CLAIMS

1. Pharmaceutical combination comprising:
   - a first conjugate comprising at least one effector molecule and a single-domain antibody (sdAb) for binding to a first cell-surface molecule, which are covalently linked to each other, directly or via a linker;
   - a second conjugate comprising a binding molecule for binding to a second cell-surface molecule and a saponin, which binding molecule and the saponin are covalently linked to each other, directly or via a linker, wherein the saponin is a monodesmosidic triterpene glycoside or a bidesmosidic triterpene glycoside, wherein the second cell-surface molecule is the same as or different from the first cell-surface molecule; and optionally
   - a pharmaceutically acceptable excipient and/or pharmaceutically acceptable diluent.

2. Pharmaceutical combination of claim 1 in the form of at least two, preferably two, pharmaceutical compositions comprising:
   - a first pharmaceutical composition comprising the first conjugate and optionally comprising a pharmaceutically acceptable excipient and/or pharmaceutically acceptable diluent; and
   - a second pharmaceutical composition comprising the second conjugate, and optionally comprising a pharmaceutically acceptable excipient and/or pharmaceutically acceptable diluent.

3. Pharmaceutical combination of claim 1 in the form of a single pharmaceutical composition comprising the first conjugate and the second conjugate, and optionally comprising a pharmaceutically acceptable excipient and/or pharmaceutically acceptable diluent.

4. Pharmaceutical combination of any one of the claims 1-3, wherein the first conjugate comprises an sdAb which is any one or more of: 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 (V_{NAR}) domain, preferably the HCAb is from *Camelidae* origin; and 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.

5. Pharmaceutical combination of any one of the claims 1-4, wherein the first conjugate comprises at least two sdAbs with a single first sdAb covalently bound to the at least one effector molecule, or with two or more sdAbs bound to the at least one effector molecule, or with all of the at least two sdAbs

bound to the at least one effector molecule, for example wherein each of the at least two sdAbs is bound to one or more of the at least one effector molecule.

6. Pharmaceutical combination of any one of the claims 1-5, wherein the sdAb comprises at least two sdAbs, which are the same sdAbs, preferably two – eight sdAbs, more preferably two – four sdAbs.