# Phase 1a/1b Study of First-in-Class B7-H4 Antibody, FPA150, as Monotherapy in Patients with Advanced Solid Tumors

#2529

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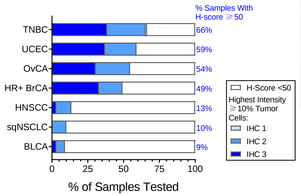
## BACKGROUND

### B7-H4 is a Member of the B7 Family of T Cell Checkpoint Ligands and Shares Significant Homology with Other Members, Including PD-L1

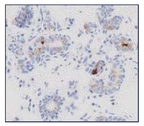
- Unlike CTLA-4 and PD-L1, B7-H4 does not appear to be a primary regulator of immune responses as B7-H4 deficient mice do not develop spontaneous autoimmune disease
- Expressed in several human tumors and expression tends to correlate with poor prognosis

### B7-H4 is Over-Expressed in Many Cancers Including Approximately 50-70% Breast and Gynecologic Cancers

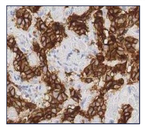
IHC Score Distrubtion [Stage III/IV Samples]




Normal Breast Tissue

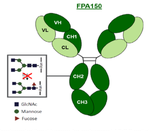


Invasive Ductal Carcinoma



Overexpression of B7-H4 in tumors relative to healthy tissues is predicted to provide a favorable therapeutic index for a B7-H4 antibody that possesses ADCC activity

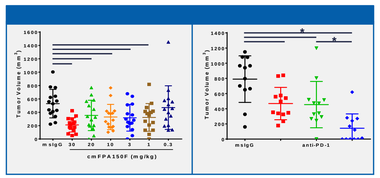
### FPA150 was Selected and Engineered to Possess Both T Cell Checkpoint Blockade and Enhanced ADCC Activities




*Produced without fucose for enhanced ADCC activity*

| FPA150 |
|---|
| Fully human IgG1κ monoclonal antibody |
| High affinity binding to B7-H4 IgV ectodomain<br>• Fully cross-reactive with rodent and cyno B7-H4 |
| T cell checkpoint blockade activity<br>• FPA150 selected for its ability to relieve suppression of T cell activation by B7-H4 |
| ADCC activity<br>• FPA150 redirects $Fc\gamma RIIIa^+$ effector cells (NK cells and Macrophages) to eliminate B7-H4-expressing tumor cells<br>• FPA150 is afucosylated and demonstrates higher affinity binding to $Fc\gamma RIIIa$ and enhanced ADCC activity |

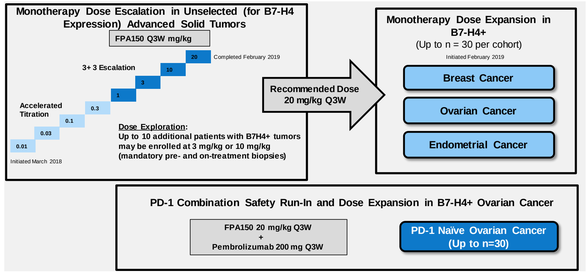
### FPA150 Demonstrates Dose-Dependent Antitumor Activity *in vivo* and Elicits Complete Tumor Regression in Combination with PD-(L)1 Blockade




- cmFPA150F is FPA150 engineered onto a mouse IgG2a Fc and is fucosylated
- cmFPA150F demonstrates anti-tumor activity as a monotherapy at doses as low as 1-3 mg/kg in the 4T1- and B16-moB7-H4 engineered models
- Treatment in combination with anti-PD-1 blockade results in complete tumor regressions at doses as low as 0.3 mg/kg

## METHODS

### First-in-Human Phase 1a/b Study of FPA150 ± Pembrolizumab in Advanced Solid Tumors




### Phase 1a Study Objectives

- Primary Objectives:
  - Safety and tolerability
  - Determination of MTD/RD
- Secondary Objectives:
  - Characterize PK profile and immunogenicity
- Exploratory Objectives:
  - Evaluate clinical benefit
  - Characterize PD profile in pre- and on-treatment biopsies and peripheral blood

## RESULTS

### Phase 1a: Baseline Demographics and Prior Therapy

| | Total (N=29) |
|---|---|
| Age, median (range) | 63 (38-84) |
| Female, n (%) | 22 (75.9) |
| ECOG, n (%)<br>0<br>1 | <br>2 (6.9)<br>27 (93.1) |
| Prior anti-cancer treatments, median (range) | 4 (1-9) |
| Disease stage at study entry<br>Stage IIIb/IV, n (%) | <br>27 (93.1) |
| Primary site of cancer, n (%)<br>Ovary<br>Bile duct/Gall bladder<br>Uterus<br>Salivary gland<br>Other | <br>12 (41.4)<br>5 (17.2)<br>2 (6.9)<br>2 (6.9)<br>8 (27.6) |

