Study Design

The Phase 1 study focused on the PK and safety of masofaniten and Enz when administered in combination to establish the RPD2 for both drugs. In vitro, masofaniten is a strong inhibitor of CYP3A4, the main enzyme involved in the metabolism of Enz. Enz exposure is reduced when administered in combination with Enz by more than the plasma level of the inhibitor. Enz is a patient inhibitor of CYP3A4, which is involved in the metabolism of masofaniten. Masofaniten plasma levels may be increased when administered in combination with Enz (thus modifying dose adjustments)

Phase 1 - Current Patient Disposition

- Out of 18 patients: 13 ongoing, 5 discontinued
- Disease progression = 3
- Brain lesions = 1 (non-related event)
- Non-cancer related death = 1 (patient with PF and 0.2 mg/m2)
- 13 have non-measurable disease
- PS 90%: 69% (11/16 pts)
- Current status: 0.5 mg/m2 (6/16 evaluable pts received prior dose escalation in mHSPC)

Conclusions

- Based on the safety of the trial and the PK data from the Phase 1 - study, the recommended Phase 2 combination doses are 600 mg masofaniten + 160 mg Enz (QD)
- Combination of masofaniten and Enz at all doses tested is safe and well tolerated
- Masofaniten has no effect on Enz exposure when administered in combination with Enz thus allowing the use of full dose per label of Enz in combination
- Enz significantly reduces masofaniten exposure (likely through induction of CYP3A4), but Enz dosing of 160 mg QD independently of the baseline level
- Rapid, deep and durable PSA reductions were observed in patients, regardless of previous chemotherapy status (60 evaluable patients received prior dose escalation in mHSPC)

Phase 2 - On the basis of encouraging Phase 1 results, an ongoing Phase 2 trial (NCT04657040) is evaluating the safety and efficacy of masofaniten + Enz in patients with mHSPC, independent of prior docetaxel exposure.