CLAIMS

1. An immunotherapeutic protein comprising one or more immunoglobulin heavy chain polypeptide comprising an Fc region component comprising at least a constant heavy chain domain 3 (CH3) domain (or at least a constant heavy domain 4 (CH4) domain), wherein said one or more polypeptide includes an amino acid substitution at a position corresponding to H429 of the amino acid sequence of human IgG1 heavy chain (Eu numbering).

2. The immunotherapeutic protein of claim 1, wherein the Fc region component comprises one or more of the follow features: 1) a constant heavy domain 3 (CH3) and a constant heavy domain 2 (CH2) of an immunoglobulin heavy chain, optionally in combination with a lower, core and/or upper hinge sequence or comprises a constant heavy domain 3 (CH3) only.

3. The immunotherapeutic protein of claim 1 or 2, wherein the immunotherapeutic protein is an immunoglobulin molecule comprising first and second immunoglobulin heavy chain polypeptides comprising an Fc region component comprising CH2 and CH3 domains so that the first and second polypeptides form, by dimerisation, an Fc fragment or Fc-like fragment.

4. The immunotherapeutic protein of claim 3, wherein the Fc region component is derived from an Ig heavy chain selected from: an IgG1 heavy chain polypeptide, an IgG2 heavy chain polypeptide, an IgG3 heavy chain polypeptide, an IgG4 heavy chain polypeptide, and an IgA heavy chain polypeptide.

5. The immunotherapeutic protein of claim 1, wherein the immunotherapeutic protein is an immunoglobulin molecule comprising first and second immunoglobulin heavy chain polypeptides comprising an Fc region component comprising CH2 and CH4 domains so that the first and second polypeptides form, by dimerisation, an Fc fragment or Fc-like fragment.

6. The immunotherapeutic protein of claim 3 or 5, wherein the immunoglobulin protein is an antibody, antibody-like molecule or antibody derivative.

7. The immunotherapeutic protein of claim 6, wherein the immunoglobulin protein comprises at least one antigen recognition structure which may specifically bind to an antigen or epitope of therapeutic significance.

8. The immunotherapeutic protein of claim 7, wherein the at least one antigen recognition structure specifically binds to a cancer-associated antigen, an autoantigen, an allergen, an antigen associated with an inflammatory disease, an antigen from a transplanted tissue or organ or an antigen of an infectious agent such as an antigen of a bacterial or viral pathogen.

9. The immunotherapeutic protein of claim 8, wherein the at least one antigen recognition structure specifically binds to one of the following:

i) a cancer-associated antigen selected from CD20, CD38 and CD52;

ii) an antigen of SARS-CoV-2 virus, Middle East respiratory syndrome coronavirus (MERS-CoV), respiratory syncytial virus (RSV) or dengue virus;

iii) an antigen of a viral pathogen selected from antigens of coronaviruses;

iv) a cell surface molecule known to induce cell activation or cell proliferation and/or stimulate an inhibitory pathway to inhibit or reduce cell responses;

v) a cell surface molecule known to induce a cellular response selected from stimulation of an inhibitory pathway to inhibit or reduce responses;

vi) an immune checkpoint molecule;

vii) an immune checkpoint molecule is selected from the group consisting of 4-1BB (CD137), cluster of differentiation (CD40, CD154), OX40 receptor (TNFRSF4, CD134), tumour necrosis factor receptor type II (TNFR2, CD120b), glucocorticoid-induced TNFR-related protein (GITR, TNFRSF18, CD357), cluster of differentiation 27 (CD27), T cell immunoglobulin and mucin-domain containing-3 (TIM-3), B and T lymphocyte attenuator (BTLA, CD272), lymphocyte activation gene-3 (LAG3, CD223), cytotoxic T-lymphocyte- associated protein 4 (CTLA4, CD152), inducible T-cell costimulatory (ICOS, CD278), cluster of differentiation 28 (CD28), TT cell immunoreceptor with Ig and ITIM domains (IGIT, Vstm3), programmed death-ligand 1 (PDL-1, CD274) and programmed cell death protein 1 (PD-1, CD279);

viii) a cell surface molecule, wherein the cell surface molecule induces cell death cell death when engaged by a ligand or the immunotherapeutic protein; and

ix) a cell surface molecule is selected from the group consisting of tumour necrosis receptor 1 (TNFR1), Fas (CD95), Death Receptor 3, Death Receptor 4, Death Receptor 5, Death Receptor 6, and cluster of differentiation (CD38).

10. The immunotherapeutic protein of any one of claims 6 to 9, wherein the immunotherapeutic protein is an antibody that forms oligomers through self-association in solution at physiological pH.

11. The immunotherapeutic protein of claim 10, wherein the immunotherapeutic protein is a hexamer.

12. The immunotherapeutic protein of claim 10 or 11, wherein the amino acid substitution at the position corresponding to H429 of the amino acid sequence of the human IgG1 heavy chain polypeptide is an H→Y substitution.

13. The immunotherapeutic protein of any one of claims 6 to 9, wherein the immunotherapeutic

protein is an antibody that forms oligomers upon binding to a relevant target through "on target" oligomerisation.

14. The immunotherapeutic protein of claim 13, wherein the immunotherapeutic protein forms a hexamer upon binding to a relevant target through "on target" oligomerisation.

