We claim:

1. An isolated human antibody or antigen-binding fragment thereof that specifically binds human angiopoietin-like protein 4 (hANGPTL4), comprising a heavy chain complementarity determining region 1 (HCDR1)/HCDR2/HCDR3 combination selected from SEQ ID NO: 28/30/32, 76/78/80, 4/6/8, 52/54/56, 100/102/104, 124/126/128, 148/150/152, 172/174/176, 196/198/200, 220/222/224, 244/246/248, 268/270/272, 292/294/296, 316/318/320, 340/342/344, 364/366/368, 388/390/392, 412/414/416, 436/438/440 and 460/462/464.

2. An isolated human antibody or antigen-binding fragment thereof that specifically binds human angiopoietin-like protein 4 (hANGPTL4), comprising a light chain complementarity determining region 1 (LCDR1)/LCDR2/LCDR3 combination selected from SEQ ID NO:36/38/40, 84/86/88, 12/14/16, 60/62/64, 108/110/112, 132/134/136, 156/158/160, 180/182/184, 204/206/208, 228/230/232, 252/254/256, 276/278/280, 300/302/304, 324/326/328, 348/350/352, 372/374/376,396/398/400, 420/422/424 and 444/446/448.

3. The antibody or antigen-binding fragment according to claim 1 or 2, comprising heavy and light chain CDR sequences HCDR1/HCDR2/HCDR3/LCDR1/LCDR2/LCDR3 comprising a CDR sequence combination selected from SEQ ID NO:28/30/32/36/38/40, 76/78/80/84/86/88, 4/6/8/12/14/16, 52/54/56/60/62/64, 100/102/104/108/110/112, 124/126/128/132/134/136, 148/150/152/156/158/160, 172/174/176/180/182/184, 196/198/200/204/206/208, 220/222/224/228/230/232, 244/246/248/252/254/256, 268/270/272/276/278/280, 292/294/296/300/302/304, 316/318/320/324/326/328, 340/342/344/348/350/352, 364/366/368/372/374/376, 388/390/392/396/398/400, 412/414/416/420/422/424, 436/438/440/444/446/448 and 460/462/464/396/398/400.

4. An isolated human antibody or antigen-binding fragment of an antibody that specifically binds human angiopoietin-like protein 4 (hANGPTL4), comprising a heavy chain variable region (HCVR) selected from SEQ ID NO:487, 90, 2, 18, 22, 26, 42, 46, 50, 66, 70, 74, 94, 98, 114, 118, 122, 138, 142, 146, 162, 166, 170, 186, 190, 194, 210, 214, 218, 234, 238, 242, 258, 262, 266, 282, 286, 290, 306, 310, 314, 330, 334, 338, 354, 358, 362, 378, 382, 386, 402, 406, 410, 426, 430, 434, 450, 454, 458, 466 and 468.

5. The antibody or antigen-binding fragment according to claim 4, further comprising a light chain variable region (LCVR) selected from SEQ ID NO:44, 92, 10, 20, 24, 34, 48, 58, 68, 72, 82, 96, 106, 116, 120, 130, 140, 144, 154, 164, 168, 178, 188, 192, 202, 212, 216, 226, 236, 240, 250, 260, 264, 274, 284, 288, 298, 308, 312, 322, 332, 336, 346, 356, 360, 370, 380, 384, 394, 404, 408, 418, 428, 432, 442, 452 and 456.

6. The antibody or antigen-binding fragment according to any one of claims 1 to 5, comprising a HCVR/LCVR sequence pair selected from SEQ ID NO:487/44, 90/92, 2/10, 18/20, 22/24, 26/34, 42/44, 46/48, 50/58, 66/68, 70/72, 74/82, 94/96, 98/106, 114/116, 118/120, 122/130, 138/140,

142/144, 146/154, 162/164, 166/168, 170/178, 186/188, 190/192, 194/202, 210/212, 214/216, 218/226, 234/236, 238/240, 242/250, 258/260, 262/264, 266/274, 282/284, 286/288, 290/298, 306/308, 310/312, 314/322, 330/332, 334/336, 338/346, 354/356, 358/360, 362/370, 378/380, 382/384, 386/394, 402/404, 406/408, 410/418, 426/428, 430/432, 434/442, 450/452, 454/456, 458/394, 466/404 and 468/408.

7. The antibody or antigen-binding fragment according to any one of claims 1 to 6, comprising a HCVR/LCVR sequence pair SEQ ID NO:487/44 or 90/92.

