

WHAT IS CLAIMED IS:

- Claim 1. A **CD137 Binding Molecule** comprising a first binding site that immunospecifically binds to an epitope of CD137, wherein said first binding site 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) said first Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **CD137 MAB-6 VL1 (SEQ ID NO:50)**; and
 - (B) said first Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **CD137 MAB-6 VH1 (SEQ ID NO:46)**.
- Claim 2. The **CD137 Binding Molecule** of claim 1, wherein said first Heavy Chain Variable Domain comprises the amino acid sequence of: **hCD137 MAB-6 VH1 (SEQ ID NO:46)**.
- Claim 3. The **CD137 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-6 VL1 (SEQ ID NO:54)**;
 - (B) **hCD137 MAB-6 VL1 (SEQ ID NO:50)**;
 - (B) **hCD137 MAB-6 VL2 (SEQ ID NO:55)**; or
 - (C) **hCD137 MAB-6 VL3 (SEQ ID NO:56)**.
- Claim 4. The **CD137 Binding Molecule** of any one of claims 1-3, wherein:
- (A) said first Heavy Chain Variable Domain comprises the amino acid sequence of: **hCD137 MAB-6 VH1 (SEQ ID NO:46)**; and
 - (B) said first Light Chain Variable Domain comprises the amino acid sequence of: **hCD137 MAB-6 VL3 (SEQ ID NO:56)**.
- Claim 5. The **CD137 Binding Molecule** of any one of claims 1-4, wherein said molecule is a bispecific molecule comprising a second binding site that immunospecifically binds a tumor antigen (**TA**), and wherein said second binding site comprises a second Light Chain Variable Domain that comprises a CDR_{L1}, CDR_{L2} and CDR_{L3}, and a second Heavy Chain Variable Domain that comprises a CDR_{H1}, CDR_{H2} and CDR_{H3}.

- Claim 6. The **CD137 Binding Molecule** of claim 5, wherein said **TA** is selected from the antigens presented in **Tables 1-2**.
- Claim 7. The **CD137 Binding Molecule** of claim 5, wherein said **TA** is PD-L1 and wherein:
- (A) said second Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **hPD-L1 MAB-2 VLx (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 **hPD-L1 MAB-2 VHx (SEQ ID NO:59)**.
- Claim 8. The **CD137 Binding Molecule** of claim 7, wherein:
- (A)
 - (1) said second Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **hPD-L1 MAB-2 VL1 (SEQ ID NO:58)**; or
 - (2) said second Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **hPD-L1 MAB-2 VL2 (SEQ ID NO:72)**;and
 - (B)
 - (1) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hPD-L1 MAB-2 VH1 (SEQ ID NO:57)**;
 - (2) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hPD-L1 MAB-2 VH2 (SEQ ID NO:67)**;
 - (3) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hPD-L1 MAB-2 VH3 (SEQ ID NO:68)**;
 - (4) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hPD-L1 MAB-2 VH2 (SEQ ID NO:69)**;

- (5) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hPD-L1 MAB-2 VH2 (SEQ ID NO:70)**; or
- (6) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hPD-L1 MAB-2 VH2 (SEQ ID NO:71)**.

Claim 9. The **CD137 Binding Molecule** of claim 8, wherein said second Heavy Chain Variable Domain comprises the amino acid sequence of:

- (A) **hPD-L1 MAB-2 VH1 (SEQ ID NO:57)**;
- (B) **hPD-L1 MAB-2 VH2 (SEQ ID NO:67)**;
- (C) **hPD-L1 MAB-2 VH3 (SEQ ID NO:68)**;
- (D) **hPD-L1 MAB-2 VH4 (SEQ ID NO:69)**;
- (E) **hPD-L1 MAB-2 VH5 (SEQ ID NO:70)**; or
- (F) **hPD-L1 MAB-2 VH6 (SEQ ID NO:71)**.

Claim 10. The **CD137 Binding Molecule** of any one of claims 8 or 9, wherein said second Light Chain Variable Domain comprises the amino acid sequence of:

- (A) **hPD-L1 MAB-2 VL1 (SEQ ID NO:58)**; or
- (B) **hPD-L1 MAB-2 VL2 (SEQ ID NO:72)**.

Claim 11. The **CD137 Binding Molecule** of claim 5, wherein the **TA** is 5T4 and wherein:

- (A) (1) said 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:93)**; and
- (2) said 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:92)**; or
- (B) (1) said 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:95)**; and
- (2) said 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:96)**.

