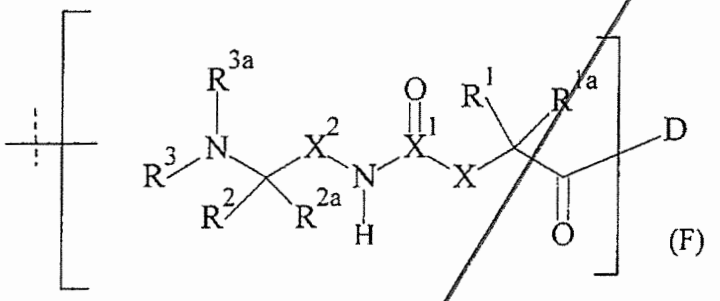
Claims

1. A pharmaceutical composition comprising one or more pharmaceutically acceptable excipient(s) and a carrier-linked VEGF neutralizing prodrug, wherein the carrier-linked prodrug comprises a covalently bound VEGF neutralizing biologically active moiety, a reversible prodrug linker moiety and a carrier group which is a hydrogel, which VEGF neutralizing biologically active is reversibly connected to a carrier through a reversible prodrug linker moiety, wherein there is optionally a spacer moiety between the carrier moiety and the reversible prodrug linker and wherein the reversible prodrug linker is of formula (F):



(F)

,

wherein

the dashed line indicates attachment to the rest of the carrier-linked prodrug, i.e. to the carrier moiety or to the optional spacer moiety;

D is a VEGF neutralizing biologically active moiety which is connected to the rest of the molecule via an aromatic amine of the corresponding VEGF neutralizing drug by forming an amide linkage;

X is $C(R^4R^{4a})$; $N(R^4)$; O; $C(R^4R^{4a})$-$C(R^5R^{5a})$; $C(R^5R^{5a})$-$C(R^4R^{4a})$; $C(R^4R^{4a})$-$N(R^6)$; $N(R^6)$-$C(R^4R^{4a})$; $C(R^4R^{4a})$-O; or O-$C(R^4R^{4a})$;

X^1 is C; or S(O);

X^2 is $C(R^7, R^{7a})$; or $C(R^7, R^{7a})$-$C(R^8, R^{8a})$;

R^1, R^{1a}, R^2, R^{2a}, R^3, R^{3a}, R^4, R^{4a}, R^5, R^{5a}, R^6, R^7, R^{7a}, R^8, R^{8a} are independently selected from the group consisting of H; and C_{1-4} alkyl;

optionally, one or more of the pair(s) R^{1a}/R^{4a}, R^{1a}/R^{5a}, R^{4a}/R^{5a}, R^{4a}/R^{5a}, R^{7a}/R^{8a} form a chemical bond;

optionally, one or more of the pair(s) R^1/R^{1a}, R^2/R^{2a}, R^4/R^{4a}, R^5/R^{5a}, R^7/R^{7a}, R^8/R^{8a} are joined together with the atom to which they are attached to form a C_{3-7} cycloalkyl; or 4- to 7-membered heterocyclyl;

optionally, one or more of the pair(s) R^1/R^4, R^1/R^5, R^1/R^6, R^4/R^5, R^7/R^8, R^2/R^3 are joined together with the atoms to which they are attached to form a ring A;

optionally, R^3/R^{3a} are joined together with the nitrogen atom to which they are attached to form a 4- to 7-membered heterocycle;

A is selected from the group consisting of phenyl; naphthyl; indenyl; indanyl; tetralinyl; C_{3-10} cycloalkyl; 4- to 7-membered heterocyclyl; and 8- to 11-membered heterobicyclyl;

provided that one hydrogen of R^1, R^{1a}, R^2, R^{2a}, R^3, R^{3a}, R^4, R^{4a}, R^5, R^{5a}, R^6, R^7, R^{7a}, R^8 or R^{8a} is replaced with a bond to connect the moiety of formula (F) with the rest of the VEGF neutralizing prodrug, i.e. to the carrier moiety or to the optional spacer moiety;

for use in a method for the treatment of one or more ocular conditions.

2. The pharmaceutical composition of claim 1, wherein the carrier is a PEG-based hydrogel.

3. The pharmaceutical composition of claim 1 or 2, wherein the treatment comprises intraocular administration of the prodrug.

