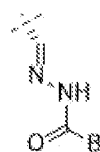


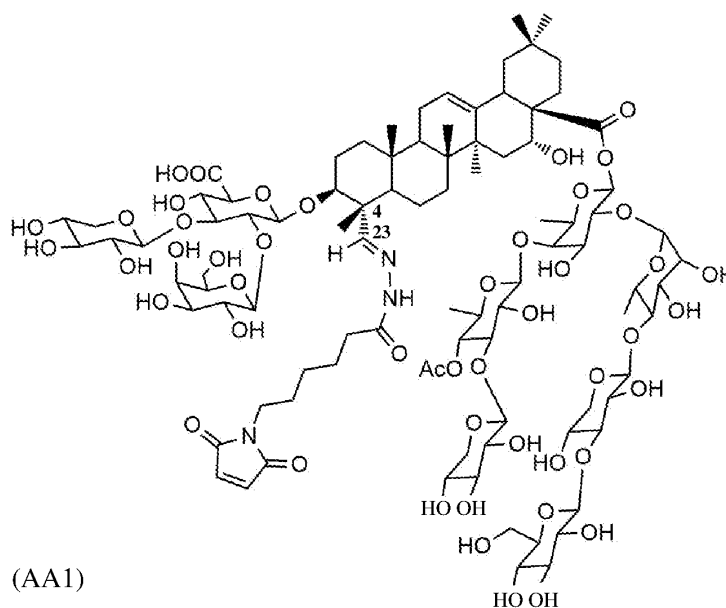
CLAIMS

1. Saponin derivative based on a saponin comprising a triterpene aglycone core structure and at least one of a first saccharide chain 'R1' and a second saccharide chain 'R2' linked to the aglycone core structure, wherein the saponin derivative comprises an aglycone core structure comprising an aldehyde functional group which has been derivatised, wherein the aldehyde functional group is transformed to a hydrazone functional group according to formula (A)

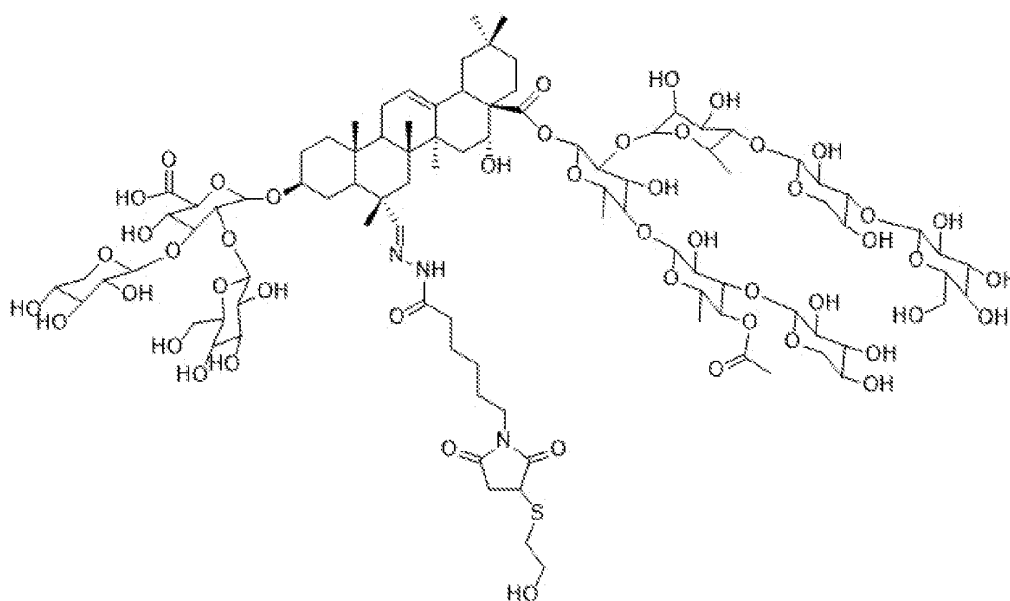


(A),

wherein B is H or B is a LINKER A, with the proviso that the saponin derivative is not the saponin derivative according to formula (AA1) and not the saponin derivative according to formula (AA2):



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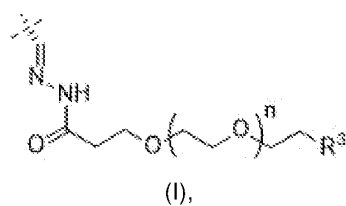
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(AA2),

or

wherein the aldehyde functional group is transformed to a hydrazone functional group
 according to formula (I)

10

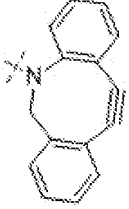
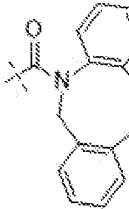
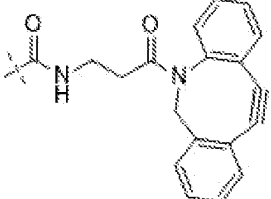
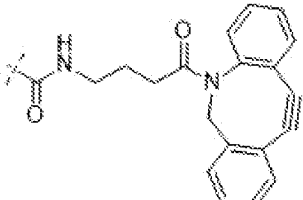


15 wherein n is an integer selected from 0-15,

R^3 is azide or R^3 is OH, or

R^3 is a cyclooctyne moiety selected from the group consisting of cyclooctyne moieties (II)a-d

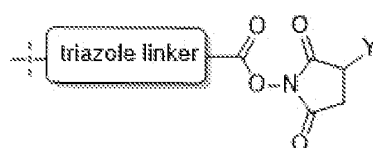
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(II)a	
(II)b	
(II)c	
(II)d	

or,

R³ is a linker according to formula (III):

