~~WHAT IS~~ CLAIM~~ED IS:~~

~~1. A composition for treating or preventing an ocular disease in a human subject, comprising a vector, the vector comprising an expression cassette, the expression cassette comprising a nucleic acid molecule or a non-pathogenic variant thereof encoding a functional or non-mutant CYP4V2 protein operably linked to one or more regulatory sequence, wherein the disease is associated with the dysfunction, dystrophy, disorder, degeneration, atrophy and/or death of ocular cells~~

~~2. A composition for preventing, arresting, slowing progression of, treating or ameliorating the dysfunction, dystrophy, disorder, degeneration, atrophy and/or death of an ocular cell, comprising a vector, the vector comprising an expression cassette, the expression cassette comprising a nucleic acid molecule or a non-pathogenic variant thereof encoding a functional or non-mutant CYP4V2 protein operably linked to one or more regulatory sequence. Diseases:~~

~~3. The composition of claim 1 or 2, wherein the ocular disease or ocular cell degeneration is an inherited retinal degeneration (IRD) or retinitis pigmentosa (RP) with bi-allelic mutation in the CYP4V2 gene~~

~~4. The composition of claim 1, 2 or 3, wherein the disease is or the ocular cell degeneration is associated with Bietti Crystalline Dystrophy (also known as Bietti Crystalline Corneoretinal Dystrophy; BCD).~~

~~5. The composition of any one of claims 1-4, wherein the vector is a viral vector, a plasmid, or a non-viral vector.~~

~~6. The composition of claim 5 , wherein the viral vector is selected from the group consisting of an adeno-associated virus (AAV) vector, an adenovirus vector, a lentivirus vector, a herpes simplex virus vector, a baculovirus vector, a sendai virus vector, and a retrovirus vector.~~

~~7. The composition of claim 5 or 6, wherein the vector is a recombinant AAV vector (rAAV).~~

~~8. The composition of claim 5, 6, or 7, wherein the AAV genome or AAV capsid protein in the rAAV is from any one of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, or another serotype or isolate or Glade of AAV, or any derivative, variant or hybrid thereof.~~

~~9. The composition of any one of claims 5-8, wherein the rAAV is a pseudotyped AAV (e.g., AAV2/5, AAV2/8, AAV2/1, AAV2/9, AAV2/6, AAV2/4, AAV2/6, AAV5/2, AAV8/1, AAV8/2, AAV2/7, AAV2/12 andAAV2/10) or a hybrid AAV (e.g., AAV-DJ, AAV-DJ/8, or AAV-DJ/9).~~

~~10. The composition of any one of claims 5-9, wherein the rAAV comprises one or more capsid mutations (e.g., Y-F, K-R, T-A, S-A and/or T-V mutations, (e.g., AAV2 with one or more capsid mutations among Y444F, Y500F, Y730F, Y252F, Y272F, Y700F, Y704F and T491V, or the corresponding mutation for a different AAV serotype, (e.g., AAV2 (Y444F +Y500F+Y730F), AAV2 (quadY-F+T-V), or AAV2/8 (Y733F)))).~~

~~11. The composition of any one of claims 5-10, wherein the serotype of the rAAV is selected or derived from the group consisting of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, Anc80, rh10 and/or ShH10.~~

~~12. The composition of any one of claims 5-11, wherein the rAAV is selected or derived from the group consisting of AAV2/5, AAV2/8, AAV2/2, AAV2 (Y444F+Y500F+Y730F), AAV2/1, AAV2/9, AAV2/8(Y733F), AAV2/6, AAV2/4, AAV2/7, AAV5, AAV2, AAV8, AAV1, AAV9, AAV6, AAV10, AAV4, AAV7, AAV12, Anc80, AAV 7m8, AAV-DJ, ShH10, AAV-PHP.B or a hybrid, a derivative or variant thereof.~~

~~13. The composition of any one of claims 5-12, wherein the rAAV vector is a single-stranded AAV vector or a self-complementary AAV (scAAV) vector.~~

~~14. The composition of claim 5, wherein the vector is a plasmid, a naked nucleic acid, liposomes (e.g., cationic or anionic liposomes), dendrimer, nanoparticle, polymers (e.g., polyplexes), lipid-polymer system, solid lipid nanoparticle, or liposome protamine/DNA lipoplex (LPD).~~

~~15. The composition of any of the preceding claims, wherein the functional or non-mutant CYP4V2 protein encoded by the nucleic acid sequence comprises a polypeptide having at least 80% amino acid sequence identity (e.g., at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity) to any of the sequences selected from the group consisting of SEQ ID NOs: 4-6.~~

~~16. The composition of any of the preceding claims, wherein the nucleic acid molecule has at least 75% sequence identity to any of the sequences in SEQ ID NO: 1, 2 or 3.~~

~~17. The composition of any of the preceding claims, wherein the nucleic acid molecule has at least 80% sequence identity to any of the sequences in SEQ ID NO: 1, 2 or 3.~~

~~18. The composition of any of the preceding claims, wherein the nucleic acid molecule comprises a sequence shown in SEQ ID NO: 1, 2, or 3.~~

~~19. The composition of any of the preceding claims, wherein the nucleic acid molecule comprises a codon-optimized sequence encoding a protein comprising an amino acid sequence selected from SEQ ID NO: 4, 5, or 6.~~

~~20. The composition of any of the preceding claims, wherein the regulatory sequence comprises a promoter.~~

~~21. The composition of claim 20, wherein the promoter is an RPE cell-specific promoter, a retinal cell-specific promoter, a corneal cell-specific promoter, an ocular cell-specific promoter or a constitutive promoter.~~

~~22. The composition of claim 20, wherein the promoter is a beta actin promoter or a viral promoter or a hybrid thereof.~~

~~23. The composition of claim 20, wherein the promoter is selected from the group consisting of a CAG promoter (hybrid CMV early enhancer/Chicken beta actin promoter, also known as CAGGS promoter, CB promoter or CBA promoter), a chicken beta actin promoter, a small CBA (smCBA) promoter, a CB^{SB} promoter, or a CBh promoter, another beta-actin promoter such as the human beta actin promoter, a elongation factor 1 alpha short (EFS) promoter, a elongation factor 1 alpha (EF-1 alpha) promoter, a CMV promoter, a PGK promoter, a UBC promoter, a GUSB promoter, a UCOE promoter, a VMD2 (vitelliform macular dystrophy 2; also known as BEST1) promoter, a RPE65 promoter, or a hybrid, a variant or a derivative thereof.~~

~~24. The composition of any of the preceding claims, wherein the regulatory sequence is a polyA signal selected from the group consisting of a bovine growth hormone polyadenylation signal (bGH polyA), a small polyA signal (SPA), a human growth hormone polyadenylation signal (hGH polyA), a SV40 polyA signal, a SV40 late polyA signal, or a derivative, a hybrid and a variant thereof.~~

~~25. The composition of any of the preceding claims, wherein the regulatory sequence comprises a Kozak sequence.~~

~~26. The composition of any of the preceding claims, wherein the regulatory sequence comprises an enhancer.~~

~~27. The composition of claim 26, wherein the enhancer is a viral enhancer, including without limitation, a WPRE enhancer, an HPRE enhancer, a CTE enhancer or a derivative or hybrid or variant thereof.~~

~~28. A composition for treating or preventing BCD or for producing a composition for treating or preventing BCD comprising a nucleic acid molecule sharing at least 80% sequence identity with any of the CYP4V2 expression cassette sequence in SEQ ID NOs: 60 to 64.~~

~~29. The composition of any of the preceding claims, wherein the composition is formulated with a pharmaceutically acceptable carrier and additional components suitable for the specific route of administration.~~

~~30. A method of treating or preventing an ocular disease in a human subject, the method comprising administering a vector to the subject, wherein the vector comprises an expression cassette, the expression cassette comprising a nucleic acid molecule or a non-pathogenic variant thereof encoding a functional or non-mutant CYP4V2 protein operably linked to one or more regulatory sequence, wherein the disease is associated with the dysfunction, dystrophy, disorder, degeneration, atrophy and/or death of ocular cells~~

~~31. A method of preventing, arresting, slowing progression of, treating or ameliorating the dysfunction, dystrophy, disorder, degeneration, atrophy and/or death of an ocular cell, the method comprising delivering a vector to the ocular cell, wherein the vector comprises an expression cassette, the expression cassette comprising a nucleic acid molecule or a non-pathogenic variant thereof encoding a functional or non-mutant CYP4V2 protein operably linked to one or more regulatory sequence.~~

~~32. The method of claim 30 or 31, wherein the ocular cells are retinal cells, corneal cells, choroidal cells, retinal pigment epithelial (RPE) cells, photoreceptor cells, and/or choroidal epithelial cells.~~

33. The method of claim 30 or 31, wherein the ocular disease or ocular cell degeneration is an inherited retinal degeneration (IRD) or retinitis pigmentosa (RP) with bi-allelic mutation in the CYP4V2 gene.

34. The method of claim 30 or 31, wherein the disease is or the ocular cell degeneration is associated with Bietti Crystalline Dystrophy (also known as Bietti Crystalline Corneoretinal Dystrophy; BCD).

35. The method of any one of claims 30-34, wherein the vector is a viral vector, a plasmid, or a non-viral vector.

36. The method of claim 35, wherein the viral vector is selected from the group consisting of an adeno-associated virus (AAV) vector, an adenovirus vector, a lentivirus vector, a herpes simplex virus vector, a baculovirus vector, a sendai virus vector, and a retrovirus vector.

37. The method of claim 36, wherein the vector is a recombinant AAV vector (rAAV).

38. The method of claim 37, wherein the rAAV comprises an AAV genome or a derivative thereof, and/or an AAV capsid protein or a derivative or variant thereof.

39. The method of claim 37 or 38, wherein the rAAV is a chimeric AAV, a shuffled AAV, or a capsid-modified AAV.

40. The method of claim 36, 37, 38 or 39, wherein the AAV genome or AAV capsid protein in the rAAV is from any one of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, or another serotype or isolate or Glade of AAV, or any derivative, variant or hybrid thereof.

41. The method of any one of claims 37-40, wherein the rAAV is a pseudotyped AAV (e.g., AAV2/5, AAV2/8, AAV2/1, AAV2/9, AAV2/6, AAV2/4, AAV2/6, AAV5/2, AAV8/1,

AAV8/2, AAV2/7, AAV2/12 andAAV2/10) or a hybrid AAV (e.g., AAV-DJ, AAV-DJ/8, or AAV-DJ/9).

42. The method of any one of claims 37-41, wherein the rAAV comprises one or more capsid mutations (e.g., Y-F, K-R, T-A, S-A and/or T-V mutations, (e.g., AAV2 with one or more capsid mutations among Y444F, Y500F, Y730F, Y252F, Y272F, Y700F, Y704F and T491V, or the corresponding mutation for a different AAV serotype, (e.g., AAV2 (Y444F +Y500F+Y730F), AAV2 (quadY-F+T-V), or AAV2/8 (Y733F)))).

43. The method of any one of claims 37-42, wherein the serotype of the rAAV is selected or derived from the group consisting of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, Anc80, rh10 and/or ShH10.

44. The method of any one of claims 37-43, wherein the rAAV is selected or derived from the group consisting of AAV2/5, AAV2/8, AAV2/2, AAV2 (Y444F+Y500F+Y730F), AAV2/1, AAV2/9, AAV2/8(Y733F), AAV2/6, AAV2/4, AAV2/7, AAV5, AAV2, AAV8, AAV1, AAV9, AAV6, AAV10, AAV4, AAV7, AAV12, Anc80, AAV-7m8, AAV-DJ, ShH10, AAV-PHP.B or a hybrid, a derivative or variant thereof.

