

1. a heavy chain polypeptide comprising the following complementarity determining regions (CDRs): a heavy chain CDR1 that is a CDR1 in SEQ ID NOs:14; a heavy chain CDR2 that is a CDR2 in SEQ ID NOs:14; a heavy chain CDR3 that is a CDR3 in SEQ ID NOs:14, and
2. a light chain polypeptide comprising the following CDRs: a light chain CDR1 that is a CDR1 in SEQ ID NOs:15; a light chain CDR2 that is a CDR2 in SEQ ID NOs:15; and a light chain CDR3 that is a CDR3 in SEQ ID NOs:15;

and

b. N-acetyl arginine, and

c. at least one of an arginine salt or proline,

wherein the pharmaceutical composition has a viscosity of less than 80 cP, and wherein the PCSK9-binding polypeptide is present at a concentration of 140 mg/mL to 260 mg/mL and the N-acetyl arginine is present at a concentration of 25 mM to 230 mM.

In another aspect, the present disclosure refers to a method of preparing a PCSK9-binding polypeptide in a pharmaceutical composition comprising at least 140 mg/mL of PCSK9-binding polypeptide, comprising adding to a pharmaceutical composition comprising the PCSK9-binding polypeptide an effective amount of N-acetyl arginine and at least one of an arginine salt or proline, such that the viscosity of the pharmaceutical composition is reduced when compared to the pharmaceutical composition lacking the N-acetyl arginine, and wherein the PCSK9-binding polypeptide is selected from the group consisting of:

a. a monoclonal antibody comprising a heavy chain polypeptide having an amino acid sequence of SEQ ID NO:1 and a light chain polypeptide having an amino acid sequence of SEQ ID NO:2 (evolocumab), or an antigen-binding fragment thereof; and

b. a monoclonal antibody, comprising:

- i. a heavy chain polypeptide comprising the following complementarity determining regions (CDRs): a heavy chain CDR1 that is a CDR1 in SEQ ID

NOs:14; a heavy chain CDR2 that is a CDR2 in SEQ ID NOs:14; a heavy chain CDR3 that is a CDR3 in SEQ ID NOs:14, and

- ii. a light chain polypeptide comprising the following CDRs: a light chain CDR1 that is a CDR1 in SEQ ID NOs:15; a light chain CDR2 that is a CDR2 in SEQ ID NOs:15; and a light chain CDR3 that is a CDR3 in SEQ ID NOs:15,

wherein the pharmaceutical composition has a viscosity of less than 80 cP, and wherein the PCSK9-binding polypeptide is present at a concentration of 140 mg/mL to 260 mg/mL and the N-acetyl arginine is present at a concentration of 25 mM to 230 mM.

In one example, the present disclosure refers to a method of formulating a therapeutic polypeptide, comprising

- a. a first concentration step, wherein the polypeptide in a first solution is concentrated;
- b. a first solution exchange step, wherein the concentrated polypeptide in the first solution is exchanged into a second solution comprising N-acetyl arginine using diafiltration;
- c. a second concentration step, wherein the polypeptide in the second solution is concentrated;
- d. a second solution exchange step, wherein the polypeptide in the concentrated second solution is exchanged into a third solution comprising N-acetyl arginine using diafiltration; and
- e. a third concentration step, wherein the polypeptide in the third solution is concentrated;

wherein the therapeutic polypeptide comprises a PCSK9-binding polypeptide that blocks binding of PCSK9 to LDLR and is selected from the group consisting of:

- i. a monoclonal antibody comprising a heavy chain having an amino acid sequence of SEQ ID NO:1 and a light chain having an amino acid sequence of SEQ ID NO:2 (evolocumab), or an antigen-binding fragment thereof; and
- ii. a monoclonal antibody, comprising:

CLAIMS

1. Use of a pharmaceutical composition in the preparation of a medicament for treating familial hypercholesterolemia, non-familial hypercholesterolemia, hyperlipidemia, heart disease, metabolic syndrome, diabetes, coronary heart disease, stroke, cardiovascular disease, Alzheimer's disease or dyslipidemia in a human subject, wherein the pharmaceutical composition comprises:
 - a. a PCSK9-binding polypeptide that selected from the group consisting of:
 - i. a monoclonal antibody comprising a heavy chain polypeptide having an amino acid sequence of SEQ ID NO:1 and a light chain polypeptide having an amino acid sequence of SEQ ID NO:2 (evolocumab), or an antigen-binding fragment thereof; and
 - ii. a monoclonal antibody, comprising:
 1. a heavy chain polypeptide comprising the following complementarity determining regions (CDRs): a heavy chain CDR1 that is a CDR1 in SEQ ID NOs:14; a heavy chain CDR2 that is a CDR2 in SEQ ID NOs:14; a heavy chain CDR3 that is a CDR3 in SEQ ID NOs:14, and
 2. a light chain polypeptide comprising the following CDRs: a light chain CDR1 that is a CDR1 in SEQ ID NOs:15; a light chain CDR2 that is a CDR2 in SEQ ID NOs:15; and a light chain CDR3 that is a CDR3 in SEQ ID NOs:15;
 - and
 - b. N-acetyl arginine, and
 - c. at least one of an arginine salt or proline,wherein the pharmaceutical composition has a viscosity of less than 80 cP, and wherein the PCSK9-binding polypeptide is present at a concentration of 140 mg/mL to 260 mg/mL and the N-acetyl arginine is present at a concentration of 25 mM to 230 mM.
2. The use of claim 1, wherein the PCSK9-binding polypeptide is a monoclonal antibody that comprises:
 - a heavy chain polypeptide comprising the following complementarity determining regions (CDRs): heavy chain CDR1, CDR2, and CDR3 having an amino acid sequence of SEQ ID NOs:7, 8, and 9, respectively; and
 - a light chain polypeptide comprising the following CDRs: light chain CDR1, CDR2, and CDR3 having an amino acid sequence of SEQ ID NOs:4, 5, and 6, respectively.

3. The use of claim 1 or 2, wherein the PCSK9-binding polypeptide concentration is 210 mg/mL.
4. The use of any of claims 1-3, wherein the pharmaceutical composition further comprises a buffer.
5. The use of any of claim 1-4, wherein the pharmaceutical composition further comprises a surfactant.
6. The use of any of claims 1-5, wherein the pharmaceutical composition further comprises proline.
7. The use of any of claims 1-6, wherein the pharmaceutical composition further comprises the arginine salt.
8. The use of any of claims 1-7, wherein the composition comprises high molecular weight aggregates or oligomers of the PCSK9-binding polypeptide at less than 3% of the PCSK9-binding polypeptide concentration.
9. The use of any of claims 1-9, wherein the pharmaceutical composition is liquid.
10. The use of any of claims 1-9, wherein the medicament is comprised in a kit, wherein the kit further comprises a delivery device selected from the group consisting of a syringe, an injector pen, a body injector, and an autoinjector.
11. The use of any one of claims 1-10, wherein the familial hypercholesterolemia is heterozygous hypercholesterolemia, homozygous hypercholesterolemia, familial defective apop lipoprotein B-100; polygenic hypercholesterolemia; remnant removal disease, or hepatic lipase deficiency.
12. The use of any one of claims 1-10, wherein the dyslipidemia is diabetes mellitus, familial combined hyperlipidemia, familial hypertriglyceridemia, or dyslipidemia secondary to one of: dietary indiscretion, hypothyroidism, drugs including estrogen and progestin therapy, beta-blockers, and thiazide diuretics; nephrotic syndrome, chronic renal failure, Cushing's syndrome, primary biliary cirrhosis, glycogen storage diseases, hepatoma, cholestasis, acromegaly, insulinoma, isolated growth hormone deficiency, and alcohol-induced hypertriglyceridemia.
13. A method of preparing a PCSK9-binding polypeptide in a pharmaceutical composition comprising at least 140 mg/mL of PCSK9-binding polypeptide, comprising adding to a pharmaceutical composition comprising the PCSK9-binding polypeptide an effective amount of N-acetyl arginine and at least one of an arginine salt or proline, such that the viscosity of the pharmaceutical composition is reduced when compared to the pharmaceutical composition lacking the N-acetyl arginine, and wherein the PCSK9-binding polypeptide is selected from the group consisting of:

- a. a monoclonal antibody comprising a heavy chain polypeptide having an amino acid sequence of SEQ ID NO:1 and a light chain polypeptide having an amino acid sequence of SEQ ID NO:2 (evolocumab), or an antigen-binding fragment thereof; and
- b. a monoclonal antibody, comprising:
 - i. a heavy chain polypeptide comprising the following complementarity determining regions (CDRs): a heavy chain CDR1 that is a CDR1 in SEQ ID NOs:14; a heavy chain CDR2 that is a CDR2 in SEQ ID NOs:14; a heavy chain CDR3 that is a CDR3 in SEQ ID NOs:14, and
 - ii. a light chain polypeptide comprising the following CDRs: a light chain CDR1 that is a CDR1 in SEQ ID NOs:15; a light chain CDR2 that is a CDR2 in SEQ ID NOs:15; and a light chain CDR3 that is a CDR3 in SEQ ID NOs:15,

wherein the pharmaceutical composition has a viscosity of less than 80 cP, and wherein the PCSK9-binding polypeptide is present at a concentration of 140 mg/mL to 260 mg/mL and the N-acetyl arginine is present at a concentration of 25 mM to 230 mM.