BGB-B167, a first-in-class 4-1BB/ CEACAM5 bispecific antibody, exhibits potent in vitro and vivo antitumor activity and superior safety profile in preclinical models

Zhuo Li[1, *], Liang Qu[2], Liu Xue[2], Jie Li[1], Qi Liu[2], Jian Sun[2], Hanzi Sun[2], Yun Chen[1], Yuanyuan Xie[2], Wanyi Wang[2], Lin Zhu[2], Penghao Wang[2], Xiaosui Zhou[2], Hongjia Hou[2], Jie Chen[1], Xinyi Liu[2], Yilu Zhang[2], Ning Liu[2], Xinyi Liang[2], Shuo Zhang[1], Xiaoyan Tang[2], Jing Song[2], Tong Zhang[1], Xiaomin Song[2], Xuesong Liu[2], Kang, Li[2], Chichi Huang[1, *]

Authors' Affiliations:

1 Research & Development, BeiGene (Shanghai) Co., Ltd., Shanghai 201200, China;

2 BeiGene (Beijing) Co., Ltd., Beijing 102206, China;

Abstract:

4-1BB (CD137) is a key costimulatory immunoreceptor and a promising therapeutic target in cancer. CEACAM5 (CEA) is a well-established tumor associated antigen overexpressed in many cancers, including colorectal, gastric, lung, pancreatic cancer, liver, breast and thyroid cancers. BGB-B167 is a novel immunoglobulin G (IgG)-based bispecific antibody targeting 4-1BB and CEA and is under clinical development for the treatment of advanced or metastatic solid tumors in humans.

BGB-B167 binds to its target proteins with high specificity and affinity. Potent and CEA-dependent functional activities were demonstrated using peripheral blood mononuclear cell (PBMC)-based immune cell activation and cytotoxicity assays. In humanized 4-1BB knock-in mice bearing human CEA-expressing tumors, BGB-B167 exhibited potent, dose-associated single-agent efficacy as well as synergistic antitumor activity in combination with anti-PD-1 antibody. BGB-B167 was well tolerated in 1-month repeat-dose toxicology study in cynomolgus monkeys.

Here, we describe the characterization of BGB-B167 with regard to preclinical proof-of-concept and basic drug-like properties. The combined dataset provides an overview on the design, mode of action, preclinical pharmacology and safety profile of BGB-B167.