Claims

1. ~~1.~~ Use of a ~~therapeutic agent~~recombinant human acid sphingomyelinase (rhASM) or modified rhASM for an acid sphingomyelinase (ASM) ~~disorder~~deficiency for the

manufacture of a medicament for treating the ~~disorder~~deficiency in a human subject, wherein

(a) the medicament is to be administered to the subject; and

(b) the level of lyso-sphingomyelin (lyso-SPM) in a biological sample collected from the subject three or more days after the administration is obtained, wherein the biological sample is whole blood, a dried blood spot, plasma, or serum, and wherein a decrease of the level of lyso-SPM compared to a reference level indicates efficacy of the medicament.

2. ~~2.~~ The use of claim 1, wherein the medicament is to be administered repeatedly to the subject.

3. ~~3.~~ The use of claim 1 or 2, wherein additional doses of the medicament ~~is~~are to be administered to the subject.

4. ~~4.~~ The use of any one of the preceding claims, wherein the reference level is the baseline lyso-SPM level of the subject before any treatment with the ~~therapeutic agent~~rhASM or modified rhASM.

5. ~~5.~~ The use of any one of ~~the preceding~~ claims 2-4, wherein the biological sample is to be collected prior to a subsequent dose.

~~6. The use of any one of the preceding claims, wherein the biological sample is whole blood, a dried blood spot, plasma, or serum.~~

6. ~~7.~~ The use of any one of claims 1-~~6~~5, wherein the ASM ~~disorder~~deficiency is Niemann-Pick Disease type B.

7. ~~8.~~ The use of any one of claims 1-~~6~~5, wherein the ASM ~~disorder~~deficiency is Niemann-Pick Disease type A.

~~9. The use of any one of the preceding claims, wherein the therapeutic agent is a recombinant human acid sphingomyelinase (rhASM).~~

8. ~~10.~~ The use of any one of the preceding claims, wherein a maintenance dose of the ~~therapeutic agent~~rhASM or modified rhASM at a dose concentration equal to or less than the highest dose concentration of the ~~therapeutic agent~~rhASM or modified rhASM is to be administered to the subject.

9. ~~11.~~ The use of any one of the preceding claims, wherein each successive dose of the ~~therapeutic agent~~rhASM or modified rhASM is to be administered two weeks after the previous dose.

10. ~~12.~~ The use of any one of the preceding claims, wherein one or more dose concentrations of the ~~therapeutic agent~~rhASM or modified rhASM are to be administered at least twice.

11. ~~13.~~ The use of any one of the preceding claims, wherein each dose of the ~~therapeutic agent~~rhASM or modified rhASM is to be administered at 0.03 mg/kg to 3 mg/kg.

12. ~~14.~~ The use of any one of the preceding claims, wherein the first dose of the ~~therapeutic agent~~rhASM or modified rhASM that the subject receives is to be administered at 0.1 mg/kg.

13. ~~15.~~ The use of claim ~~14~~12, wherein a maintenance dose of the ~~therapeutic agent~~rhASM or modified rhASM at 1, 2, or 3 mg/kg is to be administered to the subject.

14. ~~16.~~ The use of any one of the preceding claims, wherein the ~~therapeutic agent~~rhASM or modified rhASM is to be administered to the subject intravenously.

15. ~~17.~~ Use of a recombinant human acid sphingomyelinase (rhASM) for the manufacture of a medicament for treating Niemann-Pick Disease type A or type B in a human subject, wherein:

(a) a starting dose of rhASM at 0.03 or 0.1 mg/kg and subsequent doses that increase in dose concentration until reaching 3 mg/kg are to be administered to the human subject;

(b) maintenance doses are to be administered to the subject at 3 mg/kg or less; and

(c) the level of lyso-sphingomyelinase (lyso-SPM) in a biological sample collected from the subject (i) within 24 hours, (ii) within 48 hours, or (iii) 72 or more hours after administration of a dose is to be ~~measured~~obtained;

wherein the biological sample is a dried blood spot, whole blood, plasma, or serum;

wherein each dose is to be administered two weeks after the previous dose, and wherein a decrease of the level of lyso-SPM compared to a reference level indicates efficacy of the medicament.

16. ~~18.~~ The use of claim ~~17~~15, wherein the maintenance doses are to be administered at 1, 2, or 3 mg/kg.

17. ~~19.~~ The use of claim ~~17~~15 or ~~18~~16, wherein the subject has been determined prior to treatment to have an elevated level of lyso-SPM compared to a healthy control.

~~20. The use of any one of claims 15-17-19, wherein the biological sample is a dried blood spot.~~

18. ~~21. The use of any one of claims 17-20, wherein the biological sample is~~to be collected prior to a subsequent dose.

19. ~~22.~~ The use of any one of the preceding claims, wherein the subject is an adult patient.

20. ~~23.~~ The use of any one of the preceding claims, wherein the subject is a pediatric patient.