

## **Phase I Clinical Trial of CX-4945: A First-in-Class, Orally Administered Small Molecule Inhibitor of Protein Kinase CK2**

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**Introduction:** CX-4945 is a novel, orally administered small molecule designed to potently and selectively inhibit protein kinase CK2, a previously unexploited molecular target with well documented roles in many cancers. *In vitro*, CX-4945 selectively kills cancer cells by modulating key survival pathways, resulting in inhibition of proliferation, promotion of apoptosis and cell cycle arrest. Pre-clinically, CX-4945 has demonstrated single-agent potency in suppressing xenograft tumor growth with a wide therapeutic window. The objectives of this phase I study are to determine the maximum tolerated dose (MTD) and dose limiting toxicities (DLTs), to characterize the pharmacokinetics (PKs), and to study the pharmacodynamic effects of CX-4945.

**Procedures:** Eligible patients with advanced solid tumors, Castleman's disease or multiple myeloma with progressive disease, or for whom there are no available standard therapies, receive CX-4945 in successive dose cohorts at: 90, 160, 300, 460, 700 and 1000 mg per dose. Oral doses are administered twice daily for twenty-one consecutive days of a four week cycle. Therapy is continued in consenting patients until signs of intolerance to CX-4945 are observed, or there is evidence of advancing disease. Response by RECIST is determined after every 2 cycles. Serial blood and plasma samples are collected on the first and final dosing days of Cycle 1 (i.e., Day 1 and Day 21) for pharmacokinetic analysis and for pharmacodynamic biomarker evaluations (specifically, total and phosphorylated forms of p21 and Akt.)

**Results:** Thirteen patients with solid tumors (3-4 patients per cohort, from four separate dose cohorts) have received oral doses of CX-4945. These doses have been well tolerated, with no reported adverse events of grade 3 or higher. CX-4945 has demonstrated general linearity in PK parameters between the dose cohorts, with a terminal half life of approximately 25 hours at steady state.

**Conclusions:** To date, CX-4945 has shown no drug related toxicity and has dose proportional PKs. No DLTs have yet been observed, and the MTD remains to be defined in this Phase I study. Further enrollment to the planned dose escalation cohorts is ongoing.