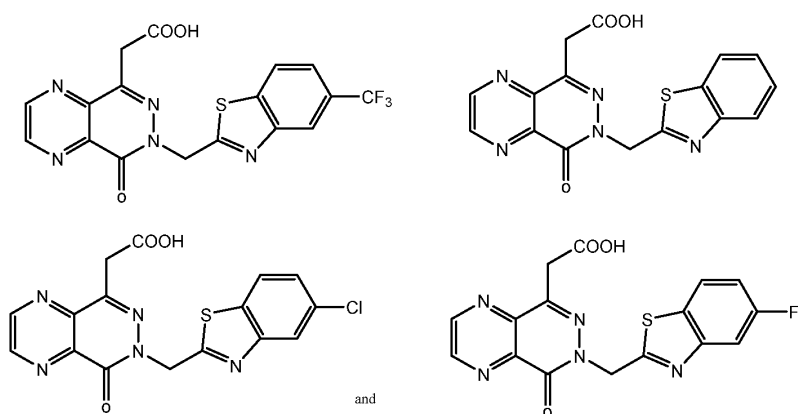


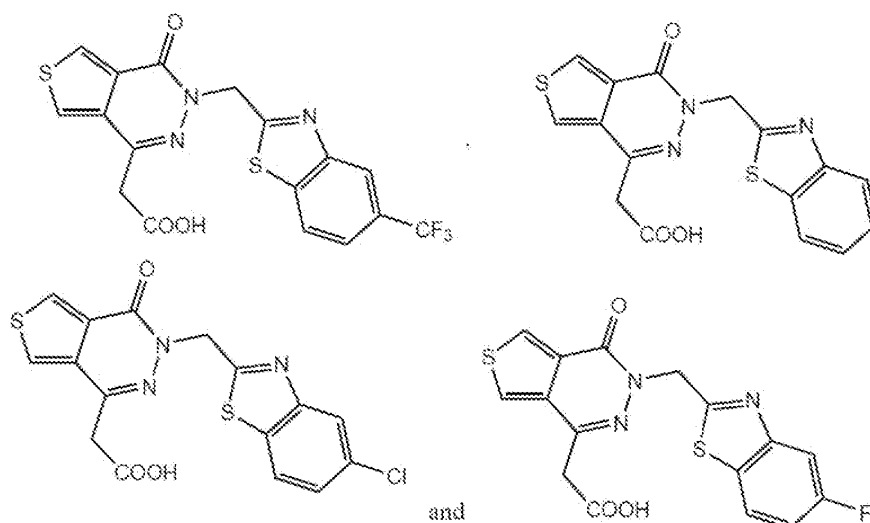
We claim:

1. An aldose reductase inhibitor for use in the treatment of a genetic and/or metabolic disorder that alters sorbitol metabolism or causes over production of sorbitol, such as SDH deficiency.
2. The aldose reductase inhibitor of claim 1, wherein the treatment decreases sorbitol accumulation.
3. The aldose reductase inhibitor of claim 1 or 2, wherein the disorder is a genetic disorder that alters metabolism of sorbitol or causes over-production of sorbitol.
4. The aldose reductase inhibitor of claim 1 or 2, wherein the disorder is genetic SDH deficiency.
5. The aldose reductase inhibitor of any one of claims 1-4, wherein the disorder includes clinical features or complications selected from the group consisting of cataracts, neuropathy, retinopathy, cardiomyopathy, nephropathy, microvascular complications, atherosclerosis and other cardiovascular complications, albuminuria, and diabetes.
6. An aldose reductase inhibitor of any one of claims 1-5, wherein the disorder is hereditary neuropathy.
7. The aldose reductase inhibitor of claim 6, wherein the hereditary neuropathy as associated with SDH deficiency.
8. The aldose reductase inhibitor of claim 6 or 7, wherein the hereditary neuropathy is Charcot–Marie–Tooth disease (CMT).
9. The aldose reductase inhibitor of claim 6 or 7, wherein the CMT is CMT-2.
10. The aldose reductase inhibitor of claim 9, wherein the CMT-2 is distal hereditary motor neuronopathy (dHMN).

