We claim:

1. A non-human animal comprising in its genome a humanized endogenous *MYOC* locus in which a region of the endogenous *MYOC* locus has been deleted and replaced with a corresponding human *MYOC* sequence,

optionally wherein the region of the endogenous *MYOC* locus comprises both a *MYOC* exonic sequence and a *MYOC* intronic sequence and the corresponding human *MYOC* sequence comprises both a *MYOC* exonic sequence and a *MYOC* intronic sequence,

wherein the non-human animal further comprises in its genome a genomically integrated expression cassette, wherein the genomically integrated expression cassette comprises:

(a) a nucleic acid encoding a chimeric Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) associated (Cas) protein comprising a nuclease-inactive Cas protein fused to one or more transcriptional activation domains; and

(b) a nucleic acid encoding a chimeric adaptor protein comprising an adaptor protein fused to one or more transcriptional activation domains, and

wherein the non-human animal further comprises one or more guide RNAs that were administered or one or more expression cassettes that encode the one or more guide RNAs, each guide RNA comprising one or more adaptor-binding elements to which the chimeric adaptor protein can specifically bind,

wherein each of the one or more guide RNAs is capable of forming a complex with the Cas protein and guiding it to a target sequence within a target gene, and

wherein at least one of the one or more guide RNAs targets the humanized endogenous MYOC locus, and

optionally wherein the one or more guide RNAs or one or more expression cassettes that encode the one or more guide RNAs are in the trabecular meshwork.

2. The non-human animal of claim 1, wherein the humanized endogenous *MYOC* locus comprises a mutation associated with glaucoma,

optionally wherein the human *MYOC* sequence comprises the mutation.

3. The non-human animal of any preceding claim, wherein the humanized endogenous *MYOC* locus comprises a Y437H mutation, and

wherein the human *MYOC* sequence comprises the Y437H mutation.

4. The non-human animal of any preceding claim, wherein the humanized endogenous *MYOC* locus comprises an endogenous *MYOC* promoter, wherein the human *MYOC* sequence is operably linked to the endogenous *MYOC* promoter, and/or

wherein at least one intron and at least one exon of the endogenous *MYOC* locus have been deleted and replaced with the corresponding human *MYOC* sequence, and/or

wherein the humanized endogenous *MYOC* locus comprises a human *MYOC* 3' untranslated region, and/or

wherein the endogenous *MYOC* 5' untranslated region has not been deleted and replaced with the corresponding human *MYOC* sequence.

5. The non-human animal of any preceding claim, wherein the humanized endogenous *MYOC* locus encodes a human myocilin protein,

optionally wherein the human myocilin protein sequence comprises the sequence set forth in SEQ ID NO: 4, and optionally wherein the human myocilin protein sequence is encoded by a coding sequence comprising the sequence set forth in SEQ ID NO: 5.

6. The non-human animal of any preceding claim, wherein the entire *MYOC* coding sequence of the endogenous *MYOC* locus has been deleted and replaced with the corresponding human *MYOC* sequence, and

wherein a region of the endogenous *MYOC* locus from the *MYOC* start codon to the *MYOC* stop codon has been deleted and replaced with the corresponding human *MYOC* sequence.

7. The non-human animal of any preceding claim, wherein a region of the endogenous *MYOC* locus from the *MYOC* start codon to the *MYOC* stop codon has been deleted and replaced with a human *MYOC* sequence comprising the corresponding human *MYOC* sequence and a human *MYOC* 3' untranslated region,

wherein the human *MYOC* sequence comprises a Y437H mutation,

wherein the endogenous *MYOC* 5' untranslated region has not been deleted and replaced with the human *MYOC* sequence, and

wherein the humanized endogenous *MYOC* locus comprises an endogenous *MYOC* promoter, wherein the human *MYOC* sequence is operably linked to the endogenous *MYOC* promoter.

