Phase 1/2 Trial of Oral Masofaniten (EPI-7386) in Combination with Enzalutamide (Enz) Compared to Enz Alone in Metastatic Castration-Resistant Prostate Cancer (mCRPC) Subjects

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Background: Masofaniten (EPI-7386), as a next generation aniten, inhibits androgen receptor (AR) activity by binding the N-terminal domain and blocking transcription, irrespective of ligand-binding domain resistance mechanisms. Preclinically, combining masofaniten + Enz results in a deeper blockade of the AR pathway and greater antitumor activity than either agent alone.

Methods: This Phase 1/2 multicenter, open-label clinical trial (NCT05075577; EU CT 2023-509336-25-00) examines mCRPC pts on androgen deprivation therapy naïve to second-generation antiandrogens (1 line of prior chemotherapy in the metastatic hormone sensitive setting allowed). Phase 1 (P1) completed enrollment; evaluated escalating doses of masofaniten + Enz; reviewed safety and pharmacokinetics (PK) endpoints of the combination to establish the recommended Phase 2 combination dose (RP2CD); and assessed possible drug-drug interactions. Currently enrolling, phase 2 (P2) is a two arm, 2:1 randomized trial evaluating antitumor activity of masofaniten + Enz versus Enz alone.

Results: P1 enrolled 18 pts in 4 cohorts; 16 are evaluable for efficacy analysis per protocol and 11 are still ongoing. 14/18 pts displayed 2+ parameters associated with Enz early treatment failure. The RP2CD was established at masofaniten 600 mg BID + Enz 160 mg QD. The RP2CD continues to be well tolerated and PK results demonstrated Enz exposure was not impacted by masofaniten while masofaniten exposure, despite being reduced by co-administration of Enz, remained in the active range seen in preclinical studies. To date, 14/16 pts achieved PSA90 (88%) regardless of previous chemotherapy status (44% pts received prior chemotherapy in the mHSPC setting). 5/16 evaluable pts showed measurable disease with 3/5 (60%) partial response and 2/5 (40%) stable disease. As data matures and the median time to PSA progression is not yet reached, the data compares favorably to historical P3 trials of Enz single agent.

Conclusions: Updated results, long term follow-up of P1 pts and a comparison to historical trials will be presented. P2 is currently enrolling in the USA, Canada, Australia, France, Belgium and Spain.

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