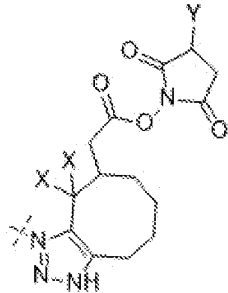
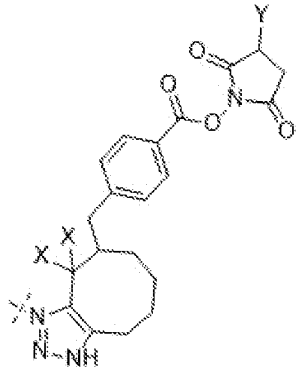
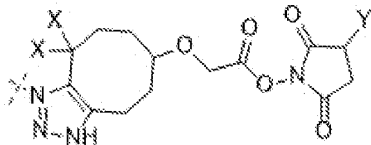
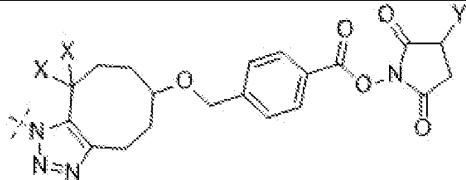
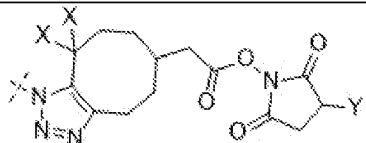
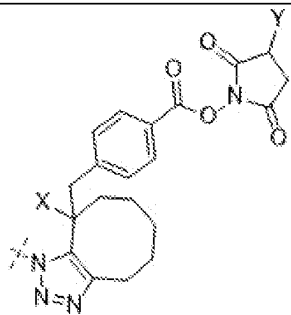
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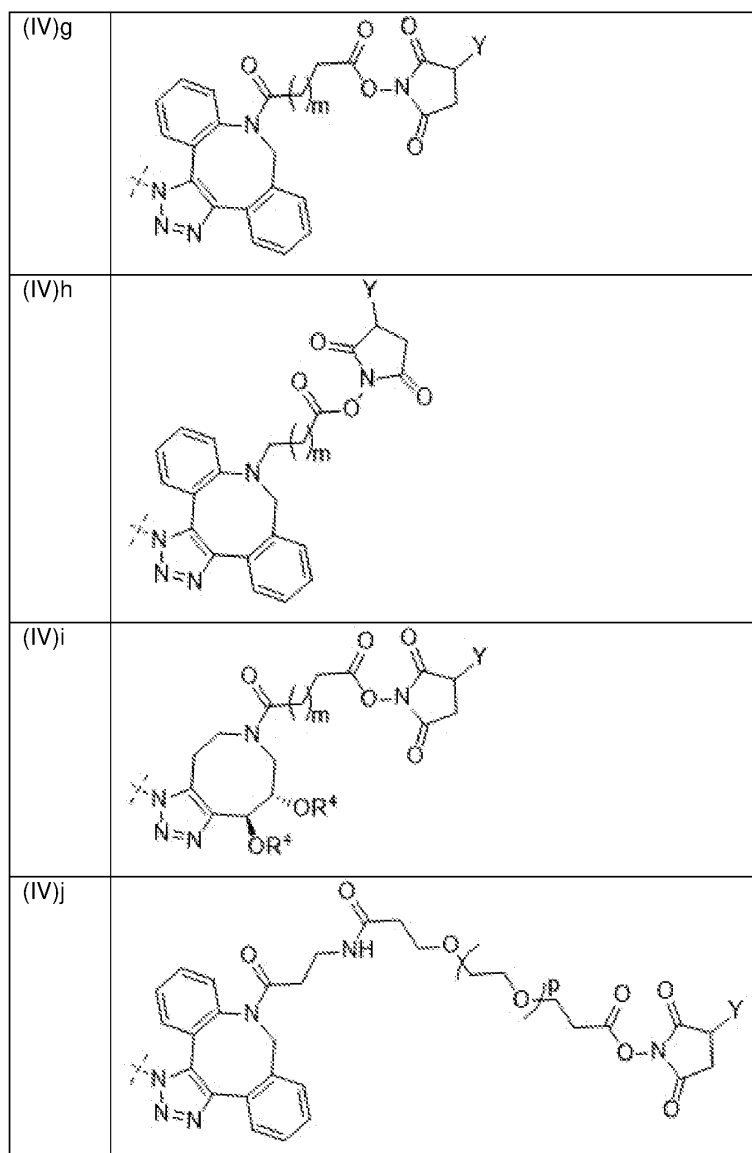
(III),

wherein Y is H or SO₂ONa,

10 and the linker according to formula (III) is selected from the group consisting of linkers (IV)a-j:

(IV)a	
(IV)b	
(IV)c	
(IV)d	
(IV)e	
(IV)f	

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wherein X is H or F, preferably F;

m is 1 or 2;

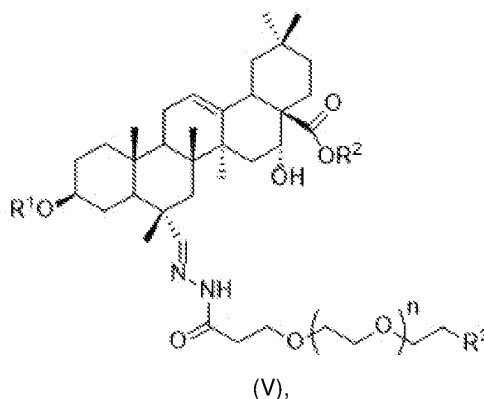
p is an integer selected from 0-5, preferably 1-4, more preferably 2-3; and

5 R⁴ is a C1-C3 alkyl chain, preferably a C1 alkyl chain.

2. Saponin derivative according to claim 1, wherein the saponin on which the saponin derivative is based is a mono-desmosidic or bi-desmosidic triterpene saponin belonging to the type of a 12,13-dehydrooleanane with the aldehyde group in position C-23 and optionally comprising a glucuronic acid group in a carbohydrate substituent at the C-3β-OH group of the saponin,
- 10 preferably a bi-desmosidic triterpene saponin belonging to the type of a 12,13-dehydrooleanane

with the aldehyde group in position C-23 and comprising a glucuronic acid group in a carbohydrate substituent at the C-3 β -OH group of the saponin.

3. Saponin derivative according to claim 1 or 2, wherein the saponin derivative is according to
5 formula (V)



wherein R¹ and R² are independently selected from hydrogen, a monosaccharide, a linear
10 oligosaccharide and a branched oligosaccharide and R³ is as defined in claim 1.

4. Saponin derivative according to any one of the claims 1-3, wherein n is an integer selected from
1-12, preferably 2-9, more preferably 3-6, most preferably n is 3.
5. Saponin derivative according to any one of the claims 1-4, wherein
15 R¹ is selected from:
- H,
 - GlcA-,
 - Glc-,
 - 20 Gal-,
 - Rha-(1→2)-Ara-,
 - Gal-(1→2)-[Xyl-(1→3)]-GlcA-,
 - Glc-(1→2)-[Glc-(1→4)]-GlcA-,
 - Glc-(1→2)-Ara-(1→3)-[Gal-(1→2)]-GlcA-,
 - 25 Xyl-(1→2)-Ara-(1→3)-[Gal-(1→2)]-GlcA-,
 - Glc-(1→3)-Gal-(1→2)-[Xyl-(1→3)]-Glc-(1→4)-Gal-,
 - Rha-(1→2)-Gal-(1→3)-[Glc-(1→2)]-GlcA-,
 - Ara-(1→4)-Rha-(1→2)-Glc-(1→2)-Rha-(1→2)-GlcA-,
 - Ara-(1→4)-Fuc-(1→2)-Glc-(1→2)-Rha-(1→2)-GlcA-,
 - 30 Ara-(1→4)-Rha-(1→2)-Gal-(1→2)-Rha-(1→2)-GlcA-,
 - Ara-(1→4)-Fuc-(1→2)-Gal-(1→2)-Rha-(1→2)-GlcA-,
 - Ara-(1→4)-Rha-(1→2)-Glc-(1→2)-Fuc-(1→2)-GlcA-,

