

CLAIMS

1. An antibody or an antigen binding fragment thereof which specifically binds to a human Programmed Death Ligand 1 (PD-L1), in which the antibody or antigen binding fragment comprises:
 - 5 a heavy chain variable region comprising a CDRH1 amino acid sequence of SEQ ID NO: 7 or SEQ ID NO: 10, a CDRH2 amino acid sequence of SEQ ID NO: 8 or SEQ ID NO: 11, and a CDRH3 amino acid sequence of SEQ ID NO: 9 or SEQ ID NO: 12; and a light chain variable region comprising a CDRL1 amino acid sequence of SEQ ID NO: 17 or SEQ ID NO: 20, a CDRL2 amino acid sequence of SEQ ID NO: 18 or SEQ ID NO: 21, and a CDRL3 amino acid sequence of SEQ ID NO: 19 or SEQ ID NO: 22.
2. An antibody or antigen binding fragment according to Claim 1, comprising of the heavy chain variable region is amino acid sequence SEQ ID NO: 13 and the light chain variable region is amino acid sequence SEQ ID NO: 23.
3. A pharmaceutical composition comprising an antibody or antigen binding fragment as
 - 15 defined in Claim 1 or 2 and a pharmaceutically acceptable excipient, diluent or carrier.
4. An antibody or an antigen binding fragment thereof which specifically binds to a human Programmed Death Ligand 1 (PD-L1), in which the antibody or antigen binding fragment comprises a heavy chain variable region comprising a CDRH3 amino acid sequence at least 95% identical to SEQ ID NO: 9 or at least 95% identical to SEQ ID NO: 12.
- 20 5. An antibody or antigen binding fragment according to Claim 4, in which the heavy chain variable region comprises a CDRH1 amino acid sequence at least 95% identical to SEQ ID NO: 7 or at least 95% identical to SEQ ID NO: 10 and/or a CDRH2 amino acid sequence at least 95% identical to SEQ ID NO: 8 or at least 95% identical to SEQ ID NO: 11.
6. An antibody or antigen binding fragment according to Claim 4 or 5, in which the heavy
 - 25 chain variable region comprises an amino acid sequence at least 90% identical to SEQ ID NO: 13.
7. An antibody or antigen binding fragment according to Claim 4, 5 or 6, in which the light chain variable region comprises a CDRL1 amino acid sequence at least 95% identical to SEQ ID NO: 17 or at least 95% identical to SEQ ID NO: 20; a CDRL2 amino acid sequence at least

95% identical to SEQ ID NO: 18 or at least 95% identical to SEQ ID NO: 21; and/or a CDRL3 amino acid sequence at least 95% identical to SEQ ID NO: 19 or at least 95% identical to SEQ ID NO: 22.

8. An antibody or antigen binding fragment thereof according to any of Claims 4 to 7, in which the light chain variable region comprises an amino acid sequence at least 95% identical to SEQ ID NO: 23.

9. An antibody or antigen binding fragment thereof that specifically binds to a human Programmed Death Ligand 1 (PD-L1), the antibody or antigen binding fragment thereof comprising a heavy chain variable (V_H) domain and a light chain variable (V_L) domain, in which:

(a) the V_H domain has an amino acid sequence that is at least 90% identical to SEQ ID NO: 13, and the V_L domain has an amino acid sequence that is at least 90% identical to SEQ ID NO: 23; or

(b) the V_H domain has an amino acid sequence of SEQ ID NO: 13 or the V_L domain has an amino acid sequence of SEQ ID NO: 23; or

(c) the V_H domain has an amino acid sequence of SEQ ID NO: 13 and the V_L domain has an amino acid sequence of SEQ ID NO: 23; or

(d) the V_H domain has a CDRH1 amino acid sequence that is at least 95% identical to SEQ ID NO: 7 or at least 95% identical to SEQ ID NO: 10, a CDRH2 amino acid sequence that is at least 95% identical to SEQ ID NO: 8 or at least 95% identical to SEQ ID NO: 11, and a CDRH3 amino acid sequence that is at least 95% identical to SEQ ID NO: 9 or at least 95% identical to SEQ ID NO: 12; or