45. The method of any one of claims 37-44, wherein the rAAV vector is a single-stranded AAV vector or a self-complementary AAV (scAAV) vector.

46. The method of any one of claims 30-34, wherein the vector is a plasmid, a naked nucleic acid, liposomes (e.g., cationic or anionic liposomes), dendrimer, nanoparticle, polymers (e.g., polyplexes), lipid-polymer system, solid lipid nanoparticle, or liposome-protamine/DNA lipoplex (LPD).

47. The method of any one of claims 30-46, wherein the functional or non-mutant CYP4V2 protein encoded by the nucleic acid sequence comprises a polypeptide having at least 80% amino acid sequence identity (e.g., at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%,

88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity) to any of the sequences selected from the group consisting of SEQ ID NOs: 4-6.

48. The method of any one of claims 30-47, wherein the nucleic acid molecule has at least 75% sequence identity to any of the sequences in SEQ ID NO: 1, 2 or 3.

49. The method of any one of claims 30-48, wherein the nucleic acid molecule has at least 80% sequence identity to any of the sequences in SEQ ID NO: 1, 2 or 3.

50. The method of any one of claims 30-49, wherein the nucleic acid molecule comprises a sequence shown in SEQ ID NO: 1, 2, or 3.

51. The method of any one of claims 30-50, wherein the nucleic acid molecule comprises a codon-optimized sequence encoding a protein comprising an amino acid sequence selected from SEQ ID NO: 4, 5, or 6.

52. The method of any one of claims 30-51, wherein the regulatory sequence comprises a promoter.

53. The method of claim 52, wherein the promoter is an RPE cell-specific promoter, a retinal cell-specific promoter, a corneal cell-specific promoter, an ocular cell-specific promoter or a constitutive promoter.

54. The method of claim 52, wherein the promoter is a beta actin promoter or a viral promoter or a hybrid thereof.

55. The method of claim 52, wherein the promoter is selected from the group consisting of a CAG promoter (hybrid CMV-early enhancer/Chicken beta actin promoter, also known as CAGGS promoter, CB promoter or CBA promoter), a chicken beta actin promoter, a small CBA (smCBA) promoter, a CB^{SB} promoter, or a CBh promoter, another beta-actin promoter such as

the human beta actin promoter, a elongation factor 1 alpha short (EFS) promoter, a elongation factor 1 alpha (EF-1 alpha) promoter, a CMV promoter, a PGK promoter, a UBC promoter, a GUSB promoter, a UCOE promoter, a VMD2 (vitelliform macular dystrophy 2; also known as BEST1) promoter, a RPE65 promoter, or a hybrid, a variant or a derivative thereof.

56. The method of any one of claims 30-55, wherein the regulatory sequence comprises a polyadenylation (polyA) signal.

57. The method of claim 56, wherein the polyA signal is a bovine growth hormone polyadenylation signal (bGH polyA), a small polyA signal (SPA), a human growth hormone polyadenylation signal (hGH polyA), a SV40 polyA signal, a SV40 late polyA signal, or a derivative, a hybrid or a variant thereof.

58. The method of any one of claims 30-57, wherein the regulatory sequence comprises a Kozak sequence.

59. The method of any one of claims 30-57, wherein the regulatory sequence comprises an enhancer.

60. The method of claim 59, wherein the enhancer is a viral enhancer, including without limitation, a WPRE enhancer, an HPRE enhancer, a CTE enhancer or a derivative or hybrid or variant thereof.

61. A method for treating or preventing BCD, the method comprising administering a vector comprising a nucleic acid molecule sharing at least 80% sequence identity with any of the CYP4V2 expression cassette sequence in SEQ ID NOs: 60 to 64.

62. The method of any one of claims 30-61, wherein the composition is formulated with a pharmaceutically acceptable carrier and additional components suitable for the specific route of administration.

~~63. A composition for use in producing a vector for treating or preventing BCD, the composition comprising a nucleic acid molecule sharing at least 80% sequence identity with any of the CYP4V2 expression cassette sequence in SEQ ID NOs: 60 to 64.~~

~~64. The method of any one of claims 30-63, wherein for in vitro treatment, the target cell is infected at a dose (MOI) of about 1 x 10^3 GC to about 1 x 10^6 GC per cell (GC: genomic copies, measuring genome containing AAV particles).~~

~~65. The method of any one of claims 30-64, wherein for in vivo administration to a subject's eye, a single administration can be on the order of from about 1 x 10^6 to 2 x 10^13 GC (e.g., a high dose range of about 1 x 10^11 GC to about 1 x 10^12 GC, a medium dose range of about 1 x 10^10 GC to about 1 x 10^11 GC, a low dose range of about 1 x 10^9 GC to about 1 x 10^10 GC, a very low dose range of about 1 x 10^6 GC to about 1 x 10^9 GC, and a very high dose range of about 1 x 10^12 GC to about 2 x 10^13 GC), or any dose within these ranges that is sufficient to provide the desired effect.~~

~~66. The method of any one of claims 30-65, wherein the administering step takes place before the onset of disease symptoms or after the onset of disease symptoms.~~

~~67. The method of any one of claims 30-66, wherein the administration and/or targeted delivery is to the eye and/or to an ocular cell.~~

~~68. The method of any one of claims 30-67, wherein the administration is by sub-retinal injection, intravitreal injection, or by implanting intravitreally a device encapsulating the vector.~~

~~69. The method of any one of claims 30-68, wherein the administration is by any other administration method that effectively delivers the vectors to the sub-retinal place, the posterior segment of the eye, the cornea, the retina, the choroid, the RPE cells, the photoreceptors or corneal epithelial cells, the CE cells of the subject.~~

~~70. The method of claim 67, wherein the administration to the eye is achieved by delivery through the bloodstream.~~

~~71. The method of any of the preceding claims, wherein the ocular cells are selected from the group consisting of retinal pigment epithelium (RPE) cells, photoreceptor cells (PRCs), corneal epithelial cells (CECs), choroidal endothelial (CE) cells, retinal cells, corneal cells, lens cells, ganglion cells, optic nerve cells, and/or choroidal cells, as well as the said types of cells derived from a stem cell (including without limitation, an iPSC, a ES cell, an MSC, an adult stem cell and/or a tissue-specific stem cell).~~

~~72. The method of any of claims 30-71, wherein the vector is formulated with a pharmaceutically acceptable carrier and additional components suitable for the specific route of administration.~~

~~73. The method of any of claims 30-72, further comprising identifying a subject having BCD or at risk of developing BCD, or having bi-allelic CYP4V2 mutation.~~

~~74. A method for treating or preventing Bietti Crystalline Dystrophy (BCD) in a human subject, the method comprising delivering to the subject's ocular cells a vector comprising a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 2 encoding a human CYP4V2 protein or a nucleic acid sequence sharing at least 90% sequence identity to the nucleic acid sequence of SEQ ID NO: 2, operably linked to one or more regulatory sequence.~~

~~75. The method of claim 74, wherein the vector is an adeno-associated virus (AAV) vector.~~

~~76. The method of claim 74 and 75, wherein the regulatory sequence is a promoter.~~

77. A nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 2 encoding a human CYP4V2 protein or a nucleic acid sequence sharing at least 90% sequence identity to the nucleic acid sequence of SEQ ID NO: 2.

78. An expression cassette comprising the nucleic acid molecule of claim 77 and one or more regulatory sequence operably linked to such nucleic acid sequence.

79. A vector comprising the nucleic acid molecule of claim 77 or the expression cassette of claim 78.

80. The vector of claim 79, wherein the vector is a viral vector or is selected from the group consisting of a recombinant adeno-associated virus (rAAV) vector, a recombinant adenovirus vector, a recombinant lentivirus vector, a recombinant herpes simplex virus vector, a recombinant baculovirus vector, a recombinant sendai virus vector, and a recombinant retrovirus vector.

81. The vector of claim 79, wherein the vector is a plasmid or a non-viral vector.

82. The vector of claim 81, wherein the non-viral vector is selected froma naked nucleic acid, liposomes (e.g., cationic or anionic liposomes), dendrimer, nanoparticle, polymers (e.g., polyplexes), lipid-polymer system, solid lipid nanoparticle, or liposome protamine/DNA lipoplex (LPD)..

83. A host cell comprising the nucleic acid molecule of claim 77 and/or the vector of any one of claims 79 to 82.

84. A method to reduce immune responses to viral vectors, preserve transduction efficiency, to lower viral vector and/or immunosuppressant dose, and/or to maximize therapeutic effect to different patients of the same genetic disease, in viral vector mediated gene therapy, comprising:

(a) establishing a pool of more than one recombinant viral vectors (e.g., rAAVs) with sufficient transduction efficiency in the target cell type for the gene therapy by creating variants with antigenic region mutations or other mutations or variants on the capsids of said viral vectors after such mutations or variants are confirmed with sufficient transduction efficiency in target cells relevant to the disease (e.g., in iPS-RPE or RPE cell lines for CYP4V2 gene therapy for BCD).

(b) detecting pre-existing neutralizing anti-viral vector antibodies (NAbs) against different viral vector serotypes and/or capsid mutations or variants in the subject in need of the gene therapy, and/or testing and comparing different viral vectors in patient-specific disease target cells (e.g., iPS-RPE cells) derived from such subject.

(c) selecting a viral vector from said pool of viral vectors with (i) sufficient transduction efficiency in the disease target cells and (ii) low cross-reactivity with the pre-existing NAbs in the subject, and/or (iii) good phenotype rescue result in the subject's patient-specific disease target cells (e.g., patient-specific iPS-RPE or RPE cell lines for CYP4V2 gene therapy for BCD), wherein such viral vector pool comprising different serotypes and/or capsid-modified viral vectors (e.g., including without limitation, capsid-mutant AAVs and/or capsid protein variant AAVs).

(d) using the viral vector selected from (c) for administration to the subject.

(e) repeating (b) through (d) (only the part relating to pre-existing NAbs) above each time the subject requires a gene therapy administration, including without limitation, a follow-up administration to the same organ (e.g., an eye or a contralateral eye), or to another organ.

85. A method of using AAV vector-mediated gene therapy in treating or preventing human retinal diseases, wherein the AAV vector comprises a nucleic acid molecule comprising a EFS promoter (SEQ ID NO: 35) and/or a small polyA (SEQ ID NO: 36) operably linked to the therapeutic transgene, or a nucleic acid molecule shares at least 90% sequence identify with SEQ ID NO: 35 or at least 85% sequence identity with SEQ ID NO: 36.

86. The method of claim 85, wherein the AAV vector is a single-stranded AAV.

~~87. The method of claim 85, wherein the AAV vector is a self-complementary AAV (scAAV).~~

~~88. A cellular disease model comprising a cell line composition comprising (a) a stem cell provided from a subject or reprogrammed from a cell provided from a subject, or (2) a cell derived from a stem cell provided from a subject or reprogrammed from a cell provided from a subject, comprising one or more mutations in a target gene.~~

~~89. The composition of claim 88, wherein the stem cell is an induced pluripotent stem (iPS) cell.~~

~~90. The composition of claim 88, wherein the stem cell is an embryonic stem (ES) cell, somatic (or adult) stem cell, tissue specific stem cell, or mesenchymal stem cell (MSC).~~

~~91. The composition of claim 88, wherein the cell provided from a subject is a somatic cell.~~

~~92. The composition of claim 88, wherein the cell provided from a subject is a skin cell, a fibroblast or a blood cell.~~

~~93. The composition of claim 88 or 92, wherein the cell provided from a subject is a skin fibroblast or a peripheral blood mononuclear cell (PBMC).~~

~~94. The composition of claim 88, wherein the cell provided from a subject is a urinary cell, a renal epithelial cell, a hair follicle, or a dermal papilla cell.~~

~~95. The composition of claim 88, wherein the cell derived from a stem cell is an ocular cell.~~

96. The composition of claim 95, wherein the ocular cell is a retinal pigment epithelial (RPE) cell, photoreceptor cell (PRC, including rod cell, cone cell and photoreceptor progenitor cell), retinal cell, corneal cell, corneal epithelial cell (CEC), optic nerve cell, lens cell, choroidal endothelial (CE) cell, optic nerve cell or choroidal cell.

