

CLAIMS

~~1. A method of generating an anti-CTLA-4 antibody with reduced binding to CTLA-4 at acidic pH, comprising replacing tyrosine with histidine within or near one or more CDR1-3 regions of at least one of a light chain and heavy chain variable region of the antibody.~~

~~2. An anti-CTLA-4 antibody variant with reduced binding to CTLA-4 at acidic pH, wherein the anti-CTLA-4 antibody comprises the amino acid sequence of Tremelimumab or Ipilimumab in which one or more tyrosine residues in at least one of a light chain and heavy chain variable region is replaced with histidine.~~

~~3.1. An anti-CTLA-4 antibody comprising a heavy chain comprising the sequence set forth in SEQ ID NO: 4, 3, 5, 6 or 8, and a light chain comprising the sequence set forth in SEQ ID NO: 2 or 4.~~

~~4.2. The anti-CTLA-4 antibody of claim 3.1, comprising a heavy chain comprising the sequence set forth in SEQ ID NO: 6, and a light chain comprising the sequence set forth in SEQ ID NO: 2.~~

~~5.3. An anti-CTLA-4 antibody comprising a heavy chain comprising the sequence set forth in one of SEQ ID NOS: 14-18, and a light chain comprising the sequence set forth in one of SEQ ID NOS: 10-12.~~

~~6.4. Use of the anti-CTLA-4 antibody of any one of the preceding claims in the manufacture of a medicament for cancer immunotherapy, wherein the anti-CTLA-4 antibody is to be used either alone or in combination with one or more other therapies.~~

~~7.5. The use of claim 6.4, wherein the other therapy is an antibody that binds to PD-1 or PD-L1.~~

~~8.6. The use of claim 7.5, wherein the anti-PD-1 antibody is Nivolumab or Pembrolizumab.~~

~~9.7. Use of an anti-CTLA-4 antibody of any one of claims 1-5 in the manufacture of a medicament for treating cancer.~~