We claim:

1. A method of treating a disorder characterized by increased levels of HER3 expression in an esophageal tract comprising:

selecting patient suffering from increased levels of HER3 expression in an esophageal tract; and

administering an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction, thereby treating the disorder.

2. The method of claim 1, wherein the disorder is selected from the group consisting of esophageal cancer and Barretts esophageal cancer.

3. The method of claim 1, wherein the antibody or fragment thereof is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.

4. The method of claim 1, wherein the antibody or fragment is formulated into a pharmaceutical composition comprising a physiologically acceptable carrier, excipient, or diluent.

5. The method of claim 4, further comprising an additional therapeutic agent.

6. The method of claim 5, wherein the additional therapeutic agent is selected from the group consisting of an HER1 inhibitor, a HER2 inhibitor, a HER3 inhibitor, a HER4 inhibitor, an mTOR inhibitor and a PI3 Kinase inhibitor.

7. The method of claim 6, wherein the additional therapeutic agent is a HER1 inhibitor selected from the group consisting of Matuzumab (EMD72000), Erbitux®/Cetuximab, Vectibix® /Panitumumab, mAb 806, Nimotuzumab, Iressa® /Gefitinib, CI-1033 (PD183805), Lapatinib (GW-572016), Tykerb® /Lapatinib Ditosylate, Tarceva® / Erlotinib HCL (OSI-774), PKI-166, and Tovok®; a HER2 inhibitor selected from the group consisting of Pertuzumab, Trastuzumab, MM-111, neratinib, lapatinib or lapatinib ditosylate /Tykerb®; a

HER3 inhibitor selected from the group consisting of, MM-121, MM-111, IB4C3, 2DID12 (U3 Pharma AG), AMG888 (Amgen), AV-203(Aveo), MEHD7945A (Genentech), MOR10703 (Novartis) and small molecules that inhibit HER3; and a HER4 inhibitor.

8. The method of claim 6, wherein the additional therapeutic agent is an mTOR inhibitor selected from the group consisting of Temsirolimus/Torisel®, ridaforolimus / Deforolimus, AP23573, MK8669, everolimus /Affinitor® .

9. The method of claim 6, wherein the additional therapeutic agent is a PI3 Kinase inhibitor selected from the group consisting of GDC 0941, BEZ235, BMK120 and BYL719.

10. A method of treating gastric cancer comprising:

selecting a patient suffering from gastric cancer; and

administering an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction, thereby treating gastric cancer.

11. The method of claim 10, wherein the antibody or fragment thereof is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.

12. The method of claim 10, wherein the antibody or fragment is formulated into a pharmaceutical composition comprising a physiologically acceptable carrier, excipient, or diluent.

13. The method of claim 12, further comprising an additional therapeutic agent.

14. The method of claim 13, wherein the additional therapeutic agent is selected from the group consisting of an HER1 inhibitor, a HER2 inhibitor, a HER3 inhibitor, a HER4 inhibitor, an mTOR inhibitor and a PI3 Kinase inhibitor.

15. The method of claim 14, wherein the additional therapeutic agent is a HER1 inhibitor selected from the group consisting of Matuzumab (EMD72000), Erbitux®/Cetuximab, Vectibix® /Panitumumab, mAb 806, Nimotuzumab, Iressa® /Gefitinib, CI-1033 (PD183805),

Lapatinib (GW-572016), Tykerb® /Lapatinib Ditosylate, Tarceva® / Erlotinib HCL (OSI-774), PKI-166, and Tovok®; a HER2 inhibitor selected from the group consisting of Pertuzumab, Trastuzumab, MM-111, neratinib, lapatinib or lapatinib ditosylate /Tykerb®; a HER3 inhibitor selected from the group consisting of, MM-121, MM-111, IB4C3, 2DID12 (U3 Pharma AG), AMG888 (Amgen), AV-203(Aveo), MEHD7945A (Genentech), MOR10703 (Novartis) and small molecules that inhibit HER3; and a HER4 inhibitor.

16. The method of claim 14, wherein the additional therapeutic agent is an mTOR inhibitor selected from the group consisting of Temsirolimus/Torisel®, ridaforolimus / Deforolimus, AP23573, MK8669, everolimus /Affinitor® .

