**Supplemental material and method**

Cell line and patient-derived xenograft studies

Cell line based and NIBIO G016 patient-derived xenograft (PDX) studies were performed internally. NIBIO G016 tumor derived from a gastric cancer patient was obtained from National Institute of Biomedical Innovation (Japan). Specific pathogen-free female CAnN.Cg-Foxn1nu/CrlCrlj mice (BALB/c nude mice) aged 4–6 weeks were purchased from Charles River Laboratories Japan, Inc. All models were established by s.c. inoculation into the right flank of the mice.

NCI-N87, KPL-4, JIMT-1, GCIY, and CFPAC-1 models were established by injecting 1 x 107, 1 x 107, 3 x 106, 4 x 106, 8.6 x 106 cells suspended with saline, respectively. Capan-1 and NIBIO-G016 models were established by inoculating tumor fragments maintained by serial passaging in host mice.

When tumor volumes reached approximately 100–200 mm3, the tumor-bearing mice were randomized into treatment and control groups based on the tumor volume, and dosing was initiated (Day 0). DS-8201a, anti-HER2 Ab, T-DM1, and control IgG-ADC were administered intravenously to the mice at a volume of 10 mL/kg. As a vehicle, saline, ABS buffer (10 mM Acetate Buffer, 5% sorbitol, pH5.5), or HBS buffer (10 mM Histidine, 10% Trehalose, 0.02% Polysorbate 20, and pH 5.5) was administered at the same volume as the ADCs. The tumor volume was defined as 1/2 × length × width2.

Other PDX studies were performed by South Texas Accelerated Research Therapeutics. Specific pathogen-free female Crl:NU(NCr)-Foxn1nu mice (athymic nude mice) aged 6–12 weeks were purchased from Charles River Laboratories International, Inc (US). ST225, ST565, and ST313 models derived from breast cancer patients were established by inoculating tumor fragments maintained by serial passaging in host mice. When tumor volumes reached approximately 100–300 mm3, the tumor-bearing mice were evaluated as mentioned above. HER2 immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) were performed by using formalin-fixed paraffin-embedded untreated-tumor samples, a HercepTest II kit (Dako A/S) and a PathVysion HER-2 DNA Probe Kit (Abbott Molecular Inc.). The staining and scoring were conducted by SRL Medisearch (Japan).