8. The non-human animal of any preceding claim, wherein:

(i) the human *MYOC* sequence at the humanized endogenous *MYOC* locus comprises a sequence at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the sequence set forth in SEQ ID NO: 87; and/or

(ii) the humanized endogenous *MYOC* locus encodes a myocilin protein comprising a sequence at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the sequence set forth in SEQ ID NO: 4; and/or

(iii) the humanized endogenous *MYOC* locus comprises a myocilin coding sequence comprising a sequence at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the sequence set forth in SEQ ID NO: 5; and/or

(iv) the humanized endogenous *MYOC* locus comprises a sequence at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the sequence set forth in SEQ ID NO: 88 or 89.

9. The non-human animal of any preceding claim, wherein the humanized endogenous *MYOC* locus does not comprise a selection cassette or a reporter gene.

10. The non-human animal of any preceding claim, wherein the non-human animal is homozygous for the humanized endogenous *MYOC* locus.

11. The non-human animal of any preceding claim, wherein the non-human animal comprises the humanized endogenous *MYOC* locus in its germline.

12. The non-human animal of any preceding claim, wherein the non-human animal is a mammal.

13. The non-human animal of claim 12, wherein the non-human animal is a rat or a mouse.

14. The non-human animal of claim 13, wherein the non-human animal is the mouse.

15. The non-human animal of any preceding claim, further comprising a second genomically integrated expression cassette that encodes one or more guide RNAs each comprising one or more adaptor-binding elements to which the chimeric adaptor protein can specifically bind,

wherein each of the one or more guide RNAs is capable of forming a complex with the Cas protein and guiding it to a target sequence within a target gene, and

wherein at least one of the one or more guide RNAs targets the humanized endogenous *MYOC* locus.

16. The non-human animal of any preceding claim, wherein the first expression cassette is integrated into a *Rosa26* locus,

the Cas protein is a Cas9 protein comprising mutations corresponding to D10A and N863A when optimally aligned with a *Streptococcus pyogenes* Cas9 protein,

the one or more transcriptional activator domains in the chimeric Cas protein comprise VP64,

the adaptor protein comprises an MS2 coat protein or a functional fragment or variant thereof,

the one or more transcriptional activation domains in the chimeric adaptor protein comprise p65 and HSF1,

the non-human animal further comprises one or more guide RNAs that were administered or one or more expression cassettes that encode the one or more guide RNAs,

the one or more guide RNAs or one or more expression cassettes that encode the one or more guide RNAs are in the trabecular meshwork,

each of the one or more guide RNAs comprises two adaptor-binding elements to which the chimeric adaptor protein can specifically bind,

the two adaptor-binding elements comprise a first adaptor-binding element within a first loop of each of the one or more guide RNAs and a second adaptor-binding element within a second loop of each of the one or more guide RNAs, and

the target sequence is within a region 200 base pairs upstream of the transcription start site and 1 base pair downstream of the transcription start site.

17. The non-human animal of any preceding claim, wherein the non-human animal is a mouse, and wherein the one or more guide RNAs target one or more guide RNA target sequences selected from SEQ ID NOS: 90-95, and

optionally wherein the non-human animal is a mouse, and wherein the one or more guide RNAs target one or more guide RNA target sequences selected from SEQ ID NOS: 93-94.

18. The non-human animal of any preceding claim, wherein the non-human animal is a mouse, and wherein the one or more guide RNAs target the guide RNA target sequence set forth in SEQ ID NO: 93.

19. The non-human animal of any preceding claim, wherein the non-human animal has at least 2-fold, at least 3-fold, at least 4-fold, at least 5-fold, at least 6-fold, at least 7-fold, at least 8-fold, at least 9-fold, at least 10-fold, at least 11-fold, at least 12-fold, at least 13-fold, at least 14-fold, or at least 15-fold increased *MYOC* mRNA or protein expression in the eye, the limbal ring, the retina, the ciliary body, or the trabecular meshwork relative to a control non-human animal that does not comprise the one or more guide RNAs or the one or more expression cassettes that encode the one or more guide RNAs.