4. The pharmaceutical composition of claim 3, wherein the intraocular administration is via intraocular injection.

5. The pharmaceutical composition of any one of claims 1 to 4, wherein the prodrug comprised in the pharmaceutical composition has a concentration of 5 to 200 mg prodrug/ml pharmaceutical composition.

6. The pharmaceutical composition of any one of claims 1 to 5, wherein the composition comprises 8 to 80 weight percent of VEGF neutralizing biologically active moiety based on the total weight of the prodrug.

7. The pharmaceutical composition of any one of claims 4 to 6, wherein the injection is carried out with an injection volume ranging from 10 to 200 µl per injection.

8. The pharmaceutical composition of any one of claims 3 to 7, wherein the time period between two intraocular administrations of the VEGF neutralizing prodrug is at least 1 month.

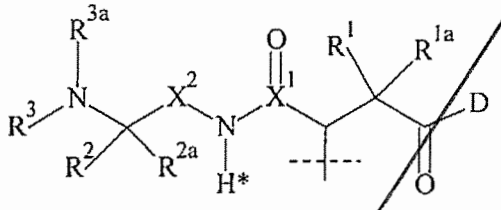
9. The pharmaceutical composition of any one of claims 1 to 8, wherein the VEGF neutralizing prodrug comprises in bound form a biologically active moiety selected from the group of drugs consisting of antisense RNA, antisense DNA, ribozymes or RNAi molecules targeting a VEGF nucleic acid; anti-VEGF aptamers, anti-VEGF

antibodies, anti-VEGF antibody fragments, DARPins and soluble VEGF receptor decoys that prevent binding of a VEGF to its cognate receptor; antisense, ribozymes, and RNAi molecules targeting a cognate VEGF receptor (VEGFR) nucleic acid; anti-VEGFR aptamers or anti-VEGFR antibodies that bind to a cognate VEGFR receptor; anti-VEGFR antibody fragments that bind to a cognate VEGFR receptor and VEGFR tyrosine kinase inhibitors.

10. The pharmaceutical composition of any one of claims 1 to 9, wherein the VEGF neutralizing prodrug comprises in bound form a biologically active moiety selected from the group consisting of ranibizumab, bevacizumab, pegaptanib, aflibercept, MP0112, KH902, ESBA1008, AL 39324, ALG-1001, and bevasiranib and/or fragments thereof.

11. The pharmaceutical composition of any one of claims 1 to 10, wherein the VEGF neutralizing prodrug comprises in bound form ranibizumab.

12. The pharmaceutical composition of any one of claims 1 to 11, wherein the the VEGF neutralizing prodrug comprises a moiety of formula (F-i):



(F-i),

wherein

D is ranibizumab;

the dashed line indicates attachment to the carrier or to the optional spacer moiety;

X is $C(R^4R^{4a})$; $N(R^4)$; O; $C(R^4R^{4a})$-$C(R^5R^{5a})$; $C(R^5R^{5a})$-$C(R^4R^{4a})$; $C(R^4R^{4a})$-$N(R^6)$; $N(R^6)$-$C(R^4R^{4a})$; $C(R^4R^{4a})$-O; or O-$C(R^4R^{4a})$;

X^1 is C; or S(O);

X^2 is $C(R^7, R^{7a})$; or $C(R^7, R^{7a})$-$C(R^8, R^{8a})$;

R^1, R^{1a}, R^2, R^{2a}, R^3, R^{3a}, R^4, R^{4a}, R^5, R^{5a}, R^6, R^7, R^{7a}, R^8, R^{8a} are independently selected from the group consisting of H; and C_{1-4} alkyl;