- Ara-(1→4)-Fuc-(1→2)-Glc-(1→2)-Fuc-(1→2)-GlcA-,
 Ara-(1→4)-Rha-(1→2)-Gal-(1→2)-Fuc-(1→2)-GlcA-,
 Ara-(1→4)-Fuc-(1→2)-Gal-(1→2)-Fuc-(1→2)-GlcA-,
 Xyl-(1→4)-Rha-(1→2)-Glc-(1→2)-Rha-(1→2)-GlcA-,
 5 Xyl-(1→4)-Fuc-(1→2)-Glc-(1→2)-Rha-(1→2)-GlcA-,
 Xyl-(1→4)-Rha-(1→2)-Gal-(1→2)-Rha-(1→2)-GlcA-,
 Xyl-(1→4)-Fuc-(1→2)-Gal-(1→2)-Rha-(1→2)-GlcA-,
 Xyl-(1→4)-Rha-(1→2)-Glc-(1→2)-Fuc-(1→2)-GlcA-,
 Xyl-(1→4)-Fuc-(1→2)-Glc-(1→2)-Fuc-(1→2)-GlcA-,
 10 Xyl-(1→4)-Rha-(1→2)-Gal-(1→2)-Fuc-(1→2)-GlcA-,
 Xyl-(1→4)-Fuc-(1→2)-Gal-(1→2)-Fuc-(1→2)-GlcA-, and
 derivatives thereof, and
 R² is selected from:
 H,
 15 Glc-,
 Gal-,
 Rha-(1→2)-[Xyl-(1→4)]-Rha-,
 Rha-(1→2)-[Ara-(1→3)-Xyl-(1→4)]-Rha-,
 Ara-,
 20 Xyl-,
 Xyl-(1→4)-Rha-(1→2)-[R¹-(→4)]-Fuc- wherein R¹ is 4E-Methoxycinnamic acid,
 Xyl-(1→4)-Rha-(1→2)-[R²-(→4)]-Fuc- wherein R² is 4Z-Methoxycinnamic acid,
 Xyl-(1→4)-[Gal-(1→3)]-Rha-(1→2)-4-OAc-Fuc-,
 Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-3,4-di-OAc-Fuc-,
 25 Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R⁵-(→4)]-3-OAc-Fuc- wherein R⁵ is 4E-Methoxycinnamic acid,
 Glc-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-4-OAc-Fuc-,
 Glc-(1→3)-Xyl-(1→4)-Rha-(1→2)-4-OAc-Fuc-,
 (Ara- or Xyl)-(1→3)-(Ara- or Xyl)-(1→4)-(Rha- or Fuc)-(1→2)-[4-OAc-(Rha- or Fuc)-(1→4)]-(Rha-
 or Fuc-),
 30 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Qui-(1→4)]-Fuc-,
 Api-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-Fuc-,
 Xyl-(1→4)-[Gal-(1→3)]-Rha-(1→2)-Fuc-,
 Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-Fuc-,
 Ara/Xyl-(1→4)-Rha/Fuc-(1→4)-[Glc/Gal-(1→2)]-Fuc-,
 35 Api-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R⁶-(→4)]-Fuc- wherein R⁶ is 5-O-[5-O-Ara/Api-3,5-
 dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid,
 Api-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R⁷-(→4)]-Fuc- wherein R⁷ is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-
 methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid,
 Api-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Rha-(1→3)]-4-OAc-Fuc-,
 40 Api-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[Rha-(1→3)]-4-OAc-Fuc-,

- 6-OAc-Glc-(1→3)-Xyl-(1→4)-Rha-(1→2)-[3-OAc-Rha-(1→3)]-Fuc-,
 Glc-(1→3)-Xyl-(1→4)-Rha-(1→2)-[3-OAc-Rha-(1→3)]-Fuc-,
 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Qui-(1→4)]-Fuc-,
 Glc-(1→3)-[Xyl-(1→4)]-Rha-(1→2)-[Qui-(1→4)]-Fuc-,
 5 Glc-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Xyl-(1→3)-4-OAc-Qui-(1→4)]-Fuc-,
 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[3,4-di-OAc-Qui-(1→4)]-Fuc-,
 Glc-(1→3)-[Xyl-(1→4)]-Rha-(1→2)-Fuc-,
 6-OAc-Glc-(1→3)-[Xyl-(1→4)]-Rha-(1→2)-Fuc-,
 Glc-(1→3)-[Xyl-(1→3)-Xyl-(1→4)]-Rha-(1→2)-Fuc-,
 10 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Xyl-(1→3)-4-OAc-Qui-(1→4)]-Fuc-,
 Api/Xyl-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[Rha-(1→3)]-4OAc-Fuc-,
 Api-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[Rha-(1→3)]-4OAc-Fuc-,
 Api/Xyl-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R⁸-(→4)]-Fuc- wherein R⁸ is 5-O-[5-O-Rha-(1→2)-Ara/Api-3,5-dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid,
 15 Api/Xyl-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R⁹-(→4)]-Fuc- wherein R⁹ is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid,
 Api/Xyl-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R¹⁰-(→4)]-Fuc- wherein R¹⁰ is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid,
 Api-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R¹¹-(→4)]-Fuc- wherein R¹¹ is 5-O-[5-O-Ara/Api-3,5-dihydroxy-
 20 6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid,
 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R¹²-(→4)]-Fuc- wherein R¹² is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid,
 Api-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R¹³-(→3)]-Fuc- wherein R¹³ is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid,
 25 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R¹⁴-(→3)]-Fuc- wherein R¹⁴ is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid
 Glc-(1→3)-[Glc-(1→6)]-Gal-, and
 derivatives thereof.
- 30 6. Saponin derivative according to any one of the claims 1-5, wherein
 R¹ is selected from:
 Gal-(1→2)-[Xyl-(1→3)]-GlcA-; and
 R² is selected from:
 Glc-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Xyl-(1→3)-4-OAc-Qui-(1→4)]-Fuc-,
 35 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[3,4-di-OAc-Qui-(1→4)]-Fuc-,
 Api-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R¹¹-(→4)]-Fuc- wherein R¹¹ is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid,
 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R¹²-(→4)]-Fuc- wherein R¹² is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid,

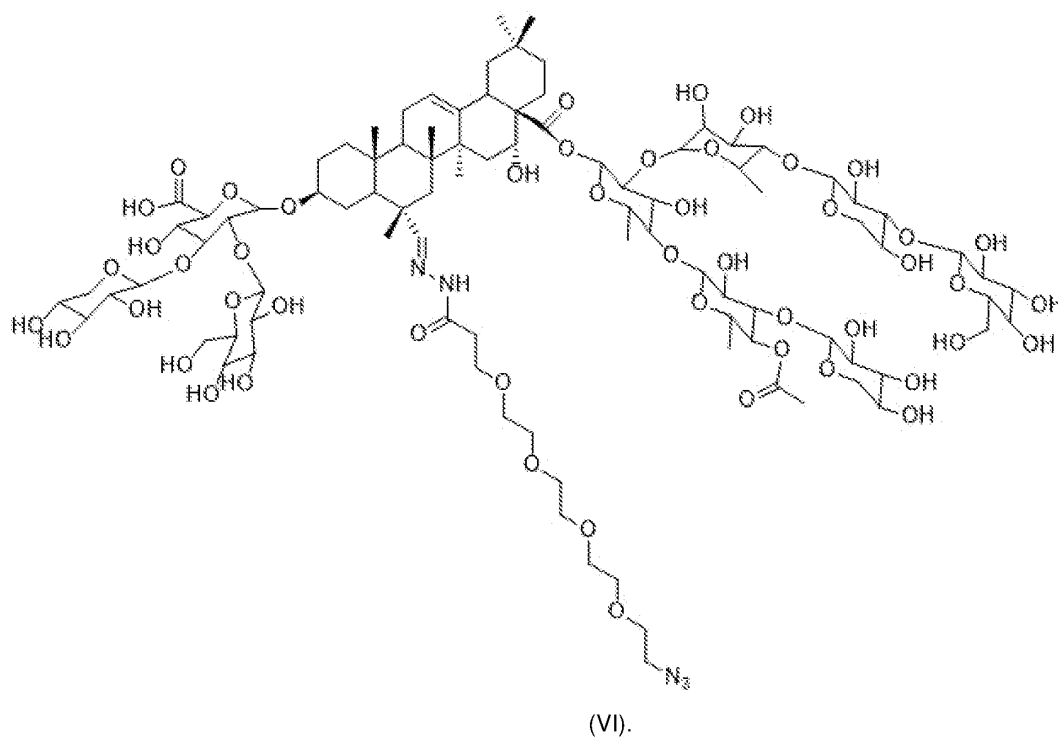
- Api-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R¹³-(→3)]-Fuc- wherein R¹³ is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid, and
 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R¹⁴-(→3)]-Fuc- wherein R¹⁴ is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid,
- 5 preferably R¹ is Gal-(1→2)-[Xyl-(1→3)]-GlcA- and R² is Glc-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Xyl-(1→3)-4-OAc-Qui-(1→4)]-Fuc-.
7. Saponin derivative according to any one of the claims 1-6, wherein the saponin derivative is a derivative of a saponin selected from the group of saponins consisting of: *Quillaja* bark saponin,
- 10 dipsacocide B, saikosaponin A, saikosaponin D, macranthoidin A, esculentoside A, phytolaccagenin, aescinate, AS6.2, NP-005236, AMA-1, AMR, alpha-Hederin, NP-012672, NP-017777, NP-017778, NP-017774, NP-018110, NP-017772, NP-018109, NP-017888, NP-017889, NP-018108, SA1641, AE X55, NP-017674, NP-017810, AG1, NP-003881, NP-017676, NP-017677, NP-017706, NP-017705, NP-017773, NP-017775, SA1657, AG2,
- 15 SO1861, GE1741, SO1542, SO1584, SO1658, SO1674, SO1832, SO1904, SO1862, QS-7, QS1861, QS-7 api, QS1862, QS-17, QS-18, QS-21 A-apio, QS-21 A-xylo, QS-21 B-apio, QS-21 B-xylo, beta-Aescin, Aescin Ia, Teaseed saponin I, Teaseedsaponin J, Assamsaponin F, Digitonin, Primula acid 1 and AS64R, preferably the saponin derivative is selected from the group consisting of a QS-21 derivative, an SO1861 derivative, an SA1641 derivative and a
- 20 GE1741 derivative, more preferably the saponin derivative is selected from the group consisting of a QS-21 derivative and an SO1861 derivative, most preferably the saponin derivative is an SO1861 derivative.
8. Saponin derivative according to any one of the claims 1-7, wherein the saponin derivative is a
- 25 compound according to formula (VI)

