

[0014] In detail, in one example, the present disclosure refers to 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 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)**;
- (B) (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)**;
- (C) (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)**;
- (D) (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)**;
- (E) (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)**;
- (F) (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

- (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)**.

[0014a] In one aspect, the present disclosure refers to a **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 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)**;
- (B) (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)**;
- (C) (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)**;
- (D) (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)**;

- (E) (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)**;
 - (F) (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)**;
 - (G) (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)**;
 - (H) (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)**;
 - (I) (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
- (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 VH1D** (SEQ ID NO:86).

[0015] The disclosure further concerns such a **CD137 x TA** Binding Molecule, wherein the first Heavy Chain Variable Domain comprises the amino acid sequence of:

- (A) **hCD137 MAB-3** (SEQ ID NO:77); or
- (B) **hCD137 MAB-4** (SEQ ID NO:92);

and/or wherein the first Light Chain Variable Domain comprises the amino acid sequence of:

- (A) **hCD137 MAB-3** (SEQ ID NO:82); or
- (B) **hCD137 MAB-4** (SEQ ID NO:93).

[0016] The disclosure further concerns such a **CD137 x TA** Binding Molecule, wherein the 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 VH1F** (SEQ ID NO:209);
- (H) **hCD137 MAB-3 VH1G** (SEQ ID NO:210); or
- (I) **hCD137 MAB-4 VH1** (SEQ ID NO:92).

[0017] The disclosure further concerns such **CD137 x TA** Binding Molecules, wherein the 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 VL4** (SEQ ID NO:211);
- (G) **hCD137 MAB-3 VL5** (SEQ ID NO:212);
- (H) **hCD137 MAB-3 VL6** (SEQ ID NO:213);

[0032] The disclosure further concerns such a **CD137 x TA** Binding Molecule, 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, or SEQ ID NO:196;**
- (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, or SEQ ID NO:201;**
- (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.**

[0033] The disclosure further concerns such a **CD137 x TA** Binding Molecule, 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.**

[0034] In one aspect, the present disclosure further refers to a pharmaceutical composition comprising any of the above-described **CD137 x TA** Binding Molecules and a physiologically acceptable carrier.

[0035] The disclosure further concerns the use of any of the above-described **CD137 x TA** Binding Molecules or such pharmaceutical composition in the treatment of a disease or condition associated with or characterized by the expression of the tumor antigen (TA), and particularly wherein the disease or condition associated with or characterized by the expression of the tumor antigen (TA) is cancer. In one aspect, the present disclosure refers to the use of any of the above-described **CD137 x TA** Binding Molecules or pharmaceutical composition in the manufacture of a medicament for the treatment of a cancer.

[0036] In another example, the present disclosure further refers to 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 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)**;
- (B) (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)**;
- (C) (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)**;
- (D) (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)**;
- (E) (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)**;
- (F) (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)**;
- (G) (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)**;
- (H) (1) the 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) the 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)**;

- (I) (1) the 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) the 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)**;
- (J) (1) the 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) the 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)**;
- (K) (1) the 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) the 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)**;
- (L) (1) the 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) the 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) the 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) the 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)**.

[0036a] In one aspect, the present disclosure refers to a 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 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)**;

- (B) (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)**;
- (C) (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)**;
- (D) (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)**;
- (E) (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)**;
- (F) (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)**;
- (G) (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)**;

- (H) (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)**;
- (I) (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
- (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 VH1D (SEQ ID NO:86)**.

[0037] The disclosure further concerns the example of such a CD137 binding molecule, wherein the Heavy Chain Variable Domain comprises the amino acid sequence of:

- (A) **hCD137 MAB-3 (SEQ ID NO:77)**; or
- (B) **hCD137 MAB-4 (SEQ ID NO:92)**.

- (P) **hCD137 MAB-4 VL1 (SEQ ID NO:94)**; or
(Q) **hCD137 MAB-4 VL2 (SEQ ID NO:95)**.

[0041] The disclosure further concerns the example of such CD137 binding molecules, wherein the molecule is an antibody or an antigen binding fragment thereof

[0042] In one aspect, the present disclosure further refers to a pharmaceutical composition comprising any of the above-described CD137 Binding Molecules, and a physiologically acceptable carrier.

[0043] The disclosure further concerns the use of any of the above-described CD137 Binding Molecules, or such pharmaceutical composition, in the treatment of a disease or condition associated with a suppressed immune system or characterized by the expression of a tumor antigen (TA). In one aspect, the present disclosure refers to the use of any of the above-described CD137 Binding Molecules, or pharmaceutical composition, in the manufacture of a medicament for the treatment of a cancer.

[0044] The disclosure further concerns such use wherein the condition associated with a suppressed immune system or characterized by the expression of the tumor antigen (TA) is cancer.

[0044a] In one example, the present disclosure refers to 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)**.

[0045] The disclosure further concerns 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) the 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) the 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)**.

[0046] The disclosure further concerns the example of such HER2/neu Binding Molecules wherein:

- (A) (1) the 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) the 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) the 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) the 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) the 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) the 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)**.

[0047] The disclosure further concerns the example of such HER2/neu Binding Molecules wherein the 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)**.

[0048] The disclosure further concerns the example of such HER2/neu Binding Molecules wherein the 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)**.

[0049] The disclosure further concerns the example of such HER2/neu Binding Molecules wherein the molecule is an antibody or an antigen binding fragment thereof.