8. An isolated human antibody or antigen-binding fragment thereof that specifically binds hANGPTL4, comprising heavy and light chain CDR sequences contained within the HCVR/LCVR sequence pair of the antibody or antigen-binding fragment according to claim 6 or 7.

9. An antibody or antigen-binding fragment thereof which competes for binding to hANGPTL4 with the antibody or antigen-binding fragment according to any one of claims 3, 6 and 7.

10. An antibody or antigen-binding fragment thereof which binds the same epitope as the antibody or antigen-binding fragment according to any one of claims 3, 6, 7 and 9.

11. The antibody or antigen-binding fragment according to any one of claims 3, 6 and 7, wherein the antibody or antigen-binding fragment cross-reacts with cynomolgus monkey ANGPTL4 and rhesus monkey ANGPTL4.

12. An isolated antibody or antigen-binding fragment thereof that specifically binds human angiopoietin-like protein 4 (hANGPTL4), comprising:

(a) a heavy chain complementarity determining region 3 (HCDR3) comprising an amino cid sequence of the formula X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 - X^9 - X^{10} - X^{11} - X^{12} - X^{13} - X^{14} - X^{15} - X^{16} - X^{17} - X^{18} - X^{19} - X^{20} (SEQ ID NO:471), wherein X^1 is Ala, X^2 is Arg or Lys, X^3 is Gly or Glu, X^4 is Gly, Asp or absent, X^5 is Asp or absent, X^6 is Leu, Arg or absent, X^7 is Arg or Ser, X^8 is Phe, Gly or Arg, X^9 is Leu, His or Asn, X^{10} is Asp, Pro or Tyr, X^{11} is Trp, Tyr or Phe, X^{12} is Leu, Phe, Val or Asp, X^{13} is Ser, Tyr or Gly, X^{14} is Ser, Tyr or Asp, X^{15} is Tyr, X^{16} is Phe or Gly, X^{17} is Leu or absent, X^{18} is Asp, X^{19} is Tyr, Val or Phe, and X^{20} is Trp; and

(b) a light chain complementarity determining region 3 (LCDR3) comprising an amino acid sequence of the formula X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 - X^9 - X^{10} (SEQ ID NO:474), wherein X^1 is Gln, X^2 is Asn or Gln, X^3 is Tyr or Leu, X^4 is Asn, His, Ser or Asp, X^5 is Thr or Ser, X^6 is Ala or Tyr, X^7 is Pro, Ser or Phe, X^8 is Leu or Arg, X^9 is Thr, and X^{10} is Phe.

13. The antibody or antigen-binding fragment of claim 12, further comprising:

(c) a HCDR1 comprising an amino acid sequence of the formula X^1 - X^2 - X^3 - X^4 - X^5 -

X^6 - X^7 - X^8 (SEQ ID NO:469), wherein X^1 is Gly, X^2 is Gly or Phe, X^3 is Ser or Thr, X^4 is Phe, X^5 is Ser, X^6 is Ile, Ser or Thr, X^7 is His or Tyr, and X^8 is His, Gly or Asp;

(d) a HCDR2 comprising an amino acid sequence of the formula X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 (SEQ ID NO:470), wherein X^1 is Ile, X^2 is Asn, Ser or Gly, X^3 is His, Phe, Ser or Val, X^4 is Arg, Asp or Ala, X^5 is Gly, X^6 is Gly or absent, X^7 is Ser, Asn or Asp, and X^8 is Thr or Lys;

(e) a LCDR1 comprising an amino acid sequence of the formula X^1 - X^2 - X^3 - X^4 - X^5 - X^6 (SEQ ID NO:472), wherein X^1 is Gln, X^2 is Gly or Ser, X^3 is Ile, X^4 is Ser or Asn, X^5 is Asp, Ser or Arg, and X^6 is Tyr or Trp; and

(f) a LCDR2 comprising an amino acid sequence of the formula X^1 - X^2 - X^3 (SEQ ID NO:473), wherein X^1 is Ala or Lys, X^2 is Ala, and X^3 is Ser.

14. An isolated human antibody or antigen-binding fragment thereof that specifically binds human angiopoietin-like protein 4 (hANGPTL4), comprising a heavy chain variable region (HCVR) encoded by nucleotide sequence segments derived from V_H, D_H and J_H germline gene segments, and a light chain variable region (LCVR) encoded by nucleotide sequence segments derived from V_K and J_K germline gene segments, wherein the HCVR and the LCVR are encoded by nucleotide sequence segments derived from a combination of (i) V_H4-34, D_H3-3, J_H4, V_K1-27 and J_K4; or (ii) V_H3-30, D_H5-12, J_H6, V_K1-9 and J_K4.