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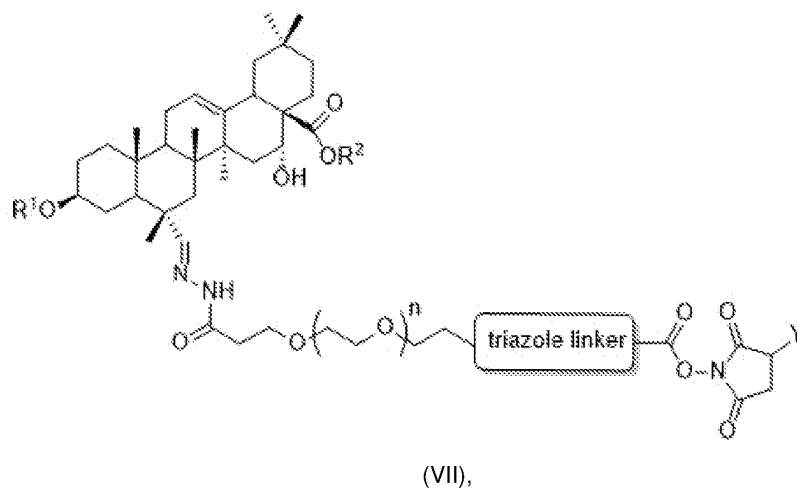
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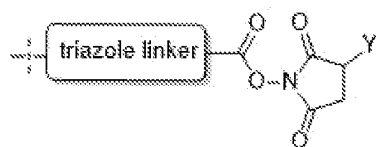


- 5 9. Saponin derivative according to any one of the claims 1-7, wherein the saponin derivative is according to formula (VII)



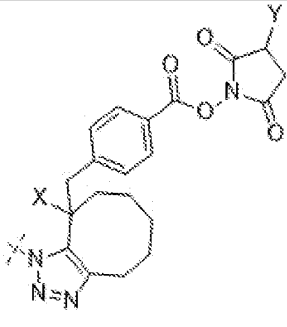
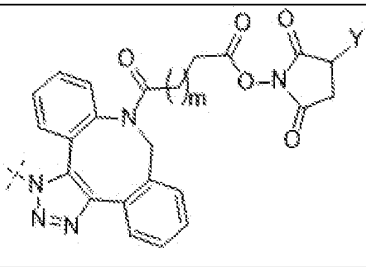
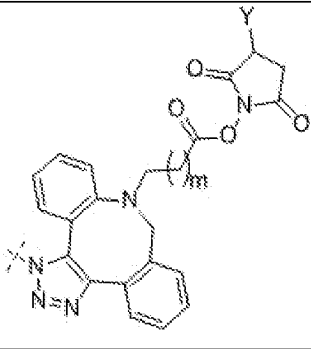
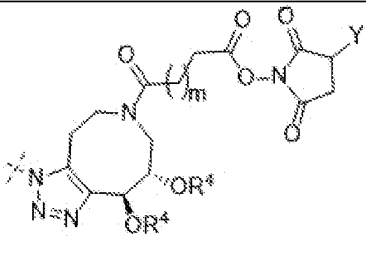
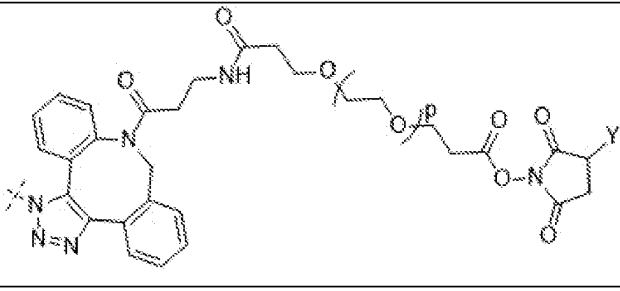
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wherein R^1 and R^2 are independently selected from hydrogen, a monosaccharide, a linear oligosaccharide and a branched oligosaccharide of claim 5 or 6,
 n is an integer selected from 0-14, preferably n is 3,
 $Y = H$ or SO_2ONa ,



the linker (formula (III)) is selected from the group consisting of linkers (IV)a-j:

(IV)a	
(IV)b	
(IV)c	
(IV)d	
(IV)e	

(IV)f	
(IV)g	
(IV)h	
(IV)i	
(IV)j	

wherein X = H or F, preferably F;

m is 1 or 2;

p is an integer selected from 0-5, preferably 1-4, more preferably 2-3; and

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R⁴ is a C1-C3 alkyl chain, preferably a C1 alkyl chain.

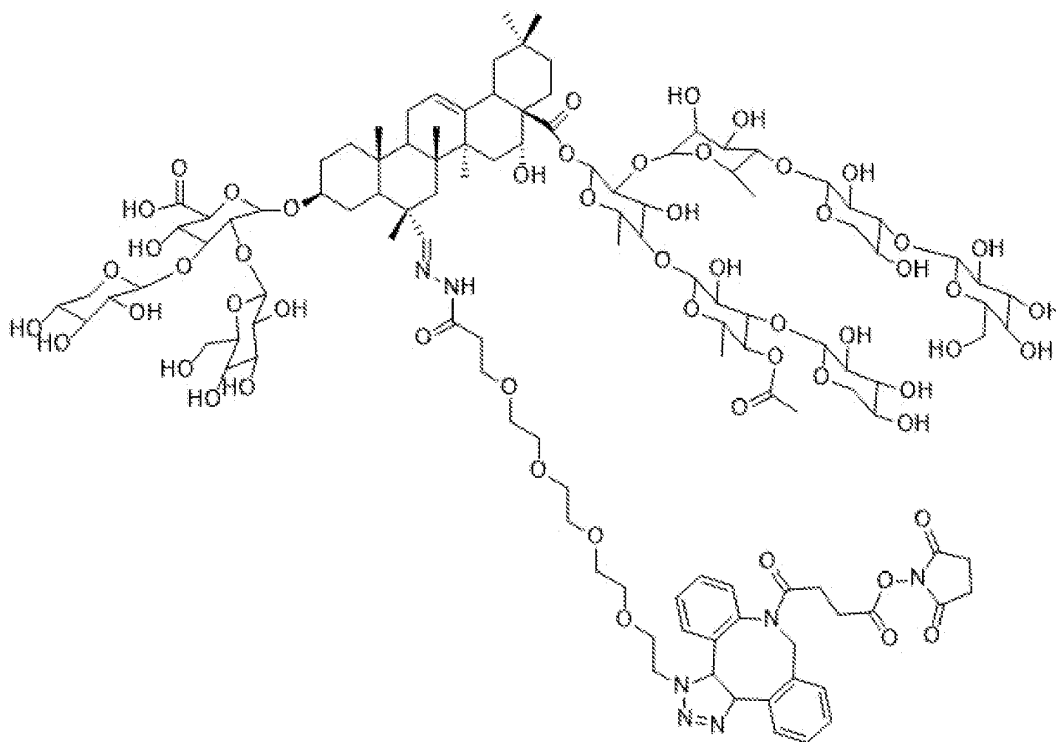
10. Saponin derivative according to any one of the claims 1-7 or 9, wherein Y = H.

