CLAIMS

1. An isolated antibody molecule capable of binding to human Programmed Death-1 (PD-1), comprising:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 33;

(b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 32;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 224, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 33; or

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 224; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 32.

2. The antibody molecule of claim 1, wherein said antibody molecule is a humanized antibody molecule, and/or a monospecific antibody molecule or a bispecific antibody molecule.

3. The antibody molecule of claim 1 or 2, which has:

a VH comprising at least one, two, three, or four framework (FW) regions comprising the amino acid sequence of any of SEQ ID NOs: 147, 151, 153, 157, 160, 162, 166, or 169, or an amino acid sequence at least 90% identical thereto, or having no more than two amino acid substitutions, insertions or deletions compared to the amino acid sequence of any of SEQ ID NOs: 147, 151, 153, 157, 160, 162, 166, or 169; and/or

a VL comprising at least one, two, three, or four framework regions comprising the amino acid sequence of any of SEQ ID NOs: 174, 177, 181, 183, 185, 187, 191, 194, 196, 200, 202, 205, or 208, or an amino acid sequence at least 90% identical thereto, or having no more than two amino acid substitutions, insertions or deletions compared to the amino acid sequence of any of SEQ ID NOs: 174, 177, 181, 183, 185, 187, 191, 194, 196, 200, 202, 205, or 208.

4. The antibody molecule of any of claims 1-3, which comprises:

a VH comprising an amino acid sequence of SEQ ID NO: 38, 50, 82, or 86, or an amino acid sequence of at least 85% identical to any of SEQ ID NOs: 38, 50, 82, or 86; and/or

a VL comprising an amino acid sequence of SEQ ID NO: 42, 46, 54, 58, 62, 66, 70, 74, or 78, or an amino acid sequence at least 85% identical to any of SEQ ID NOs: 42, 46, 54, 58, 62, 66, 70, 74, or 78.

5. The antibody molecule of any one of claims 1-4, which comprises:

a VH comprising an amino acid sequence chosen from SEQ ID NO: 38; SEQ ID NO: 50, SEQ ID NO: 82, or SEQ ID NO: 86; and/or

a VL comprising an amino acid sequence chosen from SEQ ID NO: 42, SEQ ID NO: 46, SEQ ID NO: 54; SEQ ID NO: 58; SEQ ID NO: 62; SEQ ID NO: 66; SEQ ID NO: 70; SEQ ID NO: 74, or SEQ ID NO: 78.

6. The antibody molecule of any of claims 1-4, which comprises:

a heavy chain comprising an amino acid sequence chosen from SEQ ID NO: 40, SEQ ID NO: 91, SEQ ID NO: 52, SEQ ID NO: 102, SEQ ID NO: 84, or SEQ ID NO: 88; and/or

a light chain comprising an amino acid sequence chosen from SEQ ID NO: 44, SEQ ID NO: 48, SEQ ID NO: 56, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 68, SEQ ID NO: 72, SEQ ID NO:76, or SEQ ID NO: 80.

7. The antibody molecule of any of claims 1-4, which comprises:

(a) a VH comprising the amino acid sequence of SEQ ID NO: 38 and a VL comprising the amino acid sequence of SEQ ID NO: 42;

(b) a VH comprising the amino acid sequence of SEQ ID NO: 38 and a VL comprising the amino acid sequence of SEQ ID NO: 66;

(c) a VH comprising the amino acid sequence of SEQ ID NO: 38 and a VL comprising the amino acid sequence of SEQ ID NO: 70;

(d) a VH comprising the amino acid sequence of SEQ ID NO: 50 and a VL comprising the amino acid sequence of SEQ ID NO: 70;

(e) a VH comprising the amino acid sequence of SEQ ID NO: 38 and a VL comprising the amino acid sequence of SEQ ID NO: 46;

(f) a VH comprising the amino acid sequence of SEQ ID NO: 50 and a VL comprising the amino acid sequence of SEQ ID NO: 46;

(g) a VH comprising the amino acid sequence of SEQ ID NO: 50 and a VL comprising the amino acid sequence of SEQ ID NO: 54;

(h) a VH comprising the amino acid sequence of SEQ ID NO: 38 and a VL comprising the amino acid sequence of SEQ ID NO: 54;

(i) a VH comprising the amino acid sequence of SEQ ID NO: 38 and a VL comprising the amino acid sequence of SEQ ID NO: 58;

