

EGFR x MET tsAb: Differentiated MET biparatopic design with optimal MET inhibitory activity to pursue best-in-class opportunity

Lead author: Yanzhou Zhang

Abstract

Acquired resistant mutation after small molecule inhibitor treatment in non-small cell lung cancer (NSCLC) develops invariably through mutations in EGFR or through activation of compensatory pathways such as MET. BG-T187 is a tri-specific antibody (TsAb) targeting EGFR and MET with a differentiated MET biparatopic designation designed to treat tumors driven by activated EGFR and/or MET signaling. Stronger antiproliferative effects and MET signaling inhibition by BG-T187 compared to traditional EGFR/MET bi-specific antibody were observed in vitro. Additionally, potent in vivo anti-tumor activity was observed upon BG-T187 treatment of human tumor xenograft models driven by EGFR activation mutation and/or MET amplification. Interestingly, stronger anti-tumor activity of BG-T187 than that of traditional EGFR/MET bi-specific antibody was observed in xenograft models with MET amplification. Through a comprehensive assessment of EGFR on-target toxicity risk, we demonstrated that BG-T187 show better HEK_n selectivity than EGFR/MET bi-specific antibody, indicating potential lower on-target toxicity risk of BG-T187. Collectively, our findings represent a novel EGFR/MET tri-specific antibody with differentiated MET biparatopic and pursue best-in-class potential.