17. The method of claim 14, wherein the additional therapeutic agent is a PI3 Kinase inhibitor selected from the group consisting of GDC 0941, BEZ235, BMK120 and BYL719.

18. A method of treating head and neck cancer comprising:

selecting a patient suffering from cancer the head and neck; and

administering an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction, thereby treating head and neck cancer.

19. The method of claim 18, wherein the antibody or fragment thereof is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.

20. The method of claim 18, wherein the antibody or fragment is formulated into a pharmaceutical composition comprising a physiologically acceptable carrier, excipient, or diluent.

21. The method of claim 20, further comprising an additional therapeutic agent.

22. The method of claim 21, wherein the additional therapeutic agent is selected from the group consisting of an HER1 inhibitor, a HER2 inhibitor, a HER3 inhibitor, a HER4 inhibitor, an mTOR inhibitor and a PI3 Kinase inhibitor.

23. The method of claim 22, wherein the additional therapeutic agent is a HER1 inhibitor selected from the group consisting of Matuzumab (EMD72000), Erbitux®/Cetuximab, Vectibix® /Panitumumab, mAb 806, Nimotuzumab, Iressa® /Gefitinib, CI-1033 (PD183805), Lapatinib (GW-572016), Tykerb® /Lapatinib Ditosylate, Tarceva® / Erlotinib HCL (OSI-774), PKI-166, and Tovok®; a HER2 inhibitor selected from the group consisting of Pertuzumab, Trastuzumab, MM-111, neratinib, lapatinib or lapatinib ditosylate /Tykerb®; a HER3 inhibitor selected from the group consisting of, MM-121, MM-111, IB4C3, 2DID12 (U3 Pharma AG), AMG888 (Amgen), AV-203(Aveo), MEHD7945A (Genentech), MOR10703 (Novartis) and small molecules that inhibit HER3; and a HER4 inhibitor.

24. The method of claim 22, wherein the additional therapeutic agent is an mTOR inhibitor selected from the group consisting of Temsirolimus/Torisel®, ridaforolimus / Deforolimus, AP23573, MK8669, everolimus /Affinitor® .

25. The method of claim 22, wherein the additional therapeutic agent is a PI3 Kinase inhibitor selected from the group consisting of GDC 0941, BEZ235, BMK120 and BYL719.

26. A method of treating benign prostate hypoplasia comprising:

selecting a patient suffering from benign prostate hypoplasia; and

administering an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction, thereby treating benign prostate hypoplasia.

27. The method of claim 26, wherein the antibody or fragment thereof is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.

28. The method of claim 26, wherein the antibody or fragment is formulated into a pharmaceutical composition comprising a physiologically acceptable carrier, excipient, or diluent.

29. The method of claim 28, further comprising an additional therapeutic agent.

30. The method of claim 29, wherein the additional therapeutic agent is selected from the group consisting of an HER1 inhibitor, a HER2 inhibitor, a HER3 inhibitor, a HER4 inhibitor, an mTOR inhibitor and a PI3 Kinase inhibitor.

31. The method of claim 330, wherein the additional therapeutic agent is a HER1 inhibitor selected from the group consisting of Matuzumab (EMD72000), Erbitux®/Cetuximab, Vectibix® /Panitumumab, mAb 806, Nimotuzumab, Iressa® /Gefitinib, CI-1033 (PD183805), Lapatinib (GW-572016), Tykerb® /Lapatinib Ditosylate, Tarceva® / Erlotinib HCL (OSI-774), PKI-166, and Tovok®; a HER2 inhibitor selected from the group consisting of Pertuzumab, Trastuzumab, MM-111, neratinib, lapatinib or lapatinib ditosylate /Tykerb®; a HER3 inhibitor selected from the group consisting of, MM-121, MM-111, IB4C3, 2DID12 (U3 Pharma AG), AMG888 (Amgen), AV-203(Aveo), MEHD7945A (Genentech), MOR10703 (Novartis) and small molecules that inhibit HER3; and a HER4 inhibitor.

32. The method of claim 30, wherein the additional therapeutic agent is an mTOR inhibitor selected from the group consisting of Temsirolimus/Torisel®, ridaforolimus / Deforolimus, AP23573, MK8669, everolimus /Affinitor® .

