CLAIMS

1. A pharmaceutical composition comprising about 40 to about 500 mg per dose of an antibody or an antigen-binding fragment thereof which specifically binds human proprotein convertase subtilisin/kexin type 9 (hPCSK9) together with a pharmaceutically acceptable excipient or carrier.

2. The pharmaceutical composition of claim 1, comprising about 50 mg, about 100 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 350mg, about 400 mg, about 450 mg, or about 500 mg of the antibody or antigen-binding fragment thereof.

3. The pharmaceutical composition of any one of claims 1-2, comprising an effective dose of an antibody or an antigen-binding fragment thereof which specifically binds hPCSK9, wherein the dose is sufficient for sustained reduction of low-density lipoprotein (LDL-C) levels over a period of at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23 or at least 28 days after administration.

4. The pharmaceutical composition of any one of claims 1 to 3, wherein the antibody or antigen-binding fragment thereof has one or more of the following features:

a. reduction of low-density lipoprotein (LDL-C) levels of at least about -25% to about -40% relative to a predose level with a sustained reduction over at least a 14 day period following biweekly administration of a dose of about 50 mg;

b. reduction of LDL-C of at least about -50% to about -65% relative to a predose level with a sustained reduction over at least a 14 day-period following biweekly administration of a dose of about 100 mg;

c. reduction of LDL-C of at least about -60 % to at least about -75% relative to a predose level with a sustained reduction over at least a 14 day-period following biweekly administration of a dose of about 150 mg;

d. reduction of LDL-C of at least about 40% to about 75% relative to a predose level with a sustained reduction over at least a 28 day period following administration of a dose of about 200 mg every 4 weeks;

e. reduction of LDL-C of at least about -50 % to about -75% relative to a predose level with a sustained reduction over at least a 28 day-period following administration of a dose of about 300 mg every 4 weeks;

f. increase of serum HDL cholesterol levels of at least 2-5.5% relative to a predose level following biweekly administration of a dose of about 150 mg;

g. little or no measurable effect on troponin levels, following administration of a dose of about 50-300 mg every 2-4 weeks; or

h. increase of one or more of: total-cholesterol levels, ApoB levels, non HDL-C levels, or Apo-B/ApoA-1 ratio, upon administration to a subject.

5. The pharmaceutical composition of any one of claims 1-4, wherein the antibody or antigen-binding fragment thereof is capable of overcoming statin resistance when administered to a subject with statin-resistant hypercholesterolemia.

6. The pharmaceutical composition of any one of claims 1-5, wherein the antibody or antigen-binding fragment thereof comprises heavy and light chain CDR sequences from the HCVR and LCVR amino acid sequence pair having SEQ ID NOs: 90/92.

7. The pharmaceutical composition of any one of claims 1-6 wherein the composition is a liquid formulation.

8. The pharmaceutical composition of claim 7, wherein the liquid formulation is an injection solution comprising about 40 mg to about 200 mg of the antibody or antigen-binding fragment per 1 ml volume.

9. The pharmaceutical composition of claim 8, wherein the injection solution comprises about 40 mg, about 50 mg, about 75 mg, about 100 mg, about 150 mg or about 200 mg of the antibody or antigen-binding fragment per 1 ml volume.

10. A unit dosage form comprising the pharmaceutical composition of any one of claims 1-9.

11. The unit dosage form of claim 10, comprising about 40 mg, about 50 mg, about 75 mg, about 100 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, or about 500 mg of the antibody or antigen-binding fragment.

12. The unit dosage form of any one of claims 10 or 11 comprising the antibody or antigen binding fragment as a liquid formulation in a hermetically sealed container.

13. The unit dosage form of claim 12, wherein the container is selected from the group consisting of a vial, a sachette, a pre-filled syringe, a pre-filled autoinjector, a cartridge, a reusable syringe, and a reusable applicator.

14. The unit dosage form of any of claims 10-13, wherein the quantity of the antibody or antigen binding fragment is indicated on the hermetically-sealed container.

15. An article of manufacture comprising the pharmaceutical composition of any one of claims 1-9 and a container.

16. The article of manufacture of claim 15 comprising one or more of the following components:

a. one or more unit dosage forms according to claims 10-14;

c. instructions for use; and

c. a device for application of the antibody such as a syringe.

17. The article of manufacture of claim 16 further comprising one or more unit dosage forms comprising an HMG-CoA reductase inhibitor.

18. The article of manufacture of any of claims 16-17 comprising sufficient unit dosage forms for a weekly, bi-weekly, or every 4 week administration regime.

19. The pharmaceutical composition of any one of claims 1 to 18 for use in the treatment of a disease or condition in which PCSK9 expression or activity causes an impact.

20. The pharmaceutical composition of claim 19, wherein the disease or condition is selected from the group consisting of: elevated total cholesterol levels, elevated low-density lipoprotein cholesterol (LDL-C) levels, hyperlipidemia, dyslipidemia, atherosclerosis, hypercholesterolemia, primary hypercholesterolemia, familial hypercholesterolemia, and hypercholesteremia which is uncontrolled by statins

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A pharmaceutical composition comprising 40 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 250 mg, 300 mg, 350mg, 400 mg, 450 mg or 500mg of an antibody or an antigen-binding fragment thereof which specifically binds human proprotein convertase subtilisin/kexin type 9 (hPCSK9) together with a pharmaceutically acceptable excipient or carrier, wherein the antibody or antigen-binding fragment thereof comprises the three heavy chain CDRs set forth in SEQ ID NOs: 76, 78, and 80 and the three light chain CDRs set forth in SEQ ID NOs: 84, 86, and 88.