(j) a VH comprising the amino acid sequence of SEQ ID NO: 38 and a VL comprising the amino acid sequence of SEQ ID NO: 62;

(k) a VH comprising the amino acid sequence of SEQ ID NO: 50 and a VL comprising the amino acid sequence of SEQ ID NO: 66;

(l) a VH comprising the amino acid sequence of SEQ ID NO: 38 and a VL comprising the amino acid sequence of SEQ ID NO: 74;

(m) a VH comprising the amino acid sequence of SEQ ID NO: 38 and a VL comprising the amino acid sequence of SEQ ID NO: 78;

(n) a VH comprising the amino acid sequence of SEQ ID NO: 82 and a VL comprising the amino acid sequence of SEQ ID NO: 70;

(o) a VH comprising the amino acid sequence of SEQ ID NO: 82 and a VL comprising the amino acid sequence of SEQ ID NO: 66; or

(p) a VH comprising the amino acid sequence of SEQ ID NO: 86 and a VL comprising the amino acid sequence of SEQ ID NO: 66.

8. The antibody molecule of any of claims 1-7, which comprises:

(a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 91 and a light chain comprising the amino acid sequence of SEQ ID NO: 44;

(b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 91 and a light chain comprising the amino acid sequence of SEQ ID NO: 56;

(c) a heavy chain comprising the amino acid sequence of SEQ ID NO: 91 and a light chain comprising the amino acid sequence of SEQ ID NO: 68;

(d) a heavy chain comprising the amino acid sequence of SEQ ID NO: 91 and a light chain comprising the amino acid sequence of SEQ ID NO: 72;

(e) a heavy chain comprising the amino acid sequence of SEQ ID NO: 102 and a light chain comprising the amino acid sequence of SEQ ID NO: 72;

(f) a heavy chain comprising the amino acid sequence of SEQ ID NO: 40 and a light chain comprising the amino acid sequence of SEQ ID NO: 44;

(g) a heavy chain comprising the amino acid sequence of SEQ ID NO: 40 and a light chain comprising the amino acid sequence of SEQ ID NO: 48;

(h) a heavy chain comprising the amino acid sequence of SEQ ID NO: 52 and a light chain comprising the amino acid sequence of SEQ ID NO: 48;

(i) a heavy chain comprising the amino acid sequence of SEQ ID NO: 52 and a light chain comprising the amino acid sequence of SEQ ID NO: 56;

(j) a heavy chain comprising the amino acid sequence of SEQ ID NO: 40 and a light chain comprising the amino acid sequence of SEQ ID NO: 56;

(k) a heavy chain comprising the amino acid sequence of SEQ ID NO: 40 and a light chain comprising the amino acid sequence of SEQ ID NO: 60;

(l) a heavy chain comprising the amino acid sequence of SEQ ID NO: 40 and a light chain comprising the amino acid sequence of SEQ ID NO: 64;

(m) a heavy chain comprising the amino acid sequence of SEQ ID NO: 52 and a light chain comprising the amino acid sequence of SEQ ID NO: 68;

(n) a heavy chain comprising the amino acid sequence of SEQ ID NO: 40 and a light chain comprising the amino acid sequence of SEQ ID NO: 68;

(o) a heavy chain comprising the amino acid sequence of SEQ ID NO: 52 and a light chain comprising the amino acid sequence of SEQ ID NO: 72;

(p) a heavy chain comprising the amino acid sequence of SEQ ID NO: 40 and a light chain comprising the amino acid sequence of SEQ ID NO: 72;

(q) a heavy chain comprising the amino acid sequence of SEQ ID NO: 40 and a light chain comprising the amino acid sequence of SEQ ID NO: 76;

(r) a heavy chain comprising the amino acid sequence of SEQ ID NO: 40 and a light chain comprising the amino acid sequence of SEQ ID NO: 80;

(s) a heavy chain comprising the amino acid sequence of SEQ ID NO: 84 and a light chain comprising the amino acid sequence of SEQ ID NO: 72;

(t) a heavy chain comprising the amino acid sequence of SEQ ID NO: 84 and a light chain comprising the amino acid sequence of SEQ ID NO: 68; or

(u) a heavy chain comprising the amino acid sequence of SEQ ID NO: 88 and a light chain comprising the amino acid sequence of SEQ ID NO: 68.