5 11. Saponin derivative according to any one of claims 1-7, 9 or 10, wherein the linker is selected from the group consisting of linkers (IV)g-(IV)j, preferably the linker is linker (IV)g or (IV)h, more preferably the linker is linker (IV)g.

12. Saponin derivative according to any one of claims 1-7 or 9-11, wherein m = 1.

10

13. Saponin derivative according to any one of claims 1-7 or 9-12, wherein the saponin derivative is a compound according to formula (VIII)



15

(VIII).

14. First pharmaceutical composition comprising the saponin derivative according to any one of claims 1-13 and optionally a pharmaceutically acceptable excipient and/or diluent.

20 15. First pharmaceutical combination comprising:

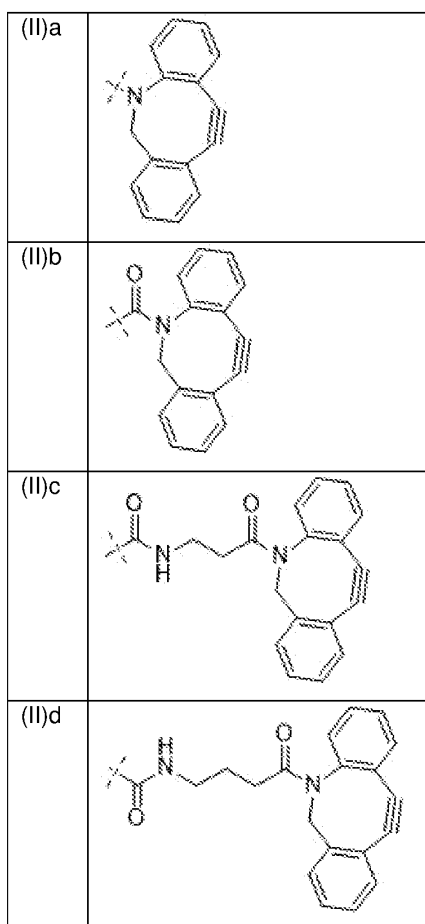
(a) the first pharmaceutical composition of claim 14; and

- (b) a second pharmaceutical composition comprising any one or more of: a conjugate of a cell-surface molecule binding-molecule and an effector moiety, an antibody-effector moiety conjugate, a receptor-ligand – effector moiety conjugate, an antibody-toxin conjugate, a receptor-ligand – toxin conjugate, an antibody-drug conjugate, a receptor-ligand – drug conjugate, an antibody-oligonucleotide conjugate and a receptor-ligand – oligonucleotide conjugate, and optionally comprising a pharmaceutically acceptable excipient and/or diluent.
16. Third pharmaceutical composition comprising the saponin derivative of any one of the claims 1-13 and further comprising any one or more of: a conjugate of a cell-surface molecule binding-molecule and an effector moiety, such as an antibody-effector moiety conjugate, a receptor-ligand – effector moiety conjugate, an antibody-toxin conjugate, a receptor-ligand – toxin conjugate, an antibody-drug conjugate, a receptor-ligand – drug conjugate, an antibody-nucleic acid conjugate and a receptor-ligand – nucleic acid conjugate, and optionally comprising a pharmaceutically acceptable excipient and/or diluent.
17. First pharmaceutical combination of claim 15 or the third pharmaceutical composition of claim 16, wherein the second pharmaceutical composition or the third pharmaceutical composition comprises any one or more of an antibody-toxin conjugate, a receptor-ligand – toxin conjugate, an antibody-oligonucleotide conjugate or a receptor-ligand – oligonucleotide conjugate, wherein preferably the toxin is a protein toxin.
18. First pharmaceutical combination of claim 15 or 17 or the third pharmaceutical composition of claim 16 or 17, wherein the saponin derivative is the saponin derivative according to claim 13.
19. First pharmaceutical composition of claim 14, first pharmaceutical combination of any one of the claims 15, 17 and 18 or the third pharmaceutical composition of any one of the claims 16-18, for use as a medicament.
20. First pharmaceutical composition of claim 14, first pharmaceutical combination of any one of the claims 15, 17 and 18 or the third pharmaceutical composition of any one of the claims 16-18, for use in the treatment or prophylaxis of a cancer or an auto-immune disease.
21. *In vitro* or *ex vivo* method for transferring a molecule from outside a cell to inside said cell, preferably into the cytosol of said cell, comprising the steps of:
- a) providing a cell;
 - b) providing the molecule for transferring from outside the cell into the cell provided in step a);
 - c) providing a saponin derivative according to any one of the claims 1-13;
 - d) contacting the cell of step a) *in vitro* or *ex vivo* with the molecule of step b) and the saponin

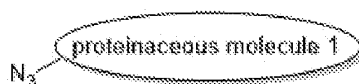
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derivative of step c), therewith establishing the transfer of the molecule from outside the cell into said cell.

22. Saponin conjugate based on a saponin derivative according to any one of the claims 1-7,
 5 wherein R^3 is a cyclooctyne moiety selected from the group consisting of cyclooctyne moieties (II)a-d,



- and wherein the cyclooctyne moiety is transformed to a triazole functional group through reaction
 10 with a first proteinaceous molecule ('proteinaceous molecule 1') comprising an azide functional group according to formula (IX)



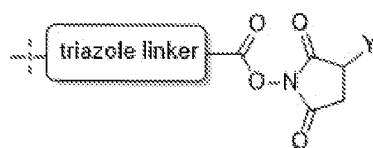
(IX);

15

or

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wherein R³ is a linker according to formula (III):



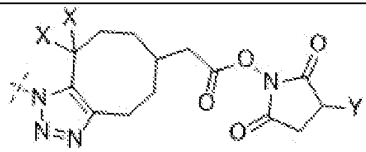
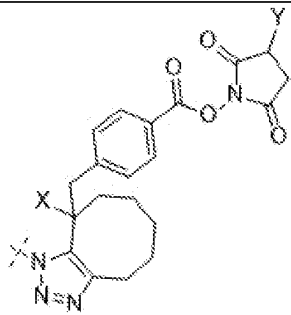
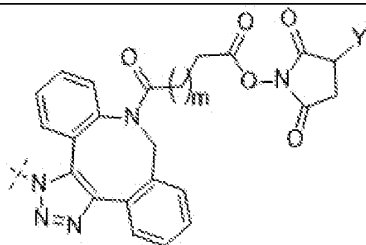
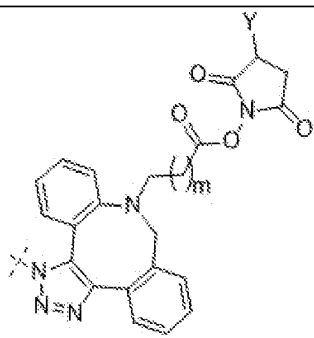
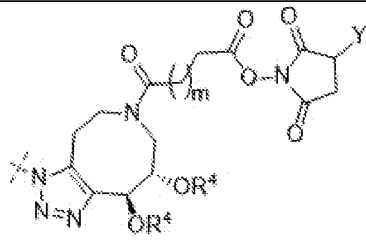
(III),

