levels). Such antibodies would preferably also possess good physical-chemical properties to facilitate development, manufacturing, or formulation.

Summary

In one aspect of the present disclosure, there is provided an antibody, or antigen-binding fragment thereof, comprising a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein the HCVR comprises the complementarity determining regions (CDRs) HCDR1, HCDR2 and HCDR3 and the LCVR comprises the CDRs LCDR1, LCDR2 and LCDR3, wherein the amino acid sequence of HCDR1 is given by SEQ ID NO: 1, the amino acid sequence of HCDR2 is given by SEQ ID NO: 2, the amino acid sequence of HCDR3 is given by SEQ ID NO: 3, the amino acid sequence of LCDR1 is given by SEQ ID NO: 4, the amino acid sequence of LCDR2 is given by SEQ ID NO: 5, and the amino acid sequence of LCDR3 is given by SEQ ID NO: 6, wherein said antibody, or antigen binding fragment thereof, binds to human PCSK9.

In another aspect of the present disclosure, there is provided an antibody comprising two heavy chains (HCs) and two light chains (LCs) wherein the amino acid sequence of each HC is given by SEQ ID NO: 9, and the amino acid sequence of each LC is given by SEQ ID NO: 10.

In yet another aspect of the present disclosure, there is provided an antibody consisting of two heavy chains and two light chains, wherein the amino acid sequence of each heavy chain is given by SEQ ID NO:9, and the amino acid sequence of each light chain is given by SEQ ID NO:10.

In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising an antibody or antigen-binding fragment as described herein and one or more pharmaceutically acceptable carriers, diluents or excipients.

In another aspect of the present disclosure, there is provided a use of an effective amount of an antibody or antigen-binding fragment as described herein in the manufacture of a medicament for treating hyperlipidemia or hypercholesterolemia.

In yet another aspect of the present disclosure, there is provided an antibody or antigen-binding fragment as described herein for use in therapy.

In a further aspect of the present disclosure, there is provided an antibody or antigen-binding fragment as described herein for use in the treatment of hyperlipidemia or hypercholesterolemia.

Description

The present invention provides an antibody, or antigen-binding fragment thereof, comprising a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein the HCVR comprises the complementarity determining regions (CDRs) HCDR1, HCDR2 and HCDR3 and the LCVR comprises the CDRs LCDR1, LCDR2 and LCDR3, wherein the amino acid sequence of HCDR1 is given by SEQ ID NO: 1, the amino acid sequence of HCDR2 is given by SEQ ID NO: 2, the amino acid sequence of HCDR3 is given by SEQ ID NO: 3, the amino acid sequence of LCDR1 is given by SEQ ID NO: 4, the amino acid sequence of LCDR2 is given by SEQ ID NO: 5, and the amino acid sequence of LCDR3 is given by SEQ ID NO: 6, wherein said antibody or antigen-binding fragment thereof binds to human PCSK9. In an embodiment, the present invention provides an antibody, or antigen-binding fragment thereof, comprising a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein the amino acid sequence of the HCVR is given by SEQ ID NO: 7 and the amino acid sequence of the LCVR is given by SEQ ID NO: 8, wherein said antibody or antigen-binding fragment thereof binds to human PCSK9. In another embodiment, the present invention provide an antibody, or antigen-binding fragment thereof, comprising two heavy chain variable regions (HCVRs) and two light chain variable regions wherein the amino acid sequence of each HCVR is given by SEQ ID NO: 7 and the amino acid sequence of each LCVR is given by SEQ ID NO: 8.