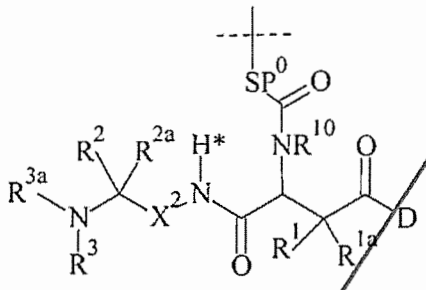
optionally, one or more of the pair(s) R^{1a}/R^{4a}, R^{1a}/R^{5a}, R^{4a}/R^{5a}, R^{4a}/R^{5a}, R^{7a}/R^{8a} form a chemical bond;

optionally, one or more of the pair(s) R^1/R^{1a}, R^2/R^{2a}, R^4/R^{4a}, R^5/R^{5a}, R^7/R^{7a}, R^8/R^{8a} are joined together with the atom to which they are attached to form a C_{3-7} cycloalkyl; or 4- to 7-membered heterocyclyl;

optionally, one or more of the pair(s) R^1/R^4, R^1/R^5, R^1/R^6, R^4/R^5, R^7/R^8, R^2/R^3 are joined together with the atoms to which they are attached to form a ring A;
optionally, R^3/R^{3a} are joined together with the nitrogen atom to which they are attached to form a 4- to 7-membered heterocycle;
A is selected from the group consisting of phenyl; naphthyl; indenyl; indanyl; tetralinyl; C_{3-10} cycloalkyl; 4- to 7-membered heterocyclyl; and 8- to 11-membered heterobicyclyl;
optionally, the moiety of formula (F-i) is further substituted, provided that the hydrogel marked with the asterisk in formula (F-i) is not replaced by a substituent and that R^3 and R^{3a} are independently of each other H or are connected to N through an SP^3-hybridized carbon atom.

13. The pharmaceutical composition of claims 12, wherein X^1 is C.

14. The pharmaceutical composition of claim 12 or 13, wherein the VEGF neutralizing prodrug comprises a moiety of formula (f-ii)

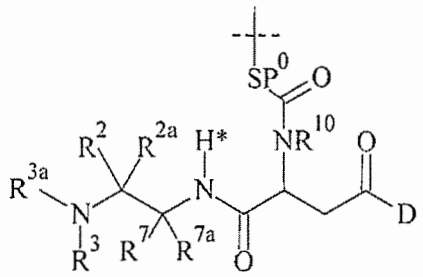


(F-ii),

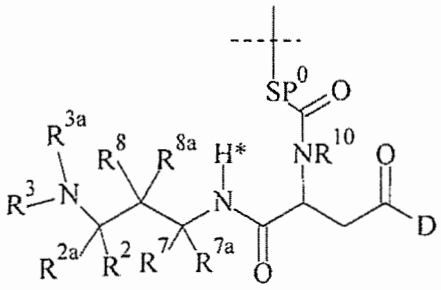
wherein
the dashed line indicates attachment to the carrier;
R^1, R^{1a}, R^2, R^{2a}, R^3, R^{3a}, X^2 and D are used as defined in claim 12;
R^{10} is selected from H and C_{1-6} alkyl;
SP^0 is a spacer moiety;
and wherein the moiety of formula (F-ii) is optionally further substituted, provided that the hydrogel marked with the asterisk in formula (F-ii) is not replaced by a substituent and that R^3 and R^{3a} are independently of each other H or are connected to N through an SP^3-hybridized carbon atom.

15. The pharmaceutical composition of any one of claims 12 to 14, wherein R^1 and R^{1a} are both H.

16. The pharmaceutical composition of any one of claims 12 to 15, wherein the VEGF neutralizing prodrug comprises a moiety of formula (F-iiia) or (F-iiib):



(F-iiia),



(F-iiib),

wherein

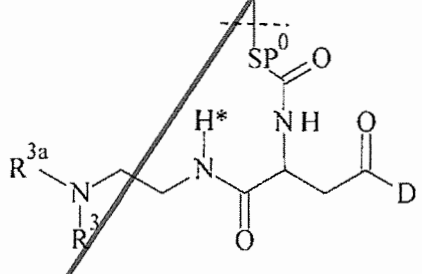
the dashed line indicates attachment to the carrier;

R^2, R^{2a}, R^3, R^{3a}, R^7, R^{7a}, R^8, R^{8a}, X^2 and D are used as defined in claim 12;

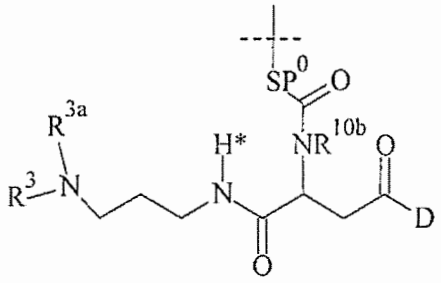
R^{10} and SP^0 are used as defined in claim 14;

and wherein the moiety of formula (F-iiia) or (F-iiib) is optionally further substituted, provided that the hydrogen marked with the asterisk in formula (F-iiia) and (F-iiib) is not replaced by a substituent and that R^3 and R^{3a} are independently of each other H or are connected to N through an SP^3-hybridized carbon atom.