5

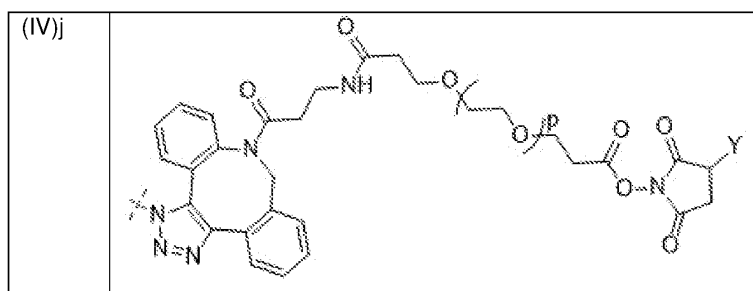
wherein Y is H or SO₂ONa, preferably H,

the linker according to formula (III) is selected from the group consisting of linkers (IV)a-j:

(IV)a	
(IV)b	
(IV)c	
(IV)d	

(IV)e	
(IV)f	
(IV)g	
(IV)h	
(IV)i	

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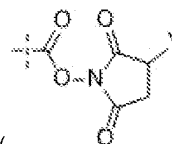


wherein X is H or F, preferably F;

m is 1 or 2;

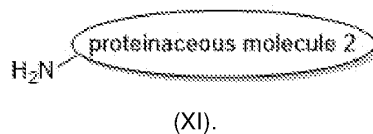
p is an integer selected from 0-5, preferably 1-4, more preferably 2-3;

- 5 R⁴ is a C1-C3 alkyl chain, preferably a C1 alkyl chain; and



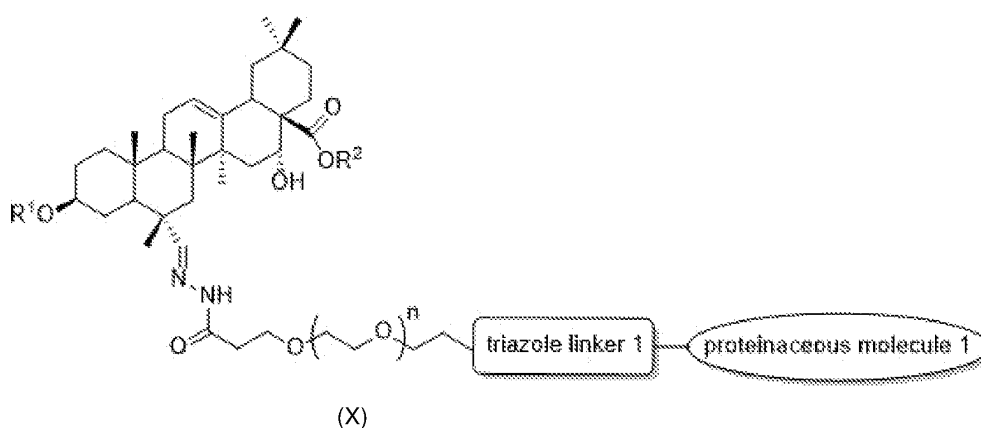
wherein the *N*-hydroxy succinimide active ester functional group () is transformed to an amide functional group (-C(O)-N(H)-) through reaction with a second proteinaceous molecule ('proteinaceous molecule 2') comprising an amine functional group according to formula (XI)

10



23. Saponin conjugate according to claim 22, wherein the saponin conjugate is according to formula (X),

15



- 20 wherein R¹ and R² are independently selected from hydrogen, a monosaccharide, a linear oligosaccharide and a branched oligosaccharide,

n is an integer selected from 0-15,

the triazole linker 1 is selected from the group of triazole linkers (XI)a-d,

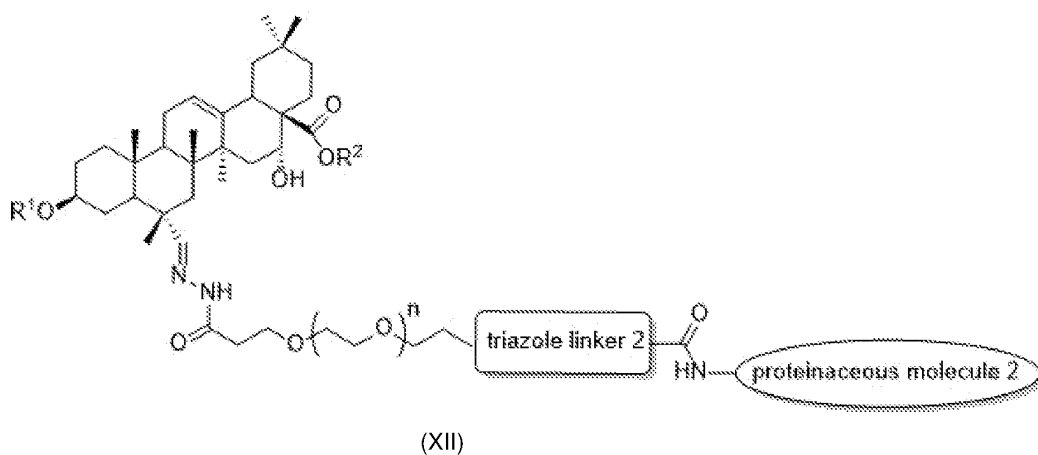
(XI)a	
(XI)b	
(XI)c	
(XI)d	

5 or

wherein the saponin conjugate is according to formula (XII),

10

15



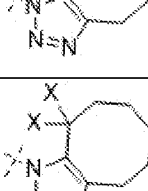
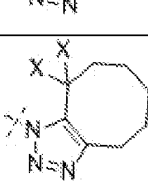
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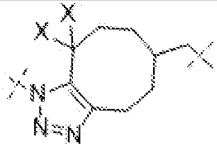
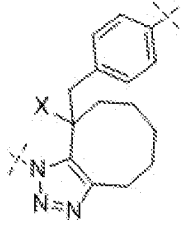
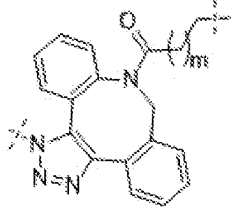
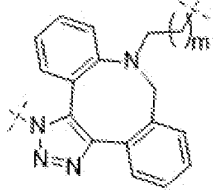
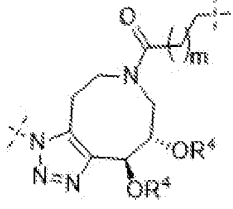
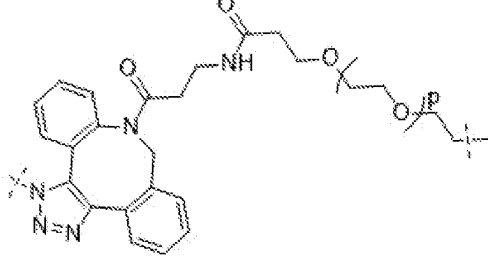
wherein R¹ and R² are independently selected from hydrogen, a monosaccharide, a linear oligosaccharide and a branched oligosaccharide of claim 5 or 6,

n is an integer selected from 0-15,

the triazole linker 2 is selected from the group consisting of triazole linkers (XIII)a-j

10

(XIII)a	
(XIII)b	
(XIII)c	
(XIII)d	

(XIII)e	
(XIII)f	
(XIII)g	
(XIII)h	
(XIII)i	
(XIII)j	

wherein X is H or F, preferably F;

