CLAIMS

1. A siRNA molecule for use in the treatment and/or prevention of a retinal disease related to neovascularization ~~an eye condition~~ characterised by increased expression and/or activity of NRARP wherein said molecule specifically targets at least one sequence selected from the group consisting of SEQ ID NO. 1 to SEQ ID NO. 9.

~~2. A siRNA molecule for use in the treatment and/or prevention of an eye condition characterised by increased expression and/or activity of NRARP according to claim 1, wherein said eye condition is related to neovascularization.~~

~~3~~2. A siRNA molecule for use in the treatment and/or prevention of a retinal disease related to neovascularization ~~an eye condition~~ characterised by increased expression and/or activity of NRARP according to claim~~s~~ 1 ~~or 2~~, wherein said ~~eye condition~~ retinal disease is selected from age-related macular degeneration (AMD), ischemic retinopathy, diabetic macular edema (DME), proliferative diabetic retinopathy (PDR), diabetic retina ischemia (DRI), diabetic retinal edema (DRE), myopic neovascularization and retinopathy of prematurity (ROP) and combinations thereof.

~~4~~3. A siRNA molecule for use in the treatment and/or prevention of a retinal disease related to neovascularization ~~an eye condition~~ characterised by increased expression and/or activity of NRARP according to any preceding claim wherein said siRNA comprises a 19 nucleotide double-stranded region.

~~5~~4. A siRNA molecule for use in the treatment and/or prevention of a retinal disease related to neovascularization ~~an eye condition~~ characterised by increased expression and/or activity of NRARP according to claim ~~4~~ 3 wherein said siRNA is blunt-ended.

~~6~~5. A siRNA molecule for use in the treatment and/or prevention of a retinal disease related to neovascularization ~~an eye condition~~

characterised by increased expression and/or activity of NRARP according to any preceding claim wherein said siRNA comprises or consists of at least one sequence selected from the group consisting of SEQ ID NO. 10 to SEQ ID NO. 18.

~~7~~6. A siRNA molecule for use in the treatment and/or prevention of a retinal disease related to neovascularization ~~an eye condition~~ characterised by increased expression and/or activity of NRARP according to any preceding claim, wherein said siRNA comprises or consists of a sense strand which comprises or consists of at least one sequence selected from the group consisting of SEQ ID NO. 10 to SEQ ID NO. 18, and an antisense strand which is complementary to the sense strand.

~~8~~7. A siRNA molecule for use in the treatment and/or prevention of a retinal disease related to neovascularization ~~an eye condition~~ characterised by increased expression and/or activity of NRARP according to any preceding claim, wherein at least one nucleotide comprises a chemical modification.

~~9~~8. A siRNA molecule for use in the treatment and/or prevention of a retinal disease related to neovascularization ~~an eye condition~~ characterised by increased expression and/or activity of NRARP according to claim ~~8~~7, wherein said chemical modification of a nucleotide is selected from: 2’-O-methyl modification, 2’-fluoro modification, introduction of phosphorothioate modified nucleotides, substitution of uracil with 5-Propynyluracil, substitution of uracil with 5'-methyluridine, substitution of uracyl ribose nucleotides with 4’-thioribose and substitution of uracyl ribose nucleotides with deoxythymidine nucleotides and combinations thereof.

~~10~~9. A siRNA molecule for use in the treatment and/or prevention of a retinal disease related to neovascularization ~~an eye condition~~ characterised by increased expression and/or activity of NRARP according to claims ~~8~~7 or ~~9~~8 wherein said chemical modification is on the sense strand, the antisense strand or on both.

~~11~~10. A siRNA molecule for use in the treatment and/or prevention of a retinal disease related to neovascularization ~~an eye condition~~ characterised by increased expression and/or activity of NRARP according to any of claims ~~8~~ 7 to ~~10~~ 9 wherein said siRNA comprises at least one sequence selected from the group consisting of SEQ ID NO. 19 ~~-~~ to SEQ ID NO. 66.