17. The pharmaceutical composition of any one of claims 12 to 16, wherein the VEGF neutralizing prodrug comprises a moiety of formula (F-iva) or (F-ivb):



(F-iva),



(F-ivb),

wherein

the dashed line indicates attachment to the carrier;

R^3 and R^{3a} are used as defined in claim 12;

R^{10b} is C_{1-6} alkyl;

and wherein the moiety of formula (F-iva) or (F-ivb) is optionally further substituted, provided that the hydrogen marked with the asterisk is not replaced by a substituent and that R^3 and R^{3a} are independently of each other H or are connected to N through an SP^3-hybridized carbon atom.

18. The pharmaceutical composition of any one of claims 12 to 17, wherein R^3 is H and R^{3a} is methyl.

19. The pharmaceutical composition of any one of claims 12 to 17, wherein R^3 and R^{3a} of are both H.

20. The pharmaceutical composition of any one of claims 12 to 17, wherein R^3 is H and R^{3a} is methyl.

21. The pharmaceutical composition of any one of claims 1 to 20, wherein the ocular condition is a disease characterized by ocular neovascularization.

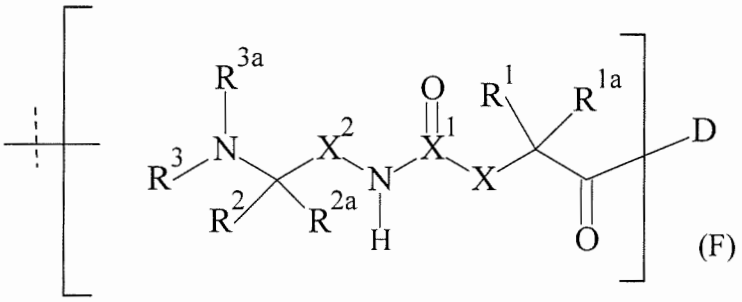
22. The pharmaceutical composition of claim 21, wherein the intraocular neovascularization is an ocular disease selected from the group consisting of optic disc neovascularization, iris neovascularization, retinal neovascularization, choroidal neovascularization, corneal neovascularization, vitreal neovascularization, glaucoma, pannus, pterygium, macular edema, macular degeneration, age-related macular degeneration, diabetic retinopathy, diabetic retinal ischemia, diabetic macular edema, vascular retinopathy, retinal degeneration, retrolental fibroplasias, retinoblastoma, retinopathy of prematurity of macular degeneration, corneal graft neovascularization, central retinal vein occlusion, pathological myopia, ocular tumors, uveitis, inflammatory diseases of the eye, and proliferative vitreoretinopathy.

23. The pharmaceutical composition of any one of claims 1 to 22, wherein the pharmaceutical composition further comprises one or more drug(s) in its/their free form selected from the group consisting of antisense RNA, antisense DNA, ribozymes or RNAi molecules targeting a VEGF nucleic acid; anti-VEGF aptamers, anti-VEGF antibodies, anti-VEGF antibody fragments, DARPins, anticalins, lipocalins, and soluble VEGF receptor decoys that prevent binding of a VEGF to its cognate receptor; antisense, ribozymes, and RNAi molecules targeting a cognate VEGF receptor (VEGFR) nucleic acid; anti-VEGFR aptamers or anti-VEGFR antibodies that bind to a cognate VEGFR receptor; anti-VEGFR antibody fragments that bind to a cognate VEGFR receptor and VEGFR tyrosine kinase inhibitors.

