

What is claimed is:

1. A method of treating a subject having or at risk of developing homocystinuria or hyperhomocysteinemia, the method comprising:
 - 5 administering a therapeutically effective amount of formulation comprising a modified human cystathionine- γ -lyase (CGL) enzyme comprising at least the following substitutions relative to a native human CGL amino acid sequence (SEQ ID NO: 1): isoleucine at position 59, leucine at position 63, methionine at position 91, aspartic acid at position 119, arginine at position 268, glycine at position 311, valine at position 339, and serine at position 353;
 - 10 wherein the formulation is administered at an enzyme dose of about 0.05 mg/kg to about 4 mg/kg at a frequency of one dose per day to one dose per month.
2. The method of claim 1, wherein the enzyme is bound to one or more PEG units.
3. The method of claim 1 or 2, wherein the formulation further comprises a pharmaceutically acceptable carrier.
- 15 4. The method of any one of claims 1-3, wherein the formulation is 2 mL of a liquid supplied in a 5 mL vial.
5. The method of any one of claims 1-4, wherein the formulation comprises an enzyme concentration of about 1 mg/mL to about 50 mg/mL.
6. The method of any one of claims 1-5, wherein the formulation comprises an enzyme
20 concentration of about 1 to about 20 mg/mL.
7. The method of any one of claims 1-6, wherein the formulation is administered intravenously or subcutaneously.
8. The method of any one of claims 1-7, wherein the formulation is administered one dose per week.
- 25 9. The method of any one of claims 1-8, wherein the formulation is administered intravenously for four weeks, followed by subcutaneous administration in subsequent weeks.
10. The method of any one of claims 1-9, wherein the formulation is administered to the subject at a dose of about 0.1 mg/kg to about 1 mg/kg.
11. The method of any one of claims 1-10, wherein the formulation is administered once a
30 week at a dose of about 0.1 mg/kg to about 1 mg/kg.

12. The method of any one of claims 1-11, wherein the formulation is administered to the subject at a dose of about 0.15 mg/kg, about 0.45 mg/kg, or about 1 mg/kg.
13. The method of any one of claims 1-12, wherein the formulation is diluted in saline prior to intravenously administering to the subject.
- 5 14. The method of any one of claims 1-13, wherein the subject is a human patient.
15. The method of any one of claims 1-14, wherein the subject has a total plasma homocysteine level greater than 80 μM prior to initiating therapy with administering the formulation.
16. The method of any one of claims 1-15, wherein the subject is at least 12 years of age.
- 10 17. The method of any one of claims 1-16, wherein the subject is maintained on an individualized diet.
18. The method of any one of claims 1-17, wherein the subject is maintained on a methionine-restricted diet.
19. The method of any one of claims 1-18, wherein the method reduces total plasma
- 15 homocysteine levels.
20. The method of any one of claims 1-19, wherein the method reduces total plasma homocysteine levels to less than or equal to about 80 μM .
21. The method of any one of claims 1-20, wherein the method reduces total plasma homocysteine levels to less than or equal to about 50 μM .
- 20 22. The methods of any one of claims 1-21, wherein the method reduces total plasma homocysteine levels to less than or equal to about 15 μM .