ANG1005: Results of a phase I study in patients with recurrent malignant glioma

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Background:
ANG1005, created from Angiochem’s Engineered Peptide Compound (EPC) platform, has a novel mode of action targeting the low density lipoprotein receptor (LDLR) present in malignant glioma.

Methods:
Patients with recurrent malignant glioma, adequate organ function, and ECOG ≤2 were selected. Exclusion criteria included prior treatment with another EPC compound. Patients were stratified by tumor volume for dose escalation (≥300 mg/m²) or expansion (≥420 mg/m²). Doses 300 - 700 mg/m² were administered as a 2-h infusion on an outpatient basis. Primary end points were safety and tolerability, with secondary end points including efficacy and PK.

Results:
1. Safety and Tolerability:
- ANG1005 was safe and well tolerated. The majority of adverse events were related to anti-tumor activity; grade 3-4 occurred in 5% or fewer.
- No evidence of CNS toxicity and/or immunogenicity

2. Pharmacokinetics:
- Pharmacokinetic analysis was performed for ANG1005 and paclitaxel. ANG1005 exhibited a dose-dependent accumulation in plasma over multiple infusions.

3. Efficacy:
- Stabilization of disease was observed in 42% of patients. Median TTP was 24 weeks in responders (≥ SDC).

4. Final Phase I results support further development of ANG1005 and lend complementary clinical evidence to the EPiC platform.

Conclusion:
ANG1005 is safe and well tolerated; no evidence of CNS toxicity and/or immunogenicity. ANG1005 has a linear bioavailability; no evidence of accumulation after repeat dosing. ANG1005 has a favorable pharmacologic effect on GBM known as demonstrated by a lack of growth when placed in neurosphere culture conditions. ANG1005 is safe and well tolerated; no evidence of CNS toxicity and/or immunogenicity. ANG1005 has a linear bioavailability; no evidence of accumulation after repeat dosing. ANG1005 has a favorable pharmacologic effect on GBM known as demonstrated by a lack of growth when placed in neurosphere culture conditions.