CLAIMS

~~We Claim:~~

~~1. A method of treating homocystinuria in a subject, said method comprising administering to a subject~~1. Use of a composition comprising an isolated human truncated cystathionine beta synthase (htCBS) mutant polypeptide in the manufacture of a medicament for the treatment of homocystinuria in a subject, wherein the ~~isolated htCBS polypeptide mutant has been PEGylated, and wherein the isolated htCBS mutant polypeptide~~composition is to be administered ~~in a dose between about 0.01 and about 10 mg/kg at least once a week.~~to the subject, and wherein:

~~2. The method of claim 1, wherein~~(a) the ~~PEG is a low molecular weight linear PEG.~~

~~3. The method of claim 1, wherein the PEG is a high molecular weight four arm branched PEG.~~

~~4. The method of claim 1, wherein the dose is an amount selected from the group consisting of: about 0.05, about 0.1, about 0.5, about 1, and about 5 mg/kg.~~

~~5. The method of claim 1, wherein the dose is about 0.4 mg/kg.~~

~~6. The method of claim 1, wherein~~ isolated htCBS mutant polypeptide ~~is co-administered with betaine.~~comprises amino acids 2-413 of the amino acid sequence of SEQ ID NO:13 and has been PEGylated with an ME-200GS PEG molecule ; and

~~7. The method of claim 1, wherein betaine is administered prior to~~(b) the isolated htCBS mutant polypeptide~~.~~

~~8. The method of claim 1, wherein the htCBS mutant polypeptide is administered at least twice a week.~~

~~9. The method of claim 1, wherein the subject is a human.~~

~~10. The method of claim 1, wherein the isolated htCBS mutant polypeptide is PEGylated with at least one selected from the group consisting of: ME-200GS, ME-200MA0B, ME-400MA, GL4-400MA, and ME-050GS.~~

is to be~~11. A method of increasing the cystathionine and/or cysteine in a subject, said method comprising administering to a subject a composition comprising an isolated~~

~~human truncated cystathionine beta synthase (htCBS) mutant polypeptide, wherein said isolated htCBS mutant polypeptide has been PEGylated, and is~~ administered in a dose between ~~about~~ 0.~~01~~33 mg/kg and ~~about~~ 10 mg/kg at least once a week for at least six weeks.

2. Use of~~12. The method of claim 11, wherein the htCBS mutant polypeptide is administered at least twice a week.~~

~~13. The method of claim 11, wherein the subject is a human.~~

~~14. The method of claim 11, wherein the PEG is a low molecular weight linear PEG.~~

~~15. The method of claim 11, wherein the PEG is a high molecular weight four arm branched PEG.~~

~~16. The method of claim 11, wherein the isolated htCBS mutant polypeptide is PEGylated with at least one selected from the group consisting of: ME-200GS, ME-200MA0B, ME-400MA, GL4-400MA, and ME-050GS.~~

~~17. The method of claim 11, wherein the dose is an amount selected from the group consisting of: about 0.05, about 0.1, about 0.5, about 1, and about 5 mg/kg.~~

~~18. The method of claim 11, wherein the dose is about 0.4 mg/kg.~~

~~19. The method of claim 11, wherein the amount of cystathionine is increased to above 0.008 µM.~~

~~20. The method of claim 19, wherein the amount of cystathionine is increased to between 0.005-0.35 µM.~~

~~21. The method of claim 19, wherein the amount of cysteine is increased to above 140 µM.~~

~~22. The method of claim 19, wherein the amount of cysteine is increased to between 200 µM to 400 µM.~~

~~23. The method of claim 11, wherein isolated htCBS mutant polypeptide is co-administered with betaine.~~

~~24. The method of claim 11, wherein betaine is administered prior to administration of the isolated htCBS mutant polypeptide.~~

