**SUPPLEMENTARY MATERIALS AND METHODS**

**Xenograft studies**

Cell line-derived xenograft (CDX) studies: MDA-MB-453 studies by single administration and MDA-MB-231 study were performed internally. Models were established by injecting 1–2 × 107 cells (MDA-MB-453) and 5 × 106 cells (MDA-MB-231) suspended in Matrigel subcutaneously into female CAnN.Cg-Foxn1nu/CrlCrlj mice (Charles River Laboratories Japan, Inc.). HCC1569 study was performed by ProQinase GmbH. The model was established by injecting 5 × 106 cells suspended in Matrigel/PBS (1:1) orthotopically into the mammary fat pad of female CAnN.Cg-Foxn1nu/Crl mice (Charles River Germany GmbH). MDA-MB-453 study by multiple administration was performed by vivoPharm LLC. The model was established by inoculating a tumor fragment, which was maintained in host mice, subcutaneously into female CB-17/IcrHsd-Prkdscid mice (Harlan Laboratories Inc.).

Patient-derived xenograft (PDX) studies: ST565 and ST941 studies were performed by South Texas Accelerated Research Therapeutics. Models were established by inoculating tumor fragments derived from a breast cancer patient, which were maintained in host mice, subcutaneously into female Crl:NU(NCr)-Foxn1nu mice (Charles River Laboratories International, Inc.). NIBIO-G016 study was performed internally. NIBIO-G016 tumor that was derived from a gastric cancer patient was provided by Dr. Taisei Nomura (National Institute of Biomedical Innovation, Health, and Nutrition), who originally established this model. The model for the study was established by inoculating a tumor fragment, which was maintained in host mice, subcutaneously into female CAnN.Cg-Foxn1nu/CrlCrlj mice.

Group assignment and treatment initiation were carried out when the tumor volume reached approximately 100–300 mm3 (CDX models) and 200–400 mm3 (PDX models). The control group was administered PBS, saline, or 10 mM histidine buffer containing 10% Trehalose and 0.02% Polysorbate 20 (pH 5.5).

**Immunohistochemistry (IHC)**

HER3 IHC was performed using formalin-fixed paraffin-embedded tumor slides prepared from untreated xenograft models. The slides were processed using a pretreatment module PT link and an autostainer Link 48 (DAKO). The slides were deparaffinized and pretreated with Envision FLEX TRS High pH followed by endogenous peroxidase blocking and protein blocking. Then, the slides were sequentially incubated with anti-HER3 antibody (Cell Signaling Technology, Inc., Cat. No. 12708; final concentration of 2 µg/mL) as a primary antibody for 60 min, HRP Labelled Polymer Anti-Rabbit as a secondary antibody for 30 min, and the liquid DAB+ for 10 min. The slides were finally counterstained with hematoxylin for 5 min and mounted. All reagents except the primary antibody were obtained from DAKO. Images were captured by NanoZoomer-XR (Hamamatsu Photonics, Japan).