We claim:

1. A composition for use in expressing retinoschisin in a cell or for use in integrating a coding sequence for a retinoschisin protein or fragment thereof into a target genomic locus in a cell, comprising:

(a) a nucleic acid construct comprising the coding sequence for the retinoschisin protein or fragment thereof for integration into the target genomic locus; and

(b) a nuclease agent or a nucleic acid encoding the nuclease agent, wherein the nuclease agent targets a nuclease target sequence in the target genomic locus,

wherein the target genomic locus is in an endogenous *RS1* locus,

wherein integration of the nucleic acid construct into the endogenous *RS1* locus prevents transcription of the endogenous *RS1* gene downstream of the integration site,

wherein the integration of the nucleic acid construct into the endogenous *RS1* locus in the cell reduces or eliminates expression of the endogenous retinoschisin protein and replaces it with expression of the retinoschisin protein or fragment thereof encoded by the nucleic acid construct, and

wherein the coding sequence comprises exons 2-6 of human *RS1* or degenerate variants thereof.

2. The composition for use of claim 1, wherein the nucleic acid construct does not comprise a promoter that drives expression of the retinoschisin protein or fragment thereof.

3. The composition for use of claim 1 or 2, wherein:

(I) the nucleic acid construct comprises a fragment or portion of the first intron of human *RS1* located 5’ of the coding sequence; and/or

(II) the nucleic acid construct comprises a polyadenylation signal sequence located 3’ of the coding sequence; and/or

(III) the nucleic acid construct comprises a splice acceptor site located 5’ of the coding sequence, optionally wherein the splice acceptor site is from intron 1 of human *RS1*.

4. The composition for use of any one of claims 1-3, wherein the nucleic acid construct is for homology-independent targeted integration into a target genomic locus, wherein

the nucleic acid construct comprises the coding sequence for a retinoschisin protein or fragment thereof flanked on each side by a nuclease target sequence for a nuclease agent.

5. The composition for use of claim 4, wherein the nuclease target sequence in the target genomic locus is identical to the nuclease target sequence in the nucleic acid construct, and wherein the nuclease target sequence in the target genomic locus is destroyed if the nucleic acid construct is inserted in the correct orientation but is reformed if the nucleic acid construct is inserted into the target genomic locus in the opposite orientation.

6. The composition for use of claim 4 or 5, wherein the coding sequence for the retinoschisin protein or fragment thereof comprises complementary DNA (cDNA) comprising exons 2-6 of human *RS1* or degenerate variants thereof,

wherein the nucleic acid construct does not comprise a promoter that drives expression of the retinoschisin protein or fragment thereof,

wherein the nucleic acid construct comprises a polyadenylation signal sequence located 3' of the coding sequence,

wherein the nucleic acid construct comprises a splice acceptor site located 5' of the coding sequence, and

wherein the nuclease target sequence in the nucleic acid construct is identical to a nuclease target sequence for integration into the target genomic locus, wherein the nuclease target sequence in the target genomic locus is destroyed if the nucleic acid construct is inserted in the correct orientation but is reformed if the nucleic acid construct is inserted into the target genomic locus in the opposite orientation.

7. The composition for use of any one of claims 1-3, wherein the nucleic acid construct is for homologous recombination with a target genomic locus, wherein the nucleic acid construct comprises the coding sequence for a retinoschisin protein or fragment thereof flanked by homology arms on each side, optionally wherein the coding sequence and homology arms are further flanked on each side by a nuclease target sequence for a nuclease agent, and optionally wherein each homology arm is between about 25 nucleotides and about 2.5 kb in length.

8. The composition for use of claim 7, wherein the retinoschisin protein or fragment thereof is a human retinoschisin protein or fragment thereof,

wherein the coding sequence for the retinoschisin protein or fragment thereof comprises complementary DNA (cDNA) comprising exons 2-6 of human *RS1* or degenerate variants thereof,

wherein the nucleic acid construct does not comprise a promoter that drives expression of the retinoschisin protein or fragment thereof,

wherein the nucleic acid construct comprises a polyadenylation signal sequence located 3' of the coding sequence,

wherein the nucleic acid construct comprises a splice acceptor site located 5' of the coding sequence, and

wherein each homology arm is between about 25 nucleotides and about 2.5 kb in length.

