CLAIMS

1. An isolated antibody molecule capable of binding to human T-cell immunoglobulin domain and mucin domain 3 (TIM-3), comprising:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 10; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14;

(b) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 4; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8;

(c) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 25; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14;

(d) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 24; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8;

(e) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 31; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14; or

(f) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 30; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8.

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

3. The antibody molecule of claim 1 or 2, wherein said antibody molecule has a first binding specificity for TIM-3 and a second binding specificity for PD-1, 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 or a half antibody or antigen binding fragment of a half antibody.

4. The antibody molecule of any of claims 1-3, which is a Fab, F(ab')2, Fv, or a single chain Fv fragment (scFv); or comprises

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

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

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

a VH comprising an amino acid sequence chosen from SEQ ID NO: 1, 16, 26, 32, 36, 44, 48, 52, 60, 68, 72, 76, 80, 84, 92, or 100, or an amino acid sequence at least 85% identical to any of SEQ ID NOs: 1, 16, 26, 32, 36, 44, 48, 52, 60, 68, 72, 76, 80, 84, 92, or 100; and/or

a VL comprising an amino acid sequence chosen from SEQ ID NO: 2, 20, 40, 56, 64, 88, 96, or 104, or an amino acid sequence at least 85% identical to any of SEQ ID NOs: 2, 20, 40, 56, 64, 88, 96, or 104.

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

a VH comprising an amino acid sequence chosen from SEQ ID NO: 1, 16, 26, 32, 36, 44, 48, 52, 60, 68, 72, 76, 80, 84, 92, or 100; and/or

a VL comprising an amino acid sequence chosen from SEQ ID NO: 2, 20, 40, 56, 64, 88, 96, or 104.

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

a heavy chain comprising an amino acid sequence chosen from SEQ ID NO: 18, 121,_28, 34, 38, 116, 46, 50, 54, 62, 70, 74, 78, 82, 86, 94, or 102; and/or

a light chain comprising an amino acid sequence chosen from SEQ ID NO: 22, 42, 58, 66, 90, 98, or 106.

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

(a) a VH comprising the amino acid sequence of SEQ ID NO: 1 and a VL comprising the amino acid sequence of SEQ ID NO: 2;

(b) a VH comprising the amino acid sequence of SEQ ID NO: 16 and a VL comprising the amino acid sequence of SEQ ID NO: 20;

(c) a VH comprising the amino acid sequence of SEQ ID NO: 26 and a VL comprising the amino acid sequence of SEQ ID NO: 20;

(d) a VH comprising the amino acid sequence of SEQ ID NO: 32 and a VL comprising the amino acid sequence of SEQ ID NO: 20;

(e) a VH comprising the amino acid sequence of SEQ ID NO: 36 and a VL comprising the amino acid sequence of SEQ ID NO: 40;

(f) a VH comprising the amino acid sequence of SEQ ID NO: 44 and a VL comprising the amino acid sequence of SEQ ID NO: 40;

(g) a VH comprising the amino acid sequence of SEQ ID NO: 48 and a VL comprising the amino acid sequence of SEQ ID NO: 40;

(h) a VH comprising the amino acid sequence of SEQ ID NO: 36 and a VL comprising the amino acid sequence of SEQ ID NO: 20;

(i) a VH comprising the amino acid sequence of SEQ ID NO: 16 and a VL comprising the amino acid sequence of SEQ ID NO: 40;

(j) a VH comprising the amino acid sequence of SEQ ID NO: 52 and a VL comprising the amino acid sequence of SEQ ID NO: 56;

(k) a VH comprising the amino acid sequence of SEQ ID NO: 60 and a VL comprising the amino acid sequence of SEQ ID NO: 56;

(l) a VH comprising the amino acid sequence of SEQ ID NO: 52 and a VL comprising the amino acid sequence of SEQ ID NO: 64;

(m) a VH comprising the amino acid sequence of SEQ ID NO: 60 and a VL comprising the amino acid sequence of SEQ ID NO: 64;

(n) a VH comprising the amino acid sequence of SEQ ID NO: 68 and a VL comprising the amino acid sequence of SEQ ID NO: 64;