(e) the V_H domain has a CDRH1 amino acid sequence comprising 3, 2, or 1 amino acid substitutions to SEQ ID NO: 7 or SEQ ID NO: 10, a CDRH2 amino acid sequence comprising 4 or fewer amino acid substitutions to SEQ ID NO: 8 or SEQ ID NO: 11, and a CDRH3 amino acid sequence comprising 6 or fewer amino acid substitutions to SEQ ID NO: 9 or SEQ ID NO: 12, or

(f) the V_H domain has a CDRH1 amino acid sequence of SEQ ID NO: 7 or SEQ ID NO: 10, a CDRH2 amino acid sequence of SEQ ID NO: 8 or SEQ ID NO: 11, and a CDRH3 amino acid sequence of SEQ ID NO: 9 or SEQ ID NO: 12; or

(g) the V_L domain has a CDRL1 amino acid sequence that is at least 95% identical to SEQ ID NO: 17 or at least 95% identical to SEQ ID NO: 20, a CDRL2 amino acid sequence that is at least 95% identical to SEQ ID NO: 18 or at least 95% identical to SEQ ID NO: 21, and a CDRL3 amino acid sequence that is at least 95% identical to SEQ ID NO: 19 and at least 95% identical to SEQ ID NO: 22; or

(h) the V_L domain has a CDRL1 amino acid sequence of SEQ ID NO: 17 or SEQ ID NO: 20, a CDRL2 amino acid sequence of SEQ ID NO: 18 or SEQ ID NO: 21, and a CDRL3 amino acid sequence of SEQ ID NO: 19 or SEQ ID NO: 22; or

(i) the V_L domain has a CDRL1 amino acid sequence comprising 3 or fewer amino acid substitutions to SEQ ID NO: 17 or SEQ ID NO: 20, a CDRL2 amino acid sequence comprising 2 or 1 amino acid substitutions to SEQ ID NO: 18 or SEQ ID NO: 21, and a CDRL3 amino acid sequence comprising 4 or fewer amino acid substitutions to SEQ ID NO: 19 or SEQ ID NO: 22, or

(j) the V_H domain has a CDRH1 amino acid sequence that is at least 95% identical to SEQ ID NO: 7 or at least 95% identical to SEQ ID NO: 10, a CDRH2 amino acid sequence that is at least 95% identical to SEQ ID NO: 8 or at least 95% identical to SEQ ID NO: 11, and a CDRH3 amino acid sequence that is at least 95% identical to SEQ ID NO: 9 or at least 95% identical to SEQ ID NO: 12; and the V_L domain has a CDRL1 amino acid sequence that is at least 95% identical to SEQ ID NO: 17 or at least 95% identical to SEQ ID NO: 20, a CDRL2 amino acid sequence that is at least 95% identical to SEQ ID NO: 18 or at least 95% identical to SEQ ID NO: 21, and a CDRL3 amino acid sequence that is at least 95% identical to SEQ ID NO: 19 or at least 95% identical to SEQ ID NO: 22; or

(k) the V_H domain has a CDRH1 amino acid sequence comprising 3, 2, or 1 amino acid substitutions to SEQ ID NO: 7 or SEQ ID NO: 10, a CDRH2 amino acid sequence comprising 4 or fewer amino acid substitutions to SEQ ID NO: 8 or SEQ ID NO: 11, and a CDRH3 amino acid sequence comprising 6 or fewer amino acid substitutions to SEQ ID NO: 9 or SEQ ID NO: 12, and the V_L domain has a CDRL1 amino acid sequence comprising 3 or fewer amino acid substitutions to SEQ ID NO: 17 or SEQ ID NO: 20, a CDRL2 amino acid sequence comprising 2 or 1 amino acid substitutions to SEQ ID NO: 18 or SEQ ID NO: 21, and a CDRL3 amino acid sequence comprising 4 or fewer amino acid substitutions to SEQ ID NO: 19 or SEQ ID NO: 22, or

