

WHAT IS CLAIMED IS:

- Claim 1. A **CD137 x TA** Binding Molecule, wherein said Binding Molecule is capable of specific binding to an epitope of CD137 and an epitope of a tumor antigen (TA), and wherein said **CD137 x TA** Binding Molecule comprises a first Light Chain Variable Domain that comprises a CDR_{L1}, CDR_{L2} and CDR_{L3}, and a first Heavy Chain Variable Domain that comprises a CDR_{H1}, CDR_{H2} and CDR_{H3}; and wherein,
- (A) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL15 (SEQ ID NO:222)**; and
 - (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
 - (B) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL14 (SEQ ID NO:221)**; and
 - (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
 - (C) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL11 (SEQ ID NO:218)**; and
 - (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
 - (D) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL10 (SEQ ID NO:217)**; and
 - (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;

- (E) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL6 (SEQ ID NO:213)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
- (F) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL4 (SEQ ID NO:211)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
- (G) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL (SEQ ID NO:75)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH (SEQ ID NO:74)**;
- (H) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-4 VL (SEQ ID NO:91)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-4 VH (SEQ ID NO:90)**;
- (I) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-5 VL (SEQ ID NO:97)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-5 VH (SEQ ID NO:96)**;
- (J) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL (SEQ ID NO:75)**; and

- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1A (SEQ ID NO:83)**;
- (K) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL (SEQ ID NO:75)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
- (L) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL (SEQ ID NO:75)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1C (SEQ ID NO:85)**;
- or
- (M) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL (SEQ ID NO:75)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1D (SEQ ID NO:86)**.

Claim 2. The **CD137 x TA** Binding Molecule of claim 2, wherein said first Heavy Chain Variable Domain comprises the amino acid sequence of:

- (A) **hCD137 MAB-3 VH1E (SEQ ID NO:208)**;
- (B) **hCD137 MAB-3 VH1B (SEQ ID NO:84)**;
- (C) **hCD137 MAB-3 VH1A (SEQ ID NO:83)**;
- (D) **hCD137 MAB-3 VH1 (SEQ ID NO:76)**;
- (E) **hCD137 MAB-3 VH1C (SEQ ID NO:85)**;
- (F) **hCD137 MAB-3 VH1D (SEQ ID NO:86)**;
- (G) **hCD137 MAB-3 (SEQ ID NO:77)**; or
- (H) **hCD137 MAB-4 VH1 (SEQ ID NO:92)**.

- Claim 3. The **CD137 x TA** Binding Molecule of any one of claims 1-2, wherein said first Light Chain Variable Domain comprises the amino acid sequence of:
- (A) **hCD137 MAB-3 VL15 (SEQ ID NO:222);**
 - (B) **hCD137 MAB-3 VL14 (SEQ ID NO:221);**
 - (C) **hCD137 MAB-3 VL1 (SEQ ID NO:87);**
 - (D) **hCD137 MAB-3 VL2 (SEQ ID NO:88);**
 - (E) **hCD137 MAB-3 VL3 (SEQ ID NO:89);**
 - (F) **hCD137 MAB-3 (SEQ ID NO:82);**
 - (G) **hCD137 MAB-4 VL1 (SEQ ID NO:94);** or
 - (H) **hCD137 MAB-4 VL2 (SEQ ID NO:95).**
- Claim 4. The **CD137 x TA** Binding Molecule of any one of claims 1-3, wherein said tumor antigen (**TA**) is selected from the group of tumor antigens consisting of: 19.9; oncofetal protein 5T4; antigen 4.2; A33; AFP; ALCAM; BAGE; beta-catenin; CA125; Carboxypeptidase M; B1;CD5; CD19; CD20; CD22; CD23; CD25; CD27; CD30; CD33; CD36; CD46; CD52; CD79a/CD79b; CD123; CD317; CEA; CEACAM5; CEACAM6; CO-43; CO-514; CTLA-1; CTLA-4; Cytokeratin 8; E1 series; EGF-R; an Ephrin receptor; Erb; F3; FC10.2; a GAGE GD2; GD3; GD49; GM2; GM3; GICA 19-9; gp37; gp75; gp100; HER-2/neu; human B-lymphoma antigen-CD20; human milk fat globule antigen; human papillomavirus-E6/human papillomavirus-E7; HMW-MAA; I antigen; ITGB6; IL13R α 2; JAM-3; KID3; KID31; KS 1/4 pan-carcinoma antigen; KS 1/4; KSA; L6; L20; LEA; LUCA-2; M1:22:25:8; M18; M39; a MAGE; MART; Myl; MUC-1; MUM-1; N-acetylglucosaminyltransferase; neoglycoprotein; NS-10; OFA-1; OFA-2; Oncostatin M; p15; PSA; PSMA; PEMA; PIPA; prostatic acid phosphate; R24; ROR1; SSEA-1; SSEA-3; SSEA-4; sTn; T cell receptor derived peptide; TAG-72; TL5; TNF- α receptor; TNF- β receptor; TNF- γ receptor; TRA-1-85; Transferrin Receptor; TSTA; and VEGF-R.
- Claim 5. The **CD137 x TA** Binding Molecule of claim 4, wherein said tumor antigen (**TA**) is HER2/neu and wherein said **CD137 x TA** Binding Molecule comprises a second Light Chain Variable Domain that comprises a CDR_{L1}, CDR_{L2} and CDR_{L3}, and a first Heavy Chain Variable Domain that comprises a CDR_{H1}, CDR_{H2} and CDR_{H3}; and wherein

