CLAIMS

1. Use of an anti-PCSK9 antibody or antigen-binding fragment thereof in the manufacture of a medicament for lowering cholesterol level in a human subject, wherein the anti-PCSK9 antibody or antigen-binding fragment thereof is to be administered at a dose of 15 mg to 3500 mg,

wherein the anti-PCSK9 antibody or antigen-binding fragment thereof comprises a heavy chain variable region VH and a light chain variable region VL, wherein

(a) the VH comprises a combination of HCDR1, HCDR2 and HCDR3, wherein HCDR1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 10; HCDR2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 17; HCDR3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 19; and

(b) the VL comprises a combination of LCDR1, LCDR2 and LCDR3, wherein LCDR1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 4; LCDR2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 5; LCDR3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 6,

wherein the medicament is to be administered once at an interval equal to or greater than once every four weeks (Q4W), once every four weeks (Q4W), once every five weeks (Q5W), once every six weeks (Q6W), once every seven weeks (Q7W), once every eight weeks (Q8W), once every nine weeks (Q9W), once every ten weeks (Q10W), once every eleven weeks (Q11W), once every twelve weeks (Q12W), once every 4 months, once every 5 months, once every 6 months, once every 7 months, or once a year.

2. Use of an anti-PCSK9 antibody or antigen-binding fragment thereof in the manufacture of a medicament for preventing or treating hypercholesterolemia in a human subject, wherein the anti-PCSK9 antibody or antigen-binding fragment thereof is to be administered at a dose of 15 mg to 3500 mg,

wherein the anti-PCSK9 antibody or antigen-binding fragment thereof comprises a heavy chain variable region VH and a light chain variable region VL, wherein

(a) the VH comprises a combination of HCDR1, HCDR2 and HCDR3, wherein HCDR1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 10; HCDR2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 17; HCDR3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 19; and

(b) the VL comprises a combination of LCDR1, LCDR2 and LCDR3, wherein LCDR1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 4; LCDR2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 5; LCDR3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 6,

wherein the medicament is to be administered once at an interval equal to or greater than once

every four weeks (Q4W), once every four weeks (Q4W), once every five weeks (Q5W), once every six weeks (Q6W), once every seven weeks (Q7W), once every eight weeks (Q8W), once every nine weeks (Q9W), once every ten weeks (Q10W), once every eleven weeks (Q11W), once every twelve weeks (Q12W), once every 4 months, once every 5 months, once every 6 months, once every 7 months, or once a year.

3. Use of an anti-PCSK9 antibody or antigen-binding fragment thereof in the manufacture of a medicament for preventing or treating a cholesterol-related disease in a human subject, wherein the anti-PCSK9 antibody or antigen-binding fragment thereof is to be administered at a dose of 15 mg to 3500 mg,

wherein the anti-PCSK9 antibody or antigen-binding fragment thereof comprises a heavy chain variable region VH and a light chain variable region VL, wherein

(a) the VH comprises a combination of HCDR1, HCDR2 and HCDR3, wherein HCDR1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 10; HCDR2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 17; HCDR3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 19; and

(b) the VL comprises a combination of LCDR1, LCDR2 and LCDR3, wherein LCDR1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 4; LCDR2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 5; LCDR3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 6,

wherein the medicament is to be administered once at an interval equal to or greater than once every four weeks (Q4W), once every four weeks (Q4W), once every five weeks (Q5W), once every six weeks (Q6W), once every seven weeks (Q7W), once every eight weeks (Q8W), once every nine weeks (Q9W), once every ten weeks (Q10W), once every eleven weeks (Q11W), once every twelve weeks (Q12W), once every 4 months, once every 5 months, once every 6 months, once every 7 months, or once a year.

4. The use according to any one of claims 1–3, wherein

(a) the heavy chain variable region VH comprises or consists of an amino acid sequence set forth in SEQ ID NO: 30; and

(b) the light chain variable region VL comprises or consists of an amino acid sequence set forth in SEQ ID NO: 24.

5. The use according to any one of claims 1–4, wherein

(a) the heavy chain comprises or consists of an amino acid sequence set forth in SEQ ID NO: 41; and

(b) the light chain comprises or consists of an amino acid sequence set forth in SEQ ID NO: 35.

6. The use according to any one of claims 1–5, wherein the cholesterol is LDL-cholesterol.

7. The use according to any one of claims 1–6, wherein the anti-PCSK9 antibody or antigen-binding fragment thereof is to be administered at a dose of 25 mg to 3000 mg, 50 mg to 2500 mg, 75 mg to 2000 mg, 100 mg to 2000 mg, 200 mg to 2000 mg, 250 mg to 1500 mg, 300 mg to 1000 mg, 450 mg to 1000 mg, 600 mg to 1000 mg, 350 mg to 900 mg, 400 mg to 800 mg, 450 mg to 700 mg, 300 mg to 600 mg, or 450 mg to 600 mg.