11. The aldose reductase inhibitor of any one of claims 1-10, wherein the aldose reductase inhibitor is a compound of any one of Formulas (I)-(VI) or salt thereof.
12. The aldose reductase inhibitor of any one of claims 1-10, wherein the aldose reductase inhibitor is a zopolrestat or salt thereof, or epalrestat or salt thereof.
13. The aldose reductase inhibitor of any one of claims 1-10, wherein the aldose reductase inhibitor is a compound of Formula (II) or salt thereof.
14. The aldose reductase inhibitor of claim 13, wherein the aldose reductase inhibitor is selected from the following or salts thereof



15. The aldose reductase inhibitor of any one of claims 1-10, wherein the aldose reductase inhibitor is a compound of Formula (III).
16. The aldose reductase inhibitor of claim 15, wherein the aldose reductase inhibitor is selected from the following or salts thereof

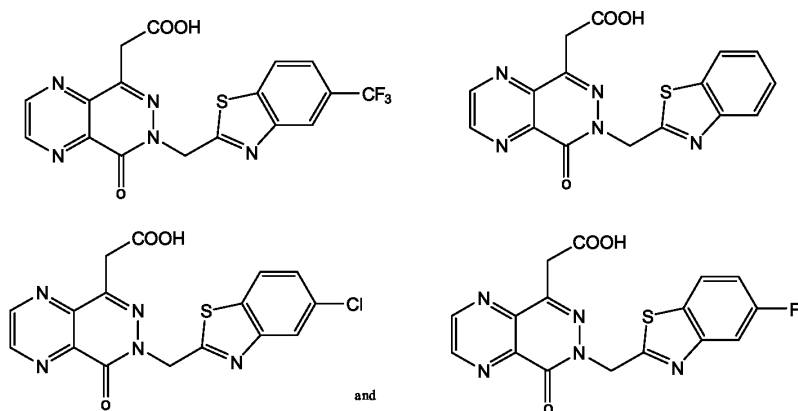


17. The aldose reductase inhibitor of any one of claims 1-16, wherein the disease or disorder is in a human.
18. The aldose reductase inhibitor of claim 17, wherein the human has diabetes.
19. The aldose reductase inhibitor method of claim 18, wherein human has a complication of diabetes.
20. The aldose reductase inhibitor of any one of the preceding claims, wherein the aldose reductase inhibitor is Compound A or a salt thereof.
21. The aldose reductase inhibitor of any one of the preceding claims, wherein the aldose reductase inhibitor is Compound B or a salt thereof.
22. A method of treating a genetic and/or metabolic disorder that alters sorbitol metabolism or causes over production of sorbitol, such as SDH deficiency, in a subject, comprising administering a therapeutically effective amount of an aldose reductase inhibitor to a subject in need thereof.

23. The method of claim 22, wherein the effective amount of an aldose reductase inhibitor is sufficient to reduce sorbitol accumulation in the subject.
24. The methods of claim 22 or 23, wherein the genetic disorder is a disorder that alters metabolism of sorbitol or causes over-production of sorbitol.
25. The method of claim 22 or 23, wherein the disorder is genetic SDH deficiency.
26. The method of any one of claims 22-25, wherein the disorder includes clinical features or complications selected from the group consisting of cataracts, neuropathy, retinopathy, cardiomyopathy, nephropathy, microvascular complications, atherosclerosis and other cardiovascular complications, albuminuria, and diabetes.
27. A method of claim 22, wherein the disorder is hereditary neuropathy.
28. The method of claim 27, wherein the hereditary neuropathy is associated or caused by SDH deficiency.
29. The method of claim 27 or 28, wherein the hereditary neuropathy is Charcot-Marie-Tooth disease (CMT).
30. The method of claim 27 or 28, wherein the Charcot-Marie-Tooth neuropathy type 2 (CMT-2).
31. The method of claim 30, wherein the CMT-2 is distal hereditary motor neuronopathy (dHMN).
32. The method of any one of claims 22-31, wherein the aldose reductase inhibitor is a compound of any one of Formulas (I)-(VI) or salt thereof.
33. The method of any one of claims 22-31, wherein the aldose reductase inhibitor is a zopolrestat or salt thereof, or epalrestat or salt thereof.