9. The antibody molecule of any of claims 1-8, which is a monoclonal antibody, a Fab, a F(ab')2, an Fv, or a single chain Fv fragment (scFv); or comprises

a heavy chain constant region chosen from IgG1, IgG2, IgG3, or IgG4, and/or

a light chain constant region chosen from the light chain constant regions of kappa or lambda.

10. The antibody molecule of claim 9, which comprises:

(a) a human IgG4 heavy chain constant region with a mutation at position 228 according to EU numbering or position 108 of SEQ ID NO: 212 or 214 and a kappa light chain constant region;

(b) a human IgG4 heavy chain constant region with a Serine to Proline mutation at position 228 according to EU numbering or position 108 of SEQ ID NO: 212 or 214 and a kappa light chain constant region;

(c) a human IgG1 heavy chain constant region with an Asparagine to Alanine mutation at position 297 according to EU numbering or position 180 of SEQ ID NO: 216 and a kappa light chain constant region;

(d) a human IgG1 heavy chain constant region with an Aspartate to Alanine mutation at position 265 according to EU numbering or position 148 of SEQ ID NO: 217 and Proline to Alanine mutation at position 329 according to EU numbering or position 212 of SEQ ID NO: 217, and a kappa light chain constant region; or

(e) a human IgG1 heavy chain constant region with a Leucine to Alanine mutation at position 234 according to EU numbering or position 117 of SEQ ID NO: 218 and Leucine to Alanine mutation at position 235 according to EU numbering or position 118 of SEQ ID NO: 218, and a kappa light chain constant region.

11. The antibody molecule of any of claims 1-10, which

(a) is capable of binding to human PD-1 with a dissociation constant (K_D) of less than about 0.2 nM;

(b) binds an extracellular Ig-like domain of PD-1;

(c) is capable of reducing binding of PD-1 to PD-L1, PD-L2, or both, or a cell that expresses PD-L1, PD-L2, or both; and/or

(d) capable of enhancing an antigen-specific T cell response.

12. The antibody molecule of any of claims 1-11, wherein said antibody molecule has a first binding specificity for PD-1 and a second binding specificity for TIM-3, LAG-3, CEACAM-1, CEACAM-5, PD-L1 or PD-L2; and/or

wherein said antibody molecule comprises an antigen binding fragment of an antibody, a half antibody, or an antigen binding fragment of a half antibody.

13. A pharmaceutical composition comprising the isolated antibody molecule of any of claims 1-12 and a pharmaceutically acceptable carrier, excipient or stabilizer.

14. An isolated nucleic acid encoding the antibody heavy or VL of the antibody molecule of any of claims 1-12.

15. An isolated nucleic acid encoding heavy chain CDRs 1-3 and light chain CDRs 1-3 of claim 1, wherein said nucleic acid comprises a nucleotide sequence of SEQ ID NO: 108-120, 223, 122-132, or 133-146.

16. The nucleic acid of claim 15, further comprising:

a nucleotide sequence encoding a VH, wherein said nucleotide sequence comprises any of SEQ ID NO: 39, 51, 83, 87, 90, 95, or 101 or is at least 85% identical to any of SEQ ID NO: 39, 51, 83, 87, 90, 95, or 101; and/or

a nucleotide sequence encoding a VL, wherein said nucleotide sequence comprises any of SEQ ID NO: 43, 47, 55, 59, 63, 67, 71, 75, 79, 93, 97, 99, 104, or 106, or is at least 85% identical to any of SEQ ID NO: 43, 47, 55, 59, 63, 67, 71, 75, 79, 93, 97, 99, 104, or 106.

17. The nucleic acid of claim 16, further comprising:

a nucleotide sequence encoding a heavy chain, wherein said nucleotide sequence comprises any of SEQ ID NO: 41, 53, 85, 89, 92, 96, or 103, or is at least 85% identical to any of SEQ ID NO: 41, 53, 85, 89, 92, 96, or 103; and/or

a nucleotide sequence encoding a light chain, wherein said nucleotide sequence comprises any of SEQ ID NO: 45, 49, 57, 61, 65, 69, 73, 77, 81, 94, 98, 100, 105 or 107, or is at least 85% identical to any of SEQ ID NO: 45, 49, 57, 61, 65, 69, 73, 77, 81, 94, 98, 100, 105 or 107.

