

What is claimed is:

1. Use of a bispecific antibody in the manufacture of a medicament for treatment of a patient with breast cancer, wherein the treatment comprises inhibiting the growth of a breast cancer cell or promoting the killing of a breast cancer cell by contacting the breast cancer cell with the bispecific antibody, wherein:

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); wherein the breast cancer cell expresses HER2; and wherein HER2 undergoes rapid lysosomal targeting and degradation in the presence of the bispecific antibody.

2. The use according to claim 1, the treatment further comprising contacting the tumor cell with a cytotoxic agent.

3. The use according to claim 2, wherein the cytotoxic agent is an antibody drug conjugate (ADC) comprising a drug, toxin, or radioisotope conjugated to an antibody 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.

4. The use according to claim 2, wherein the cytotoxic agent is a radioisotope, a toxin, or a drug.

5. The use according to claim 3 or 4, wherein the drug is selected from the group consisting of a calicheamicin, an auristatin, or a maytansine-based drug.

6. The use according to 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. The use according to 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. The use according to claim 2 or claim 4, 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. The use according to any one of the preceding claims, wherein the breast cancer cell also expresses PRLR.

10. The use according to any one of the preceding claims, wherein the breast cancer cell is characterized as an IHC2+ breast cancer cell.

11. The use according to claim 9 or claim 10, wherein the breast cancer cell is a T47D cell.

12. The use according to any one of the preceding claims, wherein HER2 undergoes rapid lysosomal targeting and degradation within 4 hours of contact.

13. The use according to 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 the cytotoxic agent is an antibody drug conjugate (ADC) comprising a drug, toxin, or radioisotope conjugated to an antibody 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 anti-HER2xPRLR bispecific 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, an auristatin, or a maytansine-based drug.
19. The pharmaceutical composition of any one of claims 15-18, wherein the cytotoxic agent comprises a maytansinoid-based drug conjugated to an anti-HER2 bivalent monospecific antibody.
20. The pharmaceutical composition of claim 15 or claim 17, wherein the cytotoxic agent comprises a maytansinoid-based drug conjugated to an anti-PRLR bivalent monospecific antibody.
21. Use of a pharmaceutical composition in the manufacture of a medicament for the treatment of breast cancer, wherein the pharmaceutical composition comprises 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, and wherein the rapidly internalized cell surface receptor and the slowly internalized cell surface receptor are expressed on the same cell.

22. The use according to claim 21, further comprising a cytotoxic agent.
23. The use according to claim 22, wherein the cytotoxic agent is an antibody drug conjugate (ADC) comprising a drug, toxin, or radioisotope conjugated to an antibody 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 anti-HER2xPRLR bispecific antibody.
24. The use according to claim 22, wherein the cytotoxic agent is a radioisotope, a toxin, or a drug.
25. The use according to claim 23 or claim 24, wherein the drug is selected from the group consisting of a calicheamicin, an auristatin, or a maytansine-based drug.
26. The use according to any one of claims 22-25, wherein the cytotoxic agent comprises a maytansinoid-based drug conjugated to an anti-HER2 bivalent monospecific antibody.
27. The use according to claim 22 or claim 24, wherein the cytotoxic agent comprises a maytansinoid-based drug conjugated to an anti-PRLR bivalent monospecific antibody.