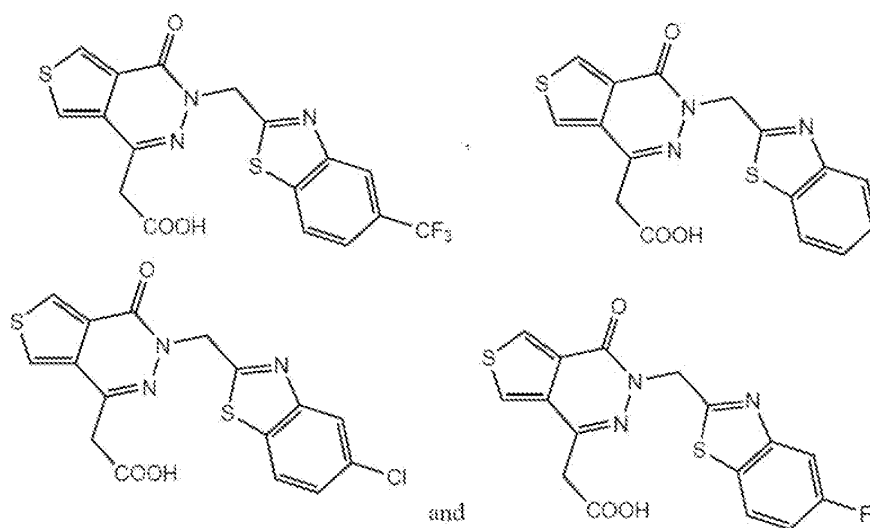
34. The method of any one of claims 22-31, wherein the aldose reductase inhibitor is a compound of Formula (II) or salt thereof.

35. The method of claim 34, wherein the aldose reductase inhibitor is selected from the following or salts thereof



36. The method of any one of claims 22-31, wherein the aldose reductase inhibitor is a compound of Formula (III).

37. The method of claim 36, wherein the aldose reductase inhibitor is selected from the following or salts thereof



38. The method of any one of claims 22-137, wherein the subject is a human.
39. The method of claim 38, wherein the subject in need thereof has diabetes.
40. The method of claim 39, wherein the subject in need thereof has a complication of diabetes.
41. The method of any one of claims 22-40, wherein the aldose reductase inhibitor is Compound A or a salt thereof.
42. The method of any one of claims 22-40, wherein the aldose reductase inhibitor is Compound B or a salt thereof.
43. Use of an aldose reductase inhibitor (ARI) for treating sorbitol-dehydrogenase (SDH) deficiency.
44. Use of an aldose reductase inhibitor (ARI) for treating a genetic disorder that alters metabolism of sorbitol or cause over-production of sorbitol.
45. Use of an aldose reductase inhibitor (ARI) for treating hereditary neuropathy.
46. An aldose reductase inhibitor (ARI) for use in the manufacture of a medicament for treating sorbitol-dehydrogenase (SDH) deficiency.
47. An aldose reductase inhibitor (ARI) for use in the manufacture of a medicament for treating a genetic disorder that alters metabolism of sorbitol or cause over-production of sorbitol.
48. An aldose reductase inhibitor (ARI) for use in the manufacture of a medicament for treating hereditary neuropathy.

49. A pharmaceutical composition for treating sorbitol-dehydrogenase (SDH) deficiency comprising administering an aldose reductase inhibitor (ARI) as an active ingredient.
50. A pharmaceutical composition for treating a genetic disorder that alters metabolism of sorbitol or cause over-production of sorbitol comprising administering an aldose reductase inhibitor (ARI) as an active ingredient.
51. A pharmaceutical composition for treating hereditary neuropathy comprising administering an aldose reductase inhibitor (ARI) as an active ingredient.