CLAIMS

1. A pegylated or unpegylated aptamer and an anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration, wherein the pegylated or unpegylated aptamer binds to C5 complement and has a sequence of SEQ ID NO: 4 and the pegylated or unpegylated aptamer and the anti-VEGF agent are for sequential or substantially simultaneous administration.

2. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to claim 1, wherein the pegylated or unpegylated aptamer or the anti-VEGF agent is administered by ocular administration, intravitreal administration, or peri-ocular administration.

3. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to claim 1 or claim 2, wherein the pegylated or unpegylated aptamer or the anti-VEGF agent is present in a depot formulation.

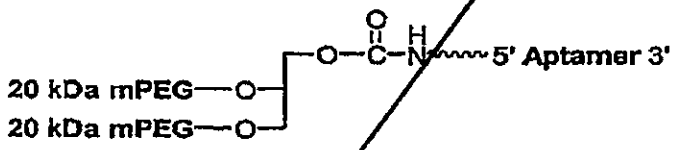
4. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to any one claims 1 to 3, wherein the pegylated or unpegylated aptamer and the anti-VEGF agent are administered in an amount effective to maintain at least the same level of visual acuity of the subject as compared to the subject's visual acuity level prior to administration of the pegylated or unpegylated aptamer or the anti-VEGF agent.

5. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to any one claims 1 to 4, wherein the pegylated or unpegylated aptamer and the anti-VEGF agent are administered in an amount effective to improve the level of visual acuity in the subject relative to the subject's level of visual acuity prior to pegylated or unpegylated aptamer or anti-VEGF agent administration.

6. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to any one of claims 1 to 5, wherein the aptamer is pegylated.

7. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to claim 6, wherein the pegylated aptamer has a sequence of SEQ ID NO: 5, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 65, or SEQ ID NO: 67.

8. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to claim 6, wherein the aptamer has the structure:



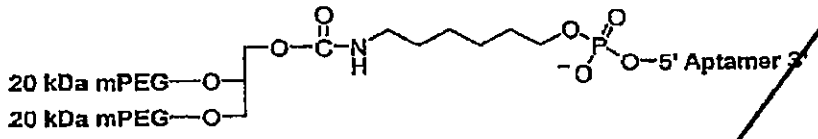
where ~~~~ indicates a linker, and

Aptamer = fCmGfCfCGfCmGmGfUfCfUfCmAmGmGfCGfCfUmGmAmGfUfCfUmGmAmGfUfUfUAfCf CfUmGfCmG-3T (SEQ ID NO:4), wherein fC and fU = 2'-fluoro nucleotides, mG and mA = 2'-OMe nucleotides, all other nucleotides are 2'-OH, and 3T indicates an inverted deoxythymidine.

9. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to claim 8, wherein the linker is an alkyl linker.

10. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to claim 9, wherein the alkyl linker comprises 2 to 18 consecutive CH_2 groups.

11. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to any one of claims 8 to 10, wherein the aptamer has the structure:



Aptamer=fCmGfCfCGfCmGmGfUfCfUfCmAmGmGfCGfCfUmGmAmGfUfCfUmGmAmGfU fUfUAfCfCfUmGfCmG-3T (SEQ ID NO: 4),

wherein fC and fU = 2'-fluoro nucleotides, and mG and mA = 2'-OMe nucleotides and all other nucleotides are 2' -OH and 3T indicates an inverted deoxy thymidine.

12. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to any one claims 1 to 11, wherein the anti-VEGF agent is an antibody or antibody fragment.

13. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to any one claims 1 to 12, wherein the anti-VEGF agent is ranibizumab or bevacizumab.

14. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to any one claims 1 to 13, wherein the aptamer and the anti-VEGF agent are present in separate compositions.

15. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to any one of claims 1 to 13, wherein the aptamer and the anti-VEGF agent are present in the same composition.

16. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to any one claims 1 to 15, wherein the macular degeneration is age-related macular degeneration (AMD).

17. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to claim 16, wherein the AMD is non-exudative AMD.

18. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing macular degeneration according to claim 16, wherein the AMD is exudative AMD.

19. Use of a pegylated or unpegylated aptamer in the manufacture of a medicament for treating, stabilizing and/or preventing macular degeneration, wherein the pegylated or unpegylated aptamer binds to C5 complement and has a sequence of SEQ ID NO: 4, and wherein the medicament is administered sequentially or substantially simultaneously with an anti-VEGF agent.

20. The use according to claim 19, wherein the medicament is administered by ocular administration, intravitreal administration, or peri-ocular administration.

21. The use according to claim 19 or claim 20, wherein the medicament is present in a depot formulation.

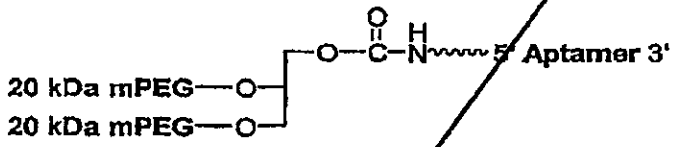
22. The use according to any one of claims 19 to 21, wherein the medicament and the anti-VEGF agent are administered in an amount effective to maintain at least the same level of visual acuity of the subject as compared to the subject's visual acuity level prior to administration of the medicament.