8. The use according to any one of claims 1–7, wherein the medicament is to be administered parenterally.

9. The use according to any one of claims 1–8, wherein an LDL-cholesterol level in the subject is decreased by > 30%, > 35%, > 40%, > 45%, > 50%, > 55%, > 60%, > 65%, > 70%, > 75%, > 80%, > 85%, or > 90% at 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 3 months, 4 months or 5 months after the medicament has been administered to the subject, compared to the LDL-cholesterol level in the subject before the medicament has been administered.

10. The use according to any one of claims 1–9, wherein a serum free PCSK-9 level in the subject is decreased by > 30%, > 35%, > 40%, > 45%, > 50%, > 55%, > 60%, > 65%, > 70%, > 75%, > 80%, > 85%, or > 90% at 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 3 months, 4 months or 5 months after the medicament has been administered to the subject compared to the serum free PCSK-9 level in the subject before the medicament has been administered.

11. The use according to any one of claims 1–10, wherein a total cholesterol level in the subject is still decreased by > 30%, > 35%, > 40%, > 45%, > 50%, > 55%, > 60%, > 65%, > 70%, > 75%, > 80%, > 85%, or > 90% at 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 3 months, 4 months or 5 months after the medicament has been administered to the subject compared to the total cholesterol level in the subject before the medicament has been administered.

12. The use according to any one of claims 1–11, wherein an apolipoprotein B level in the subject is decreased by > 30%, > 35%, > 40%, > 45%, > 50%, > 55%, > 60%, > 65%, > 70%, > 75%, > 80%, > 85%, or > 90% at 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 3 months, 4 months or 5 months after the medicament has been administered to the subject compared to the apolipoprotein B level in the subject before the medicament has been administered.

13. The use according to any one of claims 1–12, wherein a non-high-density lipoprotein cholesterol level in the subject is still decreased by > 30%, > 35%, > 40%, > 45%, > 50%, > 55%, > 60%, > 65%, > 70%, > 75%, > 80%, > 85%, or > 90% at 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 3 months, 4 months or 5 months after the medicament has been administered to the subject compared to the non-high-density lipoprotein cholesterol level in the subject before the medicament has been administered.

14. The use according to any one of claims 1–13, wherein a lipoprotein a level in the subject is decreased by > 20%, > 30%, > 35%, > 40%, > 45%, > 50%, > 55%, > 60%, > 65%, > 70%, > 75%, > 80%, > 85%, or > 90% at 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 3 months, 4 months or 5 months after the medicament has been administered to the subject compared to the lipoprotein a level in the subject before the medicament has been administered.

15. The use according to any one of claims 1–14, wherein an ApoB/ApoA1 level in the subject is decreased by > 20%, > 30%, > 35%, > 40%, > 45%, > 50%, > 55%, > 60%, > 65%, > 70%, > 75%, > 80%, > 85%, or > 90% at 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, 10 weeks, 3 months, 4 months or 5 months after the medicament has been administered to the subject compared to the ApoB/ApoA1 level in the subject before the medicament has been administered.

16. The use according to claim 1 or 3, wherein the cholesterol is serum LDL-cholesterol.

17. The use according to any one of claims 1–16, wherein the medicament is to be administered once every four weeks (Q4W), once every six weeks (Q6W), or once every eight weeks (Q8W).

18. The use according to any one of claims 1–17, wherein the subject, after the medicament has been administered, does not develop severe adverse events, particularly severe adverse events associated with the anti-PCSK9 antibody or antigen-binding fragment thereof.

19. The use according to any one of claims 1–18, wherein the subject has an incidence of adverse events comparable to a subject that has been administered a placebo.

20. The use according to claim 2, wherein the hypercholesterolemia is selected from homozygous familial hypercholesterolemia, heterozygous familial hypercholesterolemia and non-familial hypercholesterolemia.

21. The use according to any one of claims 1–20, wherein the anti-PCSK9 antibody or antigen-binding fragment thereof is comprised in a liquid antibody preparation comprising:

(i) 100 mg/mL to 200 mg/mL of the anti-PCSK-9 antibody or antigen-binding fragment thereof;

(ii) 0.2 mg/mL to 10 mg/mL of histidine;

(iii) 1% to 6% (w/v) of sorbitol and/or 50 mmol/L to 180 mmol/L of arginine or arginine salt; and

(iv) 0.05 mg/mL to 1 mg/mL of polysorbate-80 or polysorbate-20;

wherein the pH of the liquid preparation is 5.0 to 6.0.

22. The use according to any one of claims 1–21, wherein the anti-PCSK9 antibody or antigen-binding fragment thereof is comprised in a liquid antibody preparation, and the liquid antibody preparation uses water as a solvent and consists of the following compositions:

Anti-PCSK9 antibody or antigen-binding fragment thereof 150 mg/mL

Histidine 1.5 g/L

Arginine 90 mmol/L

Sorbitol 3% (w/v)

Polysorbate 80 0.3 g/L;

wherein the pH of the liquid preparation is 5.5.

23. A single pharmaceutical dosage unit, comprising an anti-PCSK9 antibody or antigen-binding fragment thereof as defined in any one of claims 1- 22 at a dose of 15 mg to 3500 mg.

24. A pharmaceutical kit, comprising the single pharmaceutical dosage unit according to claim 23.

25. The use according to claim 3, wherein the cholesterol-related disease is hyperlipidemia.