We claim:

1. A method for the treatment of a hyperproliferative disorder comprising administering a therapeutic combination as a combined formulation or by alternation to a mammal, wherein the therapeutic combination comprises a therapeutically effective amount of trastuzumab-MCC-DM1, and a therapeutically effective amount of a chemotherapeutic agent selected from a HER2 dimerization inhibitor antibody, an anti-VEGF antibody, 5-FU, carboplatin, lapatinib, ABT-869, docetaxel, GDC-0941, and GNE-390.

2. The method of claim 1 wherein the HER2 dimerization inhibitor antibody is pertuzumab.

3. The method of claim 1 wherein the anti-VEGF antibody is bevacizumab.

4. The method of claim 1 wherein the chemotherapeutic agent is 5-FU.

5. The method of claim 1 wherein the chemotherapeutic agent is carboplatin.

6. The method of claim 1 wherein the chemotherapeutic agent is lapatinib.

7. The method of claim 1 wherein the chemotherapeutic agent is ABT-869.

8. The method of claim 1 wherein the chemotherapeutic agent is docetaxel.

9. The method of claim 1 wherein the chemotherapeutic agent is GDC-0941.

10. The method of claim 1 wherein the chemotherapeutic agent is GNE-390.

11. The method of claim 1 wherein the therapeutically effective amount of trastuzumab-MCC-DM1 and the therapeutically effective amount of the chemotherapeutic agent are administered as a combined formulation.

12. The method of claim 1 wherein the therapeutically effective amount of trastuzumab-MCC-DM1 and the therapeutically effective amount of the chemotherapeutic agent are administered by alternation.

13. The method of claim 12 wherein the mammal is administered the chemotherapeutic agent and then subsequently administered trastuzumab-MCC-DM1.

14. The method of claim 12 wherein the therapeutic combination is administered at about three week intervals to a human with the hyperproliferative disorder.

15. The method of claim 12 wherein trastuzumab-MCC-DM1 is administered at intervals from about one week to three weeks to a human with the hyperproliferative disorder.

16. The method of claim 1 wherein administration of the therapeutic combination results in a synergistic effect.

17. The method of claim 1 wherein the hyperproliferative disorder is cancer.

18. The method of claim 17 wherein the hyperproliferative disorder is a cancer expressing ErbB2.

19. The method of claim 17 wherein the cancer is breast, ovary, cervix, prostate, testis, genitourinary tract, esophagus, larynx, glioblastoma, neuroblastoma, stomach, skin, keratoacanthoma, lung, epidermoid carcinoma, large cell carcinoma, non-small cell lung carcinoma (NSCLC), small cell carcinoma, lung adenocarcinoma, bone, colon, adenoma, pancreas, adenocarcinoma, thyroid, follicular carcinoma, undifferentiated carcinoma, papillary carcinoma, seminoma, melanoma, sarcoma, bladder carcinoma, liver carcinoma and biliary passages, kidney carcinoma, pancreatic, myeloid disorders, lymphoma, hairy cells, buccal cavity, nasopharyngeal, pharynx, lip, tongue, mouth, small intestine, colon-rectum, large intestine, rectum, brain and central nervous system, Hodgkin's or leukemia.

20. The method of claim 1 wherein the amount of trastuzumab-MCC-DM1 and the amount of chemotherapeutic agent are each from about 1 mg to about 1000 mg.

21. The method of claim 1 wherein the amount of trastuzumab-MCC-DM1 and the amount of chemotherapeutic agent are in a ratio of about 1:10 to about 10:1 by weight.

22. The method of claim 1 wherein the mammal is a HER2 positive patient.

23. The method of claim 1 wherein the HER2 positive patient has received trastuzumab or lapatinib therapy.

24. A pharmaceutical composition comprising trastuzumab-MCC-DM1, a chemotherapeutic agent selected from a HER2 dimerization inhibitor antibody, an anti-VEGF antibody, 5-FU, carboplatin, lapatinib, ABT-869, docetaxel, GDC-0941, and GNE-390; and one or more pharmaceutically acceptable carrier, glidant, diluent, or excipient.

