What is claimed is:

Claim 1. A Variant Chimeric 4D5 Antibody in combination with a molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint, for use in combination therapy for the treatment of cancer in a subject in need thereof, wherein:

(a) said Variant Chimeric 4D5 Antibody comprises a light chain variable domain comprising the amino acid sequence of **SEQ ID NO:4,** and a heavy chain that comprises a variant Fc Region having at least one modification in the Fc Region that enhances ADCC activity relative to a wild-type IgG1 Fc Region, wherein said heavy chain comprises an amino acid sequence selected from the group consisting of **SEQ ID NO:9**, **SEQ ID NO:11**, and **SEQ ID NO:13**; and

(b) said molecule that specifically binds a cell-surface receptor, or said ligand thereof, that regulates an immune checkpoint is an anti-PD-1 antibody or antigen-binding fragment thereof that comprises an Fc Region that exhibits reduced ADCC activity relative to a wild-type IgG1 Fc Region.

Claim 2. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to claim 1, wherein said anti-PD-1 antibody, or antigen-binding fragment thereof:

(a) comprises the three heavy chain CDRs and the three light chain CDRs of: nivolumab, pembrolizumab, pidilizumab, antibody EH12.2H7, antibody hPD-1 mAb 2, antibody hPD-1 mAb 7, antibody hPD-1 mAb 9, antibody hPD-1 mAb 15, or antibody PD-1 mAb 6-ISQ, wherein said CDRs are according to Kabat; or

(b) comprises the heavy chain variable domain and the light chain variable domain of said nivolumab, pembrolizumab, pidilizumab, antibody EH12.2H7, antibody hPD-1 mAb 2, antibody hPD-1 mAb 7, antibody hPD-1 mAb 9, antibody hPD-1 mAb 15, or antibody PD-1 mAb 6-ISQ.

Claim 3. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to claims 1 or 2, wherein said anti-PD-1 antibody or antigen-binding fragment thereof, comprises a variant Fc Region having at least one modification in the Fc Region that reduces ADCC activity.

Claim 4. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to claims 1 or 2, wherein said anti-PD-1 antibody or antigen-binding fragment thereof, comprises an IgG4 Fc Region.

Claim 5. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to claim 4, wherein said anti-PD-1 antibody or antigen-binding fragment thereof, comprises a variant IgG4 Hinge comprising a stabilizing substitution.

Claim 6. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to claim 5, wherein said anti-PD-1 antibody or antigen-binding fragment thereof, comprises a variant IgG4 Hinge comprising an S228P substitution, numbered according to Kabat.

Claim 7. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-6, wherein:

(a) said Variant Chimeric 4D5 Antibody is for administration at a dosage of 6-18 mg/kg and said anti-PD-1 antibody is for administration at a fixed dosage of 100-500 mg; or

(b) said Variant Chimeric 4D5 Antibody is for administration at a dosage of 6-18 mg/kg and said anti-PD-1 antibody is for administration at a dosage of 1-10 mg/kg.

Claim 8. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-7, wherein said Variant Chimeric 4D5 Antibody and said molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint are for administration every three weeks.

Claim 9. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for

the use according to claim 8, wherein said Variant Chimeric 4D5 Antibody is for administration at a dosage of 15 mg/kg.

Claim 10. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-9, wherein said anti-PD-1 is for administration at a dosage selected from 1 mg/kg, 2 mg/kg, 3 mg/kg, 10 mg/kg, and a fixed dosage of approximately 200 mg.

Claim 11. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-10, wherein said Variant Chimeric 4D5 Antibody and said molecule that specifically binds a cell-surface receptor, or ligand thereof, that regulates an immune checkpoint are for concurrent administration in a single pharmaceutical composition.

Claim 12. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-10, wherein said Variant Chimeric 4D5 Antibody and said molecule that specifically binds a cell-surface receptor, or ligand thereof, that regulates an immune checkpoint are for administration in separate pharmaceutical compositions within a 24-hour period of each other.