23. The use according to any one of claims 19 to 22, wherein the medicament and the anti-VEGF agent are administered in an amount effective to improve the level of visual acuity in the subject relative to the subject's level of visual acuity prior to medicament administration.

24. The use according to any one of claims 19 to 23, wherein the aptamer is pegylated.

25. The use according to claim 24, wherein the pegylated aptamer has a sequence of SEQ ID NO: 5, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 65, or SEQ ID NO: 67.

26. The use according to claim 24, wherein the aptamer has the structure:



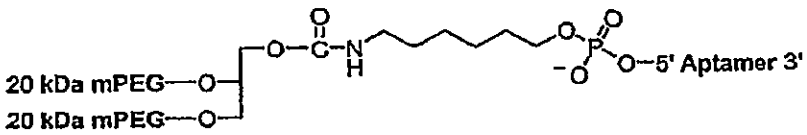
where ~~~~ indicates a linker, and

Aptamer = fCmGfCfCGfCmGmGfUfCfUfCmAmGmGfCGfCfUmGmAmGfUfCfUmGmAmGfUfUfUAfCfCfUmGfCmG-3T (SEQ ID NO:4), wherein fC and fU = 2'-fluoro nucleotides, mG and mA = 2'-OMe nucleotides, all other nucleotides are 2'-OH, and 3T indicates an inverted deoxythymidine.

27. The use according to claim 26, wherein the linker is an alkyl linker.

28. The use according to claim 27, wherein the alkyl linker comprises 2 to 18 consecutive CH_2 groups.

29. The use according to any one of claims 26 to 28, wherein the aptamer has the structure:



Aptamer=fCmGfCfCGfCmGmGfUfCfUfCmAmGmGfCGfCfUmGmAmGfUfCfUmGmAmGfU fUfUAfCfCfUmGfCmG-3T (SEQ ID NO: 4),

wherein fC and fU = 2'-fluoro nucleotides, and mG and mA = 2'-OMe nucleotides and all other nucleotides are 2' -OH and 3T indicates an inverted deoxy thymidine.

30. The use according to any one of claims 19 to 29, wherein the anti-VEGF agent is an antibody or antibody fragment.

31. The use according to any one of claims 19 to 30, wherein the anti-VEGF agent is ranibizumab or bevacizumab.

32. The use according to any one of claims 19 to 31, wherein the macular degeneration is AMD.

33. The use according to claim 32, wherein the AMD is non-exudative AMD.

34. The use according to claim 32, wherein the AMD is exudative AMD.

CLAIMS

1. A pegylated or unpegylated aptamer and an anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type age-related macular degeneration (AMD), wherein the pegylated or unpegylated aptamer binds to C5 complement and has a sequence of SEQ ID NO: 4, wherein the anti-VEGF agent is an antibody or antibody fragment directed against VEGF, and wherein the pegylated or unpegylated aptamer and the anti-VEGF agent are for sequential or substantially simultaneous administration.

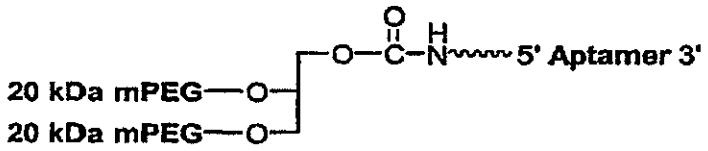
2. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type AMD according to claim 1, wherein the pegylated or unpegylated aptamer or the anti-VEGF agent is administered by ocular administration, intravitreal administration, or peri-ocular administration.

3. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type AMD according to claim 1 or claim 2, wherein the pegylated or unpegylated aptamer or the anti-VEGF agent is present in a depot formulation.

4. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type AMD according to any one claims 1 to 3, wherein the pegylated or unpegylated aptamer and the anti-VEGF agent are administered in an amount effective to maintain at least the same level of visual acuity of the subject as compared to the subject's visual acuity level prior to administration of the pegylated or unpegylated aptamer or the anti-VEGF agent.

5. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type AMD according to any one claims 1 to 4, wherein the pegylated or unpegylated aptamer and the anti-VEGF agent are administered in an amount effective to improve the level of visual acuity in the subject relative to the subject's level of visual acuity prior to pegylated or unpegylated aptamer or anti-VEGF agent administration.

6. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type AMD according to any one of claims 1 to 5, wherein the aptamer has the structure:



or a salt thereof,

where ~~~ indicates a linker, and

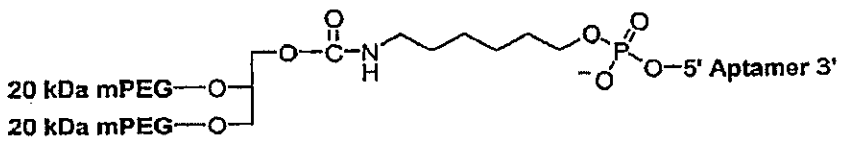
Aptamer =

fCmGfCfCGfCmGmGfUfCfUfCmAmGmGfCGfCfUmGmAmGfUfCfUmGmAmGfUfUfUAfCf CfUmGfCmG-3T (SEQ ID NO:4), wherein fC and fU = 2'-fluoro nucleotides, mG and mA = 2'-OMe nucleotides, all other nucleotides are 2'-OH, and 3T indicates an inverted deoxythymidine.

7. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type AMD according to claim 6, wherein the linker is an alkyl linker.

8. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type AMD according to claim 7, wherein the alkyl linker comprises 2 to 18 consecutive CH_2 groups.

9. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type AMD according to any one of claims 6 to 8, wherein the aptamer has the structure:



or a salt thereof,

Aptamer=fCmGfCfCGfCmGmGfUfCfUfCmAmGmGfCGfCfUmGmAmGfUfCfUmGmAmGfUfUfUAfCfCfUmGfCmG-3T (SEQ ID NO: 4),

wherein fC and fU = 2'-fluoro nucleotides, and mG and mA = 2'-OMe nucleotides and all other nucleotides are 2' -OH and 3T indicates an inverted deoxy thymidine.

10. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type AMD according to any one claims 1 to 9, wherein the anti-VEGF agent is ranibizumab or bevacizumab.

11. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type AMD according to any one claims 1 to 10, wherein the aptamer and the anti-VEGF agent are present in separate compositions.

12. The pegylated or unpegylated aptamer and anti-VEGF agent for use in a method of treating, stabilizing and/or preventing exudative type AMD according to any one of claims 1 to 10, wherein the aptamer and the anti-VEGF agent are present in the same composition.

13. Use of a pegylated or unpegylated aptamer in the manufacture of a medicament for treating, stabilizing and/or preventing exudative type AMD, wherein the pegylated or unpegylated aptamer binds to C5 complement and has a sequence of SEQ ID NO: 4, and wherein the medicament is administered sequentially or substantially simultaneously with an anti-VEGF agent that is an antibody or antibody fragment directed against VEGF.

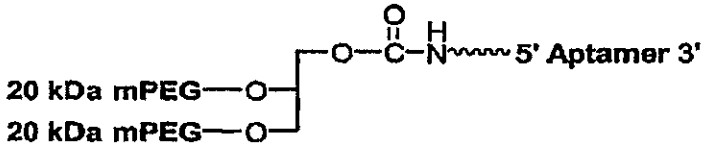
14. The use according to claim 13, wherein the medicament is administered by ocular administration, intravitreal administration, or peri-ocular administration.

15. The use according to claim 13 or claim 14, wherein the medicament is present in a depot formulation.

16. The use according to any one of claims 13 to 15, wherein the medicament and the anti-VEGF agent are administered in an amount effective to maintain at least the same level of visual acuity of the subject as compared to the subject's visual acuity level prior to administration of the medicament.

17. The use according to any one of claims 13 to 15, wherein the medicament and the anti-VEGF agent are administered in an amount effective to improve the level of visual acuity in the subject relative to the subject's level of visual acuity prior to medicament administration.

18. The use according to any one of claims 13 to 17, wherein the aptamer has the structure:



or a salt thereof,

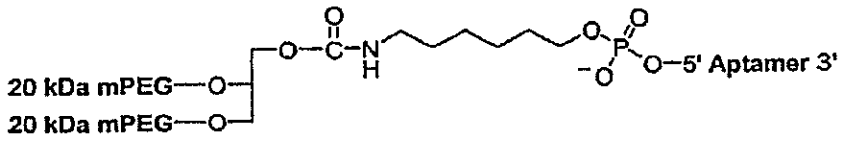
where ~~~~ indicates a linker, and

Aptamer = fCmGfCfCGfCmGmGfUfCfUfCmAmGmGfCGfCfUmGmAmGfUfCfUmGmAmGfUfUfUAfCfCfUmGfCmG-3T (SEQ ID NO:4), wherein fC and fU = 2'-fluoro nucleotides, mG and mA = 2'-OMe nucleotides, all other nucleotides are 2'-OH, and 3T indicates an inverted deoxythymidine.

19. The use according to claim 18, wherein the linker is an alkyl linker.

20. The use according to claim 19, wherein the alkyl linker comprises 2 to 18 consecutive CH_2 groups.

21. The use according to any one of claims 18 to 20, wherein the aptamer has the structure:



or a salt thereof,

Aptamer=fCmGfCfCGfCmGmGfUfCfUfCmAmGmGfCGfCfUmGmAmGfUfCfUmGmAmGfU fUfUAfCfCfUmGfCmG-3T (SEQ ID NO: 4),

wherein fC and fU = 2'-fluoro nucleotides, and mG and mA = 2'-OMe nucleotides and all other nucleotides are 2' -OH and 3T indicates an inverted deoxy thymidine.

22. The use according to any one of claims 13 to 21, wherein the anti-VEGF agent is ranibizumab or bevacizumab.