

A first-in-human Phase I/II, dose escalation, pharmacokinetic study to assess safety and tolerability of VAL201 in advanced prostate cancer

Background: Most patients with advanced prostate cancer (APC) treated with androgen deprivation therapy experience adverse side effects of castration and eventually relapse. There is a need for more effective and tolerable therapy. In prostate cancer cells, steroid hormones or epidermal growth factor trigger the association of the androgen receptor (AR) complex with Src, activating Src tyrosine kinase, stimulating DNA synthesis and G1 to S cell-cycle progression. VAL201 is a novel synthetic decapeptide which inhibits the AR/Src interaction and cancer cell progression. This first-in-human study assesses the safety, tolerability, pharmacokinetics (PK) and activity of VAL201 in patients with APC.

Methods: An accelerated titration, open label, dose-escalation, dose-expansion design to identify a maximum tolerated/administered dose (MTD/MAD) was used. VAL201 is administered subcutaneously on Days 1, 8 and 15 of a 3-week cycle, for up to 6 cycles. Dosing escalates from 0.5 mg/kg to 5.0mg/kg over 5 dose levels (DL), utilising a 3 + 3 design, with dose limiting toxicity (DLT) assessments. **Results:**Eight patients have been recruited to 4 DLs (0.5mg/kg n=1; 1.0mg/kg n=1; 2.0mg/kg n=3; 4.0mg/kg n=3, and recruitment to the final DL (5.0mg/kg) is underway. Patients had metastatic disease (n=5), locally advanced disease (n=1) or PSA relapse only (n=2). No DLT has occurred to date. Drug- related adverse events observed have been Grade 1 injection site reactions and fatigue. Median duration on trial is 85 days. Early signs of clinical activity have been observed with 5 patients showing an increase in PSA doubling time including one patient in DL4 with >30% PSA response. 5/8 patients have shown stable disease on imaging. Pharmacokinetic and pharmacodynamic analysis is ongoing and will be presented in more detail.

Conclusions: VAL201 is well-tolerated with signs of clinical activity in advanced prostate cancer. No dose limiting toxicity has been observed. The study continues recruiting to the final dose level, followed by dose-expansion.