- (l) the V_H domain has a CDRH1 amino acid sequence of SEQ ID NO: 7 or SEQ ID NO: 10, a CDRH2 amino acid sequence of SEQ ID NO: 8 or SEQ ID NO: 11, and a CDRH3 amino acid sequence of SEQ ID NO: 9 or SEQ ID NO: 12; and the V_L domain has a CDRL1 amino acid sequence of SEQ ID NO: 17 or SEQ ID NO: 20, a CDRL2 amino acid sequence of SEQ ID NO: 18 or SEQ ID NO: 21, and a CDRL3 amino acid sequence of SEQ ID NO: 19 or SEQ ID NO: 22; or
- (m) the V_H domain has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 14, and the V_L domain has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 24; or
- (n) the V_H domain has a nucleic acid sequence of SEQ ID NO: 14 and the V_L domain has a nucleic acid sequence of SEQ ID NO: 24.
10. An antibody or antigen binding fragment thereof that specifically binds to a human Programmed Death Ligand 1 (PD-L1), the antibody or antigen binding fragment thereof comprising a heavy chain and a light chain, in which:
- (a) the heavy chain has an amino acid sequence that is at least 90% identical to SEQ ID NO: 15 and the light chain has an amino acid sequence that is at least 90% identical to SEQ ID NO: 25; or
- (b) the heavy chain has an amino acid sequence of SEQ ID NO: 15 or the light chain has an amino acid sequence of SEQ ID NO: 25; or
- (c) the heavy chain has an amino acid sequence of SEQ ID NO: 15 and the light chain has an amino acid sequence of SEQ ID NO: 25; or
- (d) the heavy chain has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 16 or the light chain has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 26; or
- (e) the heavy chain has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 16 and the light chain has a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 26; or
- (f) the heavy chain has a nucleic acid sequence of SEQ ID NO: 16 or the light chain has a nucleic acid sequence of SEQ ID NO: 26; or

(g) the heavy chain has a nucleic acid sequence of SEQ ID NO: 16 and the light chain has a nucleic acid sequence of SEQ ID NO: 26.

11. An antibody or antigen binding fragment thereof according to any of Claims 1, 2 and 4 to 10, further comprising a light chain constant region.

5 12. An antibody or antigen binding fragment thereof according to Claim 11, in which the light chain constant region is a kappa light chain or a lambda light chain.

13. An antibody or antigen binding fragment thereof according to Claim 11, in which the light chain constant region has an amino acid sequence of SEQ ID NO: 207, SEQ ID NO: 209, SEQ ID NO: 211, SEQ ID NO: 213, SEQ ID NO: 215, SEQ ID NO: 217, SEQ ID NO: 219, 10 SEQ ID NO: 221, SEQ ID NO: 223, SEQ ID NO: 225, SEQ ID NO: 227, SEQ ID NO: 229, SEQ ID NO: 231, SEQ ID NO: 233, SEQ ID NO: 235, SEQ ID NO: 237, SEQ ID NO: 536, or SEQ ID NO: 538.

14. An antibody or antigen binding fragment thereof according to any Claims 1, 2 and 4 to 14, further comprising a heavy chain constant region.

15 15. An antibody or antigen binding fragment thereof according to Claim 14, in which the heavy chain constant region has an amino acid sequence of SEQ ID NO: 193, SEQ ID NO: 195, SEQ ID NO: 197, SEQ ID NO: 199, SEQ ID NO: 201, SEQ ID NO: 203, SEQ ID NO: 205, SEQ ID NO: 340, SEQ ID NO: 524, SEQ ID NO: 526, SEQ ID NO: 528, SEQ ID NO: 530, SEQ ID NO: 532 or SEQ ID NO: 534.

20 16. An antibody or antigen binding fragment thereof according to Claim 14, in which the heavy chain constant region that is an effector-null.

17. An antibody or antigen binding fragment thereof according to Claim 16, in which the effector-null heavy chain constant region is an IgG4 constant region or an IgG1 constant region.

