massively produced by the macrophages and neutrophils. Histochemistry of bone marrow aspirates and sections of spleens reveals these storage cells.

The HSR is a key homeostatic system, which is induced under conditions of metabolic stress (e.g., protein misfolding and aggregation, nutrient deprivation, oxidative or thermal stress). Its main components are the HSPs (in particular HSP70), which have significant cytoprotective properties. Heat shock protein 70 acts as molecular chaperone, assisting in the folding of newly synthesised damaged proteins, preventing protein aggregation, and targeting severely damaged proteins for degradation. Notably, the cytoprotective actions of HSP70 also include

protection against lysosomal dysfunction, cell death, and demyelination in mouse studies. Arimoclomol is a safe and well-tolerated co-inducer of HSP70 expression that acts through the activation of heat shock factor-1, the major regulator of HSP gene transcription. It is available for oral administration and show ability to cross the blood-brain barrier.

Summary

In one aspect, there is provided a use of a compound/composition comprising *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, and stereoisomers and acid addition salts thereof, in the manufacture of a medicament for the treatment of Gaucher disease (GD).

In another aspect, there is provided a use of a compound/composition comprising *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, and stereoisomers and acid addition salts thereof,

wherein the stereoisomers are selected from the group consisting of

(+)-*(R)*-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(-)-*(S)*-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(Z)-*(R)*-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(E)-(R)-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(Z)-*(S)*-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride; and

(E)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

wherein the acid addition salts are selected from the group consisting of citrate and maleate,

in the manufacture of a medicament for the treatment of Gaucher disease (GD), wherein said Gaucher disease (GD) is Gaucher disease type 1 (GD1) or Gaucher disease type 3 (GD3).

In another aspect, there is provided a use of a compound/composition comprising *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, and stereoisomers and acid addition salts thereof,

wherein the stereoisomers are selected from the group consisting of

(+)-*(R)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(-)-*(S)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(Z)-(R)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(E)-(R)-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(Z)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride; and

(E)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

wherein the acid addition salts are selected from the group consisting of citrate and maleate,

in the manufacture of a medicament for the treatment of at least one or more disease(s)/disease states selected from the group consisting of hepatomegaly, reducing liver size, splenomegaly, reducing spleen size, hepatosplenomegaly, anaemia, thrombocytopenia, and increasing haemoglobin in a patient.

A double-blind, randomized, placebo-controlled, phase 2 dose-finding trial in Gaucher disease (GD) type 1 and 3 patients naïve to enzyme and/or substrate replacement therapy, was conducted at seven

sites in India. A total of 39 patients were randomized 1:1:1:1 to receive placebo or 100mg, 200mg, or 400mg arimoclomol citrate (weight-adjusted) three times per day. The objective of the phase 2 study was to evaluate the response of the three dose levels of arimoclomol on various clinical and disease-specific biomarkers over a 6-month treatment period. Overall, 37 patients were included in the analysis set (2 patients excluded due to negative confirmatory GD genotype), of which 21 were type 1 GD and 16 were type 3 GD patients.

The data presented herewith show a dose-dependent effect of arimoclomol on certain disease-relevant clinical secondary endpoints, including liver and spleen size. Arimoclomol also demonstrated a relative reduction in serum chitotriosidase activity, and patients anemic at baseline showed a time-dependent increase in haemoglobin in the highest dose group.

The present disclosure provides an active pharmaceutical ingredient selected from *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, its

Claims

1. ~~An active pharmaceutical ingredient selected from~~Use of a compound/composition comprising *N*-[2-hydroxy-3-(1- piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, ~~its~~ and stereoisomers and ~~the~~ acid addition salts thereof, ~~for use in a method of treating~~ in the manufacture of a medicament for the treatment of Gaucher disease (GD).