15. The immunotherapeutic protein of claim 13, wherein the amino acid substitution at the position corresponding to H429 of the amino acid sequence of the human IgG1 heavy chain polypeptide is an H→F substitution.

16. The immunotherapeutic protein of claim 13, wherein the amino acid substitution at the position corresponding to H429 of the amino acid sequence of the human IgG2 heavy chain polypeptide is an H→F substitution.

17. The immunotherapeutic protein of claim 13, wherein the amino acid substitution at the position corresponding to H429 of the amino acid sequence of the human IgG3 heavy chain polypeptide is an H→F substitution.

18. The immunotherapeutic protein of any one of claims 1 to 4, wherein the immunotherapeutic protein comprises a fusion protein or protein conjugate comprising a partner polypeptide linked to an Fc region component comprising at least a CH3 domain (or at least a constant heavy domain 4 (CH4) domain).

19. The immunotherapeutic protein of claim 18, wherein the partner polypeptide is selected from:

i) a cell surface receptor polypeptide (or a fragment thereof) or a co-receptor polypeptide (or fragment thereof);

ii) a cell surface receptor polypeptide (or a fragment thereof) that is capable of binding to a structural protein of a virus such that the immunotherapeutic protein may act as a "decoy" to block viral interaction and cellular entry of a virus to a host cell;

iii) is selected from an angiotensin-converting enzyme 2 (ACE2) ectodomain, dipeptidyl peptidase 4 (DPP4, CD26), Hsp70, hepatitis A virus cellular receptor 1 (HAVCR1/TIM-1), cluster of differentiation 155 (CD155), Glucose transporter 1 (GLUT1), Proto-oncogene tyrosine-protein kinase MER (MERTK),TYRO3 Protein Tyrosine Kinase (TYRO3), AXL or cluster of differentiation 4 receptor (CD4 receptor);

iv) is selected from cytotoxic T- lymphocyte-associated protein 4 (CTLA4) (or a soluble extracellular fragment thereof), interleukin-1 receptor (IL-1R), interleukin-6 receptor (IL-6R), tumour necrosis factor receptor-2 (TNFR2, also known as CD120b) or a receptor for a cytokine of the TGF-β superfamily;

v) is a ligand for a cell surface molecule known to induce cell activation and/or proliferation and/or stimulate an inhibitory pathway to inhibit or reduce cell responses;

vi) is a ligand for an immune checkpoint molecule;

vii) is selected from the group consisting of 4-1BB (CD137), CD40 (CD154), OX40 (TNFRSF4, CD134), TNFR2 (CD120b), GITR (TNFRSF18, CD357), CD27, TIM-3, BTLA (CD272), LAG3 (CD223), CTLA4 (CD152), ICOS (CD278), CD28, TIGIT (Vstm3), PDL-1 (CD274) and PD-1 (CD279);

viii) is a ligand for a cell surface molecule which induce cell death when engaged by the ligand;

ix) is a ligand for a cell surface molecule selected from the group consisting of TNFR1, Fas, Death Receptor 3, Death Receptor 4, Death Receptor 5, Death Receptor 6, and CD38; and

x) is TNF-related apoptosis-inducing ligand (TRAIL).

20. The immunotherapeutic protein of claim 19, wherein the immunotherapeutic protein is a fusion protein that forms oligomers through self-association in solution at physiological pH.

21. The immunotherapeutic protein of claim 20, wherein the immunotherapeutic protein is a hexamer.

22. The immunotherapeutic protein of claim 20 or 21, wherein the amino acid substitution at the position corresponding to H429 of the amino acid sequence of the human IgG1 heavy chain polypeptide is an H→Y substitution.

23. The immunotherapeutic protein of claim 19, wherein the immunotherapeutic protein is a fusion protein that forms oligomers upon binding to a relevant target through "on target" oligomerisation.

24. The immunotherapeutic protein of claim 23, wherein the immunotherapeutic protein forms a hexamer upon binding to a relevant target through "on target" oligomerisation.

25. The immunotherapeutic protein of claim 23 or 24, wherein the amino acid substitution at the position corresponding to H429 of the amino acid sequence of the human IgG1 heavy chain polypeptide is an H→F substitution.

26. The use of the immunotherapeutic protein of any one of claims 1 to 25 in the manufacture of a medicament for treating or preventing a disease or condition, wherein the disease or condition is selected from autoimmune diseases and conditions, other inflammatory diseases, infectious diseases and proliferative diseases.

27. A pharmaceutical composition or medicament comprising the immunotherapeutic protein of any one of claims 1 to 25, and a pharmaceutically acceptable carrier, diluent and/or excipient.

28. A kit of parts comprising at least one immunotherapeutic protein of any one of claims 1 to 25.

29. A method of producing an immunotherapeutic protein of claim 1 to 25, comprising
1) culturing a host cell comprising a construct encoding said protein under conditions suitable for the expression of said protein, and recovering the protein from culture supernatant under conditions of:

(i) mildly acidic pH to recover immunotherapeutic protein in a monomeric form, or

(ii) substantially neutral pH to recover immunotherapeutic protein in an oligomeric form; or

2) culturing a host cell comprising a construct encoding said protein under conditions suitable for the expression of said protein, and recovering the protein from culture supernatant using a method comprising affinity chromatography using an elution buffer comprising a concentration of arginine of less than 130 mM and at less than or equal to pH 5.0.