15. An isolated nucleic acid molecule encoding the antibody or antigen-binding fragment according to any one of the preceding claims.

16. An expression vector comprising the nucleic acid molecule of claim 15.

17. A host cell comprising the expression vector of claim 16.

18. A method of producing an anti-hANGPTL4 antibody or antigen-binding fragment thereof, comprising growing the host cell of claim 17 under conditions permitting production of the antibody or fragment thereof, and recovering the antibody or fragment thereof so produced.

19. A pharmaceutical composition comprising the antibody or antigen-binding fragment according to any one of claims 1 to 14, and a pharmaceutically acceptable carrier.

20. The pharmaceutical composition of claim 19, further comprising one or more additional therapeutic agents selected from an inhibitor of HMG-CoA reductase; an inhibitor of cholesterol uptake or bile acid re-absorption, or both; an agent which increases lipoprotein catabolism; an agent which reduces the number of non-fatal heart attacks; and an activator of the LXR transcription factor.

21. The pharmaceutical composition of claim 19, further comprising one or more additional therapeutic agents selected from statin, niacin, fibrate, and anti-PCSK9 antibody.

22. A method for preventing or treating a disease or disorder which is prevented, ameliorated, improved or inhibited by reduction or inhibition of ANGPTL4 activity, comprising administering to a subject in need thereof a therapeutically effective amount of the pharmaceutical composition according to any one of claims 19 to 21.

23. The method of claim 22, wherein the disease or disorder is selected from hypertriglyceridemia, hypercholesterolemia, chylomicronemia, atherogenic dyslipidemia, a cardiovascular disease or disorder, acute pancreatitis, nonalcoholic steatohepatitis (NASH), diabetes and obesity.

24. An antibody or antigen-binding fragment according to any one of claims 1 to 14 for use to improve, ameliorate, inhibit or prevent an ANGPTL4-mediated disease or disorder.

25. The antibody or antigen-binding fragment according to claim 24, wherein the ANGPTL4-mediated disease or disorder is selected from hypertriglyceridemia, hypercholesterolemia, chylomicronemia, atherogenic dyslipidemia, a cardiovascular disease or disorder, acute pancreatitis, nonalcoholic steatohepatitis (NASH), diabetes and obesity.

26. Use of an antibody or antigen-binding fragment thereof according to any one of claims 1 to 14 in the manufacture of a medicament for use to improve, ameliorate, inhibit or prevent an ANGPTL4-mediated disease or disorder.

27. The use according to claim 26, wherein the ANGPTL4-mediated disease or disorder is selected from hypertriglyceridemia, hypercholesterolemia, chylomicronemia, atherogenic dyslipidemia, a cardiovascular disease or disorder, acute pancreatitis, nonalcoholic steatohepatitis (NASH), diabetes and obesity.

We claim:

1. An isolated human antibody or antigen-binding fragment thereof that specifically binds human angiopoietin-like protein 4 (hANGPTL4), comprising three heavy chain complementarity determining regions, HCDR1, HCDR2 and HCDR3, and three light chain complementarity determining regions, LCDR1, LCDR2 and LCDR3, wherein the amino acid sequences of the HCDR1, HCDR2 and HCDR3 comprise SEQ ID NO:28, 30 and 32, respectively; and the amino acid sequences of the LCDR1, LCDR2 and LCDR3 comprise SEQ ID NO:36, 38 and 40, respectively.

2. The antibody or antigen-binding fragment of claim 1, comprising a heavy chain variable region (HCVR) comprising an amino acid sequence selected from the group consisting of SEQ ID NO:487, 42, 26 and 46.

3. The antibody or antigen-binding fragment of claim 1, comprising a light chain variable region (LCVR) comprising an amino acid sequence selected from the group consisting of SEQ ID NO:44, 34 and 48.

4. The antibody or antigen-binding, fragment of claim 1, comprising a HCVR/LCVR sequence pair selected from the group consisting of SEQ ID NO:487/44, 42/44, 26/34 and 46/48.

5. A pharmaceutical composition comprising the antibody or antigen-binding fragment of claim 4 and a pharmaceutically acceptable carrier.

6. A pharmaceutical composition comprising the antibody or antigen-binding fragment of claim 1 and a pharmaceutically acceptable carrier.