2. Use of a compound/composition comprising ~~An active pharmaceutical ingredient selected from~~ *N*-[2-hydroxy-3-(1- piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, ~~its~~ and stereoisomers and ~~the~~ acid addition salts thereof, wherein the stereoisomers are selected from the group consisting of

   (+)-*(R)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

   (-)-*(S)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

   (Z)-(R)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

   (E)-(R)-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

   (Z)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride; and

   (E)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

wherein the acid addition salts are selected from the group consisting of citrate and maleate,

in the manufacture of a medicament for the treatment of ~~for use in a method of treating~~ Gaucher disease (GD), wherein said Gaucher disease (GD) is Gaucher disease type 1 (GD1) or Gaucher disease type 3 (GD3).~~wherein said active pharmaceutical ingredient is administered at 100 mg t.i.d, such as 200 mg t.i.d., such as 400 mg t.i.d.~~

3. The use of a composition of claim 2, wherein composition is selected from the group consisting of

N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate,

N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate;

(+)-(R)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;

(-)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;

(+)-(R)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate;

(-)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate;

(Z)-(R)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;

(E)-(R)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;

(Z)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;

(E)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;

(Z)-(R)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate;

(E)-(R)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate;

(Z)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate; and

(E)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate.

4. The use of claims 2-3, wherein said Gaucher disease (GD) is selected from the group consisting of: GD type 1 (GD1) or GD type 3 (GD3) with a deficient GBA enzyme activity below the lower limit of normal; GD type 1 (GD1) or GD type 3 (GD3) with a deficient GBA enzyme activity below the lower limit of normal; GD type 1 (GD1) with signs of brain involvement, such as with nonclinical signs of brain involvement; GD type 3 (GD3) with signs of brain involvement, such as with clinical signs of brain involvement; and GD type 3 (GD3) with at least 1 neurological symptom.

~~3. An active pharmaceutical ingredient selected from *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, its stereoisomers and the acid addition salts thereof, for use in a method of treating Gaucher disease (GD), wherein said active pharmaceutical ingredient is administered at 300 mg/day, such as 600 mg/day, such as 1200 mg/day.~~

~~4. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said Gaucher disease (GD) is GD type 1 (GD1) or GD type 3 (GD3).~~

~~5. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said Gaucher disease (GD) is GD type 1 (GD1) or GD type 3 (GD3) with a deficient GBA enzyme activity below the lower limit of normal.~~

~~6. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said Gaucher disease (GD) is GD type 1 (GD1).~~

~~7. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said Gaucher disease (GD) is GD type 1 (GD1) with signs of brain involvement, such as with nonclinical signs of brain involvement.~~

~~8. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said Gaucher disease (GD) is GD type 3 (GD3).~~

~~9. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said Gaucher disease (GD) is GD type 3 (GD3) with signs of brain involvement, such as with clinical signs of brain involvement.~~

~~10. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said Gaucher disease (GD) is GD type 3 (GD3) with at least 1 neurological symptom.~~

5. The use of claims 2-4, wherein the compound of the composition is to be administered one to three times a day.

6. The use of claim 5, wherein the compound is to be administered three times a day (t.i.d), at a per administration dose of 25 mg t.i.d. (75mg/day), 50 mg t.i.d. (150mg/day), 75 mg t.i.d. (225 mg/day), 100 mg t.i.d (300 mg/day), 150 mg t.i.d

(450 mg/day), 200 mg t.i.d (600 mg/day), 300 mg t.i.d. (900 mg/day), or 400 mg t.i.d (1200 mg/day).

~~11. An active pharmaceutical ingredient selected from *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, its stereoisomers and the acid addition salts thereof, for use in a method of treating hepatomegaly and/or reducing liver size.~~

~~12. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said method is for treating hepatomegaly and/or reducing liver size in a patient with Gaucher disease.~~

~~13. An active pharmaceutical ingredient selected from *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, its stereoisomers and the acid addition salts thereof, for use in a method of treating splenomegaly and/or reducing spleen size.~~

~~14. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said method is for treating splenomegaly and/or reducing spleen size in a patient with Gaucher disease.~~

~~15. An active pharmaceutical ingredient selected from *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, its stereoisomers and the acid addition salts thereof, for use in a method of treating hepatosplenomegaly and/or reducing liver size and reducing spleen size.~~

~~16. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said method is for treating hepatosplenomegaly and/or reducing liver size and reducing spleen size in a patient with Gaucher disease.~~

17. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said splenomegaly is splenomegaly with anaemia and thrombocytopenia.

18. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said hepatosplenomegaly is hepatosplenomegaly with anaemia and thrombocytopenia.

19. An active pharmaceutical ingredient selected from *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, its stereoisomers and the acid addition salts thereof, for use in a method of treating anaemia and/or thrombocytopenia.

20. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said method is for treating anaemia and/or thrombocytopenia in a patient with Gaucher disease.

21. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said patient with Gaucher disease is anemic.

22. An active pharmaceutical ingredient selected from *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, its stereoisomers and the acid addition salts thereof, for use in a method of increasing haemoglobin.

23. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said method is for increasing haemoglobin in a patient with Gaucher disease.

24. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said method is for increasing haemoglobin comprises administering said active pharmaceutical ingredient at a dosage of 600 mg/day

(200 mg t.i.d.) or above; such as at a dosage of 600 - 900 mg/day (200-300 mg t.i.d.) or 900-1200 mg/day (300-400 mg t.i.d.).

25. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said method is for increasing haemoglobin comprises administering said active pharmaceutical ingredient at a dosage of 600 mg/day (200 mg t.i.d.) or 1200 mg/day (400 mg t.i.d.).

26. An active pharmaceutical ingredient selected from *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, its stereoisomers and the acid addition salts thereof, for use in a method of reducing serum chitotriosidase activity.

27. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said method is for reducing serum chitotriosidase activity in a patient with Gaucher disease.

28. An active pharmaceutical ingredient selected from *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, its stereoisomers and the acid addition salts thereof, for use in a method of increasing glycosylsphingosine (lyso-Gb1).

29. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said method is for increasing glycosylsphingosine (lyso-Gb1) in a patient with Gaucher disease.

30. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said treatment dose-dependently reduces liver size.

31. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said treatment dose-dependently reduces spleen size.

~~32. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said treatment dose-dependently reduces chitotriosidase activity.~~

~~33. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said treatment time-dependently increases haemoglobin.~~

~~34. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the individual has not been treated for Gaucher disease within the preceding 4 months, such as with enzyme replacement therapy and/or substrate replacement therapy; or wherein the individual to be treated has not previously been treated for Gaucher disease, such as with enzyme replacement therapy and/or substrate replacement therapy; such as wherein the individual to be treated is naive to treatment with enzyme replacement therapy and/or substrate replacement therapy.~~

~~35. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said treatment is prophylactic, curative or ameliorating.~~

~~36. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said active pharmaceutical ingredient is the racemate of *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride.~~

~~37. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said active pharmaceutical ingredient is an optically active stereoisomer of *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride.~~

~~38. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said active pharmaceutical ingredient is an enantiomer of *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride.~~

~~39. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said active pharmaceutical ingredient is selected from the group consisting of~~

~~(+)-*(R)*-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, and~~

~~(-)-*(S)*-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride.~~

~~40. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said active pharmaceutical ingredient is selected from the group consisting of~~

~~*(Z)*-*(R)*-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, (E)-(R)-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,~~

~~*(Z)*-*(S)*-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride; and~~

~~*(E)*-*(S)*-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride.~~

~~41. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said active pharmaceutical ingredient is an acid addition salt of *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride.~~

~~42. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said active pharmaceutical ingredient is selected from the group consisting of~~

~~*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate, and~~

~~*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate.~~

~~43. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said active pharmaceutical ingredient is selected from the group consisting of~~

~~*(+)-(R)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;~~

~~*(-)-(S)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;~~

~~*(+)-(R)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate; and~~

~~*(-)-(S)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate.~~

~~44. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said active pharmaceutical ingredient is selected from the group consisting of~~

~~*(Z)-(R)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;~~

~~*(E)-(R)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;~~

~~*(Z)-(S)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;~~

(E)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride citrate;

(Z)-(R)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate;

(E)-(R)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate;

(Z)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate; and

(E)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride maleate.

45. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein said active pharmaceutical ingredient is arimoclomol.

46. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein said active pharmaceutical ingredient is arimoclomol citrate.

47. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered orally.

48. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is formulated for oral administration, such as in the form of tablets or capsules, or such as an oral powder, such as an oral powder suitable for suspension in a liquid, or such as as a suspension for oral administration.

~~49. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered daily, such as once daily, such as twice daily, such as three times daily.~~

~~50. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered three times daily (t.i.d).~~

~~51. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered at a per-administration dose of about 100 mg to about 400 mg, such as about 100 mg, 200 mg or 400 mg.~~

~~52. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered at 100 mg t.i.d., such as 200 mg t.i.d., such as 400 mg t.i.d.~~

~~53. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered at 200 mg t.i.d.~~

~~54. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered at 100 mg t.i.d.~~

~~55. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered at 400 mg t.i.d.~~

~~56. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered at a daily dosage of about 100 mg/day to about 200 mg/day, such as about 200~~

~~mg/day to about 300 mg/day, such as about 300 mg/day to about 400 mg/day, such as about 400 mg/day to about 500 mg/day, such as about 500 mg/day to about 600 mg/day, such as about 700 mg/day to about 800 mg/day, such as about 800 mg/day to about 900 mg/day, such as about 900 mg/day to about 1000 mg/day, such as about 1000 mg/day to about 1100 mg/day, such as about 1100 mg/day to about 1200 mg/day.~~

~~57. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered at a daily dosage of 300 mg/day, such as 600 mg/day, for example 1200 mg/day.~~

~~58. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered at a daily dosage of 300 mg/day.~~

~~59. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered at a daily dosage of 600 mg/day.~~

~~60. The active pharmaceutical ingredient for use according to any one of the preceding claims, wherein the active pharmaceutical ingredient is administered at a daily dosage of 1200 mg/day.~~

~~61. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered in hard capsules of 25 mg, 50 mg, and 100 mg.~~

~~62. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of ≥ 10 kg.~~

637. The use of claims 5-6The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredientcompound is to be administered to a patient with Gaucher disease in weight-adjusted dosages.

648. The active pharmaceutical ingredient for use according to any of the preceding claimsuse of claim 7, wherein the active pharmaceutical ingredient iscompound to be administered to a patient with Gaucher disease having a body weight of 10 kg to ≤ 30 kg at a dosage of 25 mg to 100 mg three times a day.

65. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of 10 kg to ≤ 30 kg at a dosage of 25 mg t.i.d., corresponding to a dosage of 75 mg/day.

66. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of 10 kg to ≤ 30 kg at a dosage of 50 mg t.i.d., corresponding to a dosage of 150 mg/day.

67. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of 10 kg to ≤ 30 kg at a dosage of 100 mg t.i.d., corresponding to a dosage of 300 mg/day.

689. The active pharmaceutical ingredient for use according to any of the preceding claimsuse of claim 7, wherein the active pharmaceutical ingredient iscompound to be administered to a patient with Gaucher disease having a body weight of 30 kg to ≤ 50 kg at a dosage of 50 mg to 200 mg three times a day.

69. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient

~~with Gaucher disease having a body weight of 30 kg to ≤ 50 kg at a dosage of 50 mg t.i.d., corresponding to a dosage of 150 mg/day.~~

~~70. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of 30 kg to ≤ 50 kg at a dosage of 100 mg t.i.d., corresponding to a dosage of 300 mg/day.~~

~~71. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of 30 kg to ≤ 50 kg at a dosage of 200 mg t.i.d., corresponding to a dosage of 600 mg/day.~~

~~72~~10. The ~~active pharmaceutical ingredient for use according to any of the preceding claims~~use of claim 7, wherein the ~~active pharmaceutical ingredient is~~compound to be administered to a patient with Gaucher disease having a body weight of 50 kg to ≤ 70 kg at a dosage of 75 mg to 300 mg three times a day.