97. The composition of claim 88, wherein the cell derived from a stem cell is a neuron cell.

98. The composition of claim 88, wherein the mutation is endogenous to the subject.

99. The composition of claim 88 or 98, wherein the mutation is introduced artificially via genetic editing or genetic manipulation.

100. The composition of claim 88, wherein the cell line comprises a plurality of mutations that are endogenous and/or exogenous to the subject.

101. The composition of claim 88, wherein the subject is a mammal.

102. The composition of claim 88, wherein the subject is a human.

103. The composition of claim 88, wherein the target gene comprises a gene set forth in Table 4.

104. The composition of claim 88, wherein the target gene comprises a mutated or defective CYP4V2, CYP1B1, MYO7A, DFNB31, USH1C, USH1G, CDH23, PCDH15, CLRN1, ACO2, AFG3L2, ATXN2, AUH, C12orf65, CISD2, FOXC1, FOXF2, LTBP2, MTPAP, MYOC, NDUFS1, NR2F1, OPA1, OPA3, OPTN, PAX6, PDGF, PITX2, POLG, SPG7, TEK, TXNRD2, WFS1, ABCA4, REP-1, RPE65, CEP290, PDE6B, RPGR, MERTK, MT-ND4, FAM47E, GBA, GCH1, HTRA2, LRRK2, PARK2, PINK1, SNCA, SYNJ1, NPC1, NPC2, CYP4A11, CYP4A22, CYP4B1, CYP4F2, CYP4F3, CYP4F8, CYP4F11, CYP4F12, CYP4F22,

~~CYP4X1, CYP4Z1, or CYP46A gene or a CYP4V2, CYP1B1, MYO7A, DFNB31, USH1C, USH1G, CDH23, PCDH15, CLRN1, ACO2, AFG3L2, ATXN2, AUH, C12orf65, CISD2, FOXC1, FOXF2, LTBP2, MTPAP, MYOC, NDUFS1, NR2F1, OPA1, OPA3, OPTN, PAX6, PDGF, PITX2, POLG, SPG7, TEK, TXNRD2, WFS1, ABCA4, REP 1, RPE65, CEP290, PDE6B, RPGR, MERTK, MT-ND4, FAM47E, GBA, GCH1, HTRA2, LRRK2, PARK2, PINK1, SNCA, SYNJ1, NPC1, NPC2, CYP4A11, CYP4A22, CYP4B1, CYP4F2, CYP4F3, CYP4F8, CYP4F11, CYP4F12, CYP4F22, CYP4X1, CYP4Z1 or CYP46A gene that encodes a protein having defective or partial function or activity.~~

~~105. The composition of claim 88, wherein the target gene is CYP4V2.~~

~~106. The composition of claim 105, wherein the cell line comprises an iPS cell.~~

~~107. The composition of claim 105, wherein the cell line comprises an iPS-RPE cell.~~

~~108. The composition of claim 105, wherein the cell line comprises an iPS-photoreceptor (iPS-PRC) cell, an iPS-corneal epithelial cell (iPS-CEC). an iPS-choroidal endothelial (CE) cell, an iPS-corneal cell, an iPS-choroidal cell, an iPS-optic nerve cell, an iPS-ocular cell or an iPS-neuron cell.~~

~~109. The composition of any one of claims 88 or 105-108, wherein the CYP4V2 mutation in the cell line is endogenous to the subject.~~

~~110. The composition of claim 88 or 109, wherein the subject has a pathologic mutation in the CYP4V2 gene or in an ortholog of the CYP4V2 gene.~~

~~111. The composition of claim 88 or 109, wherein the subject has at least one homozygous mutation or two compound heterozygous mutations set forth in Table 1.~~

~~112. The composition of claim 88, wherein the subject has inherited retinal degeneration (IRD) or retinitis pigmentosa (RP).~~

~~113. The composition of claim 88, wherein the subject has Bietti's Crystalline Dystrophy (BCD, a/k/a Bietti Crystalline Corneoretinal Dystrophy, Bietti Crystalline Retinopathy, Bietti's Retinal Dystrophy) or is at risk of developing BCD.~~

~~114. The composition of claim 88 or 105, wherein the cell line comprises at least one CYP4V2 mutation that is exogenous to the subject and is introduced artificially via genetic editing or genetic manipulation.~~

~~115. The composition of claim 88 or 114, wherein the cell line comprises an iPS cell, ES cell, MSC, tissue-specific stem cell or adult stem cell, or a RPE cell, photoreceptor cell, corneal epithelial cell. choroidal endothelial (CE) cell or choroidal cell derived from an iPS cell, ES cell, MSC, tissue specific stem cell or adult stem cell.~~

~~116. A BCD human cellular model composition or a CYP4V2 dysfunction cellular model composition comprising an iPS cell or iPS cell line, or an iPS-RPE cell or iPS-RPE cell line derived from a cell or a cell line of a BCD patient, or derived from a cell or a cell line with artificially created bi-allelic CYP4V2 mutation.~~

~~117. The composition of any one of claims 88 or 105-116, wherein the cell line has an abnormal biochemical profile in one or more compounds of the following compound groups: (i) fatty acids, (ii) ceramides, (iii) sphingomyelins, (iv) sphingosine, (v) sphinganine, (vi) hydroxy-fatty acids, (vii) corticosteroid, or (viii) proteins (other than CYP4V2) or abnormal RPE function, or higher cell atrophy, degeneration or death level as compared to a corresponding cell line of a healthy control.~~

~~118. The composition of one of claims 88 or 105-117, wherein the cell line has an abnormal biochemical profile in one or more compounds set forth in Table 2 as compared to the corresponding cell line of a healthy control.~~

~~119. A method of discovering abnormalities or phenotype in a disease cellular model, comprising evaluating and comparing the cell viability levels of the cell line of a patient (or an genetically edited or manipulated cell line comprising an exogenous mutation in the gene causing such disease) and a healthy control.~~

~~120. A method of discovering abnormalities or phenotype in a disease cellular model, comprising evaluating and comparing the RPE function levels (e.g., phagocytic activity, transepithelial resistance) of the cell line of a patient (or an genetically edited or manipulated cell line comprising an exogenous mutation in the gene causing such disease) and a healthy control, wherein the cell line is a RPE cell line (including RPE cell line derived from a stem cell).~~

~~121. The method of claim 119 or 120, wherein the comparison between cell lines are made without exposure to light.~~

~~122. The method of claim 119 or 120, wherein the comparison between cell lines are made after exposure to light.~~

~~123. The method of claim 119, 120 or 122, wherein the comparison between cell lines are made after exposure to blue light.~~

~~124. The method of claim 119, 121, 122 or 123, wherein cell viability is measured by dead/live cell ratio, sick/healthy cell ratio or similar ratios, or percentage of dead/overall cells or live/overall cells.~~

~~125. A method of discovering abnormalities or phenotype in a disease cellular model, comprising evaluating and comparing the levels of one or more compounds between the cell line~~

of a patient (or an genetically edited or manipulated cell line comprising an exogenous mutation in the gene causing such disease) and a healthy control, wherein the one or more compound is selected from the following groups: (i) fatty acids, (ii) ceramides, (iii) sphingomyelins, (iv) sphingosine, (v) sphinganine, (vi) hydroxy fatty acids, (vii) corticosteroid and/or (viii) proteins.

126. The method of claim 125, wherein one or more of the compounds evaluated is set forth in Table 2.

127. The method of claim 125 or 126, wherein the identification and/or evaluation of compound levels is performed using LC-MS, LC-MS/MS, GC-MS, GC-MS/MS, and/or FIA-MS/MS.

128. The method of claim 119, 120 or 125, wherein the disease cellular model comprises a mutated or defective gene set forth in Table 4.

129. The method of claim 119, 120 or 125, wherein the disease cellular model comprises a mutated or defective gene among the CYP4V2, CYP1B1, MYO7A, DFNB31, USH1C, USH1G, CDH23, PCDH15, CLRN1, ACO2, AFG3L2, ATXN2, AUH, C12orf65, CISD2, FOXC1, FOXF2, LTBP2, MTPAP, MYOC, NDUFS1, NR2F1, OPA1, OPA3, OPTN, PAX6, PDGF, PITX2, POLG, SPG7, TEK, TXNRD2, WFS1, ABCA4, REP-1, RPE65, CEP290, PDE6B, RPGR, MERTK, MT-ND4, FAM47E, GBA, GCH1, HTRA2, LRRK2, PARK2, PINK1, SNCA, SYNJ1, NPC1, NPC2, CYP4A11, CYP4A22, CYP4B1, CYP4F2, CYP4F3, CYP4F8, CYP4F11, CYP4F12, CYP4F22, CYP4X1, CYP4Z1, or CYP46A gene.

130. A method of screening a test agent for therapeutic efficacy against BCD, comprising:

contacting cells from an iPS-RPE cell line derived from a BCD patient or an iPS-RPE cell line comprising a mutated or defective CYP4V2 gene as a result of artificial genetic editing or manipulation with a test agent; and

evaluating the cells for normalization in levels of one or more compounds set forth in Table 2; an increase in non-defective CYP4V2 nucleic acid sequence in the cells; an increase in the amount of CYP4V2 polypeptides in the cells; and/or improved cell structure, morphology or function, or improved cell viability, as compared to before contacting by such test agent;

wherein normalization in levels of one or more compound set forth in Table 2; an increase in non-defective CYP4V2 nucleic acid sequence in the cells; an increase in the amount of CYP4V2 polypeptides in the cells; and/or improved cell structure, morphology, function or cell viability, as compared to before treatment by such test agent, is indicative of a test agent that exhibits therapeutic efficacy against BCD;

wherein the comparison among cell lines can be made after exposure to light and/or without exposure to light.

131. The method of claim 130, wherein the test agents are selected from the group consisting of nucleic acids or analogs thereof, vectors containing nucleic acid sequence or encoding polypeptides, polypeptides or analogs thereof, antibodies, chemicals, small molecules, and/or any combination thereof.

132. The method of claim 130, wherein the cells are evaluated using PCR techniques, immunoassays, sequencing, biochemical assay, function assay, cell viability assay, microscopy or combination thereof.

