GRANTED CLAIMS OF NZ 598156

CLAIMS:

1. A method of identifying a subject as suitable for treatment with an alternative glucocerebrosidase enzyme replacement therapy, the method comprising:

determining if a neutralizing antibody to a glucocerebrosidase enzyme replacement therapy is present in a sample from a subject that is currently taking or has previously received the glucocerebrosidase enzyme replacement therapy to obtain a measured value of the antibody;

comparing the measured value to a standard, wherein if the measured value is greater than the standard, the subject is identified as having tested positive for the production of the antibodies; and

selecting a subject for the alternative glucocerebrosidase enzyme replacement therapy on the basis that the subject has tested positive for the production of the antibodies.

2. The method of claim 1, wherein the subject tested positive for the production of IgE antibodies, IgM antibodies, IgG antibodies, or IgA antibodies, to the glucocerebrosidase enzyme replacement therapy the subject is currently taking or has previously taken for Gaucher disease.

3. The method of claim 1 or 2, further comprising selecting the subject on the basis that an infusion site reaction is detected.

4. The method of claim 3, wherein the infusion site reaction is detected during or within 12 hours of administration of the glucocerebrosidase enzyme replacement therapy the subject is currently taking or has previously taken for Gaucher disease.

5. The method of any one of claims 1 to 4, further comprising selecting the subject on the basis that the mean value of one or more of the parameters selected from the group consisting of hemoglobin concentration, platelet count, liver volume, spleen volume, and a skeletal parameter in the subject that is currently taking or has previously

received the glucocerebrosidase enzyme replacement therapy is lower than that obtained for a cohort of subjects with Gaucher disease treated with the alternative glucocerebrosidase enzyme replacement therapy.

6. The method of claim 5, wherein the skeletal parameter is selected from: bone mineral density (BMD), Z-score, T-score, growth of the subject, skeletal age of the subject, bone marrow burden (BMB), bone pain, or bone necrosis.

7. The method of any one of claims 1 to 6, wherein the antibody does not neutralize the enzyme activity of an alternative glucocerebrosidase enzyme replacement therapy.

8. The method of any one of claim 1 to 7, wherein the glucocerebrosidase enzyme replacement therapy the subject is currently taking or has previously taken for Gaucher disease comprises velaglucerase.

9. The method of any one of claims 1 to 7, wherein the alternative glucocerebrosidase enzyme replacement therapy comprises velaglucerase.

10. The method of any one of claims 1 to 8, wherein the alternative glucocerebrosidase enzyme replacement therapy comprises imiglucerase or uplyso.

11. The method of any one of claims 1 to 10, wherein the determining step comprises:

providing glucocerebrosidase immobilized on a surface;

contacting the sample to the immobilized glucocerebrosidase under conditions that allow the neutralizing antibody in the sample, if present, to bind to the immobilized glucocerebrosidase, thereby forming a mixture;

adding labeled glucocerebrosidase to the mixture under conditions that allow the labeled glucocerebrosidase to bind to the antibody, if present; and

detecting the label in the mixture.

12. The method of any one of claims 1 to 10, wherein the determining step comprises:

contacting the sample to labeled glucocerebrosidase under conditions that allow the neutralizing antibody in the sample, if present, to bind to the labeled glucocerebrosidase, thereby forming a mixture;

applying the mixture to a resin under conditions that allow the antibody, if present, to bind to the resin; and

detecting the label in the mixture.

13. The method of any one of claims 1 to 10, wherein the determining step comprises:

providing glucocerebrosidase immobilized on a surface;

contacting the sample to the immobilized glucocerebrosidase under conditions that allow the neutralizing antibody in the sample, if present, to bind to the immobilized glucocerebrosidase, thereby forming a mixture;

adding a labeled antibody that binds to the neutralizing antibody to the mixture under conditions that allow the labeled antibody to bind to the neutralizing antibody, if present; and

detecting the label in the mixture;

14. The method of any one of claims 1 to 10, wherein the determining step comprises:

providing a cell that expresses human macrophage mannose receptor (MMR);

contacting the sample to the cell, thereby forming a mixture;

contacting labeled glucocerebrosidase to the mixture under conditions that allow the labeled glucocerebrosidase to bind to the MMR in the absence of the neutralizing antibody;

removing unbound labeled glucocerebrosidase and labeled glucocerebrosidase bound to the cell surface; and

measuring the amount of labeled glucocerebrosidase in the cell.