20. The non-human animal of any preceding claim, wherein the non-human animal has increased intraocular pressure relative to a wild type non-human animal or a control non-human animal,

optionally wherein the non-human animal has an intraocular pressure of at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, or at least 22 mmHg, and/or

optionally wherein the non-human animal has an intraocular pressure that is at least 1, at least 2, at least 3, at least 4, at least 5, or at least 6 mmHg higher than the intraocular pressure of the control non-human animal.

21. A non-human animal cell comprising in its genome a humanized endogenous *MYOC* locus in which a region of the endogenous *MYOC* locus has been deleted and replaced with a corresponding human *MYOC* sequence,

optionally wherein the region of the endogenous *MYOC* locus comprises both a *MYOC* exonic sequence and a *MYOC* intronic sequence and the corresponding human *MYOC* sequence comprises both a *MYOC* exonic sequence and a *MYOC* intronic sequence,

wherein the non-human animal cell further comprises in its genome a genomically integrated expression cassette, wherein the genomically integrated expression cassette comprises:

(a) a nucleic acid encoding a chimeric Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) associated (Cas) protein comprising a nuclease-inactive Cas protein fused to one or more transcriptional activation domains; and

(b) a nucleic acid encoding a chimeric adaptor protein comprising an adaptor protein fused to one or more transcriptional activation domains,

wherein the non-human animal cell further comprises one or more guide RNAs that were administered or one or more expression cassettes that encode the one or more guide RNAs, each guide RNA comprising one or more adaptor-binding elements to which the chimeric adaptor protein can specifically bind,

wherein each of the one or more guide RNAs is capable of forming a complex with the Cas protein and guiding it to a target sequence within a target gene, and

wherein at least one of the one or more guide RNAs targets the humanized endogenous *MYOC* locus.

22. The non-human animal cell of claim 21, wherein the humanized endogenous *MYOC* locus comprises a mutation associated with glaucoma,

optionally wherein the human *MYOC* sequence comprises the mutation.

23. The non-human animal cell of claim 21 or 22, wherein the humanized endogenous *MYOC* locus comprises a Y437H mutation, and

wherein the human *MYOC* sequence comprises the Y437H mutation.

24. The non-human animal cell of any one of claims 21-23, wherein the humanized endogenous *MYOC* locus comprises an endogenous *MYOC* promoter, wherein the human *MYOC* sequence is operably linked to the endogenous *MYOC* promoter, and/or

wherein at least one intron and at least one exon of the endogenous *MYOC* locus have been deleted and replaced with the corresponding human *MYOC* sequence, and/or

wherein the humanized endogenous *MYOC* locus comprises a human *MYOC* 3' untranslated region, and/or

wherein the endogenous *MYOC* 5' untranslated region has not been deleted and replaced with the corresponding human *MYOC* sequence.

25. The non-human animal cell of any one of claims 21-24, wherein the humanized endogenous *MYOC* locus encodes a human myocilin protein,

optionally wherein the human myocilin protein sequence comprises the sequence set forth in SEQ ID NO: 4, and optionally wherein the human myocilin protein sequence is encoded by a coding sequence comprising the sequence set forth in SEQ ID NO: 5.

26. The non-human animal cell of any one of claims 21-25, wherein the entire *MYOC* coding sequence of the endogenous *MYOC* locus has been deleted and replaced with the corresponding human *MYOC* sequence, and

wherein a region of the endogenous *MYOC* locus from the *MYOC* start codon to the *MYOC* stop codon has been deleted and replaced with the corresponding human *MYOC* sequence.

