

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 antigen binding fragment according to Claim 1, in which the heavy chain variable region comprises an amino acid sequence at least 90% identical to SEQ ID NO: 13.
5. An antibody or antigen binding fragment thereof according to Claim 1 or 4, in which the
 - 20 light chain variable region comprises an amino acid sequence at least 95% identical to SEQ ID NO: 23.
6. 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
 - 25 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 and the V_L domain has an amino acid sequence of SEQ ID NO: 23; or

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

(d) 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

(e) 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.

7. 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 and the light chain has an amino acid sequence of SEQ ID NO: 25; or

(c) 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

(d) 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.

8. An antibody or antigen binding fragment thereof according to any of Claims 1, 2 and 4 to 7, further comprising a light chain constant region.

9. An antibody or antigen binding fragment thereof according to Claim 8, in which the light chain constant region is a kappa light chain or a lambda light chain.

10. An antibody or antigen binding fragment thereof according to Claim 8, 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, 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.

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

12. An antibody or antigen binding fragment thereof according to Claim 11, 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.

13. An antibody or antigen binding fragment thereof according to Claim 11, in which the heavy chain constant region is effector-null.

14. An antibody or antigen binding fragment thereof according to Claim 13, in which the effector-null heavy chain constant region is an IgG4 constant region or an IgG1 constant region.

15. An antibody or antigen binding fragment thereof according to any of Claims 1, 2 and 4 to 14, capable of inhibiting PD-L1-mediated suppression of T-cells
16. An antibody or antigen binding fragment thereof according to any of Claims 1, 2 and 4 to 15, in which the human PD-L1 is of SEQ ID NO: 1.
- 5 17. An antibody or antigen binding fragment thereof according to any of Claims 1, 2 and 4 to 16, 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.
18. An antibody or antigen binding fragment thereof according to any of Claims 1, 2 and 4 to 17, in which the antibody or antigen binding fragment thereof is a human antibody or
10 antigen binding fragment thereof or a humanized antibody or antigen binding fragment thereof.
19. A bispecific antibody or fusion protein (e.g. an antibody-cytokine fusion protein) comprising an antibody or antigen binding fragment thereof as defined in any of Claims 1, 2 and 4 to 18.
- 15 20. A pharmaceutical composition comprising an antibody or antigen binding fragment thereof as defined in any of Claims 4 to 19 and a pharmaceutically acceptable excipient, diluent or carrier.
21. A kit comprising an antibody or antigen binding fragment thereof as defined in any of Claims 1, 2 and 4 to 19 or a pharmaceutical composition as defined in Claim 3 or 20 and
20 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.
22. A kit according to Claim 21, which further comprises a label or instructions for use to
25 treat and/or prevent a hPD-L1 mediated disease 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.

23. 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 19.

24. Use of an antibody or antigen binding fragment thereof as defined in any of Claims 1, 2 and 4 to 19 in the manufacture of a medicament for treating or preventing a hPD-L1 mediated
5 disease in a human.

25. An antibody or antigen binding fragment thereof as defined in any of Claims 1, 2 and 4 to 19 or a pharmaceutical composition as defined in Claim 3 and 20 for use in treating or preventing a hPD-L1 mediated disease in a human.

26. Use according to Claim 24, an antibody or antigen binding fragment according to Claim
10 25 or a pharmaceutical composition for use according to Claim 25, in which the hPD-L1-mediated disease is a neurodegenerative disease or disorder.

27. Use according to Claim 26, an antibody or antigen binding fragment according to Claim 26 or a pharmaceutical composition for use according to Claim 26, in which the neurodegenerative disease or disorder is Alzheimer's disease, amyotrophic lateral sclerosis,
15 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
20 aged-related dementia.

28. Use according to Claim 28, an antibody or antigen binding fragment according to Claim 28 or a pharmaceutical composition for use according to Claim 28, in which the neurodegenerative disease or disorder is a retinal degeneration disorder.

29. Use according to Claim 28, an antibody or antigen binding fragment according to Claim
25 28 or a pharmaceutical composition for use according to Claim 28, in which the retinal degeneration disorder is age-related macular degeneration or retinitis pigmentosa.

30. Use according to any of Claims 24 and 26 to 29, an antibody or antigen binding fragment according to any of Claims 25 to 29 or a pharmaceutical composition for use

according to any of Claims 25 to 29, in which a therapeutic agent for treating or preventing the hPD-L1 mediated disease 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.

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