What is claimed is:

1. Use of a synthetic retinal derivative that provides replacement for endogenously produced 11-cis-retinal in the preparation of a medicament for treating loss or impairment of vision caused by a retinoid deficiency disorder in a patient, wherein said medicament is to be administered in a dosing regimen characterized by:

   a) administering to the patient an initial therapeutically effective dose of said medicament,

   b) refraining from administering to the patient said medicament for a resting interval of at least 1 month,

   c) administering to the patient an additional therapeutically effective dose of said medicament; wherein the initial dose is administered in a divided dose over a period of from 5 to 14 days.

2. Use of a synthetic retinal derivative that provides replacement for endogenously produced 11-cis-retinal in the preparation of a medicament for treating loss or impairment of vision caused by a retinoid deficiency disorder in a patient, wherein said medicament is to be administered in a dosing regimen characterized by:

   a) administering to the patient an initial therapeutically effective dose of said medicament,

   b) refraining from administering to the patient an additional dose of said medicament until the improvement or restoration of the patient's vision diminishes,

   c) administering to the patient another therapeutically effective dose of said medicament; wherein the initial dose is administered in a divided dose over a period of from 5 to 14 days

3. The use of claim 1, wherein the initial dose is administered in a single dose.

4. The use of claims 1 or 2, wherein the initial dose is administered in a divided dose over a period of 7 to 10 days.

5. The use of claims 1 or 2, wherein the initial dose is administered in a divided dose over a period of one week.

6. The use of claims 1 or 2, wherein the synthetic retinal derivative is a retinyl ester of 9-cis-retinal.

7. The use of claims 1 or 2, wherein the synthetic retinal derivative is a retinyl ester of 11-cis-retinal.

8. The use of claims 1 or 2, wherein the synthetic retinal derivative is 11-cis-retinal acetate.

9. The use of claims 1 or 2, wherein the synthetic retinal derivative is 9-cis-retinal acetate.

10. The use of claims 1 or 2, wherein the initial dose is administered in a divided dose over a period of two weeks.

11. The use of claims 1 or 2, wherein the initial dose is in the range of from 70 to mg/m^2 to 525 mg/m^2.

12. The use of claims 1 or 2, wherein the initial dose is in the range of from 70 mg/ m^2 to 490 mg/m^2.

13. The use of claims 1 or 2, wherein the initial dose is in the range of from 280 mg/m^2 to 490 mg/m^2.

14. The use of claims 1 or 2, wherein the initial dose is in the range of from 70 mg/m^2 to 280 mg/m^2.

15. The use of claim 5, wherein the initial dose is 280 mg/m^2.

16. The use of any one of claims 1-15, wherein the initial dose of said medicament is to be administered orally.

17. The use of any one of claims 1-15, wherein the initial dose of said medicament is to be administered by intraocular injection.

18. The use of any one of claims 1-17, wherein the resting interval is at least 3 months.

19. The use of claim 18, wherein the resting interval is at least 6 months.

20. The use of claim 18, wherein the resting interval is at least 9 months.

21. The use of claim 18, wherein the resting interval is from 3 to 6 months.

22. The use of claim 18, wherein the resting interval is from 6 to 9 months.

23. The use of claim 18, wherein the resting interval is from 3 to 9 months.

24. The use of claim 18, wherein the resting interval is from 3 months to 1 year.

25. The use of any one of claims 1-24, wherein the retinoid deficiency disorder is retinitis pigmentosa.

26. The use of any one of claims 1-24, wherein the retinoid deficiency disorder is Leber congenital amaurosis.

27. The use of any one of claims 1-24, wherein the retinoid deficiency disorder is congenital stationary night blindness.

28. The use of any one of claims 1-24, wherein the retinoid deficiency disorder is fundus albipunctatus.

29. The use of any one of claims 1-24, wherein the retinoid deficiency disorder is age-related dark adaptation.

30. The use of any one of claims 1-24, wherein the retinoid deficiency disorder is age-related macular degeneration.

31. The use of any one of claims 1-24, wherein the retinoid deficiency disorder is caused by a mutation in the LRAT gene.