24. The pharmaceutical composition of any one of claims 1 to 23, wherein the pharmaceutical composition further comprises one or more prodrug(s), which one or more prodrug(s) comprise(s) in bound form a biologically active moiety selected from the group consisting of antisense RNA, antisense DNA, ribozymes or RNAi molecules targeting a VEGF nucleic acid; anti-VEGF aptamers, anti-VEGF antibodies, anti-VEGF antibody fragments, DARPins, anticalins, lipocalins, and soluble VEGF receptor decoys that prevent binding of a VEGF to its cognate receptor; antisense, ribozymes, and RNAi molecules targeting a cognate VEGF receptor (VEGFR) nucleic acid; anti-VEGFR aptamers or anti-VEGFR antibodies that bind to a cognate VEGFR receptor; anti-VEGFR antibody fragments that bind to a cognate VEGFR receptor and VEGFR tyrosine kinase inhibitors.

Claims

1. A pharmaceutical composition comprising one or more pharmaceutically acceptable excipient(s) and a carrier-linked VEGF neutralizing prodrug, wherein the carrier-linked prodrug comprises a covalently bound VEGF neutralizing biologically active moiety, a reversible prodrug linker moiety and a carrier group which is a hydrogel, which VEGF neutralizing biologically active moiety is reversibly connected to a carrier through a reversible prodrug linker moiety, wherein there is optionally a spacer moiety between the carrier moiety and the reversible prodrug linker and wherein the reversible prodrug linker is of formula (F):



(F)

,

wherein

the dashed line indicates attachment to the rest of the carrier-linked prodrug, i.e. to the carrier moiety or to the optional spacer moiety;

D is a VEGF neutralizing biologically active moiety which is connected to the rest of the molecule via an aromatic amine of the corresponding VEGF neutralizing drug by forming an amide linkage;

X is $C(R^4R^{4a})$; $N(R^4)$; O; $C(R^4R^{4a})$-$C(R^5R^{5a})$; $C(R^5R^{5a})$-$C(R^4R^{4a})$; $C(R^4R^{4a})$-$N(R^6)$; $N(R^6)$-$C(R^4R^{4a})$; $C(R^4R^{4a})$-O; or O-$C(R^4R^{4a})$;

X^1 is C; or S(O);

X^2 is $C(R^7, R^{7a})$; or $C(R^7, R^{7a})$-$C(R^8, R^{8a})$;

R^1, R^{1a}, R^2, R^{2a}, R^3, R^{3a}, R^4, R^{4a}, R^5, R^{5a}, R^6, R^7, R^{7a}, R^8, R^{8a} are independently selected from the group consisting of H; and C_{1-4} alkyl;

optionally, one or more of the pair(s) R^{1a}/R^{4a}, R^{1a}/R^{5a}, R^{4a}/R^{5a}, R^{4a}/R^{5a}, R^{7a}/R^{8a} form a chemical bond;

optionally, one or more of the pair(s) R^1/R^{1a}, R^2/R^{2a}, R^4/R^{4a}, R^5/R^{5a}, R^7/R^{7a}, R^8/R^{8a} are joined together with the atom to which they are attached to form a C_{3-7} cycloalkyl; or 4- to 7-membered heterocyclyl;

optionally, one or more of the pair(s) R^1/R^4, R^1/R^5, R^1/R^6, R^4/R^5, R^7/R^8, R^2/R^3 are joined together with the atoms to which they are attached to form a ring A;

optionally, R^3/R^{3a} are joined together with the nitrogen atom to which they are attached to form a 4- to 7-membered heterocycle;

A is selected from the group consisting of phenyl; naphthyl; indenyl; indanyl; tetralinyl; C_{3-10} cycloalkyl; 4- to 7-membered heterocyclyl; and 8- to 11-membered heterobicyclyl;

provided that one hydrogen of R^1, R^{1a}, R^2, R^{2a}, R^3, R^{3a}, R^4, R^{4a}, R^5, R^{5a}, R^6, R^7, R^{7a}, R^8 or R^{8a} is replaced with a bond to connect the moiety of formula (F) with the rest of the VEGF neutralizing prodrug, i.e. to the carrier moiety or to the optional spacer moiety;

for use in a method for the treatment of one or more ocular conditions.

2. The pharmaceutical composition for use of claim 1, wherein the carrier is a PEG-based hydrogel.

3. The pharmaceutical composition for use of claim 1 or 2, wherein the treatment comprises intraocular administration of the prodrug.

4. The pharmaceutical composition for use of claim 4, wherein the intraocular administration is via intraocular injection.