~~25. A method of decreasing homocysteine, methionine, and/or S-adenosyl homocysteine in a subject, said method comprising administering to a subject~~ a composition comprising an isolated human truncated cystathionine beta synthase (htCBS) mutant polypeptide in the manufacture of a medicament for increasing the cystathionine and/or cysteine in a subject, wherein ~~said isolated htCBS mutant polypeptide has been PEGylated, and~~the composition is to be administered ~~in a dose between 0.01~~to the subject, and ~~10 mg/kg at least once a week.~~wherein:

~~26. The method of claim 25, wherein the PEG is a low molecular weight linear PEG.~~

~~27. The method of claim 25, wherein the PEG is a high molecular weight four arm branched PEG.~~

~~28. The method of claim 25, wherein the dose is an amount selected from~~(a) the isolated htCBS mutant polypeptide comprises amino acids 2-413 of the amino acid sequence of SEQ ID NO:13 and has been PEGylated with an ME-200GS PEG molecule; and

(b) the isolated htCBS mutant polypeptide is to be administered in a dose between 0.33 mg/kg and 10 mg/kg at least once a week for at least six weeks.

3. Use of a composition comprising an isolated human truncated cystathionine beta synthase (htCBS) mutant polypeptide in the ~~group consisting~~manufacture of~~: about 0.05, about 0.1, about 0.5, about 1, and about 5 mg/kg.~~

~~.~~

~~29. The method of claim 25, wherein the dose is about 0.4 mg/kg.~~

~~30. The method of claim 25, wherein the amount of~~ a medicament for decreasing homocysteine ~~is less than 100 µM.~~

~~31. The method of claim 30, wherein the amount of homocysteine is about 10 µM.~~

~~32. The method of claim 30, wherein the amount of,~~ methionine ~~is less than 50 µM.~~

~~33. The method of claim 32, wherein the amount of methionine is about 30 µM.~~

~~34. The method of claim 32, wherein the amount of~~, and/or S-adenosyl homocysteine ~~is decreased to less than 0.14 µM.~~in a subject, wherein the composition is to be administered to the subject, and wherein:

~~35. The method of claim 34, wherein~~(a) the ~~amount of S-adenosyl homocysteine is decreased to about 0.015 µM.~~

~~36. The method of claim 25, wherein~~ isolated htCBS ~~is co-administered~~mutant polypeptide comprises amino acids 2-413 of the amino acid sequence of SEQ ID NO:13 and has been PEGylated with ~~betaine.~~an ME-200GS PEG molecule; and

~~37. The method of claim 25, wherein betaine is administered prior to~~(b) the isolated htCBS mutant polypeptide is to be administered in a dose between 0.33 mg/kg and 10 mg/kg at least once a week for at least six weeks.

~~38. A method of treating liver disease said method comprising administering to a subject~~4. Use of a composition comprising an isolated human truncated cystathionine beta synthase (htCBS) mutant polypeptide~~, wherein said isolated htCBS mutant polypeptide has been PEGylated, and wherein the isolated htCBS mutant polypeptide is administered in a dose between 0.01 and 10 mg/kg at least once a day for at least 4 weeks.~~ in the manufacture of a medicament for the treatment of liver disease in a subject, wherein the composition is to be administered to the subject, and wherein:

~~39. The method of claim 38, wherein the PEG is a low molecular weight linear PEG.~~

~~40. The method of claim 38, wherein the PEG is a high molecular weight four arm branched PEG.~~

~~41. The method of claim 38~~(a) the isolated htCBS mutant polypeptide comprises amino acids 2-413 of the amino acid sequence of SEQ ID NO:13 and has been PEGylated with an ME-200GS PEG molecule; and

(b) the isolated htCBS mutant polypeptide is to be administered in a dose between 0.33 mg/kg and 10 mg/kg at least once a week for at least six weeks.

