Combination of bemcentinib (BGB324) – a first-in-class selective, oral AXL inhibitor – with pembrolizumab in patients with triple negative breast cancer and adenocarcinoma of the lung.

Bemcentinib (BGB324) is a first-in-class, orally bioavailable, selective, and potent AXL kinase inhibitor. AXL is overexpressed on multiple cell types in the tumour immune microenvironment including dendritic cells, T cells and tumour-associated macrophages. AXL signalling in immune cells supports tumour immune escape by downregulating dendritic cell activity, modulating tumour immune infiltration and increasing drug resistance.

Bemcentinib stimulates innate immunity & increases the effect of immune checkpoint inhibitors in vivo

In order to determine the potential for bemcentinib to stimulate innate immunity and increase the effect of immune checkpoint inhibitors in vivo, syngeneic 4T1 cells (2 × 10⁵) were implanted into the mammary pad of Balb/C mice and treatment was initiated when average tumour size reached 150 mm³. Animals were treated with control IgG or anti-CTLA4 and an anti-PD1 followed by o/n stimulation with 100 ng/ml IFN-g, and IL-12 were determined by ELISA.

M1 macrophage IL-12 was induced in tumour clearance in 5.6% of animals. Treatment was initiated when tumours bearing orthotopic 4T1 mammary tumours treated with bemcentinib + anti-PD1 expressed AXL in greater than 40% of tumour cells. AXL knockdown in M2 macrophages abrogated IL-12 response in M2 M1 polarisation.

M1 polarised monocytes isolated from PBMCs of HVs were cultured in the presence of 50 mg/ml bemcentinib then primed with 5 ng/ml IFN-g for 2 hrs followed by o/n stimulation with 100 ng/ml IFN-g. IL-12, M1 polarisation, and IL-10 were determined by ELISA.

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Safety: Bemcentinib (BGB324) in combination with pembrolizumab

Stage 1 completion expected for H2 2018

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Stage 1 completion expected for 2018.

Parallel biomarker studies under way.

Combination studies with bemcentinib & pembrolizumab in TNBC & NSCLC ongoing and recruiting.

Safety: Bemcentinib (BGB324) in combination with pembrolizumab