CLAIMS

1. A lyophilized formulation of a drug substance ~~comprising,~~ wherein:

(i) the drug substance comprises:

(a) an isolated cystathionine β-synthase (CBS) protein comprising SEQ ID NO: 1; and

(b) a PEG molecule covalently bound to the CBS protein~~.~~; and

(ii) wherein, upon reconstitution of the lyophilized formulation to a reconstituted liquid formulation, the reconstituted liquid formulation comprises:

(a) the drug substance in a concentration of about 20-30 mg/ml;

(b) about 15mM of potassium phosphate; and

(c) about 8% (w/v) trehalose.

2. The ~~drug substance~~ lyophilized formulation of claim 1, wherein the PEG molecule is ME-200GS.

3. A ~~pharmaceutical composition~~ reconstituted liquid formulation comprising:

(i) a drug substance in an amount of about 25 mg, wherein the drug substance ~~of any one of claims~~comprises:

(a) an isolated cystathionine β-synthase (CBS) protein comprising SEQ ID NO: 1; and ~~2~~

(b) a PEG molecule covalently bound to the CBS protein; and ~~a pharmaceutically acceptable excipient, adjuvant, diluent, or carrier.~~

~~A formulation~~ (ii) about 15mM of potassium phosphate;

(iii) about 8% (w/v) trehalose; and

(iv) 1mL of ~~the pharmaceutical composition~~water.

4. The reconstituted liquid formulation of claim 3, wherein the ~~formulation~~PEG molecule is ~~lyophilized.~~ ME-200GS.

~~1. The~~ 5. Use of the lyophilized formulation of claim ~~4, wherein, upon reconstitution, the~~1 or 2 or reconstituted liquid formulation ~~comprises:~~

~~(a) the drug substance in a concentration~~ of ~~about 20-30 mg/ml;~~

~~(b) about 15mM of potassium phosphate; and~~

~~(c) about 8% (w/v) trehalose.~~

~~2. A reconstituted formulation according to~~ claim ~~5, wherein a unit dose of the formulation comprises:~~

~~(a) about 25 mg of the drug substance; and~~

~~(b) 1mL of water.~~

~~A method of treating~~ 3 or 4 in the manufacture of a medicament for the treatment of homocystinuria in a subject~~, the method comprising: administering.~~

~~3.~~ 6. The use of claim 5, wherein a therapeutically effective amount of the lyophilized formulation or reconstituted liquid formulation is to be administered to the subject ~~a therapeutically effective amount of the formulation of the pharmaceutical composition of any one of claims 4-6.~~

~~The method of claim 7, wherein the therapeutically effective amount is~~at a dosage selected from the range of about 0.25mg/kg to about 10mg/kg.

7. The ~~method~~use of claim ~~8~~6, wherein the dosage is about 0.33mg/kg.

8. The ~~method~~use of claim ~~8~~6, wherein the dosage is about 0.66mg/kg.

9. The ~~method~~use of claim ~~8~~6, wherein the dosage is about 1.0mg/kg.

10. The ~~method~~use of ~~claims 8~~claim 6, wherein the dosage is about 1.5mg/kg.

11. The ~~method~~lyophilized formulation of claim 1 or 2 or reconstituted liquid formulation of claim 3 or 4 for use in a method of decreasing the level of homocysteine (Hcy) in a subject.

12. The lyophilized formulation or reconstituted liquid formulation for use of claim 11, wherein the level of Hcy is: less than about 80µM following administration; is reduced by up to 10%, up to 20%, up to 30%, up to 40%, up to 50%, up to 60%, up to 70%, up to 80%, or up to 90% following administration; or is within the range of about 10µM to about 20µM, is less than 10µM, or is about 55µM following administration.

13. The lyophilized formulation or reconstituted liquid formulation for use of claim 11 or claim 12, wherein a therapeutically effective amount of the lyophilized formulation or reconstituted liquid formulation is to be administered to the subject at a dosage selected from: the range of about 0.25mg/kg to about 10mg/kg; about 0.33mg/kg; about 0.66mg/kg; about 1.0mg/kg; about 1.5mg/kg; about 7.0mg/kg; about 10mg/kg; and less than 10mg/kg.

14. The lyophilized formulation or reconstituted liquid formulation for use of any one of claims ~~7-12, further comprising administering~~11-13, wherein at least one selected from the group consisting of: pyridoxine, vitamin B6, and betaine~~,~~ is to be administered to the subject.

15. The ~~method~~lyophilized formulation or reconstituted liquid formulation for use of any one of claims ~~7-13~~11-14, wherein the subject is on a methionine (Met)-restricted diet.

16. The ~~method~~lyophilized formulation or reconstituted liquid formulation for use of any one of claims ~~7-14~~11-15, further comprising ~~administering~~ an anti-platelet agent to be administered.

~~4.~~ 17. The ~~method of claim 15, wherein the anti-platelet agent is a warfarin blood thinner or an anti-coagulation agent.~~

~~5.~~ ~~The method~~lyophilized formulation or reconstituted liquid formulation for use of any one of claims ~~7~~11-16, wherein ~~the administering step occurs~~formulation is: (i) to be administered about once every 3 days~~.~~

6. The method of any one of claims 7-16, wherein the administering step occurs, about once per day.

7. The method of any one of claims 7-16, wherein the administering step occurs, or about once per week.

8. The method of any one of claims 7-19, wherein the administering step is repeated; or (ii) to be repeatedly administered for about 6 weeks.