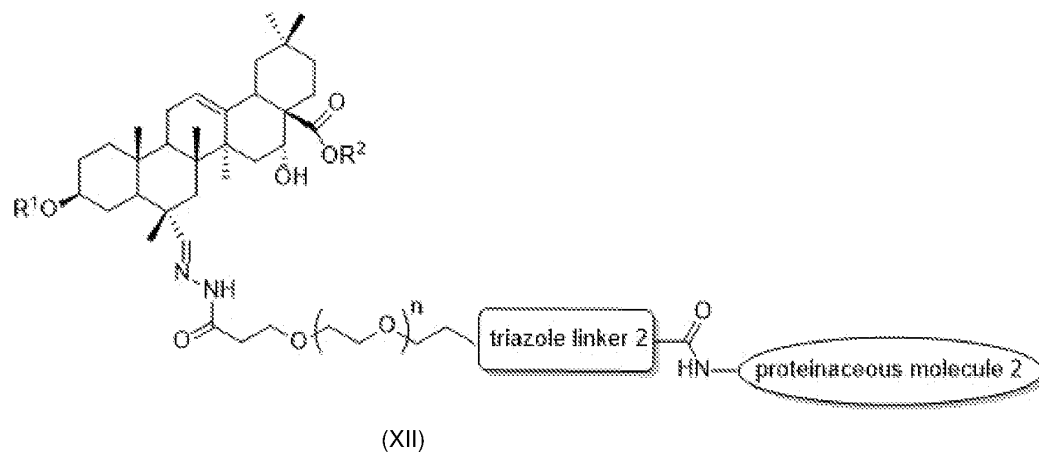
m is 1 or 2;

p is an integer selected from 0-5, preferably 1-4, more preferably 2-3; and

5 R⁴ is a C1-C3 alkyl chain, preferably a C1 alkyl chain.

24. Saponin conjugate according to claim 22 or 23, wherein n is an integer selected from 1-14, preferably 2-12, more preferably 3-9.

25. Saponin conjugate according to any one of the claims 22-24, wherein the conjugate is according to formula (XII)

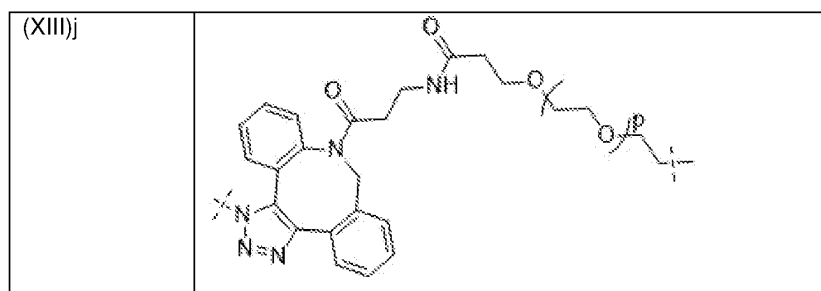


wherein R¹ and R² are independently selected from hydrogen, a monosaccharide, a linear oligosaccharide and a branched oligosaccharide of claim 5 or 6,
n is an integer selected from 0-14, preferably n is 3,
the triazole linker 2 is selected from the group consisting of triazole linkers (XIII)a-j

(XIII)a	
(XIII)b	

(XIII)c	
(XIII)d	
(XIII)e	
(XIII)f	
(XIII)g	
(XIII)h	
(XIII)i	

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wherein X is H or F, preferably F;

m is 1 or 2;

p is an integer selected from 0-5, preferably 1-4, more preferably 2-3; and

5 R⁴ is a C1-C3 alkyl chain, preferably a C1 alkyl chain.

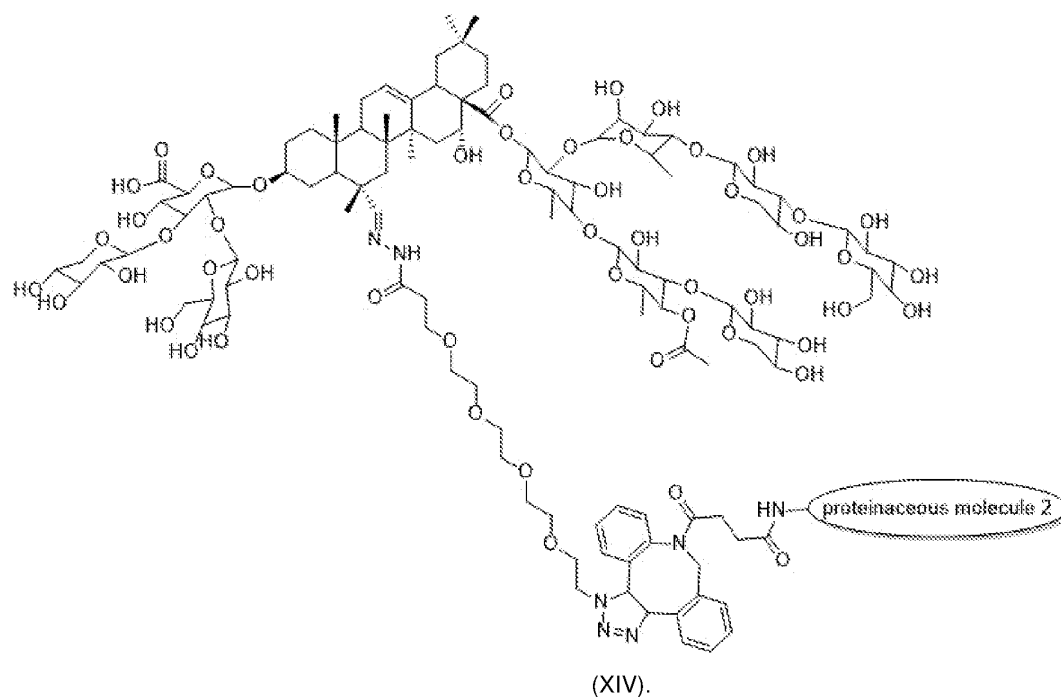
26. Saponin conjugate according to any one of claims 22-25, wherein the triazole linker 2 is selected from the group consisting of linkers (XIII)g-(XIII)j, preferably the linker is linker (XIII)g or (XIII)h, more preferably the linker is linker (XIII)g.

10

27. Saponin conjugate according to any one of claims 22-26, wherein m = 1.

28. Saponin conjugate according to any one of the claims 22-27, wherein the saponin conjugate is a compound according to formula (XIV)

15



29. Saponin conjugate according to any one of the claims 22-28, wherein the proteinaceous molecule 1 and the proteinaceous molecule 2 comprise a same first binding site for binding to a first epitope of a first cell-surface molecule, or wherein the proteinaceous molecule 1 comprises the first binding site for binding to a first epitope of a first cell-surface molecule and the proteinaceous molecule 2 comprises a second binding site for binding to a second epitope of a second cell-surface molecule, wherein the first binding site and the second binding site are different, and optionally wherein the first cell surface molecule and the second cell surface molecule are present on the same cell, preferably the first cell surface molecule and the second cell surface molecule are present on the same cell.
30. Saponin conjugate according to any one of the claims 22-29, wherein the first binding site of the proteinaceous molecule 1 and the proteinaceous molecule 2 and, if present, the second binding site of the proteinaceous molecule 2 is selected from any one or more of: an amino acid, a peptide, a protein, an antibody or a derivative or fragment thereof such as a Fab or an scFv, a single-domain antibody (sdAb), a ligand.
31. Saponin conjugate according to claim 29 or 30, wherein the first binding site of the proteinaceous molecule 1 and the proteinaceous molecule 2 and, if present, the second binding site of the proteinaceous molecule 2 is/are or comprise(s) a single-domain antibody (sdAb), preferably V_H domain derived from a heavy chain of an antibody, preferably of immunoglobulin G origin, preferably of human origin, a V_L domain derived from a light chain of an antibody, preferably of immunoglobulin G origin, preferably of human origin, a V_{HH} domain such as derived from a heavy-chain only antibody (HCAb) such as from *Camelidae* origin or *Ig-NAR* origin such as a variable heavy chain new antigen receptor (VNAR) domain, preferably the HCAb is from *Camelidae* origin, preferably the sdAb is a V_{HH} domain derived from an HCAb from *Camelidae* origin (camelid V_H) such as derived from an HCAb from camel, lama, alpaca, dromedary, vicuna, guanaco and Bactrian camel.
32. Saponin conjugate according to any one of the claims 29-31, wherein the first epitope of the first cell-surface molecule to which the first binding site can bind is a tumor-cell specific first epitope of a first tumor-cell surface molecule, more preferably a tumor-cell specific first epitope of a first tumor-cell surface receptor specifically present on a tumor cell, and wherein the second epitope of the second cell-surface molecule is a tumor-cell specific second epitope of a second tumor-cell surface molecule, more preferably a tumor-cell specific second epitope of a second tumor-cell surface receptor specifically present on a tumor cell, wherein the first cell-surface molecule and the second cell-surface molecule are present on the same cell.
33. Saponin derivative according to any one of the claims 1-13 or saponin conjugate according to any of the claims 22-32, wherein the hydrazone functional group ($=N-N(H)-C(O)-$) is hydrolysable under acidic conditions, preferably at pH 4.0 – 6.5, such that the aldehyde group