~~12~~11. A siRNA molecule for use in the treatment and/or prevention of a retinal disease related to neovascularization ~~an eye condition~~ characterised by increased expression and/or activity of NRARP according to any of claims ~~8~~ 7 to ~~11~~10, wherein said siRNA comprises or consists of a sense strand which comprises or consists of at least one sequence selected from the group consisting of SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63 and SEQ ID NO. 65, and an antisense strand which is complementary to the sense strand which is selected from the group consisting of SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64 and SEQ ID NO. 66.

~~13~~12. A siRNA molecule wherein said molecule specifically targets at least one sequence selected from the group consisting of SEQ ID NO. 1 to SEQ ID NO. 9 and reduces expression of NRARP gene when introduced in a cell and wherein said siRNA comprises a 19 nucleotide blunt-ended double-stranded structure.

~~14~~13. A siRNA molecule wherein said molecule specifically targets at least one sequence selected from the group consisting of SEQ ID NO. 1 to SEQ ID NO. 9.

~~15~~14. A siRNA molecule according to any of claims ~~13~~ 12 or ~~14~~ 13 wherein said siRNA comprises or consists of at least one sequence selected from the group consisting of SEQ ID NO. 10 to SEQ ID NO. 18.

~~16~~15. A siRNA molecule according to any of claims ~~13~~ 12 to ~~15~~14, wherein said siRNA comprises or consists of a sense strand which comprises or consists of at least one sequence selected from the group consisting of SEQ ID NO. 10 to SEQ ID NO. 18, and an antisense strand which is complementary to the sense strand.

~~17~~16. A siRNA molecule according to any of claims ~~13~~ 12 to ~~16~~15, wherein at least one nucleotide comprises a chemical modification.

~~18~~17. A siRNA molecule according to claim ~~17~~16, wherein said chemical modification of a nucleotide is selected from: 2’-O-methyl modification, 2’-fluoro modification, introduction of phosphorothioate modified nucleotides, substitution of uracil with 5-Propynyluracil, substitution of uracil with 5'-methyluridine, substitution of uracyl ribose nucleotides with 4’-thioribose and substitution of uracyl ribose nucleotides with deoxythymidine nucleotides and combinations thereof.

~~19~~18. A siRNA molecule according to claims ~~17~~ 16 or ~~18~~ 17 wherein said chemical modification is on the sense strand, the antisense strand or on both.

~~20~~19. A siRNA molecule according to any of claims ~~17~~ 16 to ~~19~~ 18 wherein said siRNA comprises at least one sequence selected from the group consisting of SEQ ID NO. 19 – SEQ ID NO. 66.

~~21~~20. A siRNA molecule according to any of claims ~~17~~ 16 to ~~20~~19, wherein said siRNA comprises or consists of a sense strand which comprises or consists of at least one sequence selected from the group consisting of SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO.

43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63 and SEQ ID NO. 65, and an antisense strand which is complementary to the sense strand which is selected from the group consisting of SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64 and SEQ ID NO. 66.

~~22~~21. Use of a siRNA molecule according to any of claims 1 to 20 ~~any preceding claim~~ in the manufacture of a medicament for the treatment of a retinal disease related to neovascularization ~~an eye condition~~ characterised by increased expression and/or activity of NRARP.

~~23. Use according to claim 22 wherein said eye condition is related to neovascularization.~~

~~24~~22. Use according to claim ~~22 or 23~~ 21 wherein said a retinal disease related to neovascularization ~~eye condition~~ is selected from age-related macular degeneration (AMD), ischemic retinopathy, diabetic macular edema (DME), proliferative diabetic retinopathy (PDR), diabetic retina ischemia (DRI), diabetic retinal edema (DRE), myopic neovascularization and retinopathy of prematurity (ROP) and combinations thereof.

~~25~~23. A pharmaceutical composition wherein said composition comprises at least a siRNA molecule described in any of claims 1 to ~~21~~20.