5. The pharmaceutical composition for use of any one of claims 1 to 4, wherein the prodrug comprised in the pharmaceutical composition has a concentration of 5 to 200 mg prodrug/ml pharmaceutical composition.

6. The pharmaceutical composition for use of any one of claims 1 to 5, wherein the composition comprises 8 to 80 weight percent of VEGF neutralizing biologically active moiety based on the total weight of the prodrug.

7. The pharmaceutical composition for use of any one of claims 4 to 6, wherein the injection is carried out with an injection volume ranging from 10 to 200 µl per injection.

8. The pharmaceutical composition for use of any one of claims 3 to 7, wherein the time period between two intraocular administrations of the VEGF neutralizing prodrug is at least 1 month.

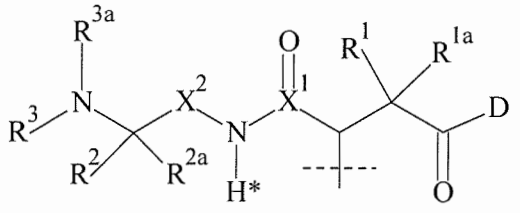
9. The pharmaceutical composition for use of any one of claims 1 to 8, wherein the VEGF neutralizing prodrug comprises in bound form a biologically active moiety selected from the group of drugs consisting of antisense RNA, antisense DNA, ribozymes or RNAi molecules targeting a VEGF nucleic acid; anti-VEGF aptamers, anti-VEGF

antibodies, anti-VEGF antibody fragments, DARPins and soluble VEGF receptor decoys that prevent binding of a VEGF to its cognate receptor; antisense, ribozymes, and RNAi molecules targeting a cognate VEGF receptor (VEGFR) nucleic acid; anti-VEGFR aptamers or anti-VEGFR antibodies that bind to a cognate VEGFR receptor; anti-VEGFR antibody fragments that bind to a cognate VEGFR receptor and VEGFR tyrosine kinase inhibitors.

10. The pharmaceutical composition for use of any one of claims 1 to 9, wherein the VEGF neutralizing prodrug comprises in bound form a biologically active moiety selected from the group consisting of ranibizumab, bevacizumab, pegaptanib, aflibercept, MP0112, KH902, ESBA1008, AL 39324, ALG-1001, and bevasiranib and/or fragments thereof.

11. The pharmaceutical composition for use of any one of claims 1 to 10, wherein the VEGF neutralizing prodrug comprises in bound form ranibizumab.

12. The pharmaceutical composition for use of any one of claims 1 to 11, wherein the the VEGF neutralizing prodrug comprises a moiety of formula (F-i):



(F-i),

wherein

D is ranibizumab;

the dashed line indicates attachment to the carrier or to the optional spacer moiety;

X is $C(R^4R^{4a})$; $N(R^4)$; O; $C(R^4R^{4a})$-$C(R^5R^{5a})$; $C(R^5R^{5a})$-$C(R^4R^{4a})$; $C(R^4R^{4a})$-$N(R^6)$; $N(R^6)$-$C(R^4R^{4a})$; $C(R^4R^{4a})$-O; or O-$C(R^4R^{4a})$;

X^1 is C; or S(O);

X^2 is $C(R^7, R^{7a})$; or $C(R^7, R^{7a})$-$C(R^8, R^{8a})$;

R^1, R^{1a}, R^2, R^{2a}, R^3, R^{3a}, R^4, R^{4a}, R^5, R^{5a}, R^6, R^7, R^{7a}, R^8, R^{8a} are independently selected from the group consisting of H; and C_{1-4} alkyl;