25. The pharmaceutical composition of claim 24 comprising a pharmaceutically acceptable glidant selected from silicon dioxide, powdered cellulose, microcrystalline cellulose, metallic stearates, sodium aluminosilicate, sodium benzoate, calcium carbonate,

calcium silicate, corn starch, magnesium carbonate, asbestos free talc, stearowet C, starch, starch 1500, magnesium lauryl sulfate, magnesium oxide, and combinations thereof.

26. The pharmaceutical composition of claim 24 wherein the amount of trastuzumab-MCC-DM1 and the amount of chemotherapeutic agent are each present from about 1 mg to about 1000 mg.

27. The pharmaceutical composition of claim 24 wherein the amount of trastuzumab-MCC-DM1 and the amount of chemotherapeutic agent are present in a ratio of about 1:10 to about 10:1 by weight.

28. The use of a therapeutic combination in the manufacture of a medicament for the treatment of cancer selected from breast, ovary, cervix, prostate, testis, genitourinary tract, esophagus, larynx, glioblastoma, neuroblastoma, stomach, skin, keratoacanthoma, lung, epidermoid carcinoma, large cell carcinoma, non-small cell lung carcinoma (NSCLC), small cell carcinoma, lung adenocarcinoma, bone, colon, adenoma, pancreas, adenocarcinoma, thyroid, follicular carcinoma, undifferentiated carcinoma, papillary carcinoma, seminoma, melanoma, sarcoma, bladder carcinoma, liver carcinoma and biliary passages, kidney carcinoma, pancreatic, myeloid disorders, lymphoma, hairy cells, buccal cavity, nasopharyngeal, pharynx, lip, tongue, mouth, small intestine, colon-rectum, large intestine, rectum, brain and central nervous system, Hodgkin's or leukemia;

wherein the therapeutic combination is administered to a mammal as a combined formulation or by alternation, and comprises a therapeutically effective amount of trastuzumab-MCC-DM1, and a therapeutically effective amount of a chemotherapeutic agent selected from a HER2 dimerization inhibitor antibody, an anti-VEGF antibody, 5-FU, carboplatin, lapatinib, ABT-869, docetaxel, GDC-0941, and GNE-390.

29. An article of manufacture for treating a hyperproliferative disorder comprising:

a) a therapeutic combination administered to a mammal as a combined formulation or by alternation, and comprising a therapeutically effective amount of trastuzumab-MCC-DM1, and a therapeutically effective amount of a chemotherapeutic agent selected from a HER2 dimerization inhibitor antibody, an anti-VEGF antibody, 5-FU, carboplatin, lapatinib, ABT-869, docetaxel, GDC-0941, and GNE-390; and

b) instructions for use.

30. A method for determining compounds to be used in combination for the treatment of cancer comprising:

a) administering a therapeutic combination of trastuzumab-MCC-DM1 and a chemotherapeutic agent selected from a HER2 dimerization inhibitor antibody, an anti-VEGF antibody, 5-FU, carboplatin, lapatinib, ABT-869, docetaxel, GDC-0941, and GNE-390 to HER2-amplified breast cancer cells, and

b) measuring inhibition of cellular proliferation wherein nonmalignant and malignant mammary cells are discriminated by cell viability.

31. The method of claim 30 wherein the HER2-amplified breast cancer cells are BT-474.

32. A method for determining a therapeutic combination to be used for the treatment of cancer comprising:

a) treating an in vitro tumor cell line with a therapeutic combination of trastuzumab-MCC-DM1, and a chemotherapeutic agent selected from a HER2 dimerization inhibitor antibody, an anti-VEGF antibody, 5-FU, carboplatin, lapatinib, ABT-869, docetaxel, GDC-0941, and GNE-390, and

b) measuring a synergistic or non-synergistic effect;

whereby a synergistic therapeutic combination for the treatment of cancer is determined.

