CLAIMS:

1. A use of a monoclonal antibody which binds human PD-1 in the manufacture of a medicament in the treatment of cancer,

wherein the IgG Fc region of the antibody is an IgG4 Fc region containing an amino acid mutation at position 228 and at least one additional amino acid mutation, wherein the at least one additional mutation causes the antibody to exhibit reduced binding to at least one Fcγ receptor relative to Fc binding of a reference IgG4 antibody having a mutation at position 228 and no other Fc region mutation, and

wherein the numbering of the residues in the IgG4 Fc region is that of the EU numbering system.

2. The use according to claim **1,** wherein the position of the at least one additional amino acid mutation is selected from the group consisting of positions 233, 234, 235, 265, 309, and 409.

3. The use according to claim **1,** wherein the IgG Fc region of the antibody contains at least two amino acid mutations in addition to the mutation at position 228.

4. The use according to claim **1,** wherein the at least one additional amino acid mutation comprises mutations at positions 233, 234, and 235.

5. The use according to claim **1,** wherein the at least one additional amino acid mutation comprises mutations at positions 233, 234, 235, and 265.

6. The use according to claim **1,** wherein the at least one additional amino acid mutation comprises mutations at positions 233, 234, 235, 265, 309, and 409.

7. The use according to claim **1,** wherein the at least one additional amino acid mutation comprises E233P, F234V and L235A.

8. The use according to claim **1,** wherein the amino acid mutation at position 228 is S228R and the at least one additional amino acid mutation comprises E233P, F234V and L235A.

9. The use according to claim **1,** wherein the binding of the IgG4 Fc region of the antibody to one or more Fcγ receptors is reduced to null.

10. The use according to claim **1,** wherein the at least one Fcγ receptor is selected from FcγRI, FcγRIIA, FcγRIIB, and Fcγ RIIIA.

11. The use according to claim **1,** wherein the antibody exhibits reduced effector function relative to the reference IgG4 antibody.

12. The use according to claim **6,** wherein the reduced effector function is antibody-dependent cell-mediated cytotoxicity (ADCC).

13. The use according to claim **1,** wherein the mutation at position 228 is S228P.

14. The use according to claim **1,** wherein the at least one additional amino acid mutation is selected from the group consisting of E233P, F234Y L235A, D265A, L309Y and R409K, or a combination thereof.

15. The use according to claim **1,** wherein the cancer is selected from lung cancer, liver cancer, stomach cancer, breast cancer, ovarian cancer, pancreatic cancer, esophageal cancer, and melanoma.

16. The use according to claim **1,** wherein the antibody exhibits anti-tumor activity.

17. The use according to claim **1,** wherein the administration of the antibody inhibits tumor progression in the subject.

18. The use according to claim **1,** wherein the administration of the antibody suppresses PD-1 mediated signal transduction.

19. A monoclonal antibody which binds human PD-1, comprising,

a PD-1 binding domain, and

an IgG4 Fc region comprising amino acid mutations at positions 228, 233, 234, and 235,

wherein the mutations at positions 233, 234, and 235 cause the antibody to exhibit reduced binding to at least one Fcγ receptor relative to Fc binding of a reference IgG4 antibody having a mutation at position 228 and no other Fc region mutation, and

wherein the numbering of the residues in the IgG4 Fc region is that of the EU numbering system.

20. The antibody of claim **19,** wherein the IgG4 Fc region comprising amino acid mutations at positions 228, 233, 234, 235, and 265.

21. The antibody of claim **19,** wherein the IgG4 Fc region comprising amino acid mutations at positions 228, 233, 234, 235, 265, 309, and 409.

22. The antibody of claim **19,** wherein the IgG4 Fc region comprising amino acid mutations of S228P, E233P, F234Y and L235A.