9. The method of any one of claims 7-19, wherein the administering step is repeated, for about 3 months.

10. The method of any one of claims 7-19, wherein the administering step is repeated, for about 6 months.

11. The method of any one of claims 7-19, wherein the administering step is repeated, for longer than 6 months.

12. The method of any one of claims 7-19, wherein the administering step is repeated, or for the remaining life span of the subject.

A method of decreasing the level of homocysteine (Hcy) in a subject, the method comprising: administering tolifespan of the subject a therapeutically effective amount of the formulation of the pharmaceutical composition of any one of claims 4-6.

13. The method of claim 25, wherein the level of Hcy is less than about 80μM following the administering step.

14. The method of claim 25, wherein the level of Hcy is reduced by up to 10% following the administering step.

~~15. The method of claim 25, wherein the level of Hcy is reduced by up to 20% following the administering step.~~

~~16. The method of claim 25, wherein the level of Hcy is reduced by up to 30% following the administering step.~~

~~17. The method of claim 25, wherein the level of Hcy is reduced by up to 40% following the administering step.~~

~~18. The method~~18. The lyophilized formulation of claim ~~25, wherein the level of Hcy is reduced by up to 50% following the administering step.~~

~~19. The method~~1 or 2 or reconstituted liquid formulation of claim ~~25, wherein the level of Hcy is reduced by up to 60% following the administering step.~~

~~20. The method of claim 25, wherein the level of Hcy is reduced by up to 70% following the administering step.~~

~~21. The method of claim 25, wherein the level of Hcy is reduced by up to 80% following the administering step.~~

~~22. The method of claim 25, wherein the level of Hcy is reduced by up to 90% following the administering step.~~

~~23. The method of any one of claims 25-35, wherein the level of Hcy is within the range of about 10μM to about 20μM following the administering step.~~

~~24. The method of any one of claims 25-35, wherein the level of Hcy is less than 10μM following the administering step.~~

~~25. The method of any one of claims 25-35, wherein the level of Hcy is about 55μM following the administering step.~~

~~26. The method of any one of claims 25-38, wherein the therapeutically effective amount is a dosage selected from the range of about 0.25mg/kg to about 10mg/kg.~~

~~27. The method of claim 39, wherein the dosage is about 0.33mg/kg.~~

~~28. The method of claim 39, wherein the dosage is about 0.66mg/kg.~~

~~29. The method of claim 39, wherein the dosage is about 1.0mg/kg.~~

~~30. The method of claim 39, wherein the dosage is about 1.5mg/kg.~~

~~31. The method of claim 39, wherein the dosage is about 7.0mg/kg.~~

~~32. The method of claim 39, wherein the dosage is about 10mg/kg.~~

~~33. The method of claim 39, wherein the dosage is less than 10mg/kg.~~

~~34. The method of any one of claims 25-46, further comprising administering at least one selected from the group consisting of: pyridoxine, vitamin B6, and betaine, to the subject.~~

~~35. The method of any one of claims 25-47, wherein the subject is on a methionine (Met)-restricted diet.~~

~~36. The method of any one of claims 25-48, further comprising administering an anti-platelet agent.~~

~~37. The method of claim 49, wherein the anti-platelet agent is a warfarin blood thinner or an anti-coagulation agent.~~

~~38. The method of any one of claims 25-50, wherein the administering step occurs about once every 3 days.~~

~~39. The method of any one of claims 25-50, wherein the administering step occurs about once per day.~~

~~40. The method of any one of claims 25-50, wherein the administering step occurs about once per week.~~

~~41. The method of any one of claims 25-50, wherein the administering step is repeated for about 6 weeks.~~

~~42. The method of any one of claims 25-50, wherein the administering step is repeated for about 3 months.~~

~~43. The method of any one of claims 25-50, wherein the administering step is repeated for about 6 months.~~

~~44. The method of any one of claims 25-50, wherein the administering step is repeated for longer than 6 months.~~

~~45. The method of any one of claims 25-50, wherein the administering step is repeated for the remaining life span of the subject.~~

~~A~~3 or 4 for use in a method of increasing the level of cysteine (Cys) in a subject~~, the method comprising: administering to the subject a therapeutically effective amount of the formulation of the pharmaceutical composition of any one of claims 4-6~~.

~~A~~19. The lyophilized formulation of claim 1 or 2 or reconstituted liquid formulation of claim 3 or 4 for use in a method of increasing the level of cystathionine (Cth) in a subject~~, the method comprising: administering to the subject a therapeutically effective amount of the formulation of the pharmaceutical~~

~~composition of any one of claims 4-6.~~.

~~A method of treating, alleviating, or preventing~~20. Use of the lyophilized formulation of claim 1 or 2 or reconstituted liquid formulation of claim 3 or 4 in the manufacture of a medicament for the treatment, alleviation, or prevention of negative clinical outcomes associated with the ocular system, skeletal system, vascular system, and/or central nervous system of a subject~~, the method comprising: administering to the subject a therapeutically effective amount of the formulation of the pharmaceutical composition of any one of claims 4-6~~.

21. The lyophilized formulation of claim 1 or 2 or reconstituted liquid formulation of claim 3 or 4 for use in a method of treating homocystinuria in a subject.