For the purpose of clarity and a concise description features are described herein as part of the same or separate embodiments, however, it will be appreciated that the scope of the invention may include embodiments having combinations of all or some of the features described.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 : Amino acid alignment of MF3178 variants.
Dots indicate the same amino acid as in MF3178 at that position. The CDR1, CDR2 and CDR3 sequences of MF3178 are in bold and underlined.

Figure 2: Increased *in vivo* tumor-targeting of bispecific over monoclonal antibody. Micro-PET imaging demonstrates that the PB4188 variant more effectively accumulates in tumors compared to the HER3 monoclonal (Fig. 2A). Gamma-counter quantification of radioactivity present in tumors confirmed that levels of PB4188 variant in the tumors were 2.5-fold higher than for the parental anti-HER3 antibody (Fig. 2B). Quantitative biodistribution for tumour uptake in the 4 mAb groups at 48 hrs. Results are expressed as a percentage of the injected dose per gram of tissue (%ID/g), error bars indicate ±S (Fig. 2C)

Figure 3A and 3B: Antibody antagonist mode dose response curves in EGFR:HER2, HER2:HER3 and HER2:HER4 assays. Reporter cells were seeded for 4hr at 37°C at 2.5K/well in the case of EGFR:HER2 or 5K/well in the case of HER2:HER3 and HER2:HER4. Antibodies were serially diluted and incubated for 3hr at 37°C prior to stimulation for 16 hrs with 10ng/ml EGF or 30 ng/ml HRG-ß2 in the case of EGFR:HER2 or HER2:HER3 and HER2:HER4, respectively. Reference stimulation curves of agonists were obtained by incubating titrations of ligands alone for 24 hrs. Each data point represents the mean and standard deviation of four replicates per dose. Data were plotted in GraphPad Prism and curve fits were performed using a log (inhibitor) vs response- variable response (4 parameters) fit to calculate IC50's.