133. A method of screening efficacy or efficiency of a formulation, vector or construct comprising a test agent for BCD, comprising:

contacting multiple cell samples from an iPS-RPE cell line derived from a BCD patient or an iPS-RPE cell line comprising a mutated or defective CYP4V2 gene as a result of artificial genetic editing or manipulation with a test agent formulated or packaged in various formulations, vectors or constructs; and

evaluating the cell samples for normalization in levels of one or more compound set forth in table 2; an increase in non-defective CYP4V2 nucleic acid sequence in the cells; an increase in the amount of CYP4V2 polypeptides in the cells; improved cell structure, morphology, function

~~or viability; and/or cell tolerance or death, as compared to before treatment by such test agent and/or to cell samples treated by the same test agent but formulated or packaged in a different formulation, vector or construct, to determine and compare the efficiency or efficacy of such formulation, vector or construct;~~

~~wherein the cells are evaluated using PCR techniques, immunoassays, sequencing, biochemical assay, cell viability assay, microscopy or combination thereof;~~

~~wherein the comparison among cell lines can be made after exposure to light and/or without exposure to light.~~

~~134. A method of screening effective and safe dosage range of a test agent for BCD, comprising:~~

~~contacting multiple cell samples from an iPS-RPE cell line derived from a BCD patient or an iPS-RPE cell line comprising a mutated or defective CYP4V2 gene as a result of artificial genetic editing or manipulation with a test agent in a different dose for each cell sample.~~

~~evaluating the cell samples for normalization in levels of one or more compound set forth in table 2; an increase in non-defective CYP4V2 nucleic acid sequence in the cells; an increase in the amount of CYP4V2 polypeptides in the cells; improved cell structure, morphology, viability or function, and/or cell tolerance or death, as compared to before treatment by such test agent and/or to cell samples treated by the same test agent but with a different dose, to determine and compare the effective and safety of different doses thereby determining a proper dosage range;~~

~~wherein the cells are evaluated using PCR techniques, immunoassays, sequencing, biochemical assay, function assay, cell viability assay, microscopy or combination thereof;~~

~~wherein the comparison among cell lines can be made after exposure to light and/or without exposure to light.~~

~~135. A method of screening or evaluating efficacy or efficiency of a delivery device or method for delivering a therapeutic agent to the retina or retinal cells comprising:~~

~~(i) contacting a cell sample from an iPS-RPE cell line derived from a BCD patient or an iPS-RPE cell line comprising a mutated or defective CYP4V2 gene as a result of artificial~~

genetic editing or manipulation with a test agent without employing the delivery device or method;

(ii) contacting another cell sample from an iPS-RPE cell line derived from a BCD patient or an iPS-RPE cell line comprising a mutated or defective CYP4V2 gene as a result of artificial genetic editing or manipulation with the test agent of the same dosage as in (i), employing the delivery device or method;

(iii) evaluating and comparing the cell samples from (i) and (ii) for normalization in levels of one or more compound set forth in Table 2; an increase in non-defective CYP4V2 nucleic acid sequence in the cells; an increase in the amount of CYP4V2 polypeptides in the cells; improved cell structure, morphology or function; cell tolerance or death; and/or the levels of the test agent in the cells, as compared to before treatment by such test agent and/or treatment by the same test agent of the same dose but without employing the delivery device or method, to determine the efficacy or efficiency of such delivery device or technique;

wherein the cells are evaluated using PCR techniques, immunoassays, sequencing, biochemical assay, function assay, cell viability, microscopy or combination thereof;

wherein the comparison among cell lines can be made after exposure to light and/or without exposure to light.

136. The method of claim 135, wherein the retinal cells are RPE cells.

137. A method of generating an isogenic control comprising genetically correcting the mutation in a patient cell line by any of the claims in gene editing therapy or RNP claims herein.

138. A method of using patient-specific iPS ocular cells to assess and suggest therapeutic effective dosage for treatment *in vivo*, the method comprising multiplyingthe optimal dose level (e.g., indicated as MOI for gene therapy *in vitro*) determined in patient-specific iPS-ocular cellular model *in vitro* by the estimated number of ocular cells (e.g., RPE cells, photoreceptor cells, or RPE cells and photoreceptor cells) targeted for treatment *in vivo* to arrive the dose level of gene therapy vectors for in vivo use (e.g., GC or gp), and such vector dose level is adjusted by a multiplier (e.g., 1 to 10 (e.g., 1 to 5 for sub-retinal injection or 5 to 10 for

~~intravitreal injection; the other factors affecting the multiplier to be applied include the size of the area targeted, and the subject being treated (e.g., the age, weight, development stage of the disease and condition of the subject to be treated, and potential immune reactions (i.e., pre-exisiting NAbs); the location and density of the ocular cells targeted for treatment) to suggest the therapeutic effective dose range for treatment *in vivo*, which can be confirmed or further refined by clinical trials.~~

~~139. The method of claim 138, wherein the method is used to assess or suggest personalized optimal dose used in treatment *in vivo* for an individual patient.~~

~~140. The method of claim 138 or 139, wherein the disease is an inherited retinal disorder (IRD) or retinitis pigmentosa (RP).~~

~~141. The method of claim 138 or 139, wherein the disease is BCD and the iPS-ocular cells are iPS-RPE cells and the ocular cells targete for treatment in vivo are RPE cells.~~

~~142. A composition comprising: (a) a CRISPR guide RNA targeting a nucleic acid sequence (the "target sequence") of or within 100 bps to the CYP4V2 gene, and (b) a functional CRISPR-associated protein (Cas).~~

~~143. The composition of claim 142, further comprising (c) a donor nucleic acid sequence comprising all or a portion of a wild-type sequence or a functional sequence of the CYP4V2 gene for correction, disruption or replacement of CYP4V2 gene or a portion thereof.~~

~~144. The composition of claim 142 or 143, wherein one or more components thereof is provided in the form of a DNA molecule encoding such component, an mRNA molecule encoding such component, a RNA molecule, a polypeptide, and/or a ribonucleoprotein (RNP) or protein-RNA complex.~~

~~145. The composition of claim 142 or 143, wherein two or more components thereof are in separate molecule or combined in one molecule or in one complex, are in separate vectors or combined in one vector, are in one or more nucleic acid complex, are in one or more RNP complex.~~

~~146. The composition of claim 143, wherein the donor nucleic acid sequence is provided in a single-stranded donor oligonucleotide (ssODN) or a vector.~~

~~147. The composition of any one of claims 142-146, wherein the vector is a plasmid, a recombinant AAV vector, a recombinant lentivirus vector, and/or a combination thereof.~~

~~148. A composition comprising a cell with a pathologic CYP4V2 mutation comprising a composition of any one of claims 142-147.~~

~~149. The composition of any one of claims 142-148, wherein (a) the CRISPR guide RNA comprising (i) a CRISPR RNA (crRNA) which comprises a protospacer element sequence that is complementary to the target sequence of or within 100 bps to a target gene (the "target gene") and a sequence that corresponds to a complementary region of the trans-activating crRNA (tracrRNA), and (ii) a tracrRNA which comprises a region that is complementary to corresponding region of the crRNA and a sequence which interacts with a CRISPR-associated protein 9 (Cas9), and (b) the functional CRISPR-associated protein comprises Cas9.~~

~~150. The composition of claim 149, wherein the protospacer element is about 20 bases, about 19 bases, about 21 bases, about 19-21 bases, about 18-22 bases, or about 16-24 bases.~~

~~151. The composition of claim 149 or 150, wherein the crRNA and the tracrRNA are in separate molecules.~~

~~152. The composition of claim 149 or 150, wherein the crRNA and the tracrRNA are combined in a single guide RNA (sgRNA).~~

~~153. The composition of claim 152, wherein the sgRNA is about 88-150 bps.~~

~~154. The composition of any one of claims 149-153, wherein the Cas9 comprises a Cas9 ortholog or a mutant Cas9 selected from: Streptococcus pyogenes (SpCas9), SpCas9 nickase (Cas9n D10A), SpCas9 (D1135E), eSpCas9, SpCas9-HF1, SpCas9 VRER, SpCas9 VQR, SpCas9EQR, Staphylococcus aureus (SaCas9), Neisseria Meningitidis, Streptococcus thermophilus, Streptococcus pneumnoniae, Campylobacter coli, Campylobacter jejuni, Streptococcus mutans, Pasteurella multocida, Bifidobacterium longum, Bacillus smithii, Treponema denticola, mycoplasma canis and enterococcus faecalis.~~

~~155. The composition of any one of claims 142-148, wherein (a) the CRISPR guide RNA comprises a crRNA which comprises a protospacer element sequence that is complementary to the target sequence of or within 100 bps to a target gene, and (b) the functional CRISPR-associated protein comprises Cpf1.~~

~~156. The composition of any one of claims 142-155, wherein the CRISPR-associated protein, Cas9, or Cpf1, further comprises one, two, three or more nuclear localization sequences (NLS) at the N-terminal and/or C-terminal, and/or a selection marker, including without limitation, GFP or EGFP.~~

~~157. The composition of claim 142, wherein the protospacer element sequence is selected from the group consisting of SEQ ID NOs: 48 to 52, or shares at least 85% sequence identity with any one of SEQ ID NO: 48 to 52 for use with a Cas protein that has NGG as protospacer adjacent motif (PAM) to target the c.802-8_810del17insGC mutation of the CYP4V2 gene.~~

~~158. The composition of claim 142, 143 or 157, wherein the donor nucleic acid sequence is selected from SEQ ID NOs: 56 and 57, or shares at least 90% sequence identity with one of~~

~~SEQ ID NO: 56, 57, or a sequence that is complementary thereof, for use to correct, disrupt or replace the c.802-8_810del17insGC mutation of the CYP4V2 gene.~~

~~159. A method of treating or preventing BCD in a subject or a cell with a mutated CYP4V2 gene, comprising:~~

~~(i) identifing the pathologic mutation in the subject or the cell through sequencing;~~

~~(ii) finding Cas related PAM sites within the region spanning from about 100 bps upstream from the first nucleotide involved in the mutation to about 100 bps downstream from the last nucleotide involved in the mutation;~~

~~(iii) identifying various protospacer element sequences targeting the CYP4V2 sequence relevant to each PAM site identified in (ii);~~

~~(iv) assessing activity level of each CRISPR guide RNA comprising a protospacer element sequence identified in (iii) and off-target editing profile based on the protospacer element sequence and PAM;~~

~~(v) selecting one or more CRISPR guide RNA design based on (iv);~~

~~(vi) designing one or more donor nucleic acid sequence based on homology-directed repair (HDR) for correcting, disrupting or replacing the targeted CYP4V2 mutation;~~

~~(vii) constructing the CRISPR guide RNA, Cas and donor nucleic acid sequence as provided in composition claims 1 to 18;~~

~~(viii) optionally validating and further selecting the components of (vii) in a cell isolated from the subject; or an iPS cell derived from the subject or a cell differentiated from a stem cell derived from the subject, or the genomic DNA isolated from the subject to assess the activity level and/or off-target editing profile; and~~

~~(ix) administering the components in (viii) to the subject or the cell via a delivery system selected from the group consisting of a ribonucleoprotein or protein-RNA complex, a vector, a protein, a nucleic acid molecule, a nanoparticle, a liposome, a micelle, a virosome, a nucleic acid complex, and/or a combination thereof, wherein the delivery is performed by electroporation or via lipid-mediated transfection, or nucleofection, or viral transduction or injection, or a combination thereof.~~

~~160. A gene editing composition for correcting or replacing the c.802-8_810del17insGC mutation in a CYP4V2 gene in a subject in vivo or in a cell in vitro, comprising:~~

~~(i) a CRISPR guide RNA comprising a protospacer element sequence selected from one of SEQ ID NO: 48 to 52 or sharing at least 80% sequence identity with one of the sequences in SEQ ID 48 to 52;~~

~~(ii) a donor nucleic acid sequence selected from one of SEQ ID NOs: 56 and 57, or shares at least 90% sequence identity with one of SEQ ID NO: 56, 57, or a sequence that is complementary thereof; and~~

~~(iii) a Cas9 protein (exemplary sequence shown in SEQ ID NO: 58), optionally containing 1, 2, 3 or more NLS, and/or a selection marker including without limitation GFP or EGFP.~~

~~161. The composition of claim 160, wherein an optional nucleotide G (SEQ ID NO: 59) is added before the protospacer element sequence.~~

~~162. The composition of claim 160 or 161, wherein the CRISPR guide RNA comprises a crRNA (exemplary sequence (excluding the 5' protospacer element sequence) shown in SEQ ID NO: 53) and a tracrRNA (exemplary sequence shown in SEQ ID NO: 54); and the protospacer element sequence is contained in the crRNA.~~

~~163. The composition of any of claims 160-162, wherein the CRISPR guide RNA comprises a single guide RNA (sgRNA) comprising the protospacer element sequence (exemplary sgRNA sequence (excluding the 5' protospacer element sequence) shown in SEQ ID NO: 55).~~