We claim:

1. Use of a therapeutic combination in the manufacture of a medicament for the treatment of a hyperproliferative disorder, wherein the therapeutic combination is to be administered as a combined formulation or by alternation to a mammal, wherein the therapeutic combination comprises a therapeutically effective amount of trastuzumab-MCC-DM1, and a therapeutically effective amount of a chemotherapeutic agent selected from GDC-0941 and GNE-390.

2. The use of claim 1, wherein the therapeutic combination consists of a therapeutically effective amount of trastuzumab-MCC-DM1, and a therapeutically effective amount of a chemotherapeutic agent selected from GDC-0941 and GNE-390.

3. The use of claim 1, wherein the therapeutic combination does not comprise pertuzumab.

4. The use of any one of the preceding claims, wherein the chemotherapeutic agent is GNE-390.

5. The use of any one of the preceding claims, wherein the chemotherapeutic agent is GDC-0941.

6. The use of any one of the preceding claims, wherein the therapeutically effective amount of trastuzumab-MCC-DM1 and the therapeutically effective amount of the chemotherapeutic agent are to be administered as a combined formulation.

7. The use of any one of claims 1 to 5, wherein the therapeutically effective amount of trastuzumab-MCC-DM1 and the therapeutically effective amount of the chemotherapeutic agent are to be administered by alternation.

8. The use of claim 7 wherein the mammal is to be administered the chemotherapeutic agent and then subsequently administered trastuzumab-MCC-DM1.

9. The use of claim 6, wherein the therapeutic combination is to be administered at about three week intervals to a human with the hyperproliferative disorder.

10. The use of any one of the preceding claims, wherein trastuzumab-MCC-DM1 is to be administered at intervals from about one week to three weeks to a human with the hyperproliferative disorder.

11. The use of claim 10, wherein the trastuzumab-MCC-DM1 is to be administered no more frequently than every 3 weeks at a dose of 2.4, 3.0 or 3.6 mg/kg intravenously.

12. The use of any one of the preceding claims, wherein the amount of trastuzumab-MCC-DM1 and the amount of chemotherapeutic agent are each from about 1 mg to about 1000 mg and the amount of trastuzumab-MCC-DM1 and the amount of chemotherapeutic agent are in a ratio of about 1:10 to about 10:1 by weight.

13. The use of any one of the preceding claims, wherein the hyperproliferative disorder is cancer expressing ErbB2.

14. The use of any one of the preceding claims, wherein the mammal is a HER2 positive patient.

15. The use of any one of the preceding claims, wherein the HER2 positive patient has received trastuzumab or lapatinib therapy.

16. A pharmaceutical composition comprising trastuzumab-MCC-DM1, a chemotherapeutic agent selected from GDC-0941 and GNE-390; and one or more pharmaceutically acceptable carrier, glidant, diluent, or excipient.

17. The pharmaceutical composition of claim 16 comprising a pharmaceutically acceptable glidant selected from silicon dioxide, powdered cellulose, microcrystalline cellulose, metallic stearates, sodium aluminosilicate, sodium benzoate, calcium carbonate, calcium silicate, corn starch, magnesium carbonate, asbestos free talc, stearowet C, starch, starch 1500, magnesium lauryl sulfate, magnesium oxide, and combinations thereof.

18. Use of a therapeutic combination in the manufacture of a medicament for the treatment of breast cancer, wherein the therapeutic combination is to be administered to a mammal as a combined formulation or by alternation, and wherein the therapeutic

combination comprises a therapeutically effective amount of trastuzumab-MCC-DM1, and a therapeutically effective amount of a chemotherapeutic agent selected from GDC-0941 and GNE-390t.

19. A method for determining a therapeutic combination of trastuzumab-MCC-DM1 and a chemotherapeutic agent selected from GDC-0941 and GNE-390, wherein the combination is to be used for the treatment of cancer comprising:

a) treating an in vitro tumor cell line with a therapeutic combination of trastuzumab-MCC-DM1, and a chemotherapeutic agent selected from GDC-0941 and GNE-390, and

b) measuring a synergistic or non-synergistic effect;

whereby a synergistic therapeutic combination for the treatment of cancer is determined.