(o) a VH comprising the amino acid sequence of SEQ ID NO: 72 and a VL comprising the amino acid sequence of SEQ ID NO: 64;

(p) a VH comprising the amino acid sequence of SEQ ID NO: 76 and a VL comprising the amino acid sequence of SEQ ID NO: 56;

(q) a VH comprising the amino acid sequence of SEQ ID NO: 80 and a VL comprising the amino acid sequence of SEQ ID NO: 56;

(r) a VH comprising the amino acid sequence of SEQ ID NO: 68 and a VL comprising the amino acid sequence of SEQ ID NO: 56;

(s) a VH comprising the amino acid sequence of SEQ ID NO: 72 and a VL comprising the amino acid sequence of SEQ ID NO: 56;

(t) a VH comprising the amino acid sequence of SEQ ID NO: 76 and a VL comprising the amino acid sequence of SEQ ID NO: 64;

(u) a VH comprising the amino acid sequence of SEQ ID NO: 80 and a VL comprising the amino acid sequence of SEQ ID NO: 64;

(v) a VH comprising the amino acid sequence of SEQ ID NO: 84 and a VL comprising the amino acid sequence of SEQ ID NO: 88;

(w) a VH comprising the amino acid sequence of SEQ ID NO: 92 and a VL comprising the amino acid sequence of SEQ ID NO: 96; or

(x) a VH comprising the amino acid sequence of SEQ ID NO: 100 and a VL comprising the amino acid sequence of SEQ ID NO: 104.

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

(a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 18 and a light chain comprising the amino acid sequence of SEQ ID NO: 22;

(b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 28 and a light chain comprising the amino acid sequence of SEQ ID NO: 22;

(c) a heavy chain comprising the amino acid sequence of SEQ ID NO: 34 and a light chain comprising the amino acid sequence of SEQ ID NO: 22;

(d) a heavy chain comprising the amino acid sequence of SEQ ID NO: 38 and a light chain comprising the amino acid sequence of SEQ ID NO: 42;

(e) a heavy chain comprising the amino acid sequence of SEQ ID NO: 46 and a light chain comprising the amino acid sequence of SEQ ID NO: 42;

(f) a heavy chain comprising the amino acid sequence of SEQ ID NO: 50 and a light chain comprising the amino acid sequence of SEQ ID NO: 42;

(g) a heavy chain comprising the amino acid sequence of SEQ ID NO: 116 and a light chain comprising the amino acid sequence of SEQ ID NO: 22;

(h) a heavy chain comprising the amino acid sequence of SEQ ID NO: 121 and a light chain comprising the amino acid sequence of SEQ ID NO: 42;

(i) a heavy chain comprising the amino acid sequence of SEQ ID NO: 54 and a light chain comprising the amino acid sequence of SEQ ID NO: 58;

(j) a heavy chain comprising the amino acid sequence of SEQ ID NO: 62 and a light chain comprising the amino acid sequence of SEQ ID NO: 58;

(k) a heavy chain comprising the amino acid sequence of SEQ ID NO: 54 and a light chain comprising the amino acid sequence of SEQ ID NO: 66;

(l) a heavy chain comprising the amino acid sequence of SEQ ID NO: 62 and a light chain comprising the amino acid sequence of SEQ ID NO: 66;

(m) a heavy chain comprising the amino acid sequence of SEQ ID NO: 70 and a light chain comprising the amino acid sequence of SEQ ID NO: 66;

(n) a heavy chain comprising the amino acid sequence of SEQ ID NO: 74 and a light chain comprising the amino acid sequence of SEQ ID NO: 66;

(o) a heavy chain comprising the amino acid sequence of SEQ ID NO: 78 and a light chain comprising the amino acid sequence of SEQ ID NO: 58;

(p) a heavy chain comprising the amino acid sequence of SEQ ID NO: 82 and a light chain comprising the amino acid sequence of SEQ ID NO: 58;

(q) a heavy chain comprising the amino acid sequence of SEQ ID NO: 70 and a light chain comprising the amino acid sequence of SEQ ID NO: 58;

(r) a heavy chain comprising the amino acid sequence of SEQ ID NO: 74 and a light chain comprising the amino acid sequence of SEQ ID NO: 58;