- (A) said second Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **HER2 MAB-1 VL (SEQ ID NO:63)**; and
- (B) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **HER2 MAB-1 VH (SEQ ID NO:62)**.

Claim 6. The **CD137 x TA** Binding Molecule of claim 5, wherein:

- (A) (1) said second Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **hHER2 MAB-1 VL1 (SEQ ID NO:67)**;
- (2) said second Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **hHER2 MAB-1 VL2 (SEQ ID NO:68)**; or
- (3) said second Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **hHER2 MAB-1 VL3 (SEQ ID NO:69)**;

and

- (B) (1) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hHER2 MAB-1 VH1 (SEQ ID NO:64)**;
- (2) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hHER2 MAB-1 VH2 (SEQ ID NO:65)**; or
- (3) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hHER2 MAB-1 VH3 (SEQ ID NO:66)**.

Claim 7. The **CD137 x TA** Binding Molecule of claim 6, wherein said second Heavy Chain Variable Domain comprises the amino acid sequence of:

- (A) **hHER2 MAB-1 VH1 (SEQ ID NO:64)**;
- (B) **hHER2 MAB-1 VH2 (SEQ ID NO:65)**; or
- (C) **hHER2 MAB-1 VH3 (SEQ ID NO:66)**.

- Claim 8. The **CD137 x TA** Binding Molecule of claim 6 or 7, wherein said second Light Chain Variable Domain comprises the amino acid sequence of:
- (A) **hHER2 MAB-1 VL1 (SEQ ID NO:67)**;
 - (B) **hHER2 MAB-1 VL2 (SEQ ID NO:68)**; or
 - (C) **hHER2 MAB-1 VL3 (SEQ ID NO:69)**.
- Claim 9. The **CD137 x TA** Binding Molecule of claim 4, wherein the tumor antigen (**TA**) is 5T4 and wherein the **CD137 x TA** Binding Molecule comprises a second Light Chain Variable Domain that comprises a CDR_{L1}, CDR_{L2} and CDR_{L3}, and a first Heavy Chain Variable Domain that comprises a CDR_{H1}, CDR_{H2} and CDR_{H3}; and wherein:
- (I) (A) the second Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **5T4 MAB-1 VL (SEQ ID NO:135)**; and
 - (B) the second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **5T4 MAB-1 VH (SEQ ID NO:134)**; or
 - (II) (A) the second Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **5T4 MAB-2 VL (SEQ ID NO:137)**; and
 - (B) the second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **5T4 MAB-2 VH (SEQ ID NO:136)**.
- Claim 10. The **CD137 x TA** Binding Molecule of claim 9, wherein the second Heavy Chain Variable Domain comprises the amino acid sequence of: **MAB-1 VH1 (SEQ ID NO:135)**.
- Claim 11. The **CD137 x TA** Binding Molecule of claim 9 or 10 wherein the second Light Chain Variable Domain comprises the amino acid sequence of: **MAB-1 VH1 (SEQ ID NO:136)**.

- Claim 12. The **CD137 x TA** Binding Molecule of any one of claims 1-11, wherein said molecule is a bispecific tetravalent Fc-bearing diabody comprising a first, a second, a third, and a fourth polypeptide chain, wherein said polypeptide chains form a covalently bonded complex.
- Claim 13. The **CD137 x TA** Binding Molecule of any one of claims 1-11, wherein said molecule is bispecific and tetravalent, and comprises a first, a second, a third, a fourth, and a fifth polypeptide chain, wherein said polypeptide chains form a covalently bonded complex.
- Claim 14. The **CD137 x TA** Binding Molecule of any one of claims 1-11, wherein said molecule is bispecific and trivalent, and comprises a first, a second, a third, and a fourth, polypeptide chain, wherein said polypeptide chains form a covalently bonded complex.
- Claim 15. The **CD137 x TA** Binding Molecule of claim 14, wherein said tumor antigen (TA) is HER2/neu and wherein:
- (A) said first polypeptide chain has the amino acid sequence of **SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, or SEQ ID NO:229**;
 - (B) said second polypeptide chain has the amino acid sequence of **SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:163, or SEQ ID NO:230**;
 - (C) said third polypeptide chain has the amino acid sequence of **SEQ ID NO:104**; and
 - (D) said fourth polypeptide chain has the amino acid sequence of **SEQ ID NO:105**.
- Claim 16. The **CD137 x TA** Binding Molecule of claim 14, wherein said tumor antigen (TA) is 5T4 and wherein:
- (A) said first polypeptide chain has the amino acid sequence of **SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, or SEQ ID NO:229**;