[0050] In one example, the present disclosure further refers to a pharmaceutical composition comprising any of the above-described HER2/neu Binding Molecules and a physiologically acceptable carrier

[0051] The disclosure further concerns the use of any of the above-described HER2/neu Binding Molecule, or such pharmaceutical composition, in the treatment of a disease or condition associated with or characterized by the expression of HER2/neu, and particularly wherein the condition associated with or characterized by the expression of HER2/neu is cancer. In one example, the present disclosure refers to use of any of the above-described HER2/neu Binding Molecule, or pharmaceutical composition, in the manufacture of a medicament for the treatment of a disease or condition associated with or characterized by the expression of HER2/neu.

[0051a] In one aspect, the present disclosure refers to use of a tumor targeting agent in the manufacture of a medicament for enhancing the activity of the tumor targeting agent, wherein the medicament is to be administered in combination with any of the above-described **CD137 x TA** Binding Molecules, or pharmaceutical composition.

[0052] The disclosure further concerns methods of enhancing the activity of a tumor targeting agent comprising administering such tumor target agent in combination with the any of the above-described **CD137 x TA** Binding Molecules, or a pharmaceutical composition comprising the same. The disclosure further concerns such methods further comprising administering a PD-1/PD-L1 checkpoint inhibitor and particularly wherein such checkpoint

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 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)**;
 - (B) (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)**;
 - (C) (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)**;
 - (D) (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)**;
 - (E) (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)**;
- (F)
 - (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)**;
- (G)
 - (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)**;
- (H)
 - (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)**;
- (I)
 - (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
- (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 VH1D (SEQ ID NO:86)**.

Claim 2. The **CD137 x TA** Binding Molecule of claim 1, 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 VH1C (SEQ ID NO:85); or**
- (E) **hCD137 MAB-3 VH1D (SEQ ID NO:86).**

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); or**
- (B) **hCD137 MAB-3 VL3 (SEQ ID NO:89).**

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 second 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) 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) 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)**.
- Claim 7. The **CD137 x TA** Binding Molecule of claim 6, wherein said second Heavy Chain Variable Domain comprises the amino acid sequence of **MAB-1 VH1 (SEQ ID NO:64)**.
- 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 **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 second Heavy Chain Variable Domain that comprises a CDR_{H1}, CDR_{H2} and CDR_{H3}; and wherein:
- (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)**.
- 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:134)**.
- 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 VL1 (SEQ ID NO:135)**.

- 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:193** and said second polypeptide has the amino acid sequence of **SEQ ID NO:198**; or said first polypeptide chain has the amino acid sequence of **SEQ ID NO:194** and said second polypeptide has the amino acid sequence of **SEQ ID NO:199**; or said first polypeptide chain has the amino acid sequence of **SEQ ID NO:195** and said second polypeptide has the amino acid sequence of **SEQ ID NO:200**; or said first polypeptide chain has the amino acid sequence of **SEQ ID NO:196** and said second polypeptide has the amino acid sequence of **SEQ ID NO:201**; or said first polypeptide chain has the amino acid sequence of **SEQ ID NO:229** and said second polypeptide has the amino acid sequence of **SEQ ID NO:230**;
 - (B) said third polypeptide chain has the amino acid sequence of **SEQ ID NO:104**; and
 - (C) 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:229**;
- (B) said second polypeptide chain has the amino acid sequence of **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 manufacture of a medicament for the treatment of a cancer.

Claim 19. 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 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)**;
- (B)
 - (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)**;
- (C)
 - (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)**;

- (D) (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)**;
- (E) (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)**;
- (F) (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)**;
- (G) (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)**;
- (H) (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)**;
- (I) (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

- (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 VH1D (SEQ ID NO:86)**.

Claim 20. The CD137 Binding Molecule of claim 19, 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 VH1C (SEQ ID NO:85)**; or
- (E) **hCD137 MAB-3 VH1D (SEQ ID NO:86)**.

Claim 21. The CD137 Binding Molecule of any one of claims 19-20, wherein said Light Chain Variable Domain comprises the amino acid sequence of:

- (A) **hCD137 MAB-3 VL15 (SEQ ID NO:222)**; or
- (B) **hCD137 MAB-3 VL3 (SEQ ID NO:89)**.

Claim 22. The CD137 Binding Molecule of any one claims 19-21, wherein said molecule is an antibody or an antigen binding fragment thereof.

Claim 23. A pharmaceutical composition comprising the CD137 Binding Molecule of any one claims 19-22, and a physiologically acceptable carrier.

Claim 24. Use of the CD137 Binding Molecule of any one of claims 19-22, or the pharmaceutical composition of claim 23, in the manufacture of a medicament for the treatment of a cancer.

Claim 25. The use of claim 18, wherein the medicament is to be administered with a tumor targeting agent.

Claim 26. The use of claim 25, wherein said tumor targeting 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 27. The use of any one of claims 18, 25 and 26, wherein the medicament is to be administered with a PD-1/PD-L1 checkpoint inhibitor.

- Claim 28. The use of claim 27, wherein said PD-1/PD-L1 checkpoint inhibitor is an anti-PD-1 antibody or an anti-PD-L1 antibody.
- Claim 29. The use of any one of claims 18 and 24-28, wherein said cancer is selected from the group consisting of: 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).