(s) a heavy chain comprising the amino acid sequence of SEQ ID NO: 78 and a light chain comprising the amino acid sequence of SEQ ID NO: 66;

(t) a heavy chain comprising the amino acid sequence of SEQ ID NO: 82 and a light chain comprising the amino acid sequence of SEQ ID NO: 66;

(u) a heavy chain comprising the amino acid sequence of SEQ ID NO: 86 and a light chain comprising the amino acid sequence of SEQ ID NO: 90;

(v) a heavy chain comprising the amino acid sequence of SEQ ID NO: 94 and a light chain comprising the amino acid sequence of SEQ ID NO: 98; or

(w) 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: 106.

10. The antibody molecule of any of claims 1-9, 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: 108 or 110 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: 108 or 110 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: 112 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: 113 and Proline to Alanine mutation at position 329 according to EU numbering or position 212 of SEQ ID NO: 113, 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: 114 and Leucine to Alanine mutation at position 235 according to EU numbering or position 118 of SEQ ID NO: 114, and a kappa light chain constant region.

11. The antibody molecule of any of claims 1-10, which has one, two, three, or all of the following properties:

(a) is capable of binding to human TIM-3 with a dissociation constant (K_D) of less than about 0.5 nM;

(b) is capable of reducing:

(i) binding of TIM-3 to phosphatidylserine (PtdSer), HMGB1, CEACAM-1, Semaphorin 4-A, or a combination thereof, or a cell that expresses PtdSer, HMGB1, CEACAM-1, Semaphorin 4-A, or a combination thereof; or

(ii) PtdSer-mediated membrane penetration of TIM-3.

(c) is capable of enhancing an antigen-specific T cell response; or

(d) binds an IgV domain of TIM-3.

12. An isolated antibody molecule that binds to the same epitope as, or an epitope that overlaps with, the epitope of a monoclonal antibody to human T-cell immunoglobulin domain and mucin domain 3 (TIM-3), wherein the monoclonal antibody comprises:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 10; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14;

(b) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 4; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8;

(c) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 25; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14;

(d) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 24; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8;

(e) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 31; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14; or

(f) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 30; and a VHCDR3 amino acid sequence of SEQ ID

NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8, wherein

(1) the antibody molecule binds to one, two, three, or all of: the two residues adjacent to the N-terminus of the A strand or Val24 and Glu25 in human TIM-3, the BC loop, the CC' loop, or the G strand of human TIM-3; and

(2) the antibody molecule has one, two, three, four, five, six, seven or all of the following properties:

(i) reduces PtdSer-dependent membrane penetration of TIM-3;

(ii) reduces binding of TIM-3 to one, two, or all of PtdSer, HMGB1, or CEACAM-1;

(iii) does not inhibit binding of TIM-3 to Galectin-9;

(iv) competes with CEACAM-1 for binding to one, two, or all of Cys58, Asn119 and Lys122 of TIM-3;

(v) reduces the formation of a hydrogen bond between Lys122 of TIM-3 and Asn42 of CEACAM-1;

(vi) competes with PtdSer for binding to the FG loop and the CC' loop of TIM-3;

(vii) competes with HMGB1 for binding to Glu62 of TIM-3; or

(viii) does not compete with Galectin-9 for binding to TIM-3.

13. The antibody molecule of claim 12, wherein the antibody molecule binds to one, two, three, four, five, six, seven, or all of the following:

(a) one, two, three, or all of: the A strand, the EF loop, the F strand, or the FG loop;

(b) one, two, three, or all of: the third residue N-terminal to the A strand or Glu23 in human TIM-3, the C strand, the C'C'' loop, or the C'' strand;

(c) one or both of residues Val24 and Glu25 adjacent to the N-terminus of the A strand; residue Thr41 within the BC loop; four, five, six, seven, or all of residues Glu121, Lys122, Phe123, Asn124, Leu125, Lys126, Leu127, and Val128 within the G strand; and three, four, five, or all of residues Gly56, Ala57, Cys58, Pro59, Val60, and Phe61 within the CC' loop;

