

Claims

1. An anti-CTLA4 antibody comprising: (a) a light chain variable region comprising (i) a complementarity determining region 1 (CDR1) comprising the amino acid sequence set forth in SEQ ID NO: 21, (ii) a CDR2 region comprising the amino acid sequence set forth in SEQ ID NO: 36, 37 or 38, and (iii) a CDR3 region comprising the amino acid sequence set forth in SEQ ID NO: 23; and, (b) a heavy chain variable region comprising (i) a CDR1 region comprising the amino acid sequence set forth in SEQ ID NO: 24, (ii) a CDR2 region comprising the amino acid sequence set forth in SEQ ID NO: 33, 34 or 35, and (iii) a CDR3 region comprising the amino acid sequence set forth in SEQ ID NO: 26.
2. The anti-CTLA4 antibody of claim 1, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 62, 63 or 64; and (b) the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 70, 71 or 72.
3. The anti-CTLA4 antibody of claim 1, wherein, (a) the light chain CDR2 region comprises the amino acid sequence set forth in SEQ ID NO: 37 and the heavy chain CDR2 region comprises the amino acid sequence set forth in SEQ ID NO: 33; (b) the light chain CDR2 region comprises the amino acid sequence set forth in SEQ ID NO: 37 and the heavy chain CDR2 region comprises the amino acid sequence set forth in SEQ ID NO: 35; or, (c) the light chain CDR2 region comprises the amino acid sequence set forth in SEQ ID NO: 38 and the heavy chain CDR2 region comprises the amino acid sequence set forth in SEQ ID NO: 35.
4. The anti-CTLA4 antibody of claim 3, wherein the heavy chain comprises the amino acid sequence set forth in SEQ ID NO: 62 and the light chain comprises the amino acid sequence set forth in SEQ ID NO: 71.
5. The anti-CTLA4 antibody of claim 3, wherein the heavy chain comprises the amino acid sequence set forth in SEQ ID NO: 64 and the light chain comprises the amino acid sequence set forth in SEQ ID NO: 71.

6. The anti-CTLA4 antibody of claim 3, wherein the heavy chain comprises the amino acid sequence set forth in SEQ ID NO: 64 and the light chain comprises the amino acid sequence set forth in SEQ ID NO: 72.
7. The anti-CTLA4 antibody of any one of claims 1-6, wherein the antibody is
5 characterized by reduced binding to soluble CTLA4.
8. An antigen binding fragment of the anti-CTLA4 antibody of any one of claims 1-7.
9. A pharmaceutical composition comprising a therapeutically effective amount of the anti-CTLA4 antibody or antigen binding fragment of any one of claims 1-8, and a physiologically acceptable carrier or excipient.
10. The pharmaceutical composition of claim 9 for use in the manufacture of a
10 medicament for treating cancer in a subject.
11. The pharmaceutical composition for use of claim 10, the medicament further comprising an additional agent selected from the group consisting of anti-PD-1 and anti-4-1BB antibodies.
12. The pharmaceutical composition for use of claim 11, wherein the anti-PD-1 or anti-
15 4-1BB antibodies, and the anti-CTLA4 antibody are combined in a single molecule as bi-specific antibodies.
13. The pharmaceutical composition for use of claim 12, wherein the pharmaceutical
20 composition induces strong deletion of Treg and local T cell activation in tumor microenvironment but minimal systemic T cell activation.