- Claim 12. The **CD137 x TA Binding Molecule** of claim 11, wherein the second Heavy Chain Variable Domain comprises the amino acid sequence of: **5T4 MAB-1 VH (SEQ ID NO:92)**.
- Claim 13. The **CD137 x TA Binding Molecule** of claim 11 or 12 wherein the second Light Chain Variable Domain comprises the amino acid sequence of: **5T4 MAB-1 VL (SEQ ID NO:93)**.
- Claim 14. The **CD137 Binding Molecule** of claim 5, wherein the **TA** is HER2 and wherein:
- (A) said second Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **hHER2-MAB-1 VLx (SEQ ID NO:79)**; and
 - (B) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hHER2-MAB-1 VHx (SEQ ID NO:78)**;
- Claim 15. The **CD137 Binding Molecule** of claim 14, 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:83)**;
 - (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:84)**; 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:85)**;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:80)**;
 - (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:81)**; 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:82).

- Claim 16. The **CD137 Binding Molecule** of claim 15, wherein said second Heavy Chain Variable Domain comprises the amino acid sequence of:
- (A) **hHER2-MAB-1 VH1** (SEQ ID NO:80);
 - (B) **hHER2-MAB-1 VH2** (SEQ ID NO:81); or
 - (C) **hHER2-MAB-1 VH3** (SEQ ID NO:82).
- Claim 17. The **CD137 Binding Molecule** of any one of claims 15 or 16, wherein said second Light Chain Variable Domain comprises the amino acid sequence of:
- (A) **hHER2-MAB-1 VL1** (SEQ ID NO:83);
 - (B) **hHER2-MAB-1 VL2** (SEQ ID NO:84); or
 - (C) **hHER2-MAB-1 VL3** (SEQ ID NO:85).
- Claim 18. The **CD137 Binding Molecule** of any one of claims 1-17, which is an antibody or a bispecific tetravalent Fc-bearing diabody, or a bispecific trivalent molecule.
- Claim 19. The **CD137 Binding Molecule** of any one of claims 1-17, wherein said molecule is bispecific and tetravalent, and comprises a first, a second, a third, and a fourth polypeptide chain, wherein said polypeptide chains form a covalently bonded complex.
- Claim 20. The **CD137 Binding Molecule** of any one of claims 1-17, 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 21. The **CD137 Binding Molecule** of claim 19, wherein said **TA** is PD-L1 and wherein:
- (A) said first and third polypeptide chains comprise the amino acid sequence of **SEQ ID NO:116**, **SEQ ID NO:118**, or **SEQ ID NO:120**; and
 - (B) said second and fourth polypeptide chains comprise the amino acid sequence of **SEQ ID NO:117**, **SEQ ID NO:119**, **SEQ ID NO:121**,

SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, or SEQ ID NO:139.

Claim 22. The **CD137 Binding Molecule** of claim 21, wherein said molecule comprises:

- (A) **SEQ ID NO:116 and SEQ ID NO:117;**
- (B) **SEQ ID NO:118 and SEQ ID NO:119;**
- (C) **SEQ ID NO:120 and SEQ ID NO:119;**
- (D) **SEQ ID NO:118 and SEQ ID NO:121;**
- (E) **SEQ ID NO:120 and SEQ ID NO:121;**
- (F) **SEQ ID NO:120 and SEQ ID NO:122;**
- (G) **SEQ ID NO:120 and SEQ ID NO:123;**
- (H) **SEQ ID NO:120 and SEQ ID NO:124;**
- (I) **SEQ ID NO:120 and SEQ ID NO:125;**
- (J) **SEQ ID NO:120 and SEQ ID NO:126; or**
- (K) **SEQ ID NO:120 and SEQ ID NO:139.**

Claim 23. The **CD137 Binding Molecule** of claim 20, wherein said **TA** is PD-L1 and wherein:

- (A) said first polypeptide chain comprises the amino acid sequence of **SEQ ID NO:127, SEQ ID NO:133, or SEQ ID NO:135;**
- (B) said second polypeptide chain comprises the amino acid sequence of **SEQ ID NO:128, SEQ ID NO:134, or SEQ ID NO:136;**
- (C) said third polypeptide chain comprises the amino acid sequence of **SEQ ID NO:129, or SEQ ID NO:131; and**
- (D) said fourth polypeptide chain comprises the amino acid sequence of **SEQ ID NO:130, SEQ ID NO:132.**

Claim 24. The **CD137 Binding Molecule** of claim 23, wherein said molecule comprises:

- (A) **SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, and SEQ ID NO:130;**
- (B) **SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:131, and SEQ ID NO:132;**
- (C) **SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:131, and SEQ ID NO:132; or**

(D) **SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:131, and SEQ ID NO:132.**

Claim 25. A pharmaceutical composition comprising the **CD137 Binding Molecule** of any one claims 1-24, and a physiologically acceptable carrier.

Claim 26. Use of the **CD137 Binding Molecule** of any one of claims 6-24, or the pharmaceutical composition of claim 25, in the treatment of a disease or condition associated with or characterized by the expression of said **TA**.