Data Cut Data: March 15 2019

### Phase 1a Treatment Emergent AEs in More than 10% of Patients

| Preferred Term, n (%) | Total (All Grades) (N=29) | Total (Grades 3 and 4) (N=29) |
|---|---|---|
| Fatigue | 7 (24.1) | 0 |
| Decreased appetite | 6 (20.7) | 1 (3.4) |
| Diarrhea | 5 (17.2) | 0 |
| Hypoalbuminemia | 5 (17.2) | 0 |
| Dehydration | 4 (13.8) | 1 (3.4) |
| Abdominal pain | 4 (13.8) | 2 (6.9) |
| Anemia | 4 (13.8) | 1 (3.4) |
| Nausea | 4 (13.8) | 0 |
| AST increased | 3 (10.3) | 2 (6.9) |
| GERD | 3 (10.3) | 0 |
| Hypokalemia | 3 (10.3) | 1 (3.4) |
| Hypomagnesemia | 3 (10.3) | 0 |
| Hyponatremia | 3 (10.3) | 1 (3.4) |
| Muscular weakness | 3 (10.3) | 0 |
| Upper Respiratory tract infection | 3 (10.3) | 0 |
| Vomiting | 3 (10.3) | 0 |

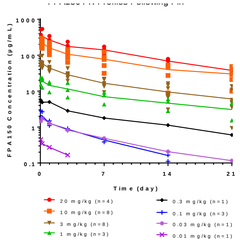
Data Cut Data: March 15 2019

## RESULTS (continued)

### Phase 1a: Summary of Safety

- There were no Dose Limiting Toxicities (DLTs)
- Treatment emergent serious adverse events (SAEs) were reported in 5 of 29 patients (17.2%) and were generally consistent with an advanced cancer population
- One patient with cholangiocarcinoma had a grade 5 SAE of acute kidney injury, not related to FPA150, in the setting of clinically progressive disease
- No SAEs were considered related to FPA150
- FPA150-related adverse events (TRAEs) were reported in 18 of 29 patients (62%)
- Grade 3 TRAE of decreased lymphocyte count in one patient
- All other TRAEs were grades 1 or 2 with diarrhea in 5 patients (17.2%) and fatigue in 4 patients (13.8%) being the most frequent
- Median of 3 (range: 1-14) FPA150 infusions and median of 44 days (range:1-274) on treatment

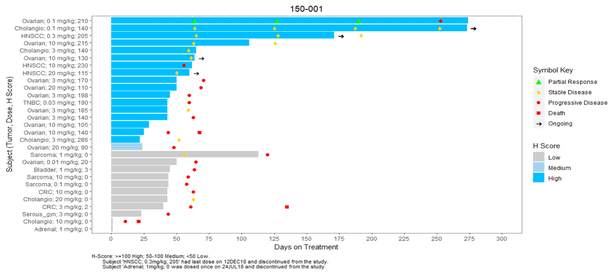
### Phase 1a Summary of Pharmacokinetics




- Typical monoclonal antibody PK profile with linear clearance for doses ≥ 0.3 mg/kg
- Elimination half-life 1-2 weeks following a single dose with minimal to no accumulation following multiple repeated Q3W dosing
- Similar FPA150 serum concentration for B7-H4 positive and negative patients
- No detectable FPA150 treatment induced anti-drug antibody
- Observed trough concentration at the RD of 20 mg/kg estimated to achieve ≥ 95% receptor saturation for both B7-H4 and FcγIIIa based on affinities

**Based on safety, PK and estimated receptor saturation for both B7-H4 and FcγIIIa of ≥ 95%, the selected RD is 20 mg/Kg Q3W**

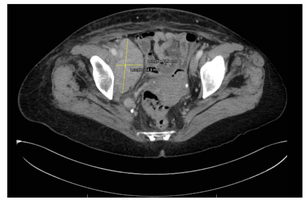
### Phase 1a: Days on Treatment and Response by B7-H4 Expression Levels



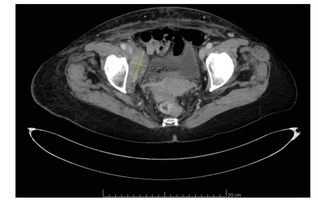

H-Score: >=100 High; 50-100 Medium; <50 Low.
Subject 'HNSCC, 0.3mg/kg, 205' had last dose on 12DEC18 and discontinued from the study.
Subject 'Adrenal, 1mg/kg, 5' was dosed once on 24JUL18 and discontinued from the study.

## RESULTS (continued)

### Confirmed Response in a Patient with Platinum-Resistant Ovarian Cancer



Baseline



Week 9

- 79 y/o woman with papillary serous ovarian ca (BRCA1+, Low tumor mutational burden, PDL1 negative) with 7 prior lines of therapy
- Disease progression after 7 months of anti-PD1 therapy (best response of SD)
- Last dose of anti-PD1 therapy was ~8 weeks prior to first dose of FPA150 on study
- Patient experienced >50% reduction in target lesion size over baseline with a duration of response of 6.2 months

## CONCLUSIONS

- FPA150 was well tolerated at doses as high as 20 mg/kg with no DLTs
- No Gr 4 TRAEs or SAEs related to FPA150
- Fatigue and diarrhea most common low grade TRAEs
- 20mg/kg Q3W selected as RD
- Typical antibody PK profile with approximately dose proportional exposure at doses ≥0.3 mg/kg with half life of 1-2 weeks
- Observed trough concentration at the RD of 20 mg/kg projected to achieve ≥ 95% receptor saturation for both B7-H4 and FcγIIIa based on affinities
- Enrollment of B7-H4+ patients (breast, ovarian and endometrial cancers) in phase 1b FPA150 monotherapy cohorts commenced in February 2019
- Based on preclinical evidence of synergy, combination of FPA150 and pembrolizumab in patients with B7-H4+ ovarian cancer has been initiated

## ACKNOWLEDGMENTS

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