A Phase I Study of $^{225}$Ac-FPI-1434 Radioimmunotherapy in Patients with IGF-1R Expressing Solid Tumors

Rosalyn A. Juergens¹, Katherine A. Zukotynski², Daniel Juneau³, Ryan Simms⁴, John Forbes⁵, Eric S. Burak⁶, John Valliant⁷, Lily Krnezich⁷, Lauren Stafford⁷, Thomas Armor⁷, Istvan Molnar⁷, Fred Saad³

¹Juravinski Cancer Centre, McMaster University, Hamilton, ON; ²Nuclear Medicine and Radiology, McMaster University, Hamilton, ON; ³Centre Hospitalier de l’Université de Montréal, Université de Montréal, Montreal, QC; ⁴Fusion Pharmaceuticals, Hamilton, ON and Boston, MA

Background

Type I insulin-like growth factor receptor (IGF-1R) is a transmembrane protein which is overexpressed in solid tumors including non–small cell lung, prostate, sarcomas, and breast cancers.

![IGF-1R](image1)

$^{[225]}$Ac-FPI-1434 is a radioimmunoconjugate consisting of a humanized monoclonal antibody (AVE1642) that binds to the external domain of IGF-1R, a proprietary bifunctional chelate, and studies in cynomolgus monkeys, and prior human experience with the unconjugated antibody, Type I insulin-like growth factor receptor (IGF-1R) is expressed on nearly all tumor types including non–small cell lung, prostate, sarcomas, and breast cancers.

![Image 2](image2)

Figure 1. Mechanism of Action

Based on anti-tumor activity of $^{[225]}$Ac-FPI-1434 in non-clinical models, favorable toxicity studies in cynomolgus monkeys, and prior human experience with the unconjugated antibody, the first-in-human trial was initiated.

![Image 3](image3)

Figure 2. Single Dose Therapeutic Efficacy in a Colorectal Cancer Tumor Xenograft Model (Colo-205)

Key Eligibility Criteria

Inclusion:
- Age ≥18 years old
- Pathologically documented, definitively diagnosed, advanced solid tumor that is refractory to all standard treatment, for which no standard treatment is available
- At least 1 measurable lesion (≥20 mm in largest diameter [≥20 mm in shortest diameter if lymph node])
- Eastern Cooperative Oncology Group (ECOG) Performance status of 0 or 1
- Life expectancy equal to or greater than 3 months as judged by the treating physician
- Adequate renal function as evidenced by a creatinine clearance ≥60 mL/min using the Cockcroft-Gault Equation
- Adequate hepatic function
- Sufficient target expression in at least one tumor lesion following the $^{[111]}$In-FPI-1547 Injection
- Dosimetry estimate of the planned $^{[225]}$Ac-FPI-1434 Injection does not exceed predetermined limits for kidney, liver and lungs

Exclusion:
- Systemic therapeutic radiopharmaceutical within 6 months prior to enrollment
- Contraindications to or inability to perform the imaging procedures required in this study
- Uncontrolled brain metastasis, including but not limited to need for treatment with steroids, surgery, or radiation therapy
- Anticancer therapy (including investigational agents) or external beam radiation therapy within 14 days of the dosing of $^{[111]}$In-FPI-1547 (6 weeks for mitomycin-C)
- Prior organ transplantation, including stem cell transplantation.
- Any prior treatment with nitrosoureas and actinomycin-D
- Clinical relevant proteinuria
- Known or suspect allergies or contraindications to the Investigational Products or any component of the investigational drug formulation
- Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, diabetes, or psychiatric/illness/social situations that would limit compliance with study requirements
- Received > 20 Gy prior radiation to large areas of the bone marrow

Study Design

- Study FPX-01-01 (NCT03746431)
- Open-label, multi-center phase I study of a single injection of Ac-225 radioimmunotherapy conjugate (option for a second dose if clinical benefit)
- Modified 3+3 dose-escalation (5 dose cohorts)
- Followed by an 8-week DLT evaluation period.

![Image 4](image4)

Study Status

Currently enrolling patients at the following locations:
- Juravinski Cancer Center (Hamilton Health Sciences) – Hamilton, Ontario
- Quebec Hospital/Laval – Quebec City, Quebec
- Université de Montreal (CHUM) – Montréal, Québec

![Image 5](image5)