9. The composition for use of any one of claims 1-3, wherein the nucleic acid construct is bidirectional and comprises:

(a) a first segment comprising a first coding sequence for a first retinoschisin protein or fragment thereof; and

(b) a second segment comprising a reverse complement of a second coding sequence for a second retinoschisin protein or fragment thereof.

10. The composition for use of claim 9, wherein the nucleic acid construct does not comprise a homology arm.

11. The composition for use of claim 9 or 10, wherein the first retinoschisin protein or fragment thereof is identical to the second retinoschisin protein or fragment thereof, and wherein the second coding sequence adopts a different codon usage from the codon usage of the first coding sequence.

12. The composition for use of any one of claims 9-11, wherein the second segment is located 3' of the first segment,

wherein both the first retinoschisin protein or fragment thereof and the second retinoschisin protein or fragment thereof are a human retinoschisin protein or fragment thereof,

wherein the first retinoschisin protein or fragment thereof is identical to the second retinoschisin protein or fragment thereof,

wherein both the first coding sequence and the second coding sequence comprise complementary DNA (cDNA) comprising exons 2-6 of human *RS1* or degenerate variants thereof,

wherein the second coding sequence adopts a different codon usage from the codon usage of the first coding sequence,

wherein the first segment comprises a first polyadenylation signal sequence located 3' of the first coding sequence, and the second segment comprises a reverse complement of a second polyadenylation signal sequence located 5' of the reverse complement of the second coding sequence,

wherein the first segment comprises a first splice acceptor site located 5' of the first coding sequence, and the second segment comprises a reverse complement of a second splice acceptor site located 3' of the reverse complement of the second coding sequence,

wherein the nucleic acid construct does not comprise a promoter that drives expression of the first retinoschisin protein or fragment thereof or the second retinoschisin protein or fragment thereof, and

wherein the nucleic acid construct does not comprise a homology arm.

13. The composition for use of any one of claims 1-12, wherein the nuclease target sequence in the target genomic locus is in the first intron in the *RS1* gene at the endogenous *RS1* locus.

14. The composition for use of any one of claims 1-13, wherein the nucleic acid construct is in a viral vector, optionally wherein the viral vector is an adeno-associated virus (AAV) viral vector, and optionally wherein the AAV is selected from the group consisting of: AAV2, AAV5, AAV8, or AAV7m8.

15. The composition for use of any one of claims 1-14, wherein the nuclease agent is a Cas protein and a guide RNA, and the nuclease target sequence is a guide RNA target sequence.

16. The composition for use of claim 15, wherein the Cas protein is a Cas9 protein.

17. The composition for use of claim 15 or 16, wherein:

(I) the composition comprises the nucleic acid encoding the Cas protein, wherein the nucleic acid comprises a DNA encoding the Cas protein, and wherein the composition comprises the DNA encoding the guide RNA, and optionally wherein the DNA encoding the Cas protein and the DNA encoding the guide RNA are in one or more viral vectors; or

(II) the composition comprises the nucleic acid encoding the Cas protein, wherein the nucleic acid comprises a messenger RNA encoding the Cas protein, wherein the composition comprises the guide RNA in the form of RNA, and optionally wherein the composition comprises the guide RNA in the form of RNA, and wherein the guide RNA and the messenger RNA encoding the Cas protein are in a lipid nanoparticle.

18. The composition for use of any one of claims 1-17, wherein the endogenous *RS1* locus comprises a mutated *RS1* gene comprising a mutation that causes X-linked juvenile retinoschisis.

19. The composition for use of any one of claims 1-18, wherein the cell is a human cell, optionally wherein the cell is a retinal cell.

20. The composition for use of any one of claims 1-19, wherein the cell is *in vivo* in an animal.

21. The composition for use of claim 20, wherein integration of the nucleic acid construct results in retinal structural restoration.