- (B) said second polypeptide chain has the amino acid sequence of **SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, or SEQ ID NO:230**;
- (C) said third polypeptide chain has the amino acid sequence of **SEQ ID NO:231**; and
- (D) said fourth polypeptide chain has the amino acid sequence of **SEQ ID NO:232**.

Claim 17. A pharmaceutical composition comprising the **CD137 x TA** Binding Molecule of any one claims 1-16, and a physiologically acceptable carrier.

Claim 18. Use of the **CD137 x TA** Binding Molecule of any one of claims 1-16, or the pharmaceutical composition of claim 17, in the treatment of a disease or condition associated with or characterized by the expression of said tumor antigen (**TA**).

Claim 19. The use of claim 18, wherein said disease or condition associated with or characterized by the expression of said tumor antigen (**TA**) is cancer.

Claim 20. A CD137 binding molecule that comprises a Light Chain Variable Domain that comprises a CDR_{L1}, CDR_{L2} and CDR_{L3}, and a Heavy Chain Variable Domain that comprises a CDR_{H1}, CDR_{H2} and CDR_{H3}; wherein:

- (A)
 - (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL15 (SEQ ID NO:222)**; and
 - (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
- (B)
 - (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL14 (SEQ ID NO:221)**; and
 - (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;

- (C) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL11 (SEQ ID NO:218)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
- (D) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL10 (SEQ ID NO:217)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
- (E) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL6 (SEQ ID NO:213)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
- (F) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL4 (SEQ ID NO:211)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
- (G) (1) said Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL (SEQ ID NO:75)**; and
- (2) said Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH (SEQ ID NO:74)**;

- (H) (1) said Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-4 VL (SEQ ID NO:91)**; and
- (2) said Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-4 VH (SEQ ID NO:90)**;
- (I) (1) said Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-5 VL (SEQ ID NO:97)**; and
- (2) said Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-5 VH (SEQ ID NO:96)**;
- (J) (1) said Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL (SEQ ID NO:75)**; and
- (2) said Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1A (SEQ ID NO:83)**;
- (K) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL (SEQ ID NO:75)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1B (SEQ ID NO:84)**;
- (L) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL (SEQ ID NO:75)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1C (SEQ ID NO:85)**; or

- (M) (1) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-3 VL (SEQ ID NO:75)**; and
- (2) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-3 VH1D (SEQ ID NO:86)**.

Claim 21. The CD137 Binding Molecule of claim 20, wherein said Heavy Chain Variable Domain comprises the amino acid sequence of:

- (A) **hCD137 MAB-3 VH1E (SEQ ID NO:208)**;
- (B) **hCD137 MAB-3 VH1B (SEQ ID NO:84)**;
- (C) **hCD137 MAB-3 VH1A (SEQ ID NO:83)**;
- (D) **hCD137 MAB-3 VH1 (SEQ ID NO:76)**;
- (E) **hCD137 MAB-3 VH1C (SEQ ID NO:85)**;
- (F) **hCD137 MAB-3 VH1D (SEQ ID NO:86)**;
- (G) **hCD137 MAB-3 (SEQ ID NO:77)**; or
- (H) **hCD137 MAB-4 VH1 (SEQ ID NO:92)**.

Claim 22. The CD137 Binding Molecule of any one of claims 20-21, wherein said Light Chain Variable Domain comprises the amino acid sequence of:

- (A) **hCD137 MAB-3 VL15 (SEQ ID NO:222)**;
- (B) **hCD137 MAB-3 VL14 (SEQ ID NO:221)**;
- (C) **hCD137 MAB-3 VL1 (SEQ ID NO:87)**;
- (D) **hCD137 MAB-3 VL2 (SEQ ID NO:88)**;
- (E) **hCD137 MAB-3 VL3 (SEQ ID NO:89)**;
- (F) **hCD137 MAB-3 (SEQ ID NO:82)**;
- (G) **hCD137 MAB-4 VL1 (SEQ ID NO:94)**; or
- (H) **hCD137 MAB-4 VL2 (SEQ ID NO:95)**.

Claim 23. The CD137 Binding Molecule of any one claims 20-22, wherein said molecule is an antibody or an antigen binding fragment thereof.

