**Supp. Figure 1** *MM-302 and trastuzumab co-localize in BT474-M3 xenograft tumors.*

Additional images from BT474-M3 human xenograft tumors at 4 h (top 2 rows) and 24 h (bottom two rows) depicting localization of MM-302 (red), trastuzumab (green), vessels (magenta) and DNA (Hoechst; blue). Yellow indicates co-localization of MM-302 and trastuzumab. Lower row in each pair represents close-up of selected region from row above.

**Supp. Figure 2** *In vivo deposition of MM-302 is specifically increased by trastuzumab or T-DM1.*

Deposition of MM-302 as evaluated by HPLC to determine total doxorubicin in BT474-M3 xenograft tumors expressed as percent of injected dose per gram of tissue (%i.d./g tissue) 24 h following injection alone or with co-administration of trastuzumab (7mg/kg), T-DM1 (7 mg/kg), a non-specific human IgG (7 mg/kg) or PBS.

**Supp. Figure 3** *Pharmacokinetics (PK) of MM-302 remains the same with or without co-administration of trastuzumab.* PK of MM-302 was measured by sampling blood from NCR/nu female mice at multiple time points post injection of MM-302 alone or MM-302 plus trastuzumab. Graph depicts measurement of doxorubicin by HPLC at the indicated timepoints from 5l of plasma diluted into 495l of 1% acetic acid/methanol buffer.

**Supp. Figure 4** *Combination of MM-302 and trastuzumab demonstrates synergistic anti-tumor activity in models of HER2-positive breast and gastric cancer.* Bliss additivity analysis of anti-tumor activity in BT474-M3 and NCI-N87 xenograft tumors treated with MM-302 alone (blue), trastuzumab alone (pink) or MM-302 and trastuzumab (green). The sum of the individual effects of MM-302 and trastuzumab produces the Bliss additive value (black); experimental results above this line (green) indicate a greater than additive effect, or synergy.