In another particular embodiment, the present invention provides an antibody, or an antigen-binding fragment thereof, comprising a heavy chain (HC) and a light chain (LC), wherein the amino acid sequence of the HC is given by SEQ ID NO: 9 and the amino acid sequence of the LC is given by SEQ ID NO: 10. In an even more particular embodiment, the present invention provides an antibody comprising two heavy chains (HCs) and two light chains (LCs) wherein the amino acid sequence of each HC is given by SEQ ID NO: 9 and the amino acid sequence of each LC is given by SEQ ID NO: 10. In a most particular embodiment, the present invention provides an antibody that consists of two HCs and two LCs, wherein the amino acid sequence of each HC is given by SEQ ID NO: 9 and the amino acid sequence of each LC is given by SEQ ID NO: 10.

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<151> 2011-09-16

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Gly Met Val Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Thr Ile Ser Ser Gly Gly Gly Tyr Thr Tyr Tyr Pro Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

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        35                  40                  45

Pro Gln Leu Leu Ile Tyr Gln Leu Ser Asn Leu Ala Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
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Gly Met Val Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Thr Ile Ser Ser Gly Gly Gly Tyr Thr Tyr Tyr Pro Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Glu Gly Ile Ser Phe Gln Gly Gly Thr Tyr Thr Tyr Val Met
            100                 105                 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr
        115                 120                 125

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Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys
        195                 200                 205

Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
    210                 215                 220

Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
225                 230                 235                 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270

Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
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Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser
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Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350

Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val
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Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
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Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
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Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
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Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Tyr Gln Asn
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Leu Glu Leu Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
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Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu

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Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
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Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
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Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
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Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
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Lys Met Ser Gly Asp Leu Leu Glu Leu Ala Leu Lys Leu Pro His Val
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Asn Leu Glu Arg Ile Thr Pro Pro Arg Tyr Arg Ala Asp Glu Tyr Gln
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Pro Pro Asp Gly Gly Ser Leu Val Glu Val Tyr Leu Leu Asp Thr Ser
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Ser Lys Cys Asp Ser His Gly Thr His Leu Ala Gly Val Val Ser Gly
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Arg Asp Ala Gly Val Ala Lys Gly Ala Ser Met Arg Ser Leu Arg Val
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Leu Asn Cys Gln Gly Lys Gly Thr Val Ser Gly Thr Leu Ile Gly Leu
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Glu Phe Ile Arg Lys Ser Gln Leu Val Gln Pro Val Gly Pro Leu Val
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Val Leu Leu Pro Leu Ala Gly Gly Tyr Ser Arg Val Leu Asn Ala Ala
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Gln Arg Leu Ile His Phe Ser Ala Lys Asp Val Ile Asn Glu Ala Trp
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Ala Arg Arg Leu Gln Ala Gln Ala Ala Arg Arg Gly Tyr Leu Thr Lys
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Ile Leu His Val Phe His Gly Leu Leu Pro Gly Phe Leu Val Lys Met
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Ser Gly Asp Leu Leu Glu Leu Ala Leu Lys Leu Pro His Val Asp Tyr
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Glu Arg Ile Thr Pro Pro Arg Tyr Arg Ala Asp Glu Tyr Gln Pro Pro
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Cys Asp Ser His Gly Thr His Leu Ala Gly Val Val Ser Gly Arg Asp
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Ala Gly Val Ala Lys Gly Ala Ser Met Arg Ser Leu Arg Val Leu Asn
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Cys Gln Gly Lys Gly Thr Val Ser Gly Thr Leu Ile Gly Leu Glu Phe
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Ile Arg Lys Ser Gln Leu Val Gln Pro Val Gly Pro Leu Val Val Leu
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Leu Pro Leu Ala Gly Gly Tyr Ser Arg Val Leu Asn Ala Ala Cys Gln
260 265 270

Arg Leu Ala Arg Ala Gly Val Val Leu Val Thr Ala Ala Gly Asn Phe
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Arg Asp Asp Ala Cys Leu Tyr Ser Pro Ala Ser Ala Pro Glu Val Ile
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Thr Val Gly Ala Thr Asn Ala Gln Asp Gln Pro Val Thr Leu Gly Thr
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Leu Gly Thr Asn Phe Gly Arg Cys Val Asp Leu Phe Ala Pro Gly Glu
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