~~73. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of 50 kg to ≤ 70 kg at a dosage of 75 mg t.i.d., corresponding to a dosage of 225 mg/day.~~

~~74. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of 50 kg to ≤ 70 kg at a dosage of 150 mg t.i.d., corresponding to a dosage of 450 mg/day.~~

~~75. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of 50 kg to ≤ 70 kg at a dosage of 300 mg t.i.d., corresponding to a dosage of 900 mg/day.~~

~~76~~11. The ~~active pharmaceutical ingredient for use according to any of the preceding claims~~use of claim 7, wherein the ~~active pharmaceutical ingredient is~~compound to be administered to a patient with Gaucher disease having a body weight of ≥ 70 kg at a dosage of 100 mg to about 400 mg three times a day.

~~77. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of ≥ 70 kg at a dosage of 100 mg t.i.d., corresponding to a dosage of 300 mg/day.~~

~~78. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of ≥ 70 kg at a dosage of 200 mg t.i.d., corresponding to a dosage of 600 mg/day.~~

~~79. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease having a body weight of ≥ 70 kg at a dosage of 400 mg t.i.d., corresponding to a dosage of 1200 mg/day.~~

~~80. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said a patient with Gaucher disease is of age ≥ 4 and ≤ 60 years.~~

~~81. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein said a patient with Gaucher disease is of age 4 to 6 years, such as 6 to 8 years, such as 8 to 10 years, such as 10 to 12 years, such as 12 to 14 years, such as 14 to 16 years, such as 16 to 18 years.~~

~~82~~12. The use of claims 5-6~~active pharmaceutical ingredient for use according to any of the preceding claims~~, wherein the ~~active pharmaceutical ingredient~~compound is to be administered to a patient with Gaucher disease in age-adjusted dosages.

~~83~~13. The use of claim 12~~active pharmaceutical ingredient for use according to any of the preceding claims~~, wherein the ~~active pharmaceutical ingredient~~compound is to be administered to a patient with Gaucher disease aged >18 years at a dosage of 100 mg to about 400 mg three times a day.

14. Use of a compound/composition comprising *N*-[2-hydroxy-3-(1- piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, and stereoisomers and acid addition salts thereof,

wherein the stereoisomers are selected from the group consisting of

(+)-*(R)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(-)-*(S)-N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(Z)-(R)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(E)-(R)-*N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

(Z)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride; and

(E)-(S)-N-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride,

wherein the acid addition salts are selected from the group consisting of citrate and maleate,

in the manufacture of a medicament for the treatment of at least one or more disease(s)/disease states selected from the group consisting of hepatomegaly, reducing liver size, splenomegaly, reducing spleen size, hepatosplenomegaly, anaemia, thrombocytopenia, and increasing haemoglobin in a patient.

15. The use of claim 14, wherein the patient has Gaucher disease.

16. The use of claim 14 or claim 15, wherein the compound of the composition is to be administered one to three times a day.

17. The use of claim 16, wherein the compound is to be administered three times a day, at a per administration dose of 25 mg t.i.d. (75mg/day), 50 mg t.i.d. (150mg/day), 75 mg t.i.d. (225 mg/day), 100 mg t.i.d (300 mg/day), 150 mg t.i.d (450 mg/day), 200 mg t.i.d (200-600 mg/day), 300 mg t.i.d. (900 mg/day), or 400 mg t.i.d (1200 mg/day).

18. The use of claim 16, wherein the compound is to be administered three times a day, at a per administration dose of 100 mg t.i.d (300 mg/day), 200 mg t.i.d (600 mg/day), 300 mg t.i.d. (900 mg/day), or 400 mg t.i.d (1200 mg/day).