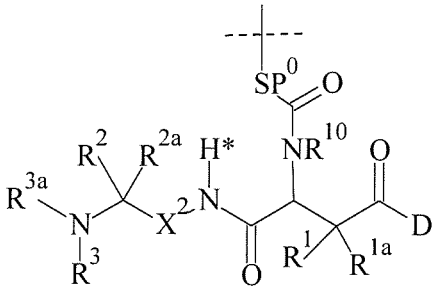
optionally, one or more of the pair(s) R^{1a}/R^{4a}, R^{1a}/R^{5a}, R^{4a}/R^{5a}, R^{4a}/R^{5a}, R^{7a}/R^{8a} form a chemical bond;

optionally, one or more of the pair(s) R^1/R^{1a}, R^2/R^{2a}, R^4/R^{4a}, R^5/R^{5a}, R^7/R^{7a}, R^8/R^{8a} are joined together with the atom to which they are attached to form a C_{3-7} cycloalkyl; or 4- to 7-membered heterocyclyl;

optionally, one or more of the pair(s) R^1/R^4, R^1/R^5, R^1/R^6, R^4/R^5, R^7/R^8, R^2/R^3 are joined together with the atoms to which they are attached to form a ring A;
optionally, R^3/R^{3a} are joined together with the nitrogen atom to which they are attached to form a 4- to 7-membered heterocycle;
A is selected from the group consisting of phenyl; naphthyl; indenyl; indanyl; tetralinyl; C_{3-10} cycloalkyl; 4- to 7-membered heterocyclyl; and 8- to 11-membered heterobicyclyl;
optionally, the moiety of formula (F-i) is further substituted, provided that the hydrogel marked with the asterisk in formula (F-i) is not replaced by a substituent and that R^3 and R^{3a} are independently of each other H or are connected to N through an SP^3-hybridized carbon atom.

13. The pharmaceutical composition for use of claims 12, wherein X^1 is C.

14. The pharmaceutical composition for use of claim 12 or 13, wherein the VEGF neutralizing prodrug comprises a moiety of formula (f-ii)

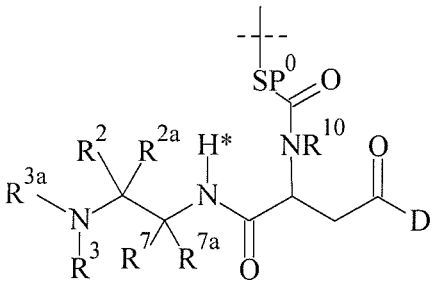


(F-ii),

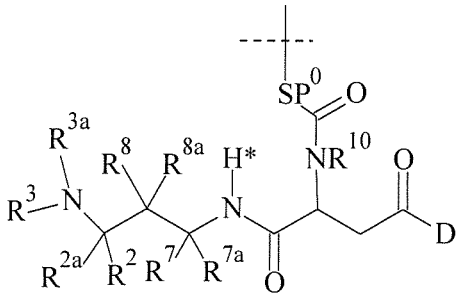
wherein
the dashed line indicates attachment to the carrier;
R^1, R^{1a}, R^2, R^{2a}, R^3, R^{3a}, X^2 and D are used as defined in claim 14;
R^{10} is selected from H and C_{1-6} alkyl;
SP^0 is a spacer moiety;
and wherein the moiety of formula (F-ii) is optionally further substituted, provided that the hydrogel marked with the asterisk in formula (F-ii) is not replaced by a substituent and that R^3 and R^{3a} are independently of each other H or are connected to N through an SP^3-hybridized carbon atom.

15. The pharmaceutical composition for use of any one of claims 12 to 14, wherein R^1 and R^{1a} are both H.

16. The pharmaceutical composition for use of any one of claims 12 to 15, wherein the VEGF neutralizing prodrug comprises a moiety of formula (F-iiia) or (F-iiib):



(F-iiia),



(F-iiib),

wherein

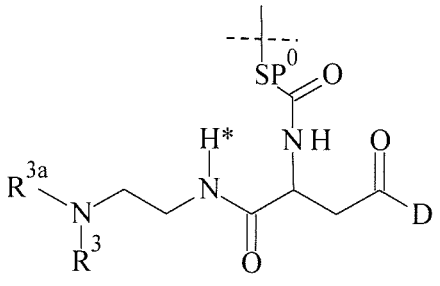
the dashed line indicates attachment to the carrier;

R^2, R^{2a}, R^3, R^{3a}, R^7, R^{7a}, R^8, R^{8a}, X^2 and D are used as defined in claim 14;

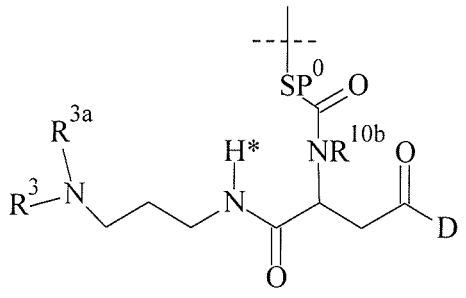
R^{10} and SP^0 are used as defined in claim 16;

and wherein the moiety of formula (F-iiia) or (F-iiib) is optionally further substituted, provided that the hydrogen marked with the asterisk in formula (F-iiia) and (F-iiib) is not replaced by a substituent and that R^3 and R^{3a} are independently of each other H or are connected to N through an SP^3-hybridized carbon atom.

