CLAIMS:

1. A method of determining the presence and/or amount of p95-~~HER2~~ and/or p95-~~HER2~~ complex in a sample, the method comprising:

(a) contacting a sample with a p95-~~HER2~~ specific antibody or a portion thereof, wherein the antibody or portion thereof binds specifically to a p95-~~HER2~~ protein fragment having a first amino acid corresponding to methionine 611 of HER2 protein, wherein the antibody or portion thereof does not bind to full length HER2, and wherein the antibody or portion thereof binds to an amino acid sequence as set forth in at least one of SEQ ID NOs: 1 and 4-7; and

(b) measuring the amount of the p95-~~HER2~~ specific antibody that binds to the sample to determine the presence and/or quantity of p95-~~HER2~~ and/or p95-~~HER2~~ complex in the sample.

2. A method for determining whether a subject with a HER2 positive cancer is likely to respond to treatment with a HER2 pathway targeted therapy, comprising:

(a) measuring an amount of p95-~~HER2~~ and/or p95-~~HER2~~ complex in a sample using a p95-HER2 specific antibody or a portion thereof, wherein the antibody or portion thereof binds specifically to a p95-~~HER2~~ protein fragment having a first amino acid corresponding to methionine 611 of HER2 protein, wherein the antibody or portion thereof does not bind to full length HER2, and wherein the antibody or portion thereof binds to an amino acid sequence as set forth in at least one of SEQ ID NOs: 1and 4-7;

(b) determining whether the amount of p95-~~HER2~~ and/or p95-~~HER2~~ complex in the sample is below or above a p95-~~HER2~~ cutoff, wherein the p95-~~HER2~~ cutoff comprises at least one of (i) a level of p95-~~HER2~~ expression at least two-fold greater than control cancer cell lines having basal levels of p95-~~HER2~~ expression or (ii) a level of p95-~~HER2~~ expression corresponding to at least a top $30^{th}$-$50^{th}$ percentile of p95-~~HER2~~ expression in a reference cohort of subjects having the HER2 positive cancer; and

(c) indicating that the subject is more likely to respond to a HER2 pathway targeted therapy targeted to the extracellular domain of HER2 if the amount of p95-~~HER2~~ in the biological sample is below the p95-~~HER2~~ cutoff as compared to if the amount of p95-~~HER2~~ in the biological sample is above the p95-~~HER2~~ cutoff.

3. The method of Claim 1 or 2, wherein the antibody is a monoclonal antibody.

4. The method of Claim 1 or 2, wherein the antibody is a polyclonal antibody.

5. The method of any one of Claims 1-4 , wherein the antibody was raised against a peptide having an amino acid sequence as set forth in at least one of SEQ ID NOs:1and 4-7.

6. The method of any one of Claims 1-5, wherein the antibody binds specifically to, was raised against, or both binds specifically to and was raised against, an amino acid sequence as set forth in SEQ ID NO:5.

7. The method of any one of Claims 1, 2, 5 and 4-6, wherein the antibody comprises one of the antibodies produced by hybridoma cell lines deposited with the ATCC having accession number PTA-9738 (p95.D3.4), PTA-9739 (p95.D8.2) and PTA-9740 (p95.D9.1).

8. The method of any one of Claims 1, 2, 5, 6 and 4-7, wherein the antibody comprises a monoclonal antibody produced by a hybridoma cell line deposited with the ATCC having accession number PTA-9740 (p95.D9.1).

9. The method any one of Claims 1-8, wherein the sample is a biological sample.

10. The method of any one of Claims 1-9, wherein the sample comprises a tissue sample or a biological fluid.

11. The method of any one of Claims 1-10, wherein the sample comprises a fixed tissue sample, a frozen tissue sample, or a tissue lysate.

12. The method of any one of Claims 1-10, wherein the sample comprises a ~~biological fluid~~ blood or plasma sample containing circulating tumor cells.

13. The method of any one of Claims 1-10, wherein the sample comprises blood, plasma, or lymph.

14. A purified antibody, or a portion thereof, that binds specifically to a p95~~-HER2~~ protein fragment having a first amino acid corresponding to methionine 611 of HER2 protein, wherein the antibody or portion thereof does not bind to full length HER2, and wherein the

antibody or portion thereof binds to an amino acid sequence as set forth in at least one of SEQ ID NOs: 1and 4-7.

15. An immunogen used to isolate an antibody to p95-~~HER2~~, wherein the immunogen has one of the sequences set forth in SEQ ID NOs: 1, 2, and 4-7.