5. The use of any one of claims 1-4, wherein the dose is an amount selected from the group consisting of: ~~about 0.05, about 0.1, about~~0.33 mg/kg, 0.~~5, about 1, and about~~ 4 mg/kg, 0.5 mg/kg~~.~~, 0.66 mg/kg, 1 mg/kg, 2 mg/kg, and 5 mg/kg.

~~42~~6. The ~~method~~use of ~~claim 38~~any one of claims 1-3, wherein isolated htCBS mutant polypeptide is to be co-administered with betaine.

7. The use of any one of claims 1-3, wherein betaine is to be administered prior to the ~~dose is about 0.4 mg/kg~~isolated htCBS mutant polypeptide.

~~43~~8. The use of claim 1 or claim 2, wherein the htCBS mutant polypeptide is to be administered at least twice a week.

9. The use of claim 2, wherein the amount of cystathionine is increased to above 0.008 µM or to between 0.005-0.35 µM.

10. The use of claim 9, wherein the amount of cysteine is increased to above 140 µM or to between 200 µM to 400 µM.

11. ~~method~~The use of claim 3, wherein the amount of homocysteine is decreased to less than 100 µM or to 10 µM.

12. ~~38~~The use of claim 11, wherein the amount of methionine is decreased to less than 50 µM or to 30 µM.

13. The use of claim 12, wherein the amount of S-adenosyl homocysteine is decreased to less than 0.14 µM or to 0.015 µM.

14. The use of claim 4, wherein damage to the liver parenchyma is reduced.

15. ~~44. A method of treating homocystinuria in a subject, the method comprising administering to a subject~~Use of a composition comprising an isolated human truncated cystathionine beta synthase (htCBS) mutant polypeptide ~~comprising a mutation at amino acid position 15 of SEQ ID NO: 3, wherein said isolated htCBS mutant polypeptide is PEGylated with an ME-200GS PEG molecule.~~

~~45. The method of claim 44, wherein the mutation is a substitution of a serine for a cysteine.~~

~~46. The method of claim 44, wherein the subject is a human.~~

~~47. The method of claim 44, wherein the composition is administered in a dose selected from the range of about 0.1 mg/kg to about 24 mg/kg.~~

~~48. The method of claim 44, wherein the composition is administered in a dose selected from a range in the group consisting of: about 0.01 mg/kg to about 0.5 mg/kg, about 0.3 mg/kg to about 0.7 mg/kg, about 0.5 mg/kg to about 0.9 mg/kg, and about 0.7 mg/kg to about 1.1 mg/kg.~~

~~49. A method of treating~~in the manufacture of a medicament for the treatment of at least one disease, disorder, or condition selected from the group consisting of osteoporosis, thinning hair, or eye defects, ~~the method comprising administering to a subject a composition comprising an isolated human truncated cystathionine B synthase (htCBS) mutant polypeptide comprising a mutation at amino acid position 15 of SEQ ID NO: 3, wherein said isolated htCBS polypeptide mutant is PEGylated with an ME-200GS PEG molecule.~~wherein the composition is to be administered to the subject, and wherein:

~~50~~(a) the isolated htCBS mutant polypeptide comprises amino acids 2-413 of the amino acid sequence of SEQ ID NO: 13, and has been PEGylated with an ME-200GS PEG molecule; and

(b) the isolated htCBS mutant polypeptide is to be administered in a dose between 0.33 mg/kg and 10 mg/kg at least once a week for at least six weeks.

16. The ~~method~~use of claim ~~49~~15, wherein the subject is not on a methionine restricted diet.

~~51~~17. The ~~method~~use of claim ~~49~~15, wherein the subject is on a methionine restricted diet.

18. The use of any one of claims 1-18, wherein the subject is a human.

19. An isolated human truncated cystathionine beta synthase (htCBS) mutant polypeptide for use in therapy, wherein the isolated htCBS mutant polypeptide comprises

amino acids 2-413 of the amino acid sequence of SEQ ID NO:13 and has been PEGylated with an ME-200GS PEG molecule.