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Opposition by: Strawman Limited
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AUXILIARY REQUEST 20

1. An antibody for use in a method of treatment wherein it is administered to enhance the reduction of plasma antigen, said antibody comprising

   (a) a human FcRn-binding domain which has a human FcRn-binding activity at pH 5.8 to pH 6.0 and at pH 7.4, wherein the human FcRn-binding activity at pH 7.0 and at 25°C is stronger than KD 2.3 µM~~3.2 µM~~, and wherein the human FcRn-binding domain is an Fc domain resulting from substituting a different amino acid for at least one amino acid in the Fc domain of a human IgG1, IgG2, IgG3 or IgG4; and

   (b) an antigen-binding domain which has a lower antigen-binding activity at pH 5.8 to pH 6.0 than at pH 7.4 and wherein the ratio of antigen-binding activity at pH 5.8 and at pH 7.4 is ~~2 or greater,~~ 10 or greater or 40 or greater in the value of KD (at pH 5.8)/KD (at pH 7.4) ~~.~~

   wherein an antibody binding to PCSK9 with an affinity at physiological pH greater than at endosomal pH and having the Fc double mutation M428L-N434S is excluded.

2. The antibody for the use of claim 1, wherein said antibody comprises an amino acid mutation of the antigen-binding domain, which comprises a substitution of histidine for at least one amino acid of the antigen-binding domain or the insertion of at least one histidine.

3. The antibody for the use of claim 1 or 2, wherein the antigen-binding domain is obtained from an antigen-binding domain library.

4. The antibody for the use of any one of claims 1 to 3, wherein the human FcRn-binding domain is a human FcRn-binding domain comprising an amino acid sequence with a substitution of a different amino acid for at least one amino acid selected from those of positions 237, 238, 239, 248, 250, 252, 254, 255, 256, 257, 258, 265, 270, 286, 289, 297, 298, 303, 305, 307, 308, 309, 311, 312, 314, 315, 317,