18. An expression vector comprising the nucleic acid of any of claims 14-17.

19. A host cell comprising the nucleic acid of any of claims 14-17.

20. A method of producing an antibody molecule or fragment thereof, comprising culturing the host cell of claim 19 under conditions suitable for gene expression.

21. A method of detecting PD-1 in a biological sample from a subject, comprising (i) contacting the sample and/or a reference sample with an isolated antibody molecule of any of claims 1-12 under conditions that allow interaction of the antibody molecule and a polypeptide of PD-1 to occur, and (ii) detecting formation of a complex between the antibody molecule and the sample and/or the subject the reference sample.

22. An antibody molecule of any of claims 1-12, or a pharmaceutical composition of claim 13, for use in the stimulation of an immune response or the treatment of a cancer or an infectious disease in a subject.

23. The antibody molecule, or pharmaceutical composition, for use as claimed in claim 22, wherein the cancer is chosen from a lung cancer, a melanoma, a renal cancer, a liver cancer, a prostate cancer, a breast cancer, a colorectal cancer, a gastric cancer, a pancreatic cancer, a thyroid cancer, a brain cancer, a uterine cancer, a nasopharyngeal cancer, a head and neck cancer, an ovarian cancer, an endometrial cancer, an endocrine cancer, or a hematological cancer, or a metastatic lesion of the cancer.

24. The antibody molecule, or pharmaceutical composition, for use as claimed in claim 23, wherein:

(a) the lung cancer is chosen from a non-small cell lung cancer (NSCLC), a lung adenocarcinoma, a squamous cell lung carcinoma, or a small cell lung cancer, or an NSCLC comprising a KRAS mutation;

(b) the melanoma is chosen from an advanced melanoma, an unresectable melanoma, a metastatic melanoma, a melanoma with a BRAF mutation, a melanoma with an NRAS mutation, a cutaneous melanoma, or an intraocular melanoma;

(c) the renal cancer is chosen from a renal cell carcinoma (RCC), a metastatic renal cell carcinoma, or a clear cell renal cell carcinoma (CCRCC);

(d) the hematologic cancer is chosen from a lymphoma, a myeloma, or a leukemia;

(e) the brain cancer is a glioblastoma;

(f) the breast cancer is a triple negative breast cancer;

(g) the liver cancer is a hepatocellular carcinoma; or

(h) the cancer is a MSI-high (high microsatellite instability) cancer.

25. The antibody molecule, or pharmaceutical composition, for use as claimed in any of claims 22-24, wherein the antibody molecule or pharmaceutical composition is to be used in combination with a second therapeutic agent or procedure.

26. The antibody molecule, or pharmaceutical composition, for use as claimed in claim 25, wherein the second therapeutic agent or procedure is chosen from one or more of chemotherapy, a targeted anti-cancer therapy, an oncolytic drug, a cytotoxic agent, an immune-based therapy, a cytokine, surgical procedure, a radiation procedure, an activator of a costimulatory molecule, an inhibitor of an inhibitory molecule, a vaccine, or a cellular immunotherapy, or

wherein the antibody molecule or pharmaceutical composition is to be administered in combination with:

(a) an agonist of a costimulatory molecule chosen from one or more of OX40, CD2, CD27, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3 or CD83 ligand; or

(b) an inhibitor of an immune checkpoint molecule chosen from one or more of PD-L1, PD-L2, CTLA-4, TIM-3, LAG-3, CEACAM-1, CEACAM-5, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 or TGFR.

27. The antibody molecule, or pharmaceutical composition, for use as claimed in any of claims 22-26, wherein the antibody molecule or pharmaceutical composition is to be used in combination with one or more of the following:

(a) an inhibitor of LAG-3;

(b) an inhibitor of TIM-3;

(c) an inhibitor of PD-L1;

(d) an agonist of GITR;

(e) an interleukin;

(f) a MEK inhibitor; or

(g) an FGFR inhibitor.

