ANG1005: Results of a phase I study in patients with advanced solid tumors and brain metastases

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Background: ANG1005, created from Angiogenics’ Engineered Peptide Compound (EPC) platform, has a novel mode of action targeting the low-density lipoprotein receptor-related protein (LRP-1) which is highly expressed on the surface of the blood-brain barrier (BBB) and angiogenesis on cancer cells. This phase I study was initiated to determine the MTD and to evaluate efficacy and tolerability of ANG1005.

Methods: Patients with advanced solid tumors, adequate organ function, ECOG 0-1 received ANG1005 by IV infusion on days 1-8 without premedication. Brain metastases were required at the maximum tolerated dose (MTD). Doses were escalated in a modified Fibonacci scheme in sequential cohorts of 1-4 patients. Study objectives included characterizing toxicity, tolerability, PK, identifying the MTD and examining evidence of efficacy and tolerability. Phase I patients (n=19) were identified and recommended highest phase II dose. Median age 54, male: 43, prior therapies: 3, brain: 2, systemic: 3, both: 1. grade 3 adverse events were transient and manageable. The dosing interval varied widely with no-toxicity. No evidence of CNS toxicity or confusion was observed in patients who received multiple doses. Only 4 patients experienced infusion related reactions and these were at a significantly higher concentration (1065 mg/m2 vs. 650 mg/m2). PK data indicate that ANG1005 bioavailability is dependent on the route of administration.

Results: 12 patients in phase I received doses of 20-720 mg/m2. 20 at 650 mg/m2, identified the MTD and recommended highest phase II dose. Median age 54, male: 43, prior therapies: 3, brain: 2, systemic: 3, both: 1. grade 3 adverse events were transient and manageable. The dosing interval varied widely with no-toxicity. No evidence of CNS toxicity or confusion was observed in patients who received multiple doses. Only 4 patients experienced infusion related reactions and these were at a significantly higher concentration (1065 mg/m2 vs. 650 mg/m2). PK data indicate that ANG1005 bioavailability is dependent on the route of administration.

Conclusions: ANG1005 is safe and well tolerated and demonstrates activity in advanced solid tumors and brain metastases, a disease for which there is currently no approved chemotherapy drug.