~~26. A method of treatment of an eye condition characterised by increased expression and/or activity of NRARP, the method comprising administering to a patient in need thereof an siRNA molecule according to any of claims 1 to 21, or a pharmaceutical composition according to claim 25.~~

~~27. A method of treatment according to claim 26 wherein said eye condition is selected from age-related macular degeneration (AMD), ischemic retinopathy, diabetic macular edema (DME), proliferative diabetic retinopathy (PDR), diabetic retina ischemia (DRI), diabetic retinal edema (DRE), myopic neovascularization and retinopathy of prematurity (ROP) and combinations thereof.~~

24. A pharmaceutical composition in the form of an eye drop comprising an siRNA molecule which specifically targets at least one sequence selected from the group consisting of SEQ ID NO. 1 to SEQ ID NO. 9.

25. A pharmaceutical composition according to claim 24 wherein said siRNA comprises a 19 nucleotide double-stranded region.

26. A pharmaceutical composition according to claim 25 wherein said siRNA is blunt-ended.

27. A pharmaceutical composition according to any of claims 24 to 26 wherein said siRNA comprises or consists of at least one sequence selected from the group consisting of SEQ ID NO. 10 to SEQ ID NO. 18.

28. A pharmaceutical composition according to any of claims 24 to 27, wherein said siRNA comprises or consists of a sense strand which comprises or consists of at least one sequence selected from the group consisting of SEQ ID NO. 10 to SEQ ID NO. 18, and an antisense strand which is complementary to the sense strand.

29. A pharmaceutical composition according to any of claims 24 to 28, wherein at least one nucleotide comprises a chemical modification.

30. A pharmaceutical composition according to claim 29, wherein said chemical modification of a nucleotide is selected from the group consisting of: 2’-O-methyl modification, 2’-fluoro modification, introduction of phosphorothioate modified nucleotides, substitution of uracil with 5-Propynyluracil, substitution of uracil with 5'-methyluridine, substitution of uracyl ribose nucleotides with 4’-

thioribose and substitution of uracyl ribose nucleotides with deoxythymidine nucleotides and combinations thereof.

31. A pharmaceutical composition according to claims 29 or 30 wherein said chemical modification is on the sense strand, the antisense strand or on both.

32. A pharmaceutical composition according to any of claims 29 to 31 wherein said siRNA comprises at least one sequence selected from the group consisting of SEQ ID NO. 19 to SEQ ID NO. 66.

33. A pharmaceutical composition according to any of claims 29 to 32, wherein said siRNA comprises or consists of a sense strand which comprises or consists of at least one sequence selected from the group consisting of SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63 and SEQ ID NO. 65, and an antisense strand which is complementary to the sense strand which is selected from the group consisting of SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64 and SEQ ID NO. 66.

34. A pharmaceutical composition according to claim 33 wherein said siRNA comprises or consists of a sense strand which comprises or consists of the nucleotide sequence of SEQ ID NO. 37, and an antisense strand which is complementary to the sense strand which comprises or consists of the nucleotide sequence of SEQ ID NO. 38.

35. A pharmaceutical composition according to any of claims 24 to 34, further comprising buffered saline solution.

36. A pharmaceutical composition according to claim 35 having a pH of about 7.0 to about 7.4.

37. A pharmaceutical composition according to any one of claims 24 to 34 in the form of a gel.

38. A pharmaceutical composition according to any of claims 24 to 37, further comprising one or more biopolymer selected from the group consisting of poly(lactide-co-glycolide), carbopol, hyaluronic acid, and polyacrylic acid.

39. A pharmaceutical composition according to any of claims 24 to 38, wherein said siRNA reduces expression of the NRARP gene when introduced into a cell.

40. A pharmaceutical composition according to any of claims 24 to 39, wherein said composition is for the treatment or prevention of retinal neovascularization.

41. A pharmaceutical composition comprising siRNA, wherein said siRNA has a sense strand which comprises or consists of the nucleotide sequence of SEQ ID NO. 37, and an antisense strand which is complementary to the sense strand.

42. An siRNA having a sense strand which comprises or consists of the nucleotide sequence of SEQ ID NO. 37, and an antisense strand which is complementary to the sense strand.

43. The siRNA of claim 42 wherein the antisense strand comprises or consists of the nucleotide sequence of SEQ ID NO. 38.