33. The method of claim 30, wherein the additional therapeutic agent is a PI3 Kinase inhibitor selected from the group consisting of GDC 0941, BEZ235, BMK120 and BYL719.

34. A method of treating gynacomastica, comprising:

selecting a patient suffering from gynacomastica; and

administering an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction, thereby treating gynacomastica,.

35. The method of claim 34, wherein the antibody or fragment thereof is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.

36. The method of claim 34, wherein the antibody or fragment is formulated into a pharmaceutical composition comprising a physiologically acceptable carrier, excipient, or diluent.

37. The method of claim 36, further comprising an additional therapeutic agent.

38. The method of claim 37, wherein the additional therapeutic agent is selected from the group consisting of an HER1 inhibitor, a HER2 inhibitor, a HER3 inhibitor, a HER4 inhibitor, an mTOR inhibitor and a PI3 Kinase inhibitor.

39. The method of claim 38, wherein the additional therapeutic agent is a HER1 inhibitor selected from the group consisting of Matuzumab (EMD72000), Erbitux®/Cetuximab, Vectibix® /Panitumumab, mAb 806, Nimotuzumab, Iressa® /Gefitinib, CI-1033 (PD183805), Lapatinib (GW-572016), Tykerb® /Lapatinib Ditosylate, Tarceva® / Erlotinib HCL (OSI-774), PKI-166, and Tovok®; a HER2 inhibitor selected from the group consisting of Pertuzumab, Trastuzumab, MM-111, neratinib, lapatinib or lapatinib ditosylate /Tykerb®; a HER3 inhibitor selected from the group consisting of MM-121, MM-111, IB4C3, 2DID12 (U3 Pharma AG), AMG888 (Amgen), AV-203(Ayeo), MEHD7945A (Genentech), MOR10703 (Novartis) and small molecules that inhibit HER3; and a HER4 inhibitor.

40. The method of claim 38, wherein the additional therapeutic agent is an mTOR inhibitor selected from the group consisting of Temsirolimus/Torisel®, ridaforolimus / Deforolimus, AP23573, MK8669, everolimus /Affinitor® .

41. The method of claim 38, wherein the additional therapeutic agent is a PI3 Kinase inhibitor selected from the group consisting of GDC 0941, BEZ235, BMK120 and BYL719.

42. A method of treating endometiosis comprising:

selecting a patient suffering from endometiosis; and

administering an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction, thereby treating endometiosis.

43. The method of claim 42, wherein the antibody or fragment thereof is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.

44. The method of claim 42, wherein the antibody or fragment is formulated into a pharmaceutical composition comprising a physiologically acceptable carrier, excipient, or diluent.

45. The method of claim 44, further comprising an additional therapeutic agent.

46. The method of claim 45, wherein the additional therapeutic agent is selected from the group consisting of an HER1 inhibitor, a HER2 inhibitor, a HER3 inhibitor, a HER4 inhibitor, an mTOR inhibitor and a PI3 Kinase inhibitor.

47. The method of claim 46, wherein the additional therapeutic agent is a HER1 inhibitor selected from the group consisting of Matuzumab (EMD72000), Erbitux®/Cetuximab, Vectibix® /Panitumumab, mAb 806, Nimotuzumab, Iressa® /Gefitinib, CI-1033 (PD183805), Lapatinib (GW-572016), Tykerb® /Lapatinib Ditosylate, Tarceva® / Erlotinib HCL (OSI-774), PKI-166, and Tovok®; a HER2 inhibitor selected from the group consisting of Pertuzumab, Trastuzumab, MM-111, neratinib, lapatinib or lapatinib ditosylate /Tykerb®; a HER3 inhibitor selected from the group consisting of, MM-121, MM-111, IB4C3, 2DID12 (U3 Pharma AG), AMG888 (Amgen), AV-203(Aveo), MEHD7945A (Genentech), MOR10703 (Novartis) and small molecules that inhibit HER3; and a HER4 inhibitor.

48. The method of claim 46, wherein the additional therapeutic agent is an mTOR inhibitor selected from the group consisting of Temsirolimus/Torisel®, ridaforolimus / Deforolimus, AP23573, MK8669, everolimus /Affinitor® .