2. The pharmaceutical composition of claim 1, wherein the antibody or antigen-binding fragment thereof comprises the heavy chain variable region (HCVR) amino acid sequence and the light chain variable region (LCVR) amino acid sequence set forth in SEQ ID NOs: 90 and 92, respectively.

3. The pharmaceutical composition of claim 1 or 2, comprising about 75 mg of the antibody or antigen-binding fragment thereof.

4. The pharmaceutical composition of claim 1 or 2, comprising about 150 mg of the antibody or antigen-binding fragment thereof.

5. The pharmaceutical composition of claim 1 or 2, comprising about 300 mg of the antibody or antigen-binding fragment thereof.

6. The pharmaceutical composition of any one of the previous claims comprising the antibody or antigen-binding fragment thereof as a liquid formulation, wherein the liquid formulation is an injectable solution of the antibody or antigen-binding fragment thereof per 1 ml volume.

7. The pharmaceutical composition of claim 6, wherein the injectable solution comprises 75 mg of the antibody or antigen-binding fragment thereof per 1 ml volume.

8. The pharmaceutical composition of claim 6, wherein the injectable solution comprises 150 mg of the antibody or antigen-binding fragment thereof per 1 ml volume.

9. The pharmaceutical composition of claim 6, wherein the injectable solution comprises 300 mg of the antibody or antigen-binding fragment thereof per 1 ml volume.

10. The pharmaceutical composition of claim 1 or 2 being comprised in a unit dosage form, wherein the unit dosage form comprises about 40 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 250 mg, 300 mg, 350 mg, 400 mg, 450 mg, or 500 mg of the antibody or antigen-binding fragment thereof.

11. The pharmaceutical composition of claim 10, wherein the unit dosage form comprises 75 mg of the antibody or antigen-binding fragment thereof.

12. The pharmaceutical composition of claim 10, wherein the unit dosage form comprises 150 mg of the antibody or antigen-binding fragment thereof.

13. The pharmaceutical composition of claim 10, wherein the unit dosage form comprises 300 mg of the antibody or antigen-binding fragment thereof.

14. The pharmaceutical composition of any one of claims 1-13, wherein the pharmaceutical composition is in a hermetically sealed container selected from the group consisting of a vial, a sachet, a pre-filled syringe, a pre-filled autoinjector, a cartridge for a reusable syringe, and an applicator.

15. The pharmaceutical composition of any one of claims 1-14, wherein the antibody or antigen-binding fragment thereof binds an epitope comprising one or more of amino acid residues at positions 238, 153, 159, and 343 of hPCSK9 (SEQ ID NO:755).

16. The pharmaceutical composition of any one of claims 1-15, wherein the antibody or antigen-binding fragment thereof is capable of achieving one or more of the following in a subject:

a) reduction of LDL-C of at least -60 % to at least -75% relative to a predose level with a sustained reduction over at least a 14 day-period when formulated at a dose of 150 mg that is suitable for administration every two weeks;

b) reduction of LDL-C of at least -50 % to -75% relative to a predose level with a sustained reduction over at least a 28 day-period when formulated at a dose of 300 mg that is suitable for administration every four weeks;

c) increase of serum HDL cholesterol levels of at least 2%, at least 2.5%, at least 3%, at least 3.5%, at least 4%, at least 4.5%, at least 5% or at least 5.5% relative to a predose level when formulated at a dose of 150 mg that is suitable for administration every two weeks;

d) increase of one or more of: total-cholesterol levels, ApoB levels, non HDL-C levels, and Apo-B/ApoA-1 ratio.

17. A pharmaceutical composition comprising 75 mg of an antibody or an antigen-binding fragment thereof which specifically binds hPCSK9, wherein the antibody or antigen-binding fragment thereof comprises the heavy chain variable region (HCVR) amino acid sequence and the light chain variable region (LCVR) amino acid sequence set forth in SEQ ID NOs: 90 and 92, respectively, and wherein the antibody or antigen-binding fragment thereof is in a 1 ml injectable solution.

18. A pharmaceutical composition comprising 150 mg of an antibody or an antigen-binding fragment thereof which specifically binds hPCSK9, wherein the antibody or antigen-binding fragment thereof comprises the heavy chain variable region (HCVR) amino acid sequence and the light chain variable region (LCVR) amino acid sequence set forth in SEQ ID NOs: 90 and 92, respectively, and wherein the antibody or antigen-binding fragment thereof is in a 1 ml injectable solution.

19. A pharmaceutical composition comprising 300 mg of an antibody or an antigen-binding fragment thereof which specifically binds hPCSK9, wherein the antibody or antigen-binding fragment thereof comprises the heavy chain variable region (HCVR) amino acid sequence and the light chain variable region (LCVR) amino acid sequence set forth in SEQ ID NOs: 90 and 92, respectively, and wherein the antibody or antigen-binding fragment thereof is in a 1 ml injectable solution.

20. The pharmaceutical composition according to any one of the previous substantially as hereinbefore described.

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