(d) residues Val24 and Glu25 adjacent to the N-terminus of the A strand; residue Thr41 within the BC loop; residues Glu121, Lys122, Phe123, Asn124, Leu125, Lys126, Leu127, and Val128 within the G strand; and residues Gly56, Ala57, Cys58, Pro59, Val60, and Phe61 within the CC' loop;

(e) one or more residues chosen from: residue Tyr26 within the A strand, residues Phe39 and Tyr40 within the BC loop; residue Ser105 within the EF loop; residues Gly106 and Ile107 within the F strand; and residues Asn119 and Asp120 within the FG loop;

(f) residue Tyr26 within the A strand, residues Phe39 and Tyr40 within the BC loop; residue Ser105 within the EF loop; residues Gly106 and Ile107 within the F strand; and residues Asn119 and Asp120 within the FG loop;

(g) one or more residues chosen from: residue Glu23 N-terminal to the A strand; residues Pro42, Ala43, Ala44, Pro45, Gly46, Asn47, Leu48, Val49, and Pro50 within the BC loop; residues Val51, Cys52, Trp53, Gly54, and Lys55 within the C strand; residues Arg73 and Asp74 with the C'C'' loop; and residues Val75, Asn76, and Tyr77 in the C" strand; and/or

(h) residue Glu23 N-terminal to the A strand; residues Pro42, Ala43, Ala44, Pro45, Gly46, Asn47, Leu48, Val49, and Pro50 within the BC loop; residues Val51, Cys52, Trp53, Gly54, and Lys55 within the C loop; residues Arg73 and Asp74 with the C'C'' strand; and residues Val75, Asn76, and Tyr77 in the C" strand.

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

15. An isolated nucleic acid encoding the antibody heavy and light chain variable regions of the antibody molecule of any of claims 1-13.

16. 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 encoding SEQ ID NOs: 3-10, 12-14, 24, 25, 30, or 31.

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

a nucleotide sequence encoding a VH, wherein said nucleotide sequence comprises any of SEQ ID NO: 11, 17, 29, 33, 37, 45, 49, 53, 61, 69, 73, 77, 81, 85, 93, 101, 115, or 120, or is at least 85% identical to any of SEQ ID NO: 11, 17, 29, 33, 37, 45, 49, 53, 61, 69, 73, 77, 81, 85, 93, 101, 115, or 120; and

a nucleotide sequence encoding a VL, wherein said nucleotide sequence comprises any of SEQ ID NO: 15, 21, 41, 57, 65, 89, 97, 105, 118, 123, 125, or 127, or is at least 85% identical to any of SEQ ID NO: 15, 21, 41, 57, 65, 89, 97, 105, 118, 123, 125, or 127.

18. 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: 19, 29, 35, 39, 47, 51, 55, 63, 71, 75, 79, 83, 87, 95, 103, 117, or 122, or is at least 85% identical to any of SEQ ID NO: 19, 29, 35, 39, 47, 51, 55, 63, 71, 75, 79, 83, 87, 95, 103, 117, or 122; and

a nucleotide sequence encoding a light chain, wherein said nucleotide sequence comprises any of SEQ ID NO: 23, 43, 59, 67, 91, 99, 107, 119, 124, 126, 128, or is at least 85% identical to any of SEQ ID NO: 23, 43, 59, 67, 91, 99, 107, 119, 124, 126, 128.

19. An expression vector comprising the nucleic acid of any of claims 15-18.

20. A host cell comprising the nucleic acid of any of claims 15-18.

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

22. A method of detecting TIM-3 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 1-13 under conditions that allow interaction of the antibody molecule and a polypeptide of TIM-3 to occur, and (ii) detecting formation of a complex between the antibody molecule and the sample and/or the reference sample.

23. An antibody molecule of any of claims 1-13, or a pharmaceutical composition of claim 14, for use in the stimulation of an immune response or the treatment of a cancer or an infectious disease in a subject.

24. The antibody molecule, or pharmaceutical composition, for use as claimed in claim 23, wherein the cancer is chosen from a lung cancer, a melanoma, a renal cancer, a liver cancer, a prostate cancer, a breast cancer, a head and neck cancer, a colorectal cancer, a pancreatic cancer, a brain cancer, a hematological cancer, or a metastatic lesion of the cancer.