17. The pharmaceutical composition for use of any one of claims 12 to 16, wherein the VEGF neutralizing prodrug comprises a moiety of formula (F-iva) or (F-ivb):



(F-iva),



(F-ivb),

wherein

the dashed line indicates attachment to the carrier;

R^3 and R^{3a} are used as defined in claim 14;

R^{10b} is C_{1-6} alkyl;

and wherein the moiety of formula (F-iva) or (F-ivb) is optionally further substituted, provided that the hydrogen marked with the asterisk is not replaced by a substituent and that R^3 and R^{3a} are independently of each other H or are connected to N through an SP^3-hybridized carbon atom.

18. The pharmaceutical composition for use of any one of claims 12 to 17, wherein R^3 is H and R^{3a} is methyl.

19. The pharmaceutical composition for use of any one of claims 12 to 17, wherein R^3 and R^{3a} of are both H.

20. The pharmaceutical composition for use of any one of claims 12 to 17, wherein R^3 is H and R^{3a} is methyl.

21. The pharmaceutical composition for use of any one of claims 1 to 20, wherein the ocular condition is a disease characterized by ocular neovascularization.

22. The pharmaceutical composition for use of claim 21, wherein the intraocular neovascularization is an ocular disease selected from the group consisting of optic disc neovascularization, iris neovascularization, retinal neovascularization, choroidal neovascularization, corneal neovascularization, vitreal neovascularization, glaucoma, pannus, pterygium, macular edema, macular degeneration, age-related macular degeneration, diabetic retinopathy, diabetic retinal ischemia, diabetic macular edema, vascular retinopathy, retinal degeneration, retrolental fibroplasias, retinoblastoma, retinopathy of prematurity of macular degeneration, corneal graft neovascularization, central retinal vein occlusion, pathological myopia, ocular tumors, uveitis, inflammatory diseases of the eye, and proliferative vitreoretinopathy.

23. The pharmaceutical composition for use of any one of claims 1 to 22, wherein the pharmaceutical composition further comprises one or more drug(s) in its/their free form selected from the group consisting of antisense RNA, antisense DNA, ribozymes or RNAi molecules targeting a VEGF nucleic acid; anti-VEGF aptamers, anti-VEGF antibodies, anti-VEGF antibody fragments, DARPins, anticalins, lipocalins, and soluble VEGF receptor decoys that prevent binding of a VEGF to its cognate receptor; antisense, ribozymes, and RNAi molecules targeting a cognate VEGF receptor (VEGFR) nucleic acid; anti-VEGFR aptamers or anti-VEGFR antibodies that bind to a cognate VEGFR receptor; anti-VEGFR antibody fragments that bind to a cognate VEGFR receptor and VEGFR tyrosine kinase inhibitors.

24. The pharmaceutical composition for use of any one of claims 1 to 23, wherein the pharmaceutical composition further comprises one or more prodrug(s), which one or more prodrug(s) comprise(s) in bound form a biologically active moiety selected from the group consisting of antisense RNA, antisense DNA, ribozymes or RNAi molecules targeting a VEGF nucleic acid; anti-VEGF aptamers, anti-VEGF antibodies, anti-VEGF antibody fragments, DARPins, anticalins, lipocalins, and soluble VEGF receptor decoys that prevent binding of a VEGF to its cognate receptor; antisense, ribozymes, and RNAi molecules targeting a cognate VEGF receptor (VEGFR) nucleic acid; anti-VEGFR aptamers or anti-VEGFR antibodies that bind to a cognate VEGFR receptor; anti-VEGFR antibody fragments that bind to a cognate VEGFR receptor and VEGFR tyrosine kinase inhibitors.