49. The method of claim 46, wherein the additional therapeutic agent is a PI3 Kinase inhibitor selected from the group consisting of GDC 0941, BEZ235, BMK120 and BYL719.

50. Use of an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction for the manufacture of a medicament for the treatment of an esophageal disorder.

51. Use of an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction for the manufacture of a medicament for the treatment of gastric cancer.

52. Use of an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction for the manufacture of a medicament for the treatment of head and neck cancer.

53. Use of an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction for the manufacture of a medicament for the treatment of benign prostatic hyperplasia (BPH).

54. Use of an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction for the manufacture of a medicament for the treatment of gynacomastica.

55. Use of an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction for the manufacture of a medicament for the treatment of endometriosis.

Claims:

1. Use of an antibody or fragment thereof that specifically binds to a HER3 receptor, such that the antibody or fragment thereof binds to a conformational epitope comprising amino acid residues within domain 2 and domain 4 of the HER3 receptor and blocks both ligand-dependent and ligand-independent signal transduction, for the manufacture of a medicament for treatment of benign prostate hyperplasia,
wherein the antibody or fragment thereof comprises sequence selected from the group consisting of:
   (a) a heavy chain variable region CDR1 of SEQ ID NO: 38; a heavy chain variable region CDR2 of SEQ ID NO: 39; a heavy chain variable region CDR3 of SEQ ID NO: 40; a light chain variable region CDR1 of SEQ ID NO: 41; a light chain variable region CDR2 of SEQ ID NO: 42; and a light chain variable region CDR3 of SEQ ID NO: 43;
   (b) a heavy chain variable region CDR1 of SEQ ID NO: 44; a heavy chain variable region CDR2 of SEQ ID NO: 45; a heavy chain variable region CDR3 of SEQ ID NO: 46; a light chain variable region CDR1 of SEQ ID NO: 47; a light chain variable region CDR2 of SEQ ID NO: 48; and a light chain variable region CDR3 of SEQ ID NO: 49;
   (c) a variable heavy chain (VH) sequence of SEQ ID NO: 51 and a variable light chain (VL) sequence of SEQ ID NO: 50;
   (d) a variable heavy chain (VH) sequence having SEQ ID NO: 141 and a variable light chain (VL) sequence having of SEQ ID NO: 140;
   (e) a variable heavy chain (VH) sequence selected from the group consisting of SEQ ID NOs. 402-423;
   (f) a variable light kappa chain (VK) sequence selected from the group consisting of SEQ ID NOs. 443-461 and SEQ ID NOs 479-480; or
   (g) a sequence selected from the group consisting of SEQ ID NOs. 487-492.

2. The use of claim 1, further comprising an additional therapeutic agent.

3. The use of claim 2, wherein the additional therapeutic agent is selected from the group consisting of an HER1 inhibitor, a HER2 inhibitor, a HER3 inhibitor, a HER4 inhibitor, an mTOR inhibitor and a PI3 Kinase inhibitor.

4. The use of claim 2, wherein the additional therapeutic agent is a HER1 inhibitor selected from the group consisting of Matuzumab (EMD72000), Cetuximab, Panitumumab, Nimotuzumab, Gefitinib, CI-1033 (PD183805), Lapatinib (GW-572016), Lapatinib Ditosylate, Erlotinib HCL (OSI-774), PKI-166, and N-[4-[(3-Chloro-4-fluorophenyl)amino]-7-[[(3"S")-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4(dimethylamino)-2-butenamidea HER2 inhibitor selected from the group consisting of Pertuzumab, Trastuzumab, MM-111, neratinib, lapatinib or lapatinib ditosylate; a HER3 inhibitor selected from the group consisting of, MM-121, MM-111, IB4C3, 2DID12 (U3 Pharma AG), AV-203 (Aveo), MEHD7945A (Genentech), MOR10703 (Novartis) and small molecules that inhibit HER3; and a HER4 inhibitor.

5. The use of claim 2, wherein the additional therapeutic agent is an mTOR inhibitor selected from the group consisting of Temsirolimus, ridaforolimus/Deforolimus, AP23573, MK8669, and everolimus.

6. The use of claim 2, wherein the additional therapeutic agent is a PI3 Kinase inhibitor selected from the group consisting of GDC 0941, BEZ235, BMK120 and BYL719.