of the saponin on which the saponin derivative is based is formed upon cleavage of the hydrazone functional group.

34. Saponin derivative according to any one of the claims 1-13 or saponin conjugate according to any of the claims 22-33, wherein the hydrazone functional group is hydrolysable *in vivo* under acidic conditions as present in endosomes and/or lysosomes of mammalian cells, preferably human cells, preferably at pH 4.0 – 6.5, and more preferably at pH $\leq$ 5.5, such that the aldehyde group of the saponin on which the saponin derivative is based is formed upon hydrolysis of the hydrazone functional group.
35. Second pharmaceutical combination, comprising:
- (a) a fourth pharmaceutical composition comprising the saponin conjugate of any one of the claims 29-34 and optionally a pharmaceutically acceptable excipient and/or diluent; and
 - (b) a fifth pharmaceutical composition comprising a conjugate comprising a cell-surface molecule binding-molecule, such as a third proteinaceous molecule ('proteinaceous molecule 3'), and an effector moiety, wherein the proteinaceous molecule 3 is the same or different from the proteinaceous molecule 1 and the proteinaceous molecule 2 present in the saponin conjugate, the proteinaceous molecule 3 comprising a third binding site for binding to a third epitope of a third cell-surface molecule, wherein the third cell-surface molecule, if different from the first cell surface molecule and/or the second cell surface molecule, is present on the same cell as the first cell surface molecule and the second cell surface molecule,
- the fifth pharmaceutical composition optionally further comprising a pharmaceutically acceptable excipient and/or diluent.
36. Second pharmaceutical combination of claim 35, comprising:
- (a) the fourth pharmaceutical composition of claim 35 comprising the saponin conjugate of any one of the claims 29-34, wherein the first epitope on the first cell-surface molecule is a tumor-cell specific first epitope on a first tumor cell-specific surface molecule, preferably a tumor-cell specific first epitope on a first cell-surface receptor specifically present at a tumor cell; and
 - (b) the fifth pharmaceutical composition of claim 35, wherein the third cell-surface molecule is a third tumor cell-specific surface molecule which is the same or different from the first tumor cell-specific surface molecule, preferably a third cell-surface receptor specifically present at a tumor cell which is the same or different from the first cell-surface receptor specifically present at said tumor cell, and wherein the third epitope is a tumor-cell specific third epitope, wherein the first epitope and the third epitope, which is the same as or different from the first epitope, are exposed at the same cell.
37. Third pharmaceutical combination, comprising:

- 5 (a) the fourth pharmaceutical composition of claim 35 or 36 comprising the saponin conjugate according to of any one of the claims 29-34 which comprises the first binding site for binding to the first epitope on the first cell-surface molecule, the fourth pharmaceutical composition optionally further comprising a pharmaceutically acceptable excipient and/or diluent; and
- 10 (b) a sixth pharmaceutical composition comprising a conjugate comprising a cell-surface molecule binding-molecule, such as a fourth proteinaceous molecule ('proteinaceous molecule 4'), and an effector moiety, wherein the proteinaceous molecule 4 comprises the first binding site for binding to the first epitope on the cell-surface molecule of (a), the sixth pharmaceutical composition optionally further comprising a pharmaceutically acceptable excipient and/or diluent,
- 15 wherein the first binding site of the proteinaceous molecule 1 or proteinaceous molecule 2 and the first binding site of the proteinaceous molecule 4 are the same, and wherein the first cell-surface molecule and the first epitope on the first cell-surface molecule, to which the proteinaceous molecule 1 or the proteinaceous molecule 2 can bind, and the first cell-surface molecule and the first epitope on the first cell-surface molecule, to which the proteinaceous molecule 4 can bind, are the same.

38. Fourth pharmaceutical combination, comprising:

- 20 (a) the fourth pharmaceutical composition of claim 37; and
- (b) the sixth pharmaceutical composition of claim 37,
- wherein the first cell-surface molecule is expressed on a tumor cell surface, and preferably the first cell-surface molecule is a tumor cell-specific surface molecule, and wherein preferably the first epitope is a first tumor-cell specific epitope.

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39. Second pharmaceutical combination or third pharmaceutical combination or fourth pharmaceutical combination according to any one of the claims 35-38, wherein the third binding site of the proteinaceous molecule 3 and/or the first binding site of the proteinaceous molecule 4 comprises or consists of an antibody or a binding derivative or binding fragment or binding domain thereof such as a F(ab')₂ fragment, Fab' fragment, Fab fragment, scFv, dsFv, scFv-Fc, reduced IgG (rlgG), minibody, diabody, triabody, tetrabody, Fc fusion protein, nanobody, variable V domain, a single-domain antibody (sdAb), preferably a V_{HH}, for example camelid V_H, or a ligand for a cell-surface molecule such as a receptor such as EGF and a cytokine, preferably a V_H domain derived from a heavy chain of an antibody, preferably of immunoglobulin G origin, preferably of human origin, a V_L domain derived from a light chain of an antibody, preferably of immunoglobulin G origin, preferably of human origin, a V_{HH} domain such as derived from a heavy-chain only antibody (HCAb) such as from *Camelidae* origin or *Ig-NAR* origin such as a variable heavy chain new antigen receptor (VNAR) domain, preferably the HCAb is from *Camelidae* origin, preferably the sdAb is a V_{HH} domain derived from an HCAb
- 30
- 35

from *Camelidae* origin (camelid V_H) such as derived from an HCAb from camel, lama, alpaca, dromedary, vicuna, guanaco and Bactrian camel.

- 5 40. A seventh pharmaceutical composition comprising the saponin conjugate of any one of the claims 22-34, and the conjugate comprising proteinaceous molecule 3 and an effector moiety of claim 35 or 36, or the conjugate comprising proteinaceous molecule 4 and an effector moiety of claim 37 or 38, and optionally further comprising a pharmaceutically acceptable excipient and/or diluent.
- 10 41. The second pharmaceutical combination or third pharmaceutical combination or fourth pharmaceutical combination of any one the claims 35-39, or the seventh pharmaceutical composition of claim 40, for use as a medicament.
- 15 42. The second pharmaceutical combination or third pharmaceutical combination or fourth pharmaceutical combination of any one the claims 35-39, or the seventh pharmaceutical composition of claim 40, for use in the treatment or prevention of a cancer or of an autoimmune disease such as rheumatoid arthritis.