**A Phase 1 Study of FPT155, a First-In-Class CD80 Extracellular Domain-Fc Fusion Protein, in Patients with Advanced Solid Tumors**

Lisa Horvath1, Jermaine Coward2, Hu Gan3, James Kuor1, Michael Millward4, Gary Richardson1, Wei Deng1, Siddhartha Mitra5, Maike Schmidt6, Hong Xiang3, Amy Prawirea1

1Chris O'Brien Lifehouse, Camperdown, NSW, Australia; 2ICON, Auchenflower, QLD, Australia; 3Olivia Newton-John Cancer Center, Heidelberg, VIC, Australia; 4Scintia Clinical Research, Randwick, NSW, Australia; 5Linear Clinical Research, Nedlands, WA, Australia; 6Cabini Hospital, Malvern, VIC, Australia; 7Five Prime Therapeutics, Inc., South San Francisco, CA, USA; 8St. Vincent's Hospital Sydney, Darlinghurst, NSW, Australia

**Background**

FPT155 is a First-In-Class CD80-Fc Fusion Protein:
- CD80 is a co-stimulatory molecule expressed on activated antigen presenting cells that binds to CD28 on T-cells.
- CD80 attaches to PD1 of T-cells.

**Methods**

- FPT155 is a Fc fusion protein composed of the extracellular domain of human CD80 fused to human IgG1 Fc.
- Mice that lack CD80 and CD28 do not reject skin allografts, which indicates that CD80 and CD28 are essential for T cell activation.
- FPT155 directly activated naive and memory T cells binding to CD28.
- FPT155 is a T-cell activator by binding to CD28, enabling the interaction of extracellular CD80 with CD28 at the immune synapse.

The Marine Stream iFPT155 Can Induce Complete Tumor Regression After a Single Dose

- mFPT155 expression and tumor killing activity in multiple tumor models, including some that are resistant to PD-L1 blockade: CT26, M24, EMTS, AS161, and WEHI-164.
- Mice that lack tumors in response to iFPT155 are protected from subsequent systemic challenge through the generation of tumor immunity.

FPT155 is NOT a CD82 superagonist:
- CD82 is an immunosuppressive molecule expressed on T cells and some cancer cells.
- Unlike TGN1412, effective T cell stimulation by FPT155 requires separate TCR engagement.

**Response Assessment**

- Tumor assessment with CT or MRI per RECIST v1.1: Assessable disease is any lesion ≥ 24 weeks after baseline or ≤ 12 weeks from the primary treatment.
- Additional assessment is any lesion ≥ 24 weeks after baseline or ≤ 12 weeks from the primary treatment.

**Dose Escalation**

- **Phase 1a Escalation**
  - Initially 0.07 mg
  - 2 dose expansions to 2 mg and 4 mg
- **Phase 1b Cohort Expansion**
  - Phase 1a Cohort Expansion (to follow Phase 1a)

**Key Inclusion Criteria**

- **Primary Criteria**
  - At least 1 measurable lesion (RECIST v1.1)
  - No prior treatment with other IO agents cannot have been initiated within 140 mg
  - Prior treatment with other IO agents cannot have been started within 140 mg
  - At least 1 manageable lesion

**Key Exclusion Criteria**

- **Primary**
  - CD80-negative tumor
  - Autoimmune disease
  - Prior treatment with anti-CTLA4

**PD1 Contribution to IO Efficacy**

- FPT155-induced PD1 upregulation is a possible mechanism of PD1 contribution to IO efficacy.

**Preliminary Pharmacokinetic Profile of FPT155 from Phase 1 Dose Escalation**

- Dose Escalation: 0.07 mg (N=3)
- DOX: 0.21 mg (N=1)
- 2 mg (N=2)
- 4 mg (N=1)

**Dose Escalation: Phase 1b Cohort Expansion**

- Patient 1 or 2: 2 mg TEAEs attributed to FPT155 over design changes to 3×3

**Conclusions**

- No DLTs, well-tolerated in dose escalation through October 2019
- FPT155 70 mg Q3W cohort currently enrolling
- No acute immunologic toxicities to date and no evidence of clinical or laboratory CRS

**Preliminary Pharmacokinetic Profile**

- Dose proportionality in increase in exposure
- 10% - 1 week, minimal accumulation with Q2W dosing

**Results**

- **Serious and Grade 3 Treatment Emergent AEs**
  - Grade 3 TEAEs: 0 patients
  - Grade 3/4 TEAEs: 0 patients

- **Phase 1a Objectives**
  - Evaluate the safety, efficacy, and pharmacodynamic (PD) parameters of FPT155 in patients with advanced solid tumors

**Preliminary Peripheral Biodistribution Results**

- **No consistent treatment emergent elevation in cytokines**
  - No dose-response between FPT155 and cytokine elevation to date

**Methods**

**FPT155-DOX (NCT04074775)**

- **Phase 1a Dose Escalation and Dose Exploration**
- **Phase 1b Cohort Expansion (to follow Phase 1a)**

**Key Inclusion Criteria**

- **Primary**
  - At least 1 measurable lesion
  - No prior treatment with other IO agents cannot have been started within 140 mg

**Key Exclusion Criteria**

- **Primary**
  - Autoimmune disease
  - Prior treatment with anti-CTLA4

**Preliminary Pharmacokinetic Profile of FPT155 from Phase 1 Dose Escalation**

- Median age 70 mg (N=3)
- Dose Escalation: 0.07 mg (N=3)
- DOX: 0.21 mg (N=3)
- 2 mg (N=3)
- 4 mg (N=3)

**Conclusions**

- No significant treatment-related changes in peripheral T cell component (data not shown)
- No clinical responses to therapy through FPT155 350 mg Q2W