A First-in-Human Phase 1 Clinical Study Evaluating Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Efficacy of the EDB+FN targeting ADC PYX-201 in Participants with Advanced Solid Tumors

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**BACKGROUND**

PYX-201 is an investigational antibody-drug conjugate (ADC) consisting of an EDB+FN-targeting monoclonal antibody engineered for site-specific conjugation to vc0101, which showed improved linker-payload stability and bystander activity in preclinical studies (2). The linker-payload vc0101 is completely synthetic and, via a cleavable linker, delivers auristatin PF-06380101 (Aur0101), a microtubule depolymerizing agent with potent anti-mitotic and cytotoxic properties. PYX-201 induced tumor regression in xenograft mouse models of non-small cell lung cancer and pancreatic cancer. In a syngeneic model of breast cancer, a mouse analog of PYX-201 induced upregulation of PD-L1 and infiltration of CD3+ T cells in tumors (2). The PYX-201-101 clinical trial is in progress in participants with advanced cancers (NCT05720117).

**STUDY DESIGN**

**Design:** Phase 1, first-in-human, open-label, multicenter, non-randomized, dose-escalation study

**Target Population:** Participants with advanced solid tumors who have relapsed, been non-responsive, or have progressed with all available therapies, with a focus on those tumor types known to have expression of the target antigen

**Sample Size:** Up to 45 subjects (including backfill enrollment) will be enrolled into the dose escalation cohorts

**INDICATIONS**

- Non-small cell lung cancer
- Head and Neck Squamous Cell Cancer
- Pancreatic Ductal Adenocarcinoma
- Ovarian cancer
- Hepatocellular Carcinoma
- Thyroid cancer
- Soft Tissue Sarcoma
- Kidney cancer
- Breast Cancer (hormone receptor positive (HR+)) and human epidermal growth factor receptor 2 (HER2+ breast cancer, HR+ and HER2+ breast cancer, triple negative breast cancer)

**OBJECTIVES**

**Primary Objective:** To determine the recommended dose(s) of PYX-201 for participants with relapsed or refractory solid tumors

**Secondary Objectives:**
- To characterize the PK profile of PYX-201 as a single agent
- To evaluate the preliminary antitumor activity of treatment with PYX-201 at the recommended dose(s) of PYX-201
- To evaluate the immunogenicity of PYX-201 as measured by the incidence of ADAs in participants treated with PYX-201

**Exploratory Objectives:**
- To explore predictive and pharmacodynamic biomarkers of response to PYX-201

**ENDPOINTS**

**Primary Endpoints:**
- Dose Limiting Toxicity rate
- Incidence of adverse events characterized overall and by type, seriousness, relationship to study treatment, timing, and severity graded according to the NCI-CTCAE Version 5.0

**Secondary Endpoints:**
- Single-dose and multiple-dose PK parameters (such as $C_{\text{max}}$, $AUC_{0-\text{INF}}$, $AUC_{\text{INF}}$, and $t_{1/2}$) for antibody and/or relevant metabolites
- Overall Response Rate
- Duration of Response
- Progression Free Survival
- Disease Control Rate (defined as Complete Response, Partial Response, or Stable Disease)
- Time to response (defined as the time from the first dose of PYX-201 to the time of response [CR/PR] first observed)
- Overall Survival
- Incidence of anti-PYX-201 antibodies

**STUDY PROGRESS**

Enrollment opened:
- February 2023

Up to 20 sites planned to be activated in the United States, Spain, Belgium and the United Kingdom

**REFERENCES**

1) Natha T, Hu M, Nomizu M. Peptide therapies for ocular surface disturbances based on fibronectin-integrin interactions. Progress in Retinal and Eye Research. 2015; 47:38-63