32. The use of any one of claims 1-24, wherein the retinoid deficiency disorder is caused by a mutation in the RPE65 gene.

What is claimed is:

1. Use of a synthetic retinal derivative that provides replacement for endogenously produced 11-cis-retinal in the preparation of a medicament for treating loss or impairment of vision caused by a retinoid deficiency disorder in a patient, wherein said medicament is to be administered in a dosing regimen characterized by:
   a) administering to the patient an initial therapeutically effective dose of said medicament,
   b) refraining from administering to the patient said medicament for a resting interval of at least 1 month,
   c) administering to the patient an additional therapeutically effective dose of said medicament; wherein the initial dose is administered in a divided dose over a period of up to two weeks.

2. The use of claim 1, wherein the initial dose is administered in a divided dose over a period of from 5 to 14 days.

3. The use of claim 1, wherein the initial dose is administered in a divided dose over a period of two weeks.

4. The use of claim 1, wherein the initial dose is administered in a divided dose over a period of 7 to 10 days.

5. The use of claim 1, wherein the initial dose is administered in a divided dose over a period of one week.

6. The use of claim 1, wherein the initial divided dose is administered in equal daily amounts over the dosing period.

7. The use of claim 1, wherein the synthetic retinal derivative is a 9-cis-retinyl ester.

8. The use of claim 1, wherein the synthetic retinal derivative is an 11-cis-retinyl ester.

9. The use of claim 1, wherein the synthetic retinal derivative is a 9-cis or 11-cis-retinyl ester of a mono- or polycarboxylic acid, optionally wherein the carboxylic acid is a C1-C22, C2-C22, C3-C22, C1-C10, C2-C10, C3-C10, C4-C10, C4-C8, C4-C6 or C4 monocarboxylic acid or polycarboxylic acid.

10. The use of claim 1, wherein the synthetic retinal derivative is a 9-cis or 11-cis-retinyl ester of

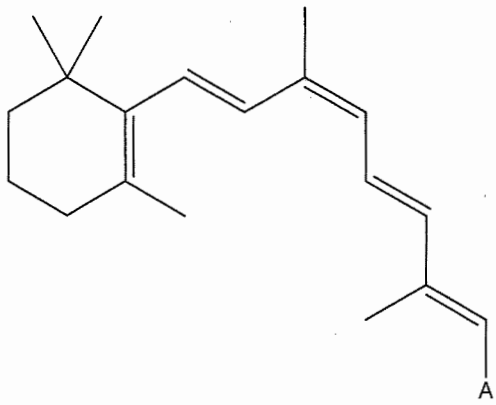
i) a dicarboxylic acid; or

ii) an acetic acid, propionic acid, butyric acid, valeric acid, caproic acid, caprylic acid, pelargonic acid, capric acid, lauric acid, oleic acid, stearic acid, palmitic acid, myristic acid or linoleic acid, oxalic acid (ethanedioic acid), malonic acid (propanedioic acid), succinic acid (butanedioic), fumaric acid (butenedioic acid), malic acid (2-hydroxybutenedioic acid), glutaric acid (pentanedioic acid), adipic acid (hexanedioic acid), pimelic acid (heptanedioic), suberic acid (octanedioic), azelaic acid (nonanedioic acid), sebacic acid (decanedioic acid), citric acid, oxaloacetic acid or ketoglutaratic acid.

11. The use of claim 1, wherein the synthetic retinal derivative is selected from 9-cis-retinal or 11-cis-retinal.

12. The use of claim 1, wherein the synthetic retinal derivative is selected from 9-cis-retinol or 11-cis-retinol.

13. The use of claim 1, wherein the synthetic retinal derivative has a structure according to formula (XIV):



(XIV)

wherein A is CH_2OR and R, together with the remainder of the molecule, forms a retinyl ester, optionally wherein R is a C1 to C24 straight chain or branched acyl group.

