

CLAIMS

1. A drug substance comprising:
 - (a) an isolated cystathionine β -synthase (CBS) protein comprising SEQ ID NO: 1;
and
 - (b) a PEG molecule covalently bound to the CBS protein.
2. The drug substance of claim 1, wherein the PEG molecule is ME-200GS.
3. A pharmaceutical composition comprising: the drug substance of any one of claims 1 and 2 and a pharmaceutically acceptable excipient, adjuvant, diluent, or carrier.
4. A formulation of the pharmaceutical composition of claim 3, wherein the formulation is lyophilized.
5. The lyophilized formulation of claim 4, wherein, upon reconstitution, 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.
6. 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.
7. A method of treating homocystinuria 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.
8. The method of claim 7, wherein the therapeutically effective amount is a dosage selected from the range of about 0.25mg/kg to about 10mg/kg.
9. The method of claim 8, wherein the dosage is about 0.33mg/kg.

10. The method of claim 8, wherein the dosage is about 0.66mg/kg.
11. The method of claim 8, wherein the dosage is about 1.0mg/kg.
12. The method of claims 8, wherein the dosage is about 1.5mg/kg.
13. The method of any one of claims 7-12, further comprising administering at least one selected from the group consisting of: pyridoxine, vitamin B6, and betaine, to the subject.
14. The method of any one of claims 7-13, wherein the subject is on a methionine (Met)-restricted diet.
15. The method of any one of claims 7-14, further comprising administering an anti-platelet agent.
16. The method of claim 15, wherein the anti-platelet agent is a warfarin blood thinner or an anti-coagulation agent.
17. The method of any one of claims 7-16, wherein the administering step occurs about once every 3 days.
18. The method of any one of claims 7-16, wherein the administering step occurs about once per day.
19. The method of any one of claims 7-16, wherein the administering step occurs about once per week.
20. The method of any one of claims 7-19, wherein the administering step is repeated for about 6 weeks.
21. The method of any one of claims 7-19, wherein the administering step is repeated for about 3 months.

22. The method of any one of claims 7-19, wherein the administering step is repeated for about 6 months.
23. The method of any one of claims 7-19, wherein the administering step is repeated for longer than 6 months.
24. The method of any one of claims 7-19, wherein the administering step is repeated for the remaining life span of the subject.
25. A method of decreasing the level of homocysteine (Hcy) 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.
26. The method of claim 25, wherein the level of Hcy is less than about 80 μ M following the administering step.
27. The method of claim 25, wherein the level of Hcy is reduced by up to 10% following the administering step.
28. The method of claim 25, wherein the level of Hcy is reduced by up to 20% following the administering step.
29. The method of claim 25, wherein the level of Hcy is reduced by up to 30% following the administering step.
30. The method of claim 25, wherein the level of Hcy is reduced by up to 40% following the administering step.
31. The method of claim 25, wherein the level of Hcy is reduced by up to 50% following the administering step.
32. The method of claim 25, wherein the level of Hcy is reduced by up to 60% following the administering step.

33. The method of claim 25, wherein the level of Hcy is reduced by up to 70% following the administering step.
34. The method of claim 25, wherein the level of Hcy is reduced by up to 80% following the administering step.
35. The method of claim 25, wherein the level of Hcy is reduced by up to 90% following the administering step.
36. The method of any one of claims 25-35, wherein the level of Hcy is within the range of about 10 μ M to about 20 μ M following the administering step.
37. The method of any one of claims 25-35, wherein the level of Hcy is less than 10 μ M following the administering step.
38. The method of any one of claims 25-35, wherein the level of Hcy is about 55 μ M following the administering step.
39. 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.
40. The method of claim 39, wherein the dosage is about 0.33mg/kg.
41. The method of claim 39, wherein the dosage is about 0.66mg/kg.
42. The method of claim 39, wherein the dosage is about 1.0mg/kg.
43. The method of claim 39, wherein the dosage is about 1.5mg/kg.
44. The method of claim 39, wherein the dosage is about 7.0mg/kg.
45. The method of claim 39, wherein the dosage is about 10mg/kg.
46. The method of claim 39, wherein the dosage is less than 10mg/kg.

47. 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.
48. The method of any one of claims 25-47, wherein the subject is on a methionine (Met)-restricted diet.
49. The method of any one of claims 25-48, further comprising administering an anti-platelet agent.
50. The method of claim 49, wherein the anti-platelet agent is a warfarin blood thinner or an anti-coagulation agent.
51. The method of any one of claims 25-50, wherein the administering step occurs about once every 3 days.
52. The method of any one of claims 25-50, wherein the administering step occurs about once per day.
53. The method of any one of claims 25-50, wherein the administering step occurs about once per week.
54. The method of any one of claims 25-50, wherein the administering step is repeated for about 6 weeks.
55. The method of any one of claims 25-50, wherein the administering step is repeated for about 3 months.
56. The method of any one of claims 25-50, wherein the administering step is repeated for about 6 months.
57. The method of any one of claims 25-50, wherein the administering step is repeated for longer than 6 months.

58. The method of any one of claims 25-50, wherein the administering step is repeated for the remaining life span of the subject.
59. 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.
60. 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.
61. A method of treating, alleviating, or preventing 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.