28. The antibody molecule, or pharmaceutical composition, for use as claimed in claim 27, wherein:

(a) the inhibitor of LAG-3 is an anti-LAG-3 antibody molecule and/or is used for the treatment of an NSCLC, a melanoma, an RCC, or a hematologic cancer;

(b) the inhibitor of TIM-3 is an anti-TIM-3 antibody molecule and/or is used for the treatment of a melanoma or an RCC;

(c) the inhibitor of PD-L1 is an anti-PD-L1 antibody molecule or chosen from YW243.55.S70, MPDL3280A, MEDI-4736, MSB-0010718C, or MDX-1105, and/or is used for the treatment of a thyroid cancer, an NSCLC, a triple negative breast cancer, a uterine cancer, or a lymphoma;

(d) the agonist of GITR is an anti-GITR antibody molecule or a fusion protein and/or is used for the treatment of an NSCLC;

(e) the interleukin is IL-15 is used for the treatment of a solid tumor;

(f) the MEK inhibitor is chosen from ARRY-142886, G02442104 (GSK1120212), RDEA436, RDEA119/BAY 869766, AS703026, G00039805 (AZD-6244 or selumetinib), BIX 02188, BIX 02189, CI-1040 (PD-184352), PD0325901, PD98059, U0126, GDC-0973 (Methanone or [3,4-

difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl][3- hydroxy-3-(25)-2-piperidinyl- 1 -azetidinyl]-), G-38963, G02443714 (AS703206), or a pharmaceutically acceptable salt or solvate thereof, and/or is used for the treatment of a triple negative breast cancer, an NSCLC, or a colorectal cancer; or

(g) the FGFR inhibitor is used for the treatment of a hepatocellular carcinoma.

29. The antibody molecule, or pharmaceutical composition, for use as claimed in any of claims 22-28, wherein the antibody molecule or pharmaceutical composition is to be used in combination with one or more of the following:

(a) a chemotherapy for the treatment of a lung cancer;

(b) an indoleamine-pyrrole 2,3-dioxygenase (IDO) inhibitor for the treatment of a lung cancer;

(c) an inhibitor of CTLA-4 for the treatment of a lung cancer or a melanoma;

(d) a cancer vaccine;

(e) one or more of: an immune-based therapy, a targeting agent, a VEGF tyrosine kinase inhibitor, an RNAi inhibitor, or an inhibitor of a downstream mediator of VEGF signaling, to treat a renal cancer;

(f) one, two or all of oxaliplatin, leucovorin, or 5-FU, for the treatment of a melanoma, a colorectal cancer, a non-small cell lung cancer, an ovarian cancer, a breast cancer, a prostate cancer, a pancreatic cancer, a hematological cancer, or a renal cell carcinoma; or

(g) a tyrosine kinase inhibitor for the treatment of a renal cancer.

30. The antibody molecule, or pharmaceutical composition, for use as claimed in claim 29, wherein:

(a) the chemotherapy is a platinum doublet therapy;

(b) the IDO inhibitor is INCB24360;

(c) the inhibitor of CTLA-4 is an anti-CTLA-4 antibody, ipilimumab, or a soluble ligand of CTLA-4, or the inhibitor of CTLA-4 is further used in combination with a BRAF inhibitor, vemurafenib, or dabrafenib;

(d) the cancer vaccine is a dendritic cell renal carcinoma (DC-RCC) vaccine;

(e) (i) the immune-based therapy comprises interleukin-2 or interferon-α; (ii) the targeting agent is a VEGF inhibitor, e.g., an anti-VEGF antibody;(iii) the VEGF tyrosine kinase inhibitor is chosen from sunitinib, sorafenib, axitinib, or pazopanib; or (iv) the inhibitor of a downstream mediator of VEGF signaling is an inhibitor of the mammalian target of rapamycin (mTOR) or temsirolimus;

(f) one, two or all of oxaliplatin, leucovorin, or 5-FU, for the treatment of a melanoma, a colorectal cancer, a non-small cell lung cancer, an ovarian cancer, a breast cancer, a prostate cancer, a pancreatic cancer, a hematological cancer, or a renal cell carcinoma; or

(g) the tyrosine kinase inhibitor is axitinib.

31. The antibody molecule, or pharmaceutical composition, for use as claimed in any of claims 22-30, wherein the subject has, or is identified as having, one or more of:

(a) a cancer that expresses PD-L1;

(b) a cancer that is positive for one, two, or all of PD-L1, CD8, IFN-γ;

(c) a cancer that is triple positive for PD-L1, CD8 and IFN-γ; or

(d) a cancer that is Tumor Infiltrating Lymphocyte (TIL) positive.

32. The antibody molecule, or pharmaceutical composition, for use as claimed in any of claims 22-31, wherein the antibody molecule or pharmaceutical composition is to be administered at a dose of about 1 to 30 mg/kg or about 1 to 5 mg/kg, and/or wherein the antibody molecule or pharmaceutical composition is to be administered once a week to once every 2, 3, or 4 weeks.