14. The use of claim 13, wherein R is a C1 to C24 straight chain or branched acyl group of

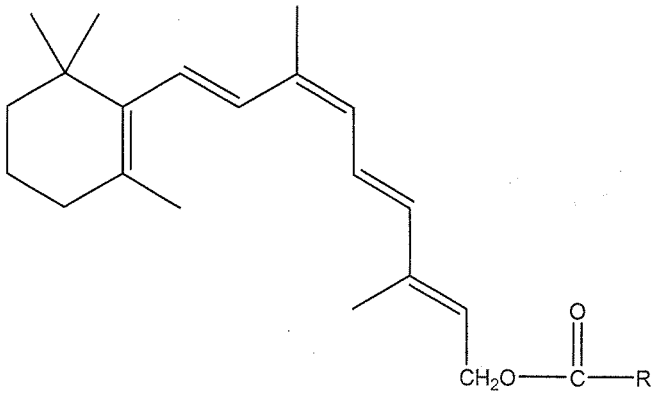
i) a dicarboxylic acid;

ii) a carboxylic acid;

iii) a hydroxyl acid; or

iv) oxalic acid (ethanedioic acid), malonic acid (propanedioic acid), succinic acid (butanedioic), fumaric acid (butenedioic acid), malic acid (2-hydroxybutenedioic acid), glutaric acid (pentanedioic acid), adipic acid (hexanedioic acid), pimelic acid (heptanedioic), suberic acid (octanedioic), azelaic acid (nonanedioic acid), sebacic acid (decanedioic acid), citric acid, oxaloacetic acid or ketoglutaratic acid.

15. The use of claim 1, wherein the synthetic retinal derivative has a structure according to formula (XXX):



(XXX)

wherein R is an alkyl group or alkenyl group and optionally C1-4 alkyl.

16. The use of claim 15, wherein R is methyl, ethyl, n-propyl, 1-methylethyl (iso-propyl), n-butyl, n-pentyl, 1,1-dimethylethyl (t-butyl), 3-methylhexyl or 2-methylhexyl.

17. The use of claim 1, wherein the synthetic retinal derivative is 11-cis-retinyl acetate.

18. The use of claim 1, wherein the synthetic retinal derivative is 9-cis-retinyl acetate.

19. The use of claim 1, wherein the synthetic retinal derivative is 9-cis-retinyl succinate.

20. The use of any one of claims 1 to 19, wherein the initial dose is in the range of from 70 mg/m^2 to 525 mg/m^2.

21. The use of any one of claims 1 to 19, wherein the initial dose is in the range of from 70 mg/m^2 to 490 mg/m^2.

22. The use of any one of claims 1 to 19, wherein the initial dose is in the range of from 280 mg/m^2 to 490 mg/m^2.

23. The use of any one of claims 1 to 19, wherein the initial dose is in the range of from 70 mg/m^2 to 280 mg/m^2.

24. The use of claim 5, wherein the initial dose is 280 mg/m^2.

25. The use of claim 1, wherein the dose in step c) is reduced from the amount of the initial dose.

26. The use of claim 1, wherein the dose in step c) is the same as the amount of the initial dose.

27. The use of claim 1, wherein the dose in step c) is increased from the amount of the initial dose.

28. The use of any one of claims 1-27, wherein the initial dose of said medicament is to be administered orally.

29. The use of claim 28, wherein said medicament comprises a lipid vehicle.

30. The use of claim 29, wherein said lipid vehicle comprises soybean oil.

31. The use of any one of claims 1-27, wherein the initial dose of said medicament is to be administered by intraocular injection.

32. The use of any one of claims 1-31, wherein the resting interval is at least 3 months.

33. The use of claim 32, wherein the resting interval is at least 6 months.

34. The use of claim 32, wherein the resting interval is at least 9 months.

35. The use of claim 32, wherein the resting interval is from 3 to 6 months.

36. The use of claim 32, wherein the resting interval is from 6 to 9 months.

37. The use of claim 32, wherein the resting interval is from 3 to 9 months.

38. The use of claim 32, wherein the resting interval is from 3 months to 1 year.

39. The use of any one of claims 1-38, wherein the retinoid deficiency disorder is retinitis pigmentosa.

40. The use of any one of claims 1-38, wherein the retinoid deficiency disorder is Leber congenital amaurosis.

41. The use of any one of claims 1-38, wherein the retinoid deficiency disorder is congenital stationary night blindness.