Claim 13. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-10, wherein one of said Variant Chimeric 4D5 Antibody and said molecule that specifically binds a cell-surface receptor, or ligand thereof, that regulates an immune checkpoint is for administration at least 24 hours, or more, after the administration of the other of said Variant Chimeric 4D5 Antibody and said molecule that specifically binds a cell-surface receptor, or ligand thereof, that regulates an immune checkpoint.

Claim 14. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-10, wherein said cancer is a cancer in which HER2/neu is expressed.

Claim 15. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to claim 14, wherein said cancer is a breast cancer, gastric cancer, prostate cancer, uterine cancer, ovarian cancer, colon cancer, endometrial cancer, adrenal carcinoma, non-small cell lung cancer, head and neck cancer, laryngeal cancer, liver cancer, renal cancer, glioblastoma, or pancreatic cancer.

Claim 16. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-15, in further combination with a third therapeutic agent selected from the group consisting of an anti-angiogenic agent, an anti-neoplastic agent, a chemotherapeutic agent, and a cytotoxic agent.

Claim 17. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to claim 16, wherein the third therapeutic agent is for concurrent administration with said Variant Chimeric 4D5 Antibody and/or said molecule that specifically binds a cell-surface receptor, or ligand thereof, that regulates an immune checkpoint.

Claim 18. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to claim 16, wherein the third therapeutic agent is for administration separately from said Variant Chimeric 4D5 Antibody and/or said molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint.

Claim 19. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-18, wherein said Variant Chimeric 4D5 Antibody is margetuximab.

Claim 20. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-19, wherein said anti-PD-1 antibody is pembrolizumab.

Claim 21. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-19, wherein said anti-PD-1 antibody is nivolumab.

Claim 22. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-19, wherein said anti-PD-1 antibody is pidilizumab.

Claim 23. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-19, wherein said anti-PD-1 antibody comprises the heavy chain variable domain of **SEQ ID NO:53** and the light chain variable domain of **SEQ ID NO:57**.

Claim 24. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-19, wherein said anti-PD-1 antibody comprises the heavy chain variable domain of **SEQ ID NO:61** and the light chain variable domain of **SEQ ID NO:65**.

Claim 25. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-19, wherein said anti-PD-1 antibody comprises the heavy chain variable domain of **SEQ ID NO:69** and the light chain variable domain of **SEQ ID NO:73**.

Claim 26. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-19, wherein said anti-PD-1 antibody comprises the heavy chain variable domain of **SEQ ID NO:77** and the light chain variable domain of **SEQ ID NO:81**.

Claim 27. The Variant Chimeric 4D5 Antibody and the molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint for the use according to any one of claims 1-19, wherein said anti-PD-1 antibody comprises the heavy chain of **SEQ ID NO:88** and the light chain of **SEQ ID NO:87**.

Claim 28. Use of a Variant Chimeric 4D5 Antibody in combination with a molecule that specifically binds a cell-surface receptor, or a ligand thereof, that regulates an immune checkpoint, in the manufacture of a medicament for the treatment of cancer in a subject in need thereof, wherein:

(a) said Variant Chimeric 4D5 Antibody comprises a light chain variable domain comprising the amino acid sequence of **SEQ ID NO:4,** and a heavy chain that comprises a variant Fc Region having at least one modification in the Fc Region that enhances ADCC activity relative to a wild-type IgG1 Fc Region, wherein said heavy chain comprises an amino acid sequence selected from the group consisting of **SEQ ID NO:9**, **SEQ ID NO:11**, and **SEQ ID NO:13**; and

(b) said molecule that specifically binds a cell-surface receptor, or said ligand thereof, that regulates an immune checkpoint is an anti-PD-1 antibody or antigen-binding fragment thereof comprises an Fc Region that exhibits reduced ADCC activity relative to a wild-type IgG1 Fc Region.