Claim 24. A pharmaceutical composition comprising the CD137 Binding Molecule of any one claims 20-23, and a physiologically acceptable carrier.

- Claim 25. Use of the CD137 Binding Molecule of any one of claims 20-23, or the pharmaceutical composition of claim 24, in the treatment of a disease or condition associated with a suppressed immune system or characterized by the expression of a tumor antigen (TA).
- Claim 26. The use of claim 25, wherein said condition associated with a suppressed immune system or characterized by the expression of said tumor antigen (TA) is cancer.
- Claim 27. A HER2/neu Binding Molecule that comprises a Light Chain Variable Domain that comprises a CDR_{L1}, CDR_{L2} and CDR_{L3}, and a Heavy Chain Variable Domain that comprises a CDR_{H1}, CDR_{H2} and CDR_{H3}; wherein:
- (A) (1) said Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **HER2 MAB-1 VL (SEQ ID NO:63)**;
- (2) said Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **hHER2 MAB-1 VL1 (SEQ ID NO:67)**;
- (3) said Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **hHER2 MAB-1 VL2 (SEQ ID NO:68)**; or
- (4) said Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **hHER2 MAB-1 VL3 (SEQ ID NO:69)**;
- and
- (B) (1) said Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **HER2 MAB-1 VH (SEQ ID NO:62)**;
- (2) said Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hHER2 MAB-1 VH1 (SEQ ID NO:64)**;
- (3) said Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hHER2 MAB-1 VH2 (SEQ ID NO:65)**; or

- (4) said Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hHER2 MAB-1 VH3** (SEQ ID NO:66).

Claim 28. The HER2/neu Binding Molecule of claim 27, wherein said Heavy Chain Variable Domain comprises the amino acid sequence of:

- (A) **HER2 MAB-1 VH** (SEQ ID NO:62)
- (B) **hHER2 MAB-1 VH1** (SEQ ID NO:64);
- (C) **hHER2 MAB-1 VH2** (SEQ ID NO:65); or
- (D) **hHER2 MAB-1 VH3** (SEQ ID NO:66).

Claim 29. The HER2/neu Binding Molecule of claim 27 or 28, wherein said Light Chain Variable Domain comprises the amino acid sequence of:

- (A) **HER2 MAB-1 VL** (SEQ ID NO:63);
- (B) **hHER2 MAB-1 VL1** (SEQ ID NO:67);
- (C) **hHER2 MAB-1 VL2** (SEQ ID NO:68); or
- (D) **hHER2 MAB-1 VL3** (SEQ ID NO:69).

Claim 30. The HER2/neu Binding Molecule of any one claims 27-29, wherein said molecule is an antibody or an antigen binding fragment thereof.

Claim 31. A pharmaceutical composition comprising the HER2/neu Binding Molecule of any one claims 27-30 and a physiologically acceptable carrier.

Claim 32. Use of the HER2/neu Binding Molecule of any one of claims 27-30, or the pharmaceutical composition of claim 31, in the treatment of a disease or condition associated with or characterized by the expression of HER2/neu.

Claim 33. The use of claim 32, wherein said condition associated with or characterized by the expression of HER2/neu is cancer.

- Claim 34. The use of any one of claims 19, 26, or 33, wherein said cancer is selected from the group consisting: bladder cancer, breast cancer, colorectal cancer, gastric cancer, glioblastoma, kidney cancer, lung cancer, melanoma, neuroblastoma, ovarian cancer, pancreatic cancer, pharyngeal cancer, prostate cancer, renal cell carcinoma, rhabdomyosarcoma, and squamous cell cancer of the head and neck (SCCHN).
- Claim 35. A method of enhancing the activity of a tumor targeting agent comprising administering said tumor target agent in combination with the **CD137 x TA** Binding Molecule of any one of claims 1-16, or the pharmaceutical composition of claim 17.
- Claim 36. A method of treating a disease or condition associated with a suppressed immune system or characterized by the expression of a tumor antigen (TA) comprising administering to a subject in need thereof of the **CD137 x TA** Binding Molecule of any one of claims 1-16, or the pharmaceutical composition of claim 17.
- Claim 37. The method of claim 36, wherein the condition associated with a suppressed immune system or characterized by the expression of the tumor antigen (TA) is cancer.
- Claim 38. The method of claim 36 or 37, further comprising administering a tumor targeting agent.
- Claim 39. The method of any one of claims 36-38, further comprising administering a PD-1/PD-L1 checkpoint inhibitor.
- Claim 40. The method of claim 35 or 38, wherein said tumor target agent is an antibody, an epitope binding fragment of an antibody, or an agent that mediates T-cell redirected killing of a target cell.
- Claim 41. The method of any one of claims 39 or 40, wherein said PD-1/PD-L1 checkpoint inhibitor is an anti-PD-1 antibody or an anti-PD-L1 antibody.