (44%)</td>
</tr>
<tr>
<td>Progressive Disease</td>
<td>2 (23%)</td>
</tr>
<tr>
<td>Disease Control Rate (95% CI)</td>
<td>77% (40%, 97%)</td>
</tr>
<tr>
<td>12-Week PFS (95% CI)</td>
<td>67% (30%, 93%)</td>
</tr>
<tr>
<td>Median Duration of Treatment, days (Range)</td>
<td>112 (42-182)</td>
</tr>
</tbody>
</table>

* Pooled across all dosing cohorts (1 at 6 mg/kg, 1 at 10 mg/kg and 1 at 15 mg/kg). All responses were confirmed (one after the data cutoff with the patient still on treatment). Investigator review was used for assessments. Data cutoff was April 1, 2016.
Metabolic Response by FDG-PET in an Additional Gastric Cancer Patient, the 4th Patient in the 15 mg/kg IHC High Cohort*

Pre Treatment

Post Treatment with 4 doses of FPA144 (15 mg/kg)

* Data from the 4th patient treated in the 15 mg/kg cohort became available after the data cutoff of April 1, 2016. The patient remains on treatment as an unconfirmed partial response by CT.
Responses are Not Confined to Homogeneously Expressing FGFR2b+ Gastric Cancer Tumors

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Best Response</th>
<th>IHC (H-score)</th>
<th>IHC 3+ (% tumor cells)</th>
<th>FISH $(FGFR2/CEP10)$ Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>605-1002</td>
<td>PR</td>
<td>265</td>
<td>80</td>
<td>16.24</td>
</tr>
<tr>
<td>605-1006</td>
<td>PR</td>
<td>210</td>
<td>30</td>
<td>22.02</td>
</tr>
<tr>
<td>011-2103</td>
<td>PR</td>
<td>70</td>
<td>10</td>
<td>4.57</td>
</tr>
<tr>
<td>605-2101</td>
<td>SD</td>
<td>250</td>
<td>60</td>
<td>13.21</td>
</tr>
<tr>
<td>607-1008</td>
<td>SD</td>
<td>150</td>
<td>40</td>
<td>16.43</td>
</tr>
<tr>
<td>605-1003</td>
<td>SD</td>
<td>60</td>
<td>15</td>
<td>30.62</td>
</tr>
<tr>
<td>605-1001</td>
<td>SD</td>
<td>45</td>
<td>10</td>
<td>7.00</td>
</tr>
<tr>
<td>607-1005</td>
<td>PD</td>
<td>250</td>
<td>70</td>
<td>27.83</td>
</tr>
<tr>
<td>605-2102</td>
<td>PD</td>
<td>180</td>
<td>30</td>
<td>38.84</td>
</tr>
</tbody>
</table>
Complete Response in a Patient with Metastatic Bladder Cancer Treated with FPA144 During Dose Escalation

- 76 year-old male with Stage 4 UBC
- Confirmed complete response (RECIST 1.1) at 3 mg/kg dose level
- FDG-PET metabolic response
- Initial tumor was IHC 2+ for FGFR2b
- Patient remains on FPA144 treatment 352 days as of April 1, 2016 data cutoff
Conclusions

- FPA144 is a targeted immunotherapy
- FPA144 is selective for the FGFR2b splice variant and appropriate patients can be identified with a proprietary IHC assay
- FPA144 was well tolerated
  - No DLTs and MTD not reached
  - No hyperphosphatemia or retinal toxicity that has been observed with small molecule kinase inhibitors targeting FGFRs
- FPA144 demonstrated monotherapy anti-tumor activity in FGFR2b+ gastric cancer patients
  - ORR in heavily pretreated patients across mixed dosing cohorts was 33%
  - Disease control was 77%
  - Duration on therapy of 112 days is significantly longer than comparable historical data
- FPA144 is advancing in development as a potential therapy for patients with cancers that express FGFR2b (including gastric and bladder cancer)
Acknowledgements

• Patients and clinicians participating in the FPA144-001 clinical trial
• The FivePrime FPA144 team