33. The antibody molecule, or pharmaceutical composition, for use as claimed in any of claims 22-32, wherein the antibody molecule or pharmaceutical composition is to be used in combination with one or more of: 1) a protein kinase C (PKC) inhibitor; 2) a heat shock protein 90 (HSP90) inhibitor; 3) an inhibitor of a phosphoinositide 3-kinase (PI3K) and/or target of rapamycin (mTOR); 4) an inhibitor of cytochrome P450, a CYP17 inhibitor, or a 17alpha-Hydroxylase/C17-20 Lyase inhibitor); 5) an iron chelating agent; 6) an aromatase inhibitor; 7) an inhibitor of p53 or an inhibitor of a p53/Mdm2 interaction; 8) an apoptosis inducer; 9) an angiogenesis inhibitor; 10) an aldosterone synthase inhibitor; 11) a smoothened (SMO) receptor inhibitor; 12) a prolactin receptor (PRLR) inhibitor; 13) a Wnt signaling inhibitor; 14) a CDK4/6 inhibitor; 15) a fibroblast growth factor receptor 2 (FGFR2)/fibroblast growth factor receptor 4 (FGFR4) inhibitor; 16) an inhibitor of macrophage colony-stimulating factor (M-CSF); 17) an inhibitor of one or more of c-KIT, histamine release, Flt3 or PKC; 18) an inhibitor of one or more of VEGFR-2, PDGFRbeta, c-KIT or Raf kinase C; 19) a somatostatin agonist and/or a growth hormone release inhibitor; 20) an anaplastic lymphoma kinase (ALK) inhibitor; 21) an insulin-like growth factor 1 receptor (IGF-1R) inhibitor; 22) a P-Glycoprotein 1 inhibitor; 23) a vascular endothelial growth factor receptor (VEGFR) inhibitor; 24) a BCR-ABL kinase inhibitor; 25) an FGFR inhibitor; 26) an inhibitor of CYP11B2; 27) a HDM2 inhibitor or an inhibitor of the HDM2-p53 interaction; 28) an inhibitor of a tyrosine kinase; 29) an inhibitor of c-MET; 30) an inhibitor of JAK; 31) an inhibitor of DAC; 32) an inhibitor of 11β-hydroxylase; 33) an inhibitor of IAP; 34) an inhibitor of PIM kinase; 35) an inhibitor of Porcupine;

36) an inhibitor of BRAF, BRAF V600E, or wild-type BRAF; 37) an inhibitor of HER3; 38) an inhibitor of MEK; or 39) an inhibitor of a lipid kinase.

34. The antibody molecule, or pharmaceutical composition, for use as claimed in any of claims 22-33, wherein the antibody molecule or pharmaceutical composition is to be used in combination with one or more of Compounds A1 to A51 as described in Table 7.

35. Use of an antibody molecule of any of claims 1-12, or a pharmaceutical composition of claim 13, in the manufacture of a medicament for the stimulation of an immune response or the treatment of a cancer or an infectious disease in a subject.

36. The use according to claim 35, wherein the cancer is chosen from a lung cancer, a melanoma, a renal cancer, a liver cancer, a prostate cancer, a breast cancer, a colorectal cancer, a gastric cancer, a pancreatic cancer, a thyroid cancer, a brain cancer, a uterine cancer, a nasopharyngeal cancer, a head and neck cancer, an ovarian cancer, an endometrial cancer, an endocrine cancer, or a hematological cancer, or a metastatic lesion of the cancer.

37. The use according to claim 36, wherein:

(a) the lung cancer is chosen from a non-small cell lung cancer (NSCLC), a lung adenocarcinoma, a squamous cell lung carcinoma, or a small cell lung cancer, or an NSCLC comprising a KRAS mutation;

(b) the melanoma is chosen from an advanced melanoma, an unresectable melanoma, a metastatic melanoma, a melanoma with a BRAF mutation, a melanoma with an NRAS mutation, a cutaneous melanoma, or an intraocular melanoma;

(c) the renal cancer is chosen from a renal cell carcinoma (RCC), a metastatic renal cell carcinoma, or a clear cell renal cell carcinoma (CCRCC);

(d) the hematologic cancer is chosen from a lymphoma, a myeloma, or a leukemia;

(e) the brain cancer is a glioblastoma;

(f) the breast cancer is a triple negative breast cancer;

(g) the liver cancer is a hepatocellular carcinoma; or

(h) the cancer is a MSI-high (high microsatellite instability) cancer.