~~164. The composition of any of claims 160-163, wherein one or more components of (i), (ii) and (iii) is provided in the form of a DNA molecule encoding such component, an mRNA molecule encoding such component, a nucleic acid molecule, a vector, a RNA molecule, a polypeptide, a ribonucleoprotein (RNP) or protein-RNA complex, and/or a combination thereof.~~

~~165. A method of treating or preventing a disease of the eye in a subject, wherein the disease is associated with a pathologic genetic or epigenetic alteration in the CYP4V2 gene, the method comprising administering a cellular composition to the subject, wherein the cellular composition comprises: retinal pigment epithelium (RPE) cells, photoreceptors or photoreceptor progenitors (PRCs), corneal epithelial cells (CECs), choroidal endothelial (CE) cells and/or other ocular cells or other cells derived from a stem cell.~~

~~166. The method of claim 165, wherein the stem cell is an embryonic stem (ES) cell, an iPC cell, an MSC, an adult stem cell or a tissue-specific stem cell.~~

~~167. The method of claim 165, wherein the stem cell is from or derived from one or more subjects not having BCD or not having a pathologic CYP4V2 gene.~~

~~168. The method of claim 165, wherein the stem cell is from or derived from one or more subjects with pathologic mutations in the CYP4V2 gene.~~

~~169. The method of any of claims 165-168, wherein the subject is a human subject.~~

~~170. A cellular composition comprising (a) a stem cell reprogrammed from a cell isolated from or a stem cell isolated from a subject affected by BCD or having pathologic mutations in the CYP4V2 gene, or (2) a cell differentiated from a stem cell isolated from a subject or reprogrammed from a cell isolated from a subject affected by BCD or having pathologic mutations in the CYP4V2 gene.~~

~~171. The composition of claim 170, wherein the stem cell reprogrammed from a cell isolated from the subject is an iPC cell.~~

~~172. The composition of claim 170, wherein the iPS cell is reprogrammed from a somatic cell from the subject.~~

~~173. The composition of claim 170, wherein the iPS cell is reprogrammed from a skin cell, a blood cell, a urinary cell, a hair cell, a fibroblast, a peripheral blood mononuclear cell (PBMC), a renal epithelial cell, a hair follicle, or a dermal papilla cell.~~

~~174. The composition of claim 170, wherein the stem cell isolated from the subject is an MSC, an adult stem cell or a tissue-specific stem cell.~~

~~175. The composition of claim 170, wherein the cell differentiated from a stem cell is an ocular cell.~~

~~176. The composition of claim 170 or 175, wherein the cell differentiated from a stem cell is an RPE cell, a PRC, a retinal cell, a corneal cell, a choroidal cell, a CEC or a CE cell.~~

~~177. The composition of claim 170, wherein the cell differentiated from a stem cell is an iPS-RPE, iPS-PRC, iPS-CEC or iPS-CE cell.~~

~~178. The composition of claim 170, wherein (i) the cell isolated from a subject affected by BCD or having pathologic mutations in the CYP4V2 gene for use to reprogram into an iPSC, (ii) the stem cell isolated from a subject or iPS cell reprogrammed from a cell isolated from a subject affected by BCD or having pathologic mutations in the CYP4V2 gene, or (iii) the cell differentiated from a stem cell isolated from a subject or an iPS cell reprogrammed from a cell isolated from a subject affected by BCD or having pathologic mutations in the CYP4V2 gene, is genetically repaired to ameliorate the effect of the mutated CYP4V2 gene.~~

~~179. The composition of claim 178, wherein genetic repair is via gene transfer therapy.~~

~~180. The composition of claim 178, wherein genetic repair is via gene transfer therapy by using any composition or method of any one of the gene therapy claims.~~

181. The composition of any of the preceding claims, wherein genetic repair is via gene editing therapy.

182. The composition of claim 181, wherein genetic repair is via gene editing therapy by using any composition or method of any one of CRISPR gene therapy claims.

183. A method of treating or preventing a disease of the eye in a subject affected by BCD or have pathologic genetic or epigenetic alterations in the CYP4V2 gene, the method comprising administering a composition of any one of the claims related to CYP4V2 autologous cellular compositions to the subject, wherein the cellular composition comprises: genetically repaired cells comprising retinal pigment epithelium (RPE) cells, photoreceptors or photoreceptor progenitors (PRCs), corneal epithelial cells (CECs), choroidal endothelial (CE) cells, and/or other ocular cells or other cells derived from a stem cell of the subject.

184. The method of claim 183, wherein the stem cell is an iPC cell, an MSC, an adult stem cell or a tissue-specific stem cell.

185. The method of claim 184, wherein the iPS cell is reprogrammed using one or more of the OCT4, SOX2, KLF4, and c-MYC transcription factors.

186. The method of any of the preceding claims, wherein the genetically repaired cells demonstrate one or more of the following: normalization in levels of one or more compound set forth in Table 2; an increase in non-defective CYP4V2 nucleic acid sequence in the cells; an increase in the amount of functional CYP4V2 polypeptides in the cells; and/or improved cell structure, morphology, viability or function, as compared to before genetic repair is performed.

187. The method of any of the preceding claims, wherein the amount of cells administered is about 1,000 to about 10 million cells in a single administration.

~~188. The method of any of the preceding claims, wherein the administration is via injection, sub-retinal injection or intravitreal injection, .~~

~~189. The method of any of the preceding claims, wherein the administration is by any other administration method that effectively delivers the cells to the sub-retinal place, the posterior segment, or the cornea of the eye of the subject.~~

~~190. The method of any of the preceding claims, wherein the cells are administered via injection of cell suspension.~~

~~191. The method of any of the preceding claims, wherein the cells are administered as part of a sheet, a matrix, a scaffold, a tissue, or a 3D retinal structure.~~

~~192. The method of any of the preceding claims, whereas the RPE cells are administered using natural and/or synthetic scaffolds to generate a functional RPE monolayer.~~

~~193. The method of any of the preceding claims, wherein the subject is a human subject.~~

~~194. A cellular composition comprising (a) a stem cell reprogrammed from a cell isolated from or a stem cell isolated from a subject affected by a disease caused by a mutated or defective gene or a gene encoding a protein having defective or partial function or activity, or (2) a cell differentiated from a stem cell isolated from a subject or reprogrammed from a cell isolated from a subject affected by a disease caused by a mutated or defective gene or a gene encoding a protein having defective or partial function or activity.~~

~~195. The composition of claim 194, wherein the stem cell reprogrammed from a cell isolated from the subject is an iPS cell.~~

~~196. The composition of claim 195, wherein the iPS cell is reprogrammed from a somatic cell of the subject.~~

~~197. The composition of claim 195 or 196, wherein the iPS cell is reprogrammed from a skin cell, a blood cell, a urinary cell, a hair cell, a fibroblast, a peripheral blood mononuclear cell (PBMC), a renal epithelial cell, a hair follicle, or a dermal papilla cell.~~

~~198. The composition of claim 194, wherein the stem cell isolated from the subject is an MSC, an adult stem cell or a tissue-specific stem cell.~~

~~199. The composition of claim 194, wherein the gene is involved in ocular development or function and/or mutation of which causes or is a risk factor to cause an ocular disease.~~

~~200. The composition of claim 194, wherein the gene is involved in neuronal development or function and/or mutation of which causes or is a risk factor to cause a neurodegenerative disease.~~

~~201. The composition of claim 194, wherein the gene is a cytochrome P450 gene.~~

~~202. The composition of claim 194, wherein the gene is one set forth in Table 4.~~

~~203. The composition of claim 194, wherein the gene comprises a mutated or defective CYP4V2, CYP1B1, MYO7A, DFNB31, USH1C, USH1G, CDH23, PCDH15, CLRN1, ACO2, AFG3L2, ATXN2, AUH, C12orf65, CISD2, FOXC1, FOXF2, LTBP2, MTPAP, MYOC, NDUFS1, NR2F1, OPA1, OPA3, OPTN, PAX6, PDGF, PITX2, POLG, SPG7, TEK, TXNRD2, WFS1, ABCA4, REP-1, RPE65, CEP290, PDE6B, RPGR, MERTK, MT-ND4, FAM47E, GBA, GCH1, HTRA2, LRRK2, PARK2, PINK1, SNCA, SYNJ1, NPC1, NPC2, CYP4A11, CYP4A22, CYP4B1, CYP4F2, CYP4F3, CYP4F8, CYP4F11, CYP4F12, CYP4F22, CYP4X1, CYP4Z1, or CYP46A gene or a CYP4V2, CYP1B1, MYO7A, DFNB31, USH1C, USH1G, CDH23, PCDH15, CLRN1, ACO2, AFG3L2, ATXN2, AUH, C12orf65, CISD2, FOXC1, FOXF2, LTBP2, MTPAP, MYOC, NDUFS1, NR2F1, OPA1, OPA3, OPTN, PAX6, PDGF, PITX2, POLG, SPG7, TEK, TXNRD2, WFS1, ABCA4, REP-1, RPE65, CEP290, PDE6B,~~

~~RPGR, MERTK, MT-ND4, FAM47E, GBA, GCH1, HTRA2, LRRK2, PARK2, PINK1, SNCA, SYNJ1, NPC1, NPC2, CYP4A11, CYP4A22, CYP4B1, CYP4F2, CYP4F3, CYP4F8, CYP4F11, CYP4F12, CYP4F22, CYP4X1, CYP4Z1 or CYP46A gene that encodes a protein having defective or partial function or activity.~~

~~204. The composition of any of the preceding claims, wherein the cell differentiated from a stem cell is any type of cell.~~

~~205. The composition of any of the preceding claims, wherein the cell differentiated from a stem cell is an ocular cell.~~

~~206. The composition of any of the preceding claims, wherein the cell differentiated from a stem cell is an RPE cell, a PRC, a retinal cell, a corneal cell, a choroidal cell, a CEC, a CE cell or an optic nerve cell.~~

~~207. The composition of any of the preceding claims, wherein the cell differentiated from a stem cell is an iPS-RPE, iPS-PRC, iPS-CEC or iPS-CE cell.~~

~~208. The composition of any of the preceding claims, wherein the cell differentiated from a stem cell is a neuron.~~

~~209. The composition of any of the preceding claims, wherein (i) the cell isolated from a subject affected by a disease caused by a mutated or defective gene or a gene encoding a protein having defective or partial function or activity for use to reprogram into an iPSC, (ii) the stem cell isolated from a subject or iPS cell reprogrammed from a cell isolated from a subject affected by a disease caused by a mutated or defective gene or a gene encoding a protein having defective or partial function or activity, or (iii) the cell differentiated from a stem cell isolated from a subject or an iPS cell reprogrammed from a cell isolated from a subject affected by a disease caused by a mutated or defective gene or a gene encoding a protein having defective or partial~~

~~function or activity, is genetically repaired to ameliorate the effect of the mutated or defective gene.~~

~~210. The composition of any of the preceding claims, wherein genetic repair is via gene transfer therapy.~~

~~211. The composition of any of the preceding claims, wherein genetic repair is via gene transfer therapy by using any composition or method of any one of the claims related to gene therapy.~~

~~212. The composition of any of the preceding claims, wherein genetic repair is via gene editing therapy.~~

~~213. The composition of any of the preceding claims, wherein genetic repair is via gene editing therapy by using any composition or method of any one of the claims related to CRISPR gene editing therapy.~~

~~214. A method of treating or preventing a disease in a subject affected by a disease caused by a mutated or defective gene or a gene encoding a protein having defective or partial function or activity set forth in Table 4, the method comprising administering a cellular composition of any one of the claims related to an autologous cell composition to the subject, wherein the cellular composition comprises: genetically repaired cells comprising retinal pigment epithelium (RPE) cells, photoreceptors or photoreceptor progenitors (PRCs), corneal epithelial cells (CECs), neurons, choroidal endothelial (CE) cells and/or other ocular cells or other cells derived from a stem cell of the subject, and wherein the mutated or defective gene in the cellular composition has been genetically repaired.~~

~~215. A method of autologously treating a subject, comprising:~~

~~(i) providing cells from a subject having a disease of the eye;~~

~~(ii) inducing pluripotency in the cells from the subject to produce iPSCs;~~

(iii) genetically repairing one or more mutations in a mutated or defective gene set forth in Table 4 in the iPSCs derived from the subject via gene editing therapy;

(iv) differentiating the iPSCs into ocular cells or other cells as needed for replacement transplantation;

(v) alternative to step (iii), genetically repair the iPS-derived cells via gene transfer therapy; and

(vi) introducing the iPS-derived cells into the subject, thereby autologously treating the subject having the disease associated with a mutated or defective gene (the "target gene").