25. The antibody molecule, or pharmaceutical composition, as claimed in claim 24, 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;

(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, a clear cell renal cell carcinoma (CCRCC), a kidney clear cell carcinoma, or a kidney papillary cell carcinoma; or

(d) the hematologic cancer is chosen from a lymphoma, a non-Hodgkin lymphoma, a myeloma, or a leukemia.

26. The antibody molecule, or pharmaceutical composition, for use as claimed in any of claims 23-25, wherein the antibody molecule or pharmaceutical composition is to be used in combination with a second therapeutic agent or procedure.

27. The antibody molecule, or pharmaceutical composition, for use as claimed in claim 26, wherein the second therapeutic agent or procedure is chosen from one or more of a 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 is to be used 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-1, PD-L1, PD-L2, CTLA-4, LAG-3, CEACAM-1, CEACAM-5, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 or TGFR.

28. The antibody molecule, or pharmaceutical composition, for use as claimed in any of claims 23-27, wherein the antibody molecule or pharmaceutical composition is to be used in combination with one or more of the following:

(a) an inhibitor of PD-1;

(b) an inhibitor of PD-L1;

(c) an inhibitor of LAG-3;

(d) an agonist of GITR;

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

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

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

(h) a MEK inhibitor for the treatment of a lung cancer, a melanoma, or a renal cancer;

(i) a cancer vaccine;

(j) one or more of:

(i) an immune-based therapy;

(ii) a targeting agent;

(iii) a VEGF tyrosine kinase inhibitor;

(iv) an RNAi inhibitor; or

(v) an inhibitor of a downstream mediator of VEGF signaling for the treatment of a renal cancer;

(k) one, two or all of oxaliplatin, leucovorin or 5-FU, for the treatment of a lung cancer, a melanoma, or a renal cancer; or

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

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

(a) the inhibitor of PD-1 is an anti-PD-1 antibody molecule or a fusion protein or chosen from MDX-1106, Merck 3475, CT-011, AMP-224, or AMP-514;

(b) the inhibitor of PD-L1 is an anti-PD-L1 antibody molecule or a fusion protein or chosen from YW243.55.S70, MPDL3280A, MEDI-4736, MSB-0010718C, or MDX-1105;

(c) the inhibitor of LAG-3 is an anti-LAG-3 antibody molecule or a fusion protein;

(d) the agonist of GITR is an anti-GITR antibody molecule or a fusion protein;

(e) the chemotherapy is a platinum doublet therapy;

(f) the IDO inhibitor is INCB24360;

(g) the inhibitor of CTLA-4 is an anti-CTLA-4 antibody, ipilimumab, or a soluble ligand of CTLA-4;

(h) the inhibitor of CTLA-4 is used further in combination with a BRAF inhibitor, vemurafenib, or dabrafenib;

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

(j) the immune-based therapy comprises interleukin-2 or interferon-α;

(k) the targeting agent is a VEGF inhibitor or an anti-VEGF antibody;

(l) the VEGF tyrosine kinase inhibitor is chosen from sunitinib, sorafenib, axitinib, or pazopanib;

(m) the inhibitor of a downstream mediator of VEGF signaling is an inhibitor of the mammalian target of rapamycin (mTOR), everolimus, or temsirolimus; or

(n) the tyrosine kinase inhibitor is axitinib.

30. The antibody molecule, or a pharmaceutical composition, for use as claimed in any of claims 23-29, wherein the subject has, or is identified as having, one or more of:

(a) a cancer that expresses TIM-3;

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

31. The antibody molecule, or a pharmaceutical composition, for use as claimed in any of claims 23-30, wherein the antibody molecule or pharmaceutical composition is to be administered at a dose of about 0.1 to 30 mg/kg, 1 to 30 mg/kg or 1 to 5 mg/kg, or, wherein the antibody molecule or

pharmaceutical composition is to be administered once a week to once every 2, 3, or 4 weeks or the antibody molecule or pharmaceutical composition is to be administered at a dose from about 10 to 20 mg/kg every other week.

32. The antibody molecule, or pharmaceutical composition, for use as claimed in any of claims 23-31, 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, *e.g.*, 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.

33. The antibody molecule, or a pharmaceutical composition, for use as claimed in any of claims 23-32, 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 6.