38. The use according to any of claims 35-37, wherein the medicament is to be used in combination with a second therapeutic agent or procedure.

39. The use according to claim 38, wherein the second therapeutic agent or procedure is chosen from one or more of chemotherapy, a targeted anti-cancer therapy, an oncolytic drug, a cytotoxic agent, an immune-based therapy, a cytokine, surgical procedure, a radiation procedure, an activator of a costimulatory molecule, an inhibitor of an inhibitory molecule, a vaccine, or a cellular immunotherapy, or

wherein the medicament is to be administered in combination with:

(a) an agonist of a costimulatory molecule chosen from one or more of OX40, CD2, CD27, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3 or CD83 ligand; or

(b) an inhibitor of an immune checkpoint molecule chosen from one or more of PD-L1, PD-L2, CTLA-4, TIM-3, LAG-3, CEACAM-1, CEACAM-5, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 or TGFR.

40. The use according to any of claims 35-39, wherein the medicament is to be used in combination with one or more of the following:

(a) an inhibitor of LAG-3;

(b) an inhibitor of TIM-3;

(c) an inhibitor of PD-L1;

(d) an agonist of GITR;

(e) an interleukin;

(f) a MEK inhibitor; or

(g) an FGFR inhibitor.

41. The use according to claim 40, wherein:

(a) the inhibitor of LAG-3 is an anti-LAG-3 antibody molecule and/or is used for the treatment of an NSCLC, a melanoma, an RCC, or a hematologic cancer;

(b) the inhibitor of TIM-3 is an anti-TIM-3 antibody molecule and/or is used for the treatment of a melanoma or an RCC;

(c) the inhibitor of PD-L1 is an anti-PD-L1 antibody molecule or chosen from YW243.55.S70, MPDL3280A, MEDI-4736, MSB-0010718C, or MDX-1105, and/or is used for the treatment of a thyroid cancer, an NSCLC, a triple negative breast cancer, a uterine cancer, or a lymphoma;

(d) the agonist of GITR is an anti-GITR antibody molecule or a fusion protein and/or is used for the treatment of an NSCLC;

(e) the interleukin is IL-15 is used for the treatment of a solid tumor;

(f) the MEK inhibitor is chosen from ARRY-142886, G02442104 (GSK1120212), RDEA436, RDEA119/BAY 869766, AS703026, G00039805 (AZD-6244 or selumetinib), BIX 02188, BIX 02189, CI-1040 (PD-184352), PD0325901, PD98059, U0126, GDC-0973 (Methanone or [3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl][3- hydroxy-3-(25)-2-piperidinyl- 1 -azetidinyl]-), G-38963, G02443714 (AS703206), or a pharmaceutically acceptable salt or solvate thereof, and/or is used for the treatment of a triple negative breast cancer, an NSCLC, or a colorectal cancer; or

(g) the FGFR inhibitor is used for the treatment of a hepatocellular carcinoma.

42. The use according to any of claims 35-41, wherein the medicament is to be used in combination with one or more of the following:

(a) a chemotherapy for the treatment of a lung cancer;

(b) an indoleamine-pyrrole 2,3-dioxygenase (IDO) inhibitor for the treatment of a lung cancer;

(c) an inhibitor of CTLA-4 for the treatment of a lung cancer or a melanoma;

(d) a cancer vaccine;

(e) one or more of: an immune-based therapy, a targeting agent, a VEGF tyrosine kinase inhibitor, an RNAi inhibitor, or an inhibitor of a downstream mediator of VEGF signaling, to treat a renal cancer;

(f) one, two or all of oxaliplatin, leucovorin, or 5-FU, for the treatment of a melanoma, a colorectal cancer, a non-small cell lung cancer, an ovarian cancer, a breast cancer, a prostate cancer, a pancreatic cancer, a hematological cancer, or a renal cell carcinoma; or

(g) a tyrosine kinase inhibitor for the treatment of a renal cancer.