216. The method of claim 214 or 215, wherein the stem cell is an iPC cell, an MSC, an adult stem cell or a tissue-specific stem cell.

217. The method of claim 216, wherein the iPS cell is reprogrammed using one or more of the OCT4, SOX2, KLF4, and c-MYC transcription factors.

218. The method of claim 214 or 215, wherein the genetically repaired cells demonstrate one or more of the following: an increase in non-defective target gene nucleic acid sequence in the cells; an increase in the amount of functional polypeptides encoded by the target gene in the cells; ; improved cell structure, morphology, viability or function, and/or improved or normalized biochemical functions in the cells, as compared to before genetic repair is performed.

219. The method of any of the preceding claims, wherein the amount of cells administered is about 1,000 to about 10 million cells in a single administration.

220. The method of any of the preceding claims, wherein the administration is via injection, sub-retinal injection, or intravitreal injection, .

221. The method of any of the preceding claims, wherein the administration is by any other administration method that effectively delivers the cells to the sub-retinal place, the

posterior segment, or the cornea of the eye of the subject, or the tissue or organ in need of the replacement cells.

222. The method of any of the preceding claims, wherein the cells are administered via injection of cell suspension.

223. The method of any of the preceding claims, wherein the cells are administered as part of a sheet, a matrix, a scaffold, a tissue or a 3D retinal structure.

224. The method of any of the preceding claims, whereas the RPE cells are administered using natural and/or synthetic scaffolds to generate a functional RPE monolayer.

225. The method of any of the preceding claims, wherein the subject is a human subject.

226. The method of any of the preceding claims, wherein the disease is associated with a genetic or epigenetic alteration or risk factor in the subject in a gene set forth in Table 4.

227. The method of any of the preceding claims, wherein the disease is photoreceptor degeneration, retinal pigment epithelium cell degeneration, retinal degeneration, cornea degeneration, and/or choroidal disorders.

228. The method of any of the preceding claims, wherein the disease is an inherited retinal degeneration (IRD).

229. The method of any of the preceding claims, wherein the disease is retinitis pigmentosa (RP).

230. The method of any of the preceding claims, wherein the disease is Bietti Crystalline Dystrophy (also known as Bietti Crystalline Corneoretinal Dystrophy; BCD).

~~231. The method of any of the preceding claims, wherein the disease is related to neurological degeneration.~~

~~232. The method of any of the preceding claims, wherein the disease is corneal dystrophy.~~

~~233. The method of any of the preceding claims, wherein the subject has BCD or is at risk of developing BCD.~~

~~234. The composition of any of the preceding claims, wherein the cells are fibroblasts, blood cells, or ocular cells.~~

~~235. The composition of any of the preceding claims, wherein the cells are obtained from urine or from hair or hair follicles.~~

~~236. The composition of any of the preceding claims, wherein the ocular cells are retinal pigment epithelial (RPE) cells, corneal epithelial cells (CECs), choroidal endothelial (CE) cells, or photoreceptor cells (PRCs).~~

~~237. The composition of any of the preceding claims, wherein the genetic or epigenetic alteration is selected from the group consisting of a mutation, an insertion, a single nucleotide polymorphism, improper methylation, improper demethylation, and combinations thereof.~~

~~238. The composition of any of the preceding claims, wherein the genetic or epigenetic alteration is a mutation.~~

~~239. The composition of any of the preceding claims, wherein the genetic or epigenetic alteration in the iPS-ocular cells from the subject has been genetically repaired using gene editing therapy.~~

~~240. The composition of any of the preceding claims, wherein the gene editing therpay method utilizes a zinc-finger nuclease, TALEN technology, or CRISPR technology.~~

~~241. The composition of any of the preceding claims, wherein the genetic or epigenetic alteration in the iPSC-ocular cells from the subject has been genetically repaired using gene transfer therapy.~~

~~242. The composition of any of the preceding claims, wherein the gene transfer therapy method utilizes a recombinant AAV vector or another viral vector or non-viral vector to deliver a healthy copy of the target gene (e.g., cDNA) to the cells to be transplanted.~~

~~243. The method of any of the preceding claims, wherein the administering step takes place before the onset of disease symptoms or after the onset of disease symptoms.~~

~~244. The method of any of the preceding claims, wherein the administration is to the eye or to another organ or tissue comprising neurons.~~

~~245. The method of any of the preceding claims, wherein the administration is by injection, sub-retinal or intravitreal injection, direct retinal injection, or.~~

~~246. The method of any of the preceding claims, wherein the administration is by any other administration method that effectively delivers the cells to the sub-retinal place, the posterior segment, or the cornea of the eye of the subject, or to the tissue or organ in need of replacement cells.~~

~~247. The method of any of the preceding claims, further comprising, prior to administering or transplanting, performing genotypic analysis on the cells to identify the presence or absence of the genetic or epigenetic alteration in one or more genes set forth in Table 4.~~

~~248. The method of any of the preceding claims, wherein the genetic or epigenetic alteration is a mutation.~~

~~249. The method of any of the preceding claims, wherein the mutation is in the CYP4V2 nucleic acid molecule.~~

~~250. The method of any of the preceding claims, further comprising, prior to administering, evaluating the eye of the subject to identify the area(s) and extent of damaged or retained photoreceptors, retinal cells, or corneal cells.~~

~~251. The method of any of the preceding claims, further comprising, following administering, monitoring the subject.~~

~~252. The method of any of the preceding claims, wherein the monitoring comprises performing non-invasive retinal imaging, corneal tests, dark adaptation, contrast sensitivity, perimetry, ERG, OCT, visual acuity tests, and/or functional studies.~~

~~253. The method of any of the preceding claims, wherein the monitoring comprises evaluating the subject for an immune response.~~

~~254. The method of any of the preceding claims, further comprising, following administering, evaluating the eye of the subject to identify the area(s) and extent of damaged or retained photoreceptors, retinal cells, or corneal cells.~~

~~255. A composition comprising: (a) a CRISPR guide RNA targeting a nucleic acid sequence (the "target sequence") of or within 100 bps to a target gene (the "target gene"), and (b) a functional CRISPR-associated protein, in a ribonucleoprotein (RNP) or protein-RNA complex.~~

~~256. The composition of claims 255, further comprising (c) a donor nucleic acid sequence comprising all or a portion of a wild-type sequence or a functional sequence of the target gene for correction or replacement of such target gene or a portion thereof.~~

~~257. A composition of claim 255 or 256, wherein the target gene is involved in ocular development or function and/or mutation of which causes or is a risk factor to cause an ocular disease.~~

~~258. A composition of claim 255 or 256, wherein the target gene is involved in neuronal development or function and/or mutation of which causes or is a risk factor to cause a neurodegenerative disease.~~

~~259. A composition of claim 255 or 256, wherein the target gene is a cytochrome P450 gene.~~

~~260. The composition of claim 255 or 256, wherein the target gene comprises a gene set forth in Table 4 that is mutated or defective, or encodes a protein having defective or partial function or activity.~~

~~261. The composition of claim 256, wherein the donor nucleic acid sequence is provided in a single-stranded donor oligonucleotide (ssODN) or a vector.~~

~~262. The composition of any one of claims 255-261, wherein (a) the CRISPR guide RNA comprising (i) a CRISPR RNA (crRNA) which comprises a protospacer element sequence that is complementary to the target sequence of or within 100 bps to a target gene and a sequence that corresponds to a complementary region of the trans-activating crRNA (tracrRNA), and (ii) a tracrRNA which comprises a region that is complementary to corresponding region of the crRNA and a sequence which interacts with a CRISPR-associated protein 9 (Cas9), and (b) the functional CRISPR-associated protein comprises Cas9.~~

~~263. The composition of claim 261 or 262, wherein the crRNA and the tracrRNA are in different nucleic acid molecules.~~

~~264. The composition of claim 261 or 262, wherein the crRNA and the tracrRNA are combined in a single guide RNA (sgRNA).~~

~~265. The composition of any one of claims 261-264, wherein the Cas9 comprises a Cas9 ortholog or a mutant Cas9 selected from: Streptococcus pyogenes (SpCas9), SpCas9 nickase (Cas9n D10A), SpCas9 (D1135E), eSpCas9, SpCas9-HF1, SpCas9 VRER, SpCas9 VQR, SpCas9EQR, Staphylococcus aureus (SaCas9), Neisseria Meningitidis, Streptococcus thermophilus, Streptococcus pneumnoniae, Campylobacter coli, Campylobacter jejuni, Streptococcus mutans, Pasteurella multocida, Bifidobacterium longum, Bacillus smithii, Treponema denticola, mycoplasma canis and enterococcus faecalis.~~

~~266. The composition of any one of claims 255-265, wherein (a) the CRISPR guide RNA comprises a crRNA which comprises a protospacer element sequence that is complementary to the target sequence of or within 100 bps to a target gene, and (b) the functional CRISPR-associated protein comprises Cpf1.~~

~~267. The composition of any one of claims 255-266, wherein the CRISPR-associated protein, Cas9, or Cpf1, further comprises one, two, three or more nuclear localization sequences (NLS) at the N-terminal and/or C-terminal, and/or a selection marker, including without limitation, GFP or EGFP.~~

~~268. The composition of any one of claims 255-267, wherein the protospacer element is 100% complementary to the target sequence or contains 1, 2, 3, 4, or 5 nucleotide mismatches corresponding to the target sequence.~~

~~269. The composition of claim 255 or 256, wherein the crRNA sequence further comprises a G nucleotide optionally added to the crRNA sequence immediately before the protospacer element.~~

~~270. The composition of any one of claims 255-269, wherein the CRISPR guide RNA, crRNA and/or the tracrRNA, or the sgRNA, is chemically modified.~~

~~271. The composition of any one of claims 255-270, wherein the wild-type version of the target gene encodes an enzyme.~~