42. The use of any one of claims 1-38, wherein the retinoid deficiency disorder is fundus albipunctatus.

43. The use of any one of claims 1-38, wherein the retinoid deficiency disorder is age-related dark adaptation.

44. The use of any one of claims 1-38, wherein the retinoid deficiency disorder is age-related macular degeneration.

45. The use of any one of claims 1-40, wherein the retinoid deficiency disorder is caused by a mutation in the LRAT gene.

46. The use of any one of claims 1-40, wherein the retinoid deficiency disorder is caused by a mutation in the RPE65 gene.

47. The use of claims 39 or 40, wherein the patient is younger than 15 years of age upon commencement of treatment.

48. The use of any one of claims 1-47, wherein the medicament is for use in improving visual acuity or visual field.

49. The use of claim 48, wherein the improvement in visual field comprises an expansion of the subject's visual field temporally and/or nasally, wherein the expansion of the patient's visual field during the first dosing period is by at least 5 degrees or at least 10 degrees nasally, and at least 20 degrees, or at least 30 degrees or at least 40 degrees temporally.

50. The use of claim 48, wherein the medicament is for use in improving visual acuity in patients with very low visual acuity.

51. The use of any one of claims 1-50, wherein the medicament comprises the synthetic retinal derivative and a lipid vehicle, and optionally wherein the synthetic retinal derivative is a 9-cis-retinyl ester formulated into an oral formulation comprising the 9-cis-retinyl ester and a lipid vehicle.

52. The use of claim 51, wherein the synthetic retinal derivative is a 9-cis-retinyl ester formulated as an orally-administered pharmaceutically acceptable composition which comprises the 9-cis-retinyl ester and soybean oil, or wherein the synthetic retinal derivative is a 9-cis-retinyl ester formulated for subcutaneous injection in soybean oil.

53. The use of claim 52, wherein the medicament comprises 9-cis-retinyl acetate in a pharmaceutically acceptable composition which comprises the 9-cis-retinyl acetate and butylated hydroxyanisole (BHA) dissolved in soybean oil, optionally wherein: (i) the 9-cis-retinyl acetate is in an amount selected from 1.25 mg/mL, 5.0 mg/mL and 20 mg/mL, and (ii) the BHA is in an amount of 0.10% w/w.

54. Use of a synthetic retinal derivative for manufacturing a medicament for improving one or more of visual acuity and visual field in a human subject having a deficiency of endogenously produced 11-cis-retinal, wherein the synthetic retinal derivative is 9-cis-retinyl acetate, wherein the medicament comprise the 9-cis-retinyl acetate in an amount selected from 1.25 mg/mL, 5.0 mg/mL, and 20 mg/mL and 0.10% w/w BHA in a soybean oil vehicle, wherein the 11-cis-retinal

deficiency is a disorder caused by a mutation in a gene selected from the LRAT gene and the RPE65 gene, and wherein the medicament is administered according to a dosing schedule that provides for

a) administering to the human subject a once-daily initial dose of 10 mg/m^2 or 40 mg/m^2 for 7 days,

b) refraining from administering to the human subject an additional therapeutically effective dose of the synthetic retinal derivative for a resting period of at least 1 month, and

c) administering to the human subject an additional therapeutically effective dose of the synthetic retinal derivative.

55. The use of claim 54, wherein the resting interval is from 1 month to 3 months.

56. The use of claims 54 or 55, wherein the mutation in the LRAT gene or RPE65 gene is associated with retinitis pigmentosa.

57. The use of claim 54 or 55, wherein the mutation in the LRAT gene or RPE65 gene is associated with Leber congenital amaurosis.

58. The use of any one of claims 54-57, wherein the visual acuity is determined by the Early Treatment of Diabetic Retinopathy Study (ETDRS) and said medicament provides an improvement in visual acuity in said subject over baseline, wherein both said baseline and said improvement are determined by said ETDRS.