~~84. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease aged >18 years at a dosage of 100 mg t.i.d., corresponding to a dosage of 300 mg/day.~~

~~85. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient with Gaucher disease aged >18 years at a dosage of 200 mg t.i.d., corresponding to a dosage of 600 mg/day.~~

~~86. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered to a patient~~

with Gaucher disease aged >18 years at a dosage of 400 mg t.i.d., corresponding to a dosage of 1200 mg/day.

87. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the maximum predicted $AUC_{0\text{-}8\ hrs}$ (High dose) is within about 80.00% to about 125.00% of a $AUC_{0\text{-}8\ hrs}$ of 6 to 9 µg-h/mL, after administration of a single dose, such as about 6 to 6.5, such as about 6.5 to 7, such as about 7 to 7.5, such as about 7.5 to 8, such as about 8 to 8.5 , such as about 8.5 to 9 µg-h/mL, after administration of a single dose.

88. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein $AUC_{0\text{-}8\ hrs,\ steady\ state}$ is within about 80.00% to about 125.00% of a $AUC_{0\text{-}8\ hrs,\ steady\ state}$ of about 1000 h ng/mL, after administration of 300 mg/day; such as within about 80.00% to about 125.00% of about 700 to 1300 h ng/mL, such as of about 800 to 1200 h ng/mL, such as of about 900 to 1100 h ng/mL, after administration of 300 mg/day.

89. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein $AUC_{0\text{-}8\ hrs,\ steady\ state}$ is within about 80.00% to about 125.00% of $AUC_{0\text{-}8\ hrs,\ steady\ state}$ of about 2000 h ng/mL, after administration of 600 mg/day, such as within about 80.00% to about 125.00% of about 1700 to 2300 h ng/mL, such as about 1800 to 2200 h ng/mL, such as about 1900 to 2100 h ng/mL after administration of 600 mg/day.

90. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein $AUC_{0\text{-}8\ hrs,\ steady\ state}$ is within about 80.00% to about 125.00% of a $AUC_{0\text{-}8\ hrs,\ steady\ state}$ of about 5100 h ng/mL, after administration of 1200 mg/day, such as within about 80.00% to about 125.00% of about 4500 to 5700 h ng/mL, such as 4500 to 4600 h ng/mL, such as 4600 to 4700 h ng/mL, such as 4700 to 4800 h ng/mL, such as 4800 to 4900 h ng/mL, such as 4900 to 5000 h ng/mL, such as 5000 to 5100 h ng/mL, such as 5100 to 5200 h ng/mL, such as 5200 to 5300 h ng/mL, such as 5300 to 5400 h ng/mL, such as 5400 to 5500 h ng/mL,

such as 5500 to 5600 h ng/mL, such as 5600 to 5700 h ng/mL after administration of 1200 mg/day.

91. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered for 1 week such as more than 1 week, such as 2 weeks or more than 2 weeks, such as 3 weeks or more than 3 weeks, such as 4 weeks or more than 4 weeks,

such as for 1 month or more than 1 month, such as 2 months or more than 2 months, such as 3 months or more than 3 months, such as 4 months or more than 4 months, such as 5 months or more than 5 months, such as 6 months or more than 6 months,

or such as for 1 year or more than 1 year.

92. The active pharmaceutical ingredient for use according to any of the preceding claims, wherein the active pharmaceutical ingredient is administered for at least 6 months, such as for at least 9 months, such as for at least 1 year, such as for at least 18 months, such as for at least 2 years, such as for at least 3 years, such as for at least 4 years, such as for at least 5 years or more.

93. A method of treating Gaucher disease (GD), said method comprising one or more steps of administering an active pharmaceutical ingredient selected from *N*-[2-hydroxy-3-(1-piperidinyl)-propoxy]-pyridine-1-oxide-3-carboximidoyl chloride, its stereoisomers and the acid addition salts thereof, to an individual in need thereof.