~~272. The composition of claim 255 or 256, wherein the target gene comprises a mutated or defective CYP4V2, CYP1B1, MYO7A, DFNB31, USH1C, USH1G, CDH23, PCDH15, CLRN1, ACO2, AFG3L2, ATXN2, AUH, C12orf65, CISD2, FOXC1, FOXF2, LTBP2, MTPAP, MYOC, NDUFS1, NR2F1, OPA1, OPA3, OPTN, PAX6, PDGF, PITX2, POLG, SPG7, TEK, TXNRD2, WFS1, ABCA4, REP-1, RPE65, CEP290, PDE6B, RPGR, MERTK, MT-ND4, FAM47E, GBA, GCH1, HTRA2, LRRK2, PARK2, PINK1, SNCA, SYNJ1, NPC1, NPC2, CYP4A11, CYP4A22, CYP4B1, CYP4F2, CYP4F3, CYP4F8, CYP4F11, CYP4F12, CYP4F22, CYP4X1, CYP4Z1, or CYP46A gene or a CYP4V2, CYP1B1, MYO7A, DFNB31, USH1C, USH1G, CDH23, PCDH15, CLRN1, ACO2, AFG3L2, ATXN2, AUH, C12orf65, CISD2, FOXC1, FOXF2, LTBP2, MTPAP, MYOC, NDUFS1, NR2F1, OPA1, OPA3, OPTN, PAX6, PDGF, PITX2, POLG, SPG7, TEK, TXNRD2, WFS1, ABCA4, REP-1, RPE65, CEP290, PDE6B, RPGR, MERTK, MT-ND4, FAM47E, GBA, GCH1, HTRA2, LRRK2, PARK2, PINK1, SNCA, SYNJ1, NPC1, NPC2, CYP4A11, CYP4A22, CYP4B1, CYP4F2, CYP4F3, CYP4F8, CYP4F11, CYP4F12, CYP4F22, CYP4X1, CYP4Z1 or CYP46A gene that encodes a protein having defective or partial function or activity.~~

~~273. The composition of any one of claims 255-272, wherein any one or more components thereof including the CRISPR guide RNA, CRISPR-associated protein, and/or the donor nucleic acid sequence, is provided separately and/or additionally in a vector, a DNA and/or an mRNA which can transcribe and/or translate into such component.~~

~~274. A pharmaceutically acceptable formulation comprising the composition of claim 255 or 273.~~

~~275. A method of treating a disease of a subject caused by a mutated or defective gene, or a gene encoding a protein having defective or partial function or activity, comprising administering to the subject a composition of any one of claims 255-274.~~

~~276. A method of treating an ocular disease or ameliorating a risk factor related thereto of a subject caused by a mutated or defective gene, or a gene encoding a protein having defective or partial function or activity, comprising administering to the subject a composition of any one of claims 255-157.~~

~~277. A method of treating a neurodegenerative disease or ameliorating a risk factor related thereto of a subject caused by a mutated or defective gene, or a gene encoding a protein having defective or partial function or activity, comprising administering to the subject a composition of any one of claims 255, 256, or 258-276.~~

~~278. A method of treating a disease or ameliorating a risk factor related thereto of a subject caused by a mutated or defective cytochrome P450 gene, or a cytochrome P450 gene encoding a protein having defective or partial function or activity, comprising administering to the subject a composition of any one of claims 255-277.~~

~~279. The method of claim 278, wherein the mutated or defective gene, or gene encoding a protein having defective or partial function or activity, disrupted, corrected or replaced is a mutated or defective version of a gene set forth in Table 4, or a version of a gene set forth in Table 4 that encodes a protein having defective or partial function or activity.~~

~~280. The method of claim 278, wherein the mutated or defective gene, or gene encoding a protein having defective or partial function or activity, is present in fibroblasts, blood, RPE,~~

photoreceptor, retinal, corneal, choroidal, ocular, optic nerve, neuron, or stem cells, or any type of cells derived from a stem cell.

281. The method of claim 278 or 279, wherein the composition therein is delivered to fibroblasts, blood, RPE, photoreceptor, retinal, corneal, choroidal, ocular, optic nerve, neuron, or stem cells, or any type of cells derived from a stem cell.

282. The method of claim 281, wherein delivery is performed by electroporation or via lipid-mediated transfection, or nucleofection, or viral transduction, or injection or a combination thereof.

283. The method of any one of claims 278-282, wherein any one or more components thereof including the CRISPR guide RNA, CRISPR-associated protein, and/or the donor nucleic acid sequence is administered to the subject or to the cells via a delivery system selected from the group consisting of a ribonucleoprotein or protein-RNA complex, a nanoparticle, a liposome, a micelle, a virosome, a nucleic acid complex, and/or a combination thereof.

284. The method of any one of claims 278-283, wherein the treatment is performed to a subject *in vivo*.

285. The method of any one of claims 278-283, wherein the treatment is performed *in vitro* in fibroblasts, blood, RPE, photoreceptor, retinal, corneal, choroidal, ocular, optic nerve, neuron, or stem cells, or any type of cells derived from a stem cell.

286. The method of claim 285, wherein the treated cells are transplanted to a subject *in vivo*, or if the treated cell is a stem cell, such stem cell is differentiated into the desired type of cells for transplantation and then the differentiated cells are transplanted into a subject *in vivo*. .

287. The method of any one of claims 278-280, wherein the mutated or defective gene, or gene encoding a protein having defective or partial function or activity, is replaced.

~~288. The method any one of claims 278-280, wherein the mutated or defective gene, or gene encoding a protein having defective or partial function or activity, has one or more mutations corrected or replaced.~~

~~289. The method of any one of claims 278-280, wherein the mutated or defective gene, or gene encoding a protein having defective or partial function or activity, is disrupted.~~

~~290. The method of any one of claims 278-280, wherein the mutated or defective gene, or gene encoding a protein having defective or partial function or activity, has 1-20, 21-40, 41-60, 61-80, 81-100, 101-1000, 1001-10000 base pairs of nucleotides or mutations disrupted, corrected or replaced.~~

~~291. The method of any one of claims 278-280, wherein a region of the mutated or defective gene, or gene encoding a protein having defective or partial function or activity, is disrupted, corrected or replaced.~~

~~292. The method of any one of claims 278-280, wherein a region of less than about 10, 8, 6, 4, 2 or 1 kb of the mutated or defective gene, or gene encoding a protein having defective or partial function or activity, is disrupted, corrected or replaced.~~

~~293. The method of any one of claims 278-280, wherein the mutated or defective gene, or gene encoding a protein having defective or partial function or activity, is disrupted, corrected or replaced via insertion and/or deletion of nucleotides.~~

~~294. The method of any one of claims 278-280, wherein the mutated or defective gene, or gene encoding a protein having defective or partial function or activity, is disrupted, corrected or replaced in one allele or both alleles.~~

295. The method of any one of claims 278-280, wherein two or more different CRISPR guide RNAs, CRISPR-associated proteins and/or donor nucleic acid sequences are used to disrupt, correct or replace one or more mutations or defects in the mutated or defective gene, or gene encoding a protein having defective or partial function.

296. The method of claim 278, wherein the subject is a mammal.

297. The method of claim 278, wherein the subject is a human.

298. The method of claim 278, wherein the method improves ocular development or function, or prevents ocular, retinal or corneal degeneration.

299. The method of claim 278, wherein the method improves neurological development or function, or prevents neural degeneration.

300. The method of claim 278, wherein the method improves expression or function of a P450 enzyme.

301. The composition of any one of claims 255, 257, 258 or 259, further comprising (c) a donor nucleic acid sequence comprising all or a portion of a target gene set forth in Table 4 with a mutation or alteration for generation of a mutated or altered target gene or a portion thereof.

302. A composition comprising a cell with a mutated or defective gene set forth in Table 4.

303. A composition comprising a cell with a mutated or defective CYP4V2, CYP1B1, MYO7A, DFNB31, USH1C, USH1G, CDH23, PCDH15, CLRN1, ACO2, AFG3L2, ATXN2, AUH, C12orf65, CISD2, FOXC1, FOXF2, LTBP2, MTPAP, MYOC, NDUFS1, NR2F1, OPA1, OPA3, OPTN, PAX6, PDGF, PITX2, POLG, SPG7, TEK, TXNRD2, WFS1, ABCA4, REP-1,

~~RPE65, CEP290, PDE6B, RPGR, MERTK, MT-ND4, FAM47E, GBA, GCH1, HTRA2, LRRK2, PARK2, PINK1, SNCA, SYNJ1, NPC1, NPC2, CYP4A11, CYP4A22, CYP4B1, CYP4F2, CYP4F3, CYP4F8, CYP4F11, CYP4F12, CYP4F22, CYP4X1, CYP4Z1, or CYP46A gene comprising a composition of any one of the claims herein~~

~~304. The composition of claim 303, wherein the vector is an AAV vector.~~

~~305. The composition of any of the preceding claims, wherein the protospacer element sequence is selected from the group consisting of SEQ ID NOs: 48 to 52, or shares at least 80% sequence identity with one of SEQ ID NO: 48 to 52 for use with a Cas protein that has NGG as protospacer adjacent motif (PAM) to target the c.802-8_810del17insGC mutation of the CYP4V2 gene.~~

~~306. The composition of any of the preceding claims, wherein the donor nucleic acid sequence is selected from SEQ ID NOs: 56 and 57, or shares at least 90% sequence identity with one of SEQ ID NO: 56 and 57, or a sequence that is complementary thereof, for use to correct, disrupt or replace the c.802-8_810del17insGC mutation of the CYP4V2 gene.~~

~~307. A method of treating a disease of a subject caused by a mutated or defective gene, or a gene encoding a protein having defective or partial function or activity, comprising administering to the subject a combination of (i) a composition targeting the existing diseased cells in the subject comprising a gene editing therapy composition or a gene transfer therapy composition, and (ii) a cellular composition comprising replacement cells.~~

~~308. The method of claim 307, wherein the subject is a human~~

~~309. The method of claim 307, wherein the disease causes degeneration in the subject's cells.~~

~~310. The method of claim 307 and 308, wherein the degeneration occurs in an RPE cells, a RPC, a CEC, a CE cell, a retinal cell, a corneal cell, a choroid cell, an optic-nerve cell, an ocular cell, a neuron, a neuronal cell, a brain cell, a liver cell, a lung cell and a cardiac cell.~~

~~311. The method of claim 307, wherein the disease is caused by a gene set forth in Table 4.~~

~~312. The method of claim 307, wherein the gene editing therapy composition is a composition of any of the gene editing therapy claims herein.~~

~~313. The method of claim 307, wherein the gene transfer therapy composition is a composition of any of the gene transfer therapy claims herein.~~

~~314. The method of claim 307, wherein the cellular composition comprises a composition of any of the cell therapy claims or the autologous cell therapy claims herein.~~

~~315. The method of claim 307, wherein the cellular composition is allogenic to the subject being treated.~~

~~316. The method of claim 307, wherein the cellular composition is autologous to the subject being treated.~~

~~317. The method of claim 307 or 314, wherein the cellular composition is genetically repaired prior to administration to the subject.~~

~~318. The method of claim 307 or 317, wherein the genetic repair is via gene editing therapy.~~

~~319. The method of claim 307 or 318, wherein the gene editing therapy is via any of the claims in the gene editing therapy claims herein.~~

~~320. The method of claim 307, 318 or 319, wherein the gene editing therapy is via any of the CRISPR RNP claims herein.~~

~~321. The method of claim 307 or 317, wherein the genetic repair is via gene transfer therapy.~~

~~322. The method of claim 307 or 321, wherein the gene transfer therapy is via any of gene transfer therapy or gene therapy claims herein.~~

~~323. The method of claim 307, wherein the compositions of (i) and (ii) are administered in a single administration.~~

~~324. The method of claim 307, wherein the compositions of (i) and (ii) are administered separately or in separate administrations.~~

~~325. The method of claim 307, wherein the replacement cells are derived from a stem cell.~~

~~326. The method of claim 307 and 325, wherein the replacement cells are derived from an iPS cell.~~

~~327. The method of claim 307 or 326, wherein the iPS cell is derived from the same subject being treated.~~

~~328. The method of claim 307 or 326, wherein the replacement cell is an iPS-RPE, iPS-PRC, iPS-CEC or iPS-CE cell.~~

~~329. The method of claim 307 or 326, wherein the replacement cell is an iPS-ocular cell.~~

~~330. The method of claim 307 or 326, wherein the replacement cell is an iPS-neuron cell.~~

~~331. The method of claim 307, wherein the method improves ocular development or function, or prevents ocular, retinal or corneal degeneration in the subject.~~

~~332. The method of claim 307, wherein the method improves neurological development or function, or prevents neural degeneration in the subject.~~

~~333. The method of claim 307, wherein the method improves expression or function of a P450 enzyme in the subject.~~

~~334. The method of any of claims 307-332, wherein the subject has suffered from ocular, retinal, corneal, choroidal or neuronal degenerations.~~

1. A vector comprising a nucleic acid molecule comprising a sequence encoding a non-mutant or functional CYP4V2 protein or a functional variant thereof having at least 96% sequence identity with any of SEQ ID NOs: 4-6 and 19-29 operably linked to at least one regulatory sequence, wherein the vector is a recombinant adeno-associated virus (rAAV) vector.