59. The use of claim 58, wherein said improvement over baseline, in one or both eyes, comprises:

an increase of up to 36 letters in said ETDRS, wherein said subject has a baseline of 20 to 50 letters in said ETDRS;

an increase of up to 7 letters in said ETDRS, wherein said subject has a baseline of 50 to 70 letters in said ETDRS; or

an increase of up to 18 letters in said ETDRS, wherein said subject has a baseline of 0 to 20 letters in said ETDRS.

60. The use of any one of claims 54-59, wherein the improvement in visual acuity of the human subject is an improvement in one or more eyes over baseline, of 1-5 EDTRS letters, at least 10 ETDRS letters, at least 15 ETDRS letters, at least 20 ETDRS letters, at least 25 ETDRS letters, at least 30 ETDRS letters, or at least 35 ETDRS letters.

61. The use of any one of claims 54-57, wherein said visual field is measured by the Goldmann Visual Field test (GVF), and said medicament provides an improvement over baseline as determined by GVF using an isopter selected from the I4e target, V4e target and a combination thereof.

62. The use of claim 61, wherein the improvement in visual field is an expansion of the human subject's visual field over baseline in one or both eyes by i) at least 5 degrees or at least 10 degrees nasally; and ii) at least 20 degrees or at least 30 degrees or at least 40 degrees temporally.

63. The use of any one of claims 54-62, wherein at least one of said visual acuity and visual field is rapidly improved over baseline following said administering in a).

64. The use of any one of claims 54-62, wherein said improving is determinable after seven days of said administering in a).

65. The use of any one of claims 54-64, wherein said improving is clinically meaningful.

66. The use of any one of claims 54-65, wherein the human subject is 20 years or older, 30 years or older, 40 years or older, 50 years or older, 60 years or older, or 70 years or older.

67. A kit for treating or ameliorating a visual disorder in a human subject associated with a deficiency in endogenously produced 11-cis-retinal, the kit comprising:

a) a synthetic retinal derivative that provides replacement for endogenously produced 11-cis-retinal,and,

b) instructions indicating a dosing schedule that provides for:

administering to the human subject an initial therapeutically effective dose of the synthetic retinal derivative that provides replacement for endogenously produced 11-cis-retinal, wherein the initial dose is administered in a divided dose over a period of up to two weeks, refraining from administering to the human subject an additional therapeutically effective dose of the synthetic retinal derivative for a resting interval of at least 1 month, and administering to the human subject an additional therapeutically effective dose of the synthetic retinal derivative.

68. The kit of claim 67, wherein the visual disorder is selected from retinitis pigmentosa, Leber congenital amaurosis, congenital stationary night blindness, fundus albipunctatus, nyctalopia, age-related impairment in dark adaptation, and age-related macular degeneration.

69. The kit of claim 68, wherein the visual disorder is selected from retinitis pigmentosa and Leber congenital amaurosis.

70. The kit of claim 69, wherein said visual disorder is caused by a mutation in the RPE65 gene or the LRAT gene.

71. The kit of any one of claims 67-70, wherein said synthetic retinal derivative comprises 9-cis-retinyl acetate.

72. The kit of claim 71, wherein said synthetic retinal derivative is formulated as a pharmaceutical formulation comprising a therapeutically effective amount of the 9-cis-retinyl acetate and butylated hydroxyanisole dissolved in soybean oil.

73. The kit of any one of claims 67-72, wherein the instructions indicate that the initial dose is administered in a divided dose over a period of 5 to 14 days, 5 days, 7 to 10 days, one week, or two weeks.

74. An orally acceptable pharmaceutical formulation comprising 9-cis-retinyl acetate and butylated hydroxyanisole dissolved in soybean oil.

75. The pharmaceutical formulation of claim 74, for use in a treatment with from 1.25 mg/m^2 to 40 mg/m^2 of 9-cis-retinyl acetate.

76. The pharmaceutical formulation of claim 74 or 75, comprising 0.10% w/w of said butylated hydroxyanisole.