43. The use according to claim 42, wherein:

(a) the chemotherapy is a platinum doublet therapy;

(b) the IDO inhibitor is INCB24360;

(c) the inhibitor of CTLA-4 is an anti-CTLA-4 antibody, ipilimumab, or a soluble ligand of CTLA-4, or the inhibitor of CTLA-4 is further used in combination with a BRAF inhibitor, vemurafenib, or dabrafenib;

(d) the cancer vaccine is a dendritic cell renal carcinoma (DC-RCC) vaccine;

(e) (i) the immune-based therapy comprises interleukin-2 or interferon-α;(ii) the targeting agent is a VEGF inhibitor, e.g., an anti-VEGF antibody;(iii) the VEGF tyrosine kinase inhibitor is chosen from sunitinib, sorafenib, axitinib, or pazopanib; or (iv) the inhibitor of a downstream mediator of VEGF signaling is an inhibitor of the mammalian target of rapamycin (mTOR) or temsirolimus;

(f) one, two or all of oxaliplatin, leucovorin, or 5-FU, for the treatment of a melanoma, a colorectal cancer, a non-small cell lung cancer, an ovarian cancer, a breast cancer, a prostate cancer, a pancreatic cancer, a hematological cancer, or a renal cell carcinoma; or

(g) the tyrosine kinase inhibitor is axitinib.

44. The use according to any of claims 35-43, wherein the subject has, or is identified as having, one or more of:

(a) a cancer that expresses PD-L1;

(b) a cancer that is positive for one, two, or all of PD-L1, CD8, IFN-γ;

(c) a cancer that is triple positive for PD-L1, CD8 and IFN-γ; or

(d) a cancer that is Tumor Infiltrating Lymphocyte (TIL) positive.

45. The use according to any of claims 35-44, wherein the medicament is to be administered at a dose of about 1 to 30 mg/kg or about 1 to 5 mg/kg, and/or wherein the medicament is to be administered once a week to once every 2, 3, or 4 weeks.

46. The use according to any of claims 35-45, wherein the medicament is to be used in combination with one or more of: 1) a protein kinase C (PKC) inhibitor; 2) a heat shock protein 90 (HSP90) inhibitor; 3) an inhibitor of a phosphoinositide 3-kinase (PI3K) and/or target of rapamycin (mTOR); 4) an inhibitor of cytochrome P450, a CYP17 inhibitor, or a 17alpha-Hydroxylase/C17-20 Lyase inhibitor); 5) an iron chelating agent; 6) an aromatase inhibitor; 7) an inhibitor of p53 or an inhibitor of a p53/Mdm2 interaction; 8) an apoptosis inducer; 9) an angiogenesis inhibitor; 10) an aldosterone synthase inhibitor; 11) a smoothened (SMO) receptor inhibitor; 12) a prolactin receptor (PRLR) inhibitor; 13) a Wnt signaling inhibitor; 14) a CDK4/6 inhibitor; 15) a fibroblast growth factor receptor 2 (FGFR2)/fibroblast growth factor receptor 4 (FGFR4) inhibitor; 16) an inhibitor of macrophage colony-stimulating factor (M-CSF); 17) an inhibitor of one or more of c-KIT, histamine release, Flt3 or PKC; 18) an inhibitor of one or more of VEGFR-2, PDGFRbeta, c-KIT or Raf kinase C; 19) a somatostatin agonist and/or a growth hormone release inhibitor; 20) an anaplastic lymphoma kinase (ALK) inhibitor; 21) an insulin-like growth factor 1 receptor (IGF-1R) inhibitor; 22) a P-Glycoprotein 1 inhibitor; 23) a vascular endothelial growth factor receptor (VEGFR) inhibitor; 24) a BCR-ABL kinase inhibitor; 25) an FGFR inhibitor; 26) an inhibitor of CYP11B2; 27) a HDM2 inhibitor or an inhibitor of the HDM2-p53 interaction; 28) an inhibitor of a tyrosine kinase; 29) an inhibitor of c-MET; 30) an inhibitor of JAK; 31) an inhibitor of DAC; 32) an inhibitor of 11β-hydroxylase; 33) an inhibitor of IAP; 34) an inhibitor of PIM kinase; 35) an inhibitor of Porcupine; 36) an inhibitor of BRAF, BRAF V600E, or wild-type BRAF; 37) an inhibitor of HER3; 38) an inhibitor of MEK; or 39) an inhibitor of a lipid kinase.

47. The use according to any of claims 35-46, wherein the medicament is to be used in combination with one or more of Compounds A1 to A51 as described in Table 7.