2. The vector of claim 1, wherein the rAAV vector comprises a VP1, VP2, or VP3 capsid protein selected from any serotype of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, or another naturally derived serotype or isolate or clade of AAV, or hybrids, variants or derivatives thereof, or

wherein the rAAV vector comprises a 5′ AAV inverted terminal repeat (ITR) or a 3′ AAV ITR selected from any one of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, or another naturally derived serotype or isolate or clade of AAV, or mutations, chimeras, variants or fusions thereof.

3. The vector of claim 1 or 2, wherein the rAAV vector is a chimeric AAV, a shuffled AAV, or a capsid-modified AAV, or

wherein the rAAV vector is a pseudotyped AAV, or

wherein the rAAV vector is a hybrid AAV.

4. The vector of any one of claims 1-3, wherein the rAAV vector comprises one or more mutations to one or more naturally derived AAV capsid proteins,

optionally wherein the one or more mutations to the AAV capsid protein comprise one or more amino acid residue Y-F, K-R, T-A, S-A or T-V substitutions.

5. The vector of any one of claims 1-4, wherein the rAAV vector is selected from the group consisting of AAV2/5, AAV2/8, AAV2/2, AAV2 (Y444F+Y500F+Y730F), AAV2/1, AAV2/9, AAV2/8(Y733F), AAV2/6, AAV2/4, AAV2/7, AAV5, AAV2, AAV8, AAV1, AAV9, AAV6, AAV10, AAV3, AAV4, AAV7, AAV11, AAV12, Anc80, AAV 7m8, AAV-DJ, ShH10, AAV-PHP.B, rh10, and a hybrid, a derivative or variant thereof, or

wherein the rAAV vector is a single-stranded AAV vector or a self-complementary AAV (scAAV) vector.

6. The vector of any one of claims 1-5, wherein the nucleic acid molecule has at least 76% sequence identity with any of SEQ ID NOs: 1 – 3.

7. The vector of any one of claims 1-6, wherein the regulatory sequence comprises a promoter,

optionally wherein the promoter is a retinal pigment epithelium (RPE) cell-specific promoter, a photoreceptor-specific promoter, a retinal cell-specific promoter, a corneal cell-specific promoter, an ocular cell-specific promoter, a cell-specific promoter, a tissue-specific promoter, a constitutive promoter, a ubiquitous promoter, a regulated promoter, an inducible promoter, or a derivative or hybrid thereof, or

optionally wherein the promoter is selected from the group consisting of a CAG promoter (also known as CAGGS promoter, CB promoter or CBA promoter), a chicken beta actin

promoter, a small CBA (smCBA) promoter, a CB^{SB} promoter, a CBh promoter, a beta-actin promoter, a human beta actin promoter, an elongation factor 1 alpha short (EFS) promoter, an elongation factor 1 alpha (EF-1 alpha or EF-1α) promoter, a cytomegalovirus (CMV) promoter, a PGK promoter, a UBC promoter, a GUSB promoter, a UCOE promoter, a VMD2 (vitelliform macular dystrophy 2; also known as BEST1) promoter, an RPE65 promoter, a GRK1 promoter, a human interphotoreceptor retinoid-binding protein proximal (IRBP) promoter, a 235 nt fragment of the hIRBP promoter, an RPGR proximal promoter, the red opsin promoter, a red-green opsin promoter, the blue opsin promoter, the mouse opsin promoter, a rhodopsin (Rho) promoter, a beta phosphodiesterase (PDE) promoter, a retinitis pigmentosa (RP1) promoter, the NXNL2/NXNL1 promoter, a retinal degeneration slow/peripherin 2 (Rds/perphZ) promoter, a IRBP/GNAT2 promoter (hIRBP enhancer fused to cone transducin alpha promoter), an Rds (retinal degeneration slow) promoter, an hPDE6b promoter, a VEcad promoter (VE-cadherin/Cadherin 5 (CDH5)/CD144 promoter), a calcium-sensitive promoter, an NFAT promoter, a zinc-inducible sheep metalioihionine (MX) promoter, a dexamethasone (Dex)-inducible mouse mammary tumor virus (MMTV) promoter, a T7 polymerase promoter system, an ecdysone insect promoter, a tetracycline-repressible system, a tetracycline-inducible system, an RU486-inducible system, and a rapamycin-inducible system, a hybrid, a variant and a derivative thereof.

8. The vector of any one of claims 1-7, wherein the regulatory sequence comprises a Kozak sequence, or

wherein the regulatory sequence comprises an enhancer,

optionally wherein the enhancer comprises a post-transcriptional regulatory element (PRE), an internal ribosome entry site (IRES), an intron regulatory sequence, a mini-intron splice donor/splice acceptor (SD-SA), or a constitutive transport element (CTE), or

optionally wherein the enhancer is selected from the group consisting of a woodchuck hepatitis virus post-transcriptional regulatory element (WPRE) enhancer, an Hepatitis B Virus post-transcriptional regulatory element (HPRE or HBVPRE) enhancer, an IRBP enhancer, a Mason-Pfizer Monkey Virus CTE enhancer, an Avian Leukemia Virus CTE enhancer, a cytomegalovirus (CMV) immediate early enhancer, and an SV40 enhancer.

9. The vector of any one of claims 1-8, wherein the regulatory sequence comprises a polyadenylation (polyA) signal,

optionally wherein the polyA signal is selected from the group consisting of a bovine growth hormone polyadenylation signal (bGH polyA), a small polyA signal (SPA), a human growth hormone polyadenylation signal (hGH polyA), an SV40 polyA signal, an SV40 early polyA signal, an SV40 late polyA signal, a derivative and a hybrid thereof.

10. The vector of any one of claims 1-9, wherein the regulatory sequence comprises an upstream enhancer (USE) operably linked to a polyA signal,

optionally wherein the USE is selected from the group consisting of SV40 late 2xUSE, HIV-1 (Human immunodeficiency virus 1) USE, GHV (Ground squirrel hepatitis virus) USE, Adenovirus (L3) USE, hTHGB (Human prothrombin) USE, and an hC2 (Human C2 complement gene) USE.

11. The vector of any one of claims 1-10, where in the regulatory sequence comprises an intron sequence, a UTR sequence, a splice site sequence, an upstream regulatory domain sequence, a response element sequence, an inducible element sequence, an origin of replication sequence, an internal ribosome entry sites (IRES) sequence, a transcription initiation sequence, a termination sequence, an RNA processing sequence, a junction sequence, or a linker sequence, or

wherein the regulatory sequence is heterologous or homologous relative to the CYP4V2 coding sequence whose expression said regulatory sequence regulates, or

wherein the regulatory sequence comprises a tissue-specific or cell-specific microRNA (miRNA) target sequence.

12. The vector of any one of claims 1-11, wherein any part of the vector shares at least 43% sequence identity with any of the CYP4V2 expression cassette sequences in SEQ ID NOs: 60 to 64 or at least 43% sequence identity with any of the following sequences: nucleotide (nt) 237 –

nt 3579 of SEQ ID NO 60; nt 166 – nt 3515 of SEQ ID NO 61; nt 166 – nt 3515 of SEQ ID NO 62; nt 166 – nt 3515 of SEQ ID NO 63; or nt 130 – nt 2097 of SEQ ID NO 64.

13. The vector of any one of claims 1-12, wherein the vector is formulated with a pharmaceutically acceptable carrier and additional components suitable for a specific route of administration.

14. A cell comprising the vector of any one of claims 1-13,
optionally wherein the cell is a mammalian cell or an insect cell,
optionally wherein the cell is an HEK293 cell,
optionally wherein the cell is a retinal pigment epithelial (RPE) cell, a photoreceptor cell, a photoreceptor progenitor cell, a choroidal cell, a retinal cell, an induced pluripotent stem (iPS) cell, or a stem cell, of or derived from a human subject suffering from Bietti's Crystalline Dystrophy (BCD, a/k/a Bietti Crystalline Corneoretinal Dystrophy, Bietti Crystalline Retinopathy, Bietti's Retinal Dystrophy), or retinitis pigmentosa (RP) or inherited retinal degeneration (IRD) with CYP4V2 mutations.

15. Use of the cell of claim 14 in the manufacture of a medicament for treating, arresting or preventing Bietti's Crystalline Dystrophy (BCD, a/k/a Bietti Crystalline Corneoretinal Dystrophy, Bietti Crystalline Retinopathy, Bietti's Retinal Dystrophy), or retinitis pigmentosa (RP) or inherited retinal degeneration (IRD) with CYP4V2 mutations in a human subject in need thereof, wherein a therapeutically effective amount of the cell is to be delivered to the human subject's eye.

16. Use of the vector of any one of claims 1-13 in the manufacture of a medicament for treating, arresting or slowing progression of, rescuing or ameliorating the dysfunction, function loss, dystrophy, disorder, degeneration, atrophy or preventing the death of an ocular cell of a human subject who has Bietti's Crystalline Dystrophy (BCD, a/k/a Bietti Crystalline Corneoretinal Dystrophy, Bietti Crystalline Retinopathy, Bietti's Retinal Dystrophy), or retinitis

pigmentosa (RP) or inherited retinal degeneration (IRD) with CYP4V2 mutations, wherein a therapeutically effective amount of the vector is to be delivered to the ocular cell,

optionally wherein the ocular cell is a retina cell, a retinal pigment epithelial (RPE) cell, a photoreceptor cell (rod or cone), a choroidal epithelial cell, a corneal epithelium cell, a choroidal cell, a corneal cell, a retina bipolar cell, a photoreceptor progenitor cell, a ganglion cell, or an optic-nerve cell.

17. Use of the vector of any one of claims 1-13 in the manufacture of a medicament for treating, arresting or preventing Bietti's Crystalline Dystrophy (BCD, a/k/a Bietti Crystalline Corneoretinal Dystrophy, Bietti Crystalline Retinopathy, Bietti's Retinal Dystrophy), or retinitis pigmentosa (RP) or inherited retinal degeneration (IRD) with CYP4V2 mutations in a human subject in need thereof, wherein a therapeutically effective amount of the vector is to be delivered to one or more ocular cells of the human subject,

wherein the one or more ocular cells are selected from retinal pigment epithelial (RPE) cells, one or more choroidal cells, and one or more photoreceptor cells of the human subject.

18. Use of the vector of any one of claims 1-13 in the manufacture of a medicament for treating, arresting, or preventing a human subject’s disease which is associated with the atrophy, dystrophy, dysfunction, degeneration or death of an ocular cell, wherein a therapeutically effective amount of the vector is to be delivered to the ocular cell of the human subject,

wherein the ocular cell is an RPE cell.

19. Use of the vector of any one of claims 1-13 in the manufacture of a medicament for treating, arresting or preventing a human subject’s disease which is associated with the atrophy, dystrophy, dysfunction, degeneration or death of an ocular cell, wherein a therapeutically effective amount of RPE cell, photoreceptor progenitor cell or stem cell is to be delivered to the human subject's eye,

wherein said RPE cell, photoreceptor progenitor cell or stem cell comprises the vector.

20. The cell of claim 14 or the vector of any one of claims 1-13, for use in therapy.