34. Use of an antibody molecule of any of claims 1-13, or a pharmaceutical composition of claim 14, 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.

35. The use according to claim 34, wherein the cancer is chosen from a lung cancer, a melanoma, a renal cancer, a liver cancer, a prostate cancer, a breast cancer, a head and neck cancer, a

colorectal cancer, a pancreatic cancer, a brain cancer, a hematological cancer, or a metastatic lesion of the cancer.

36. The use according to claim 35, 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;

(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, a clear cell renal cell carcinoma (CCRCC), a kidney clear cell carcinoma, or a kidney papillary cell carcinoma; or

(d) the hematologic cancer is chosen from a lymphoma, a non-Hodgkin lymphoma, a myeloma, or a leukemia.

37. The use according to any of claims 34-36, wherein the medicament is to be used in combination with a second therapeutic agent or procedure.

38. The use according to claim 37 wherein the second therapeutic agent or procedure is chosen from one or more of a 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 used 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-1, PD-L1, PD-L2, CTLA-4, LAG-3, CEACAM-1, CEACAM-5, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 or TGFR.

39. The use according to any of claims 34-38, wherein the medicament is to be used in combination with one or more of the following:

(a) an inhibitor of PD-1;

(b) an inhibitor of PD-L1;

(c) an inhibitor of LAG-3;

(d) an agonist of GITR;

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

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

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

(h) a MEK inhibitor for the treatment of a lung cancer, a melanoma, or a renal cancer;

(i) a cancer vaccine;

(j) one or more of:

(i) an immune-based therapy;

(ii) a targeting agent;

(iii) a VEGF tyrosine kinase inhibitor;

(iv) an RNAi inhibitor; or

(v) an inhibitor of a downstream mediator of VEGF signaling for the treatment of a renal cancer;

(k) one, two or all of oxaliplatin, leucovorin or 5-FU, for the treatment of a lung cancer, a melanoma, or a renal cancer; or

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

40. The use according to claim 39, wherein:

(a) the inhibitor of PD-1 is an anti-PD-1 antibody molecule or a fusion protein or chosen from MDX-1106, Merck 3475, CT-011, AMP-224, or AMP-514;

(b) the inhibitor of PD-L1 is an anti-PD-L1 antibody molecule or a fusion protein or chosen from YW243.55.S70, MPDL3280A, MEDI-4736, MSB-0010718C, or MDX-1105;

(c) the inhibitor of LAG-3 is an anti-LAG-3 antibody molecule or a fusion protein;

(d) the agonist of GITR is an anti-GITR antibody molecule or a fusion protein;

(e) the chemotherapy is a platinum doublet therapy;

(f) the IDO inhibitor is INCB24360;

(g) the inhibitor of CTLA-4 is an anti-CTLA-4 antibody, ipilimumab, or a soluble ligand of CTLA-4;

(h) the inhibitor of CTLA-4 is used further in combination with a BRAF inhibitor, vemurafenib, or dabrafenib;

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

(j) the immune-based therapy comprises interleukin-2 or interferon-α;

(k) the targeting agent is a VEGF inhibitor or an anti-VEGF antibody;

(l) the VEGF tyrosine kinase inhibitor is chosen from sunitinib, sorafenib, axitinib, or pazopanib;

(m) the inhibitor of a downstream mediator of VEGF signaling is an inhibitor of the mammalian target of rapamycin (mTOR), everolimus, or temsirolimus; or

(n) the tyrosine kinase inhibitor is axitinib.

41. The use according to any of claims 34-40, wherein the subject has, or is identified as having, one or more of:

(a) a cancer that expresses TIM-3;

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

42. The use according to any of claims 34-41, wherein the medicament is to be administered at a dose of about 0.1 to 30 mg/kg, 1 to 30 mg/kg or 1 to 5 mg/kg, or, wherein the medicament is to be administered once a week to once every 2, 3, or 4 weeks or the medicament is to be administered at a dose from about 10 to 20 mg/kg every other week.

43. The use according to any of claims 34-42, 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, *e.g.*, 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.

44. The use according to any of claims 34-43, wherein the medicament is to be used in combination with one or more of Compounds A1 to A51 as described in Table 6.