27. The non-human animal cell of any one of claims 21-26, wherein a region of the endogenous *MYOC* locus from the *MYOC* start codon to the *MYOC* stop codon has been deleted and replaced with a human *MYOC* sequence comprising the corresponding human *MYOC* sequence and a human *MYOC* 3' untranslated region,

wherein the human *MYOC* sequence comprises a Y437H mutation,

wherein the endogenous *MYOC* 5' untranslated region has not been deleted and replaced with the human *MYOC* sequence, and

wherein the humanized endogenous *MYOC* locus comprises an endogenous *MYOC* promoter, wherein the human *MYOC* sequence is operably linked to the endogenous *MYOC* promoter.

28. The non-human animal cell of any one of claims 21-27, wherein:

(i) the human *MYOC* sequence at the humanized endogenous *MYOC* locus comprises a sequence at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the sequence set forth in SEQ ID NO: 87; and/or

(ii) the humanized endogenous *MYOC* locus encodes a myocilin protein comprising a sequence at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the sequence set forth in SEQ ID NO: 4; and/or

(iii) the humanized endogenous *MYOC* locus comprises a myocilin coding sequence comprising a sequence at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the sequence set forth in SEQ ID NO: 5; and/or

(iv) the humanized endogenous *MYOC* locus comprises a sequence at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the sequence set forth in SEQ ID NO: 88 or 89.

29. The non-human animal cell of any one of claims 21-28, wherein the humanized endogenous *MYOC* locus does not comprise a selection cassette or a reporter gene.

30. The non-human animal cell of any one of claims 21-29, wherein the non-human animal cell is homozygous for the humanized endogenous *MYOC* locus.

31. The non-human animal cell of any one of claims 21-30, wherein the non-human animal cell is a mammal cell.

32. The non-human animal cell of claim 31, wherein the non-human animal cell is a rat cell or a mouse cell.

33. The non-human animal cell of claim 32, wherein the non-human animal cell is the mouse cell.

34. The non-human animal cell of any one of claims 21-33, further comprising a second genomically integrated expression cassette that encodes one or more guide RNAs each comprising one or more adaptor-binding elements to which the chimeric adaptor protein can specifically bind,

wherein each of the one or more guide RNAs is capable of forming a complex with the Cas protein and guiding it to a target sequence within a target gene, and

wherein at least one of the one or more guide RNAs targets the humanized endogenous *MYOC* locus.

35. The non-human animal cell of any one of claims 21-34, wherein the first expression cassette is integrated into a *Rosa26* locus,

the Cas protein is a Cas9 protein comprising mutations corresponding to D10A and N863A when optimally aligned with a *Streptococcus pyogenes* Cas9 protein,

the one or more transcriptional activator domains in the chimeric Cas protein comprise VP64,

the adaptor protein comprises an MS2 coat protein or a functional fragment or variant thereof,

the one or more transcriptional activation domains in the chimeric adaptor protein comprise p65 and HSF1,

the non-human animal cell further comprises one or more guide RNAs that were administered or one or more expression cassettes that encode the one or more guide RNAs,

the one or more guide RNAs or one or more expression cassettes that encode the one or more guide RNAs are in the trabecular meshwork,

each of the one or more guide RNAs comprises two adaptor-binding elements to which the chimeric adaptor protein can specifically bind,

the two adaptor-binding elements comprise a first adaptor-binding element within a first loop of each of the one or more guide RNAs and a second adaptor-binding element within a second loop of each of the one or more guide RNAs, and

the target sequence is within a region 200 base pairs upstream of the transcription start site and 1 base pair downstream of the transcription start site.

36. The non-human animal cell of any one of claims 21-35, wherein the non-human animal cell is a mouse cell, and wherein the one or more guide RNAs target one or more guide RNA target sequences selected from SEQ ID NOS: 90-95, and

optionally wherein the non-human animal cell is a mouse cell, and wherein the one or more guide RNAs target one or more guide RNA target sequences selected from SEQ ID NOS: 93-94.

37. The non-human animal cell of any one of claims 21-36, wherein the non-human animal cell is a mouse cell, and wherein the one or more guide RNAs target the guide RNA target sequence set forth in SEQ ID NO: 93.