A Phase 1/2 Dose Escalation and Expansion Study of Cabiralizumab (cabira; FPA-008), an anti-CSF1R antibody, in Tenosynovial Giant Cell Tumor (TGCT, Diffuse Pigmented Villonodular Synovitis D-PVNS)

Kamalesh Sankhala, Jean-Yves Blay, Kristen Ganjoo, Antoine Italiano, Bass Hassan, Tae Min Kim, Vinod Ravi, Philippe Cassier, Piotr Rutkowski, Neil Sankar, Ibrahim Qazi, Robert Sikorski, Helen Collins, Charlie Zhang, Ellyn Shocron, Hans Gelderblom

Sarcoma Oncology Center, Santa Monica, California; Centre Léon Bérard, Lyon, France; Stanford University, Stanford, California; Institut Bergonié, Bordeaux, France; Oxford Haematology and Cancer Centre, Sarcoma Unit, University of Oxford, United Kingdom; Seoul National University, Seoul, South Korea; The University of Texas MD Anderson Cancer Center, Houston, Texas; Centre Léon Bérard, Lyon, France; Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; Five Prime Therapeutics, South San Francisco, California; Leids Universitair Medisch Centrum, Leiden, Netherlands

Background: TGCT is a proliferative, neoplastic joint disease that presents as single nodule (local) or multiple nodules (diffuse D-TGCT). Localized overexpression of colony stimulating factor 1 (CSF1) leads to recruitment of cells expressing the CSF1 receptor (CSF1R), formation of a tumor and inflammation of joints and tendons. Cabira is a monoclonal antibody that inhibits the interaction of the CSF1 and IL-34 ligands with their shared receptor CSF1R.

Methods: This Ph 1/2 study is evaluating safety and efficacy of cabira monotherapy administered IV Q 2wk for 6 mo in patients (pts) with D-TGCT. Eligible pts have inoperable D-TGCT or tumor for which resection would cause unacceptable morbidity. Response is evaluated by MRI, pt reported outcomes, and Ogilvie-Harris (O-H) score (which combines pain, synovitis, range of motion and functional capacity on a scale of 0-12).

Results: As of 15 Dec 2016, 22 pts received ≥ 1 dose of cabira at 1, 2 or 4mg/kg. Dose-related exposure increase and significant reduction in target peripheral monocytes were observed. No dose limiting toxicity was identified. 4 mg/kg was chosen for Ph2 based on efficacy, tolerability, and PK. AEs ≥ Gr 2 (> 10%) were CK elevation 46%, rash and other skin disorders 36%, fatigue 23%, and periorbital/peripheral/face edema 18% each. Gr 3 AEs in ≥ 2 pt were CK elevation (n = 8) and periorbital edema (n = 2). Four drug-related SAEs were reported in 3 pts; hypertension, fever, CRP elevation, and myocarditis.

AEs of CK elevation were asymptomatic, improved to < 2X ULN after protocol mandated drug discontinuation and are a known on-target effect of CSF1R inhibition. An amendment was made during Phase 2 to allow dosing with higher CK levels

Activity at 4 mg/kg was: 1PR and 1 CK discontinuation in 3 pts in Ph1; 4 PRs in 7 evaluable pts with 6 additional ongoing in Ph2. Positive functional status improvements by O-H score were noted in objective responders (from 2 to 7).

Conclusions: The initial demonstration of objective and functional activity supports further development of cabiralizumab in pts with D-TGCT. Updated data from the ongoing Ph2 will be presented. NCT02471716.