Claim 27. A **PD-L1 Binding Molecule** comprising 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) said Light Chain Variable Domain CDR_{L1}, CDR_{L2}, and CDR_{L3} are the Light Chain CDRs of **hPD-L1 MAB-2 VL2 (SEQ ID NO:72)**;

and

(B) (1) said Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hPD-L1 MAB-2 VH2 (SEQ ID NO:67)**;

(2) said Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hPD-L1 MAB-2 VH3 (SEQ ID NO:68)**

(3) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hPD-L1 MAB-2 VH4 (SEQ ID NO:69)**

(4) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hPD-L1 MAB-2 VH5 (SEQ ID NO:70)**; or

(5) said second Heavy Chain Variable Domain CDR_{H1}, CDR_{H2}, and CDR_{H3} are the Heavy Chain CDRs of **hPD-L1 MAB-2 VH6 (SEQ ID NO:71)**.

Claim 28. The **PD-L1 Binding Molecule** of claim 27, wherein said Heavy Chain Variable Domain comprises the amino acid sequence of:

(A) **hPD-L1 MAB-2 VH2 (SEQ ID NO:67)**;

- (B) **hPD-L1 MAB-2 VH3 (SEQ ID NO:68);**
- (C) **hPD-L1 MAB-2 VH4 (SEQ ID NO:69);**
- (D) **hPD-L1 MAB-2 VH5 (SEQ ID NO:70);** or
- (E) **hPD-L1 MAB-2 VH6 (SEQ ID NO:71).**

- Claim 29. The **PD-L1 Binding Molecule** of any one of claims 27-28, wherein said Light Chain Variable Domain comprises the amino acid sequence of **hPD-L1 MAB-2 VL2 (SEQ ID NO:72)**.
- Claim 30. The **PD-L1 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 **PD-L1 Binding Molecule** of any one claims 27-30, and a physiologically acceptable carrier.
- Claim 32. Use of the **PD-L1 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 a suppressed immune system or characterized by the expression of PD-L1.
- Claim 33. The use of claim 32, wherein said disease or condition associated with a suppressed immune system or characterized by the expression of PD-L1 is cancer.
- Claim 34. The use of any one of claims 26, or 33, wherein said cancer is selected from the group consisting: bladder cancer, bone cancer, a brain and spinal cord cancer, breast cancer, cervical cancer, colorectal cancer, gallbladder or bile duct cancer, gastric cancer, glioblastoma, head and neck cancer, hepatocellular carcinoma, kidney cancer, leukemia, liver cancer, lung cancer, melanoma, neuroblastoma, non-small cell lung cancer (NSCLC), ovarian cancer, pancreatic cancer, pharyngeal cancer, prostate cancer, renal cell carcinoma, rhabdomyosarcoma, skin cancer, squamous cell cancer of the head and neck (SCCHN), stomach cancer, testicular cancer, thymic carcinoma, and uterine cancer.
- Claim 35. A method of enhancing the activity of a tumor targeting agent comprising administering said tumor target agent in combination with the **CD137 Binding**

Molecule of any one of claims 1-24, the **PD-L1 Binding Molecule** of any one of claims 27-30, or the pharmaceutical composition of any one of claims 25 or 31. Claim 36. A method of treating a disease or condition associated with a suppressed immune system or characterized by the expression of a **TA** comprising administering to a subject in need thereof of the **CD137 Binding Molecule** of any one of claims 1-24, the **PD-L1 Binding Molecule** of any one of claims 27-30, or the pharmaceutical composition of claim 25 or 31.

- Claim 37. The method of claim 36, wherein the condition associated with a suppressed immune system or characterized by the expression of the **TA** is cancer.
- Claim 38. The method of claim 36 or 37, further comprising administering a tumor targeting agent.
- Claim 39. 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 40. The method of any one of claims 36-38, wherein the cancer is selected from the group consisting: bladder cancer, bone cancer, a brain and spinal cord cancer, breast cancer, cervical cancer, colorectal cancer, gallbladder or bile duct cancer, gastric cancer, glioblastoma, head and neck cancer, hepatocellular carcinoma, kidney cancer, leukemia, liver cancer, lung cancer, melanoma, neuroblastoma, non-small cell lung cancer (NSCLC), ovarian cancer, pancreatic cancer, pharyngeal cancer, prostate cancer, renal cell carcinoma, rhabdomyosarcoma, skin cancer, squamous cell cancer of the head and neck (SCCHN), stomach cancer, testicular cancer, thymic carcinoma, and uterine cancer.
- Claim 41. A nucleic acid encoding the **CD137 Binding Molecule** of any one of claims 1-24, or the **PD-L1 Binding Molecule** of any one of claims 27-30.
- Claim 42. An expression vector comprising a nucleic acid according to claim 41.
- Claim 43. A cell comprising a nucleic acid according to claim 41 or an expression vector according to claim 42.

Claim 44. The cell according to claim 43, wherein said cell is a mammalian cell.