25 18. An antibody or antigen binding fragment thereof according to any of Claims 1, 2 and 4 to 17, capable of inhibiting PD-L1-mediated suppression of T-cells

19. An antibody or antigen binding fragment thereof according to any of Claims 1, 2 and 4 to 18, in which the human PD-L1 is of SEQ ID NO: 1.

20. An antibody or antigen binding fragment thereof according to any of Claims 1, 2 and 4 to 19, which competes for binding to the human PD-L1 with an antibody comprising a V_H amino acid sequence of SEQ ID NO: 13 and the V_L amino acid sequence of SEQ ID NO: 23.
21. An antibody or antigen binding fragment thereof according to any of Claims 1, 2 and 4 to 20, in which the antibody or antigen binding fragment thereof is a human antibody or antigen binding fragment thereof or a humanized antibody or antigen binding fragment thereof.
22. A bispecific antibody or fusion protein (e.g. an antibody-cytokine fusion protein) comprising an antibody or fragment thereof as defined in any of Claims 1, 2 and 4 to 21.
23. A pharmaceutical composition comprising an antibody or antigen binding fragment thereof as defined in any of Claims 4 to 22 and a pharmaceutically acceptable excipient, diluent or carrier.
24. A kit comprising an antibody or antigen binding fragment thereof as defined in any of Claims 1, 2 and 4 to 22 or a pharmaceutical composition as defined in Claim 3 or 23 and optionally further comprising a therapeutic agent comprising an immune checkpoint inhibitor, an immune stimulator, a chemokine receptor antagonist, a targeted kinase inhibitor, an angiogenesis inhibitor, a chemokine, a cytokine, a bi-specific molecule or a cell-based therapy.
25. A kit according to Claim 24, which further comprises a label or instructions for use to treat and/or prevent a hPD-L1 mediated disease or condition in a human, optionally in which the label or instructions comprise a marketing authorization number; optionally in which the kit comprises an IV or injection device that comprises the antibody or antigen binding fragment.
26. A vector comprising a nucleic acid encoding an antibody or antigen binding fragment thereof as defined in any of Claims 1, 2 and 4 to 22.
27. Use of an antibody or antigen binding fragment thereof as defined in any of Claims 1, 2 and 4 to 22 in the manufacture of a medicament for treating or preventing a hPD-L1 mediated disease or condition in a human.

28. An antibody or antigen binding fragment thereof as defined in any of Claims 1, 2 and 4 to 22 or a pharmaceutical composition as defined in Claim 3 and 23 for use in treating or preventing a hPD-L1 mediated disease or condition in a human.

29. Use according to Claim 27 or 28, in which the hPD-L1-mediated disease or condition is a neurodegenerative disease, disorder or condition.

30. Use according to Claim 29, in which the neurodegenerative disease, disorder or condition is Alzheimer's disease, amyotrophic lateral sclerosis, Parkinson's disease, Huntington's disease, primary progressive multiple sclerosis, secondary progressive multiple sclerosis, corticobasal degeneration, Rett syndrome, anterior ischemic optic neuropathy, glaucoma, uveitis, depression, trauma-associated stress or post-traumatic stress disorder, frontotemporal dementia, Lewy body dementias, mild cognitive impairments, posterior cortical atrophy, primary progressive aphasia and progressive supranuclear palsy or aged-related dementia.

31. Use according to Claim 29, in which the neurodegenerative disease, disorder or condition is a retinal degeneration disorder.

32. Use according to Claim 31, in which the retinal degeneration disorder is age-related macular degeneration or retinitis pigmentosa.

33. Use according to any of Claim 27 to 32, in which a therapeutic agent for treating or preventing the hPD-L1 mediated disease or condition is to be administered, the therapeutic agent comprising an immune checkpoint inhibitor, an immune stimulator, a chemokine receptor antagonist, a targeted kinase inhibitor, an angiogenesis inhibitor, a chemokine, a cytokine, a bi-specific molecule or a cell-based therapy.