## Abstract
Complete Results from Phase I Dose Escalation Study of MetMAb, a Monovalent Antagonist Antibody to the Receptor Met, Dosed as Single Agent and in Combination with bevacizumab in Patients with Advanced Solid Malignancies

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### Body

Background: The receptor tyrosine kinase Met and/or its ligand, hepatocyte growth factor (HGF), are frequently over-expressed in cancers. Aberrant activation this pathway can enhance invasion, proliferation, and survival and may promote angiogenesis.

MetMAb was uniquely engineered as a recombinant, humanized, monovalent monoclonal antibody to act as an antagonist of HGF-induced Met signaling. Materials and Methods: This study consisted of two phases: a Phase Ia dose-escalation and expansion at the recommended Phase2 dose (RP2D; 15mg/kg IV Q3W); and a Phase Ib testing MetMAb (10mg/kg or 15mg/kg IV Q3W) in combination with bevacizumab (15mg/kg Q3W). Serum was collected for evaluation of pharmacodynamic biomarkers, including IL8 and HGF. Results: 34 patients have been treated in Phase Ia and 9 patients in Phase Ib. MetMAb has a half-life of approximately 11 days, and there are no apparent PK interactions with bevacizumab. MetMAb was generally well tolerated. The most frequent treatment-related adverse events included: fatigue, peripheral edema and hypoalbuminemia. In the Ib section, no Gr3-5 drug-related toxicities were observed; a Gr1, dose-limiting toxicity of hematoptysis was observed in cohort 2 in a patient who had central-necrosis of pulmonary metastases. A patient with gastric carcinoma achieved a complete response after 4 cycles of MetMAb; this patient came off study after 10 cycles and continues to have a complete response as of 560 days following the last dose. Conclusions: MetMAb, when administered as a single-agent, or in combination with bevacizumab was generally safe and well tolerated. Phase2 trials testing MetMAb in combination with bevacizumab and paclitaxel (in triple negative breast cancer) and with erlotinib (in NSCLC) are currently ongoing.