15. Use of glucocerebrosidase in the manufacture of a medicament for the treatment of Gaucher disease, comprising identifying a subject as suitable for treatment with an alternative glucocerebrosidase enzyme replacement in accordance with the method of any one of claims 1 to 14.

16. A pharmaceutical composition comprising velaglucerase, a lyoprotectant, a buffer salt, and a stabilizing agent.

17. The pharmaceutical composition of claim 16, wherein the lyoprotectant comprises a carbohydrate.

18. The pharmaceutical composition of claim 17, wherein the carbohydrate is sucrose.

19. The pharmaceutical composition of claim 16, wherein the buffer salt comprises citrate, citrate acid, or both.

20. The pharmaceutical composition of claim 19, wherein the citrate is sodium citrate.

21. The pharmaceutical composition of claim 16, wherein the stabilizing agent comprises polysorbate.

22. The pharmaceutical composition of claim 21, wherein the polysorbate is polysorbate 20.

23. The pharmaceutical composition of claim 16, wherein the composition is a lyophilized composition.

24. The pharmaceutical composition of claim 23, wherein the moisture content of the lyophilized composition is 1% to 6%.

25. The pharmaceutical composition of claim 23, wherein the moisture content of the lyophilized composition is 3% to 5%.

26. The pharmaceutical composition of claim 16, wherein the composition is a liquid composition.

27. The pharmaceutical composition of claim 16, comprising velaglucerase, citric acid, polysorbate 20, sodium citrate, and sucrose.

28. The pharmaceutical composition of claim 16, wherein the composition is a reconstituted solution.

29. The pharmaceutical composition of claim 28, comprising about 2.5 mg/mL or about 40 U/mL of velaglucerase, about 50 mg/mL sucrose, about 12.9 mg/mL sodium citrate dihydrate, about 1.3 mg/mL citric acid monohydrate, and about 0.11 mg/mL polysorbate 20.

30. The pharmaceutical composition of claim 28, wherein the composition is reconstituted with Sterile Water for Injection.

31. The pharmaceutical composition of claim 30, further comprising sodium chloride.

32. The pharmaceutical composition of claim 16, wherein the composition is compatible with parenteral administration.

33. The pharmaceutical composition of claim 32, wherein the parenteral administration is intravenous, intradermal, or subcutaneous administration.

34. The pharmaceutical composition of claim 16, comprising one or more of a sterile diluent, an antibacterial or antifungal agent, an antioxidant agent, a chelating agent, a buffer, or an agent for the adjustment of tonicity.

35. The pharmaceutical composition of claim 34, wherein the sterile diluent is selected from the group consisting of Sterile Water for Injection, a saline solution, a fixed oil, polyethylene glycol, glycerine, and propylene glycol.

36. The pharmaceutical composition of claim 34, wherein the antibacterial or antifungal agent is selected from the group consisting of benzyl alcohol, methyl paraben, chlorobutanol, phenol, ascorbic acid, and thimerosal.

37. The pharmaceutical composition of claim 34, wherein the antioxidant agent comprises ascorbic acid or sodium bisulfite.

38. The pharmaceutical composition of claim 34, wherein the chelating agent comprises ethylenediaminetetraacetic acid.

39. The pharmaceutical composition of claim 34, wherein the buffer comprises acetate, citrate, or phosphate.

40. The pharmaceutical composition of claim 34, wherein the agent for the adjustment of tonicity comprises sodium chloride or dextrose.

41. The pharmaceutical composition of claim 16, comprising a solvent or dispersion medium.

42. The pharmaceutical composition of claim 41, wherein the solvent or dispersion medium comprises water, ethanol, polyol, or a suitable mixture thereof.

43. The pharmaceutical composition of claim 16, comprising lecithin or a surfactant.

44. The pharmaceutical composition of claim 16, comprising a pharmaceutically acceptable carrier selected from the group consisting of Sterile Water for Injection, physiological saline, bacteriostatic water, CREMOPHOR EL™, and phosphate buffered saline (PBS).

45. The pharmaceutical composition of claim 16, comprising an isotonic agent.

46. The pharmaceutical composition of claim 45, wherein the isotonic agent is a sugar, a polyalcohol, or sodium chloride.

47. The pharmaceutical composition of claim 46, wherein the sugar is sucrose.

48. The pharmaceutical composition of claim 46, wherein the polyalcohol is mannitol or sorbitol.

49. The pharmaceutical composition of claim 16, comprising an agent that delays absorption.

50. The pharmaceutical composition of claim 49, wherein the agent that delays absorption is aluminum monostearate or gelatin.