16. The immunogen according to Claim ~~14~~15, wherein said immunogen has the sequence set forth in SEQ ID NO:5.

17. The antibody of Claim 14, wherein the antibody is a polyclonal antibody.

18. The antibody of Claim 14, wherein the antibody is a monoclonal antibody.

19. The antibody of Claim 14, wherein the antibody was raised against a peptide having a sequence as set forth in any one of SEQ ID NOs:1 and 4-7.

20. The antibody of Claim 14, wherein the antibody comprises an antibody produced by a hybridoma cell line deposited with the ATCC having accession number PTA-9738 (p95.D3.4), PTA-9739 (p95.D8.2), or PTA-9740 (p95.D9.1).

21. The method of any one of Claims 1-13, wherein the step of measuring the amount of p95-~~HER2~~ and/or p95-~~HER2~~ complex in the sample comprises the steps of:

(i) contacting the sample with a p95-~~HER2~~ binding composition comprising a purified p95-~~HER2~~ specific antibody or a portion thereof, wherein the antibody or portion thereof binds specifically to a p95-~~HER2~~ protein fragment having a first amino acid corresponding to methionine 611 of HER2 protein, wherein the antibody or portion thereof does not bind to full length HER2, and wherein the antibody or portion thereof binds to an amino acid sequence as set forth in at least one of SEQ ID NOs: 1, 2, and 4-7;

(ii) contacting the p95-~~HER2~~ binding composition with a tagged binding composition, wherein the tagged binding composition comprises a molecular tag attached thereto via a cleavable linkage, and wherein the tagged binding composition specifically binds to the p95-~~HER2~~ binding composition;

(iii) cleaving the cleavable linker of the tagged binding composition, thereby releasing the molecular tag; and

(iv) quantitating the released molecular tag to determine the amount of p95~~-HER2~~ or p95~~-HER2~~ complex in the sample.

22. The method of any one of Claims 1-13 and 21, wherein the sample comprises a carcinoma.

23. The method of any one of Claims 1-13, 21, and 22, wherein the sample comprises at least one of a bone cancer, a brain cancer, an endocrine system cancer, a gastrointestinal cancer, a gynecological cancer, a~~n androlgical~~ penile cancer, a prostate cancer, a testicular cancer, a head and neck cancer, a ~~respiratory~~ lung cancer, a thyroid cancer, a urinary tract cancer, or a metastatic carcinoma.

24. The method of any one of Claims 1-13, 21, and 22, wherein the sample comprises breast cancer.

25. The method of any one of Claims 1-13 and 21-24, wherein the sample comprises metastatic breast cancer.

26. The method of any one of Claims 1-13 and 21-25, wherein the sample comprises a HER2 positive cancer.

27. The method of any one of Claims 2-13 and 21-26, wherein the HER2 pathway targeted therapy comprises a HER2 acting agent.

28. The method of any one of Claims ~~1~~2-13 and 21-27, wherein the HER2 pathway targeted therapy comprises trastuzumab, pertuzumab, or a combination thereof.

29. The method of any one of Claims ~~1~~2-13 and 21-28, wherein the HER2 pathway targeted therapy comprises is trastuzumab as part of a combination therapy.

30. The method of Claim 29, wherein the combination therapy further comprises at least one of cytarabine, melphalan, topotecan, fludarabine, etoposide, idarubicin, daunorubicin, mitoxantrone, cisplatin, paclitaxel, or cyclophosphamide.

31. The method of any one of Claims 2-13 and 21-30, wherein the response to the HER2 pathway targeted agent is measured as at least one of overall survival rate, time to

progression, ~~disease-free survival,~~ progression-free survival, ~~time to distant reoccurrence,~~ hazard ratio, and/or ~~objective tumor response or clinical benefit~~ using the RECIST criteria.

32. The method of any one of Claims 2-13 and 21-31, wherein the control cancer cells comprise SKBR3 and/or MCF7.

33. The method of any one of Claims 2-13 and 21-32, further comprising:

~~(v)~~ ——indicating that the subject is more likely to respond to a HER2 pathway targeted therapy targeted to the intracellular domain of HER2 if the amount of p95-~~HER2~~ in the biological sample is above the p95-~~HER2~~ cutoff as compared to a HER2 pathway targeted therapy targeted to the extracellular domain of HER2.

34. The method of any one of Claims 2-13 and 21-33, wherein the HER2 pathway targeted agent targeted to the intracellular domain of HER2 comprises a tyrosine kinase inhibitor.

35. The method of any one of Claims 2-13 and 21-34, wherein the HER2 pathway targeted agent targeted to the intracellular domain of HER2 comprises at least one of lapatinib, canertinib, mubritinib, AEE-788, HKI-272, BIBW-2992, or BMS-599626.