

WHAT IS CLAIMED IS:

1. A bispecific antibody for use in a method of inhibiting the growth of a breast cancer cell or promoting the killing of a breast cancer cell, the method comprising contacting a breast cancer cell with a bispecific antibody, wherein:

(a) the bispecific antibody comprises a first antigen-binding domain that specifically binds a tumor target (T), and a second antigen-binding domain that specifically binds an internalizing effector protein (E), wherein T is HER2 and E is a prolactin receptor (PRLR);

(b) the breast cancer cell expresses HER2; and

(c) HER2 undergoes rapid and complete lysosomal targeting and degradation in the presence of the bispecific antibody.

2. A bispecific antibody for use in the method of claim 1, the method further comprising contacting the tumor cell with a cytotoxic agent.

3. A bispecific antibody for use in the method of claim 2, wherein:

(a) the cytotoxic agent is an antibody drug conjugate (ADC) comprising a drug, toxin or radioisotope conjugated to an antigen-binding protein that specifically binds HER2, preferably wherein the antigen-binding portion of the ADC binds an epitope on HER2 that does not overlap with the epitope on HER2 recognized by the first antigen-binding domain of the bispecific antibody; and/or

(b) the antigen-binding protein of the ADC is an antibody.

4. A bispecific antibody for use in the method of claim 2, wherein the cytotoxic agent is a radioisotope, a toxin, or a drug.

5. A bispecific antibody for use in the method of claim 3 or 4, wherein the drug is selected from the group consisting of a calicheamicin, auristatin or a maytansine-based drug.

6. A bispecific antibody for use in the method of any one of claims 1-5, wherein the binding affinity of the bispecific antibody for PRLR is less than the binding affinity of the bispecific antibody for HER2.

7. A bispecific antibody for use in the method of any one of claims 2-6, wherein the cytotoxic agent is an antibody drug conjugate (ADC) and the ADC comprises a maytansine-based drug conjugated to an anti-HER2 bivalent monospecific antibody

8. A bispecific antibody for use in the method of any one of claims 2-7, wherein the cytotoxic agent is an antibody drug conjugate (ADC) and the ADC comprises a maytansine-based drug conjugated to an anti-PRLR bivalent monospecific antibody.

9. A bispecific antibody for use in the the method of any one of the preceding claims, wherein the breast cancer cell also expresses PRLR.

10. A bispecific antibody for use in the method of any one of the preceding claims, wherein the breast cancer cell is characterized as an IHC2+ breast cancer cell.

11. A bispecific antibody for use in the method of claim 9 or claim 10, wherein the breast cancer cell is a T47D cell.

12. A bispecific antibody for use in the method of any one of the preceding claims, wherein HER2 undergoes rapid and complete lysosomal targeting and degradation within 4 hours of contact.

13. A bispecific antibody for use in the method of any one of the preceding claims, wherein the bispecific antibody does not change the expression levels or surface turnover rates of PRLR by the breast cancer cell.

14. A pharmaceutical composition comprising an anti-HER2xPRLR bispecific antibody that binds to (i) PRLR, which is a rapidly internalized cell surface receptor and (ii) HER2, which is a slowly internalized cell surface receptor, wherein the rapidly internalized cell surface receptor and the slowly internalized cell surface receptor are expressed on the same cell.

15. The pharmaceutical composition of claim 14, further comprising a cytotoxic agent.

16. The pharmaceutical composition of claim 15, wherein:

(a) the cytotoxic agent is an antibody drug conjugate (ADC) comprising a drug, toxin or radioisotope conjugated to an antigen-binding protein that specifically binds the HER2, preferably wherein the antigen-binding portion of the ADC binds an epitope on HER2 that does not overlap with the epitope on HER2 recognized by the anti-HER2xPRLR bispecific antibody; and/or

(b) the antigen-binding protein of the ADC is an antibody.

17. The pharmaceutical composition of claim 15, wherein the cytotoxic agent is a radioisotope, a toxin, or a drug.

18. The pharmaceutical composition of claim 16 or claim 17, wherein the drug is selected from the group consisting of a calicheamicin, auristatin, or maytansine-based drug.

19. The pharmaceutical composition of any one of claims 15-18, wherein said cytotoxic agent comprises a maytansinoid-based drug conjugated to an anti-HER2 bivalent monospecific antibody

20. The pharmaceutical composition of any one of claims 15-18, wherein said cytotoxic agent comprises a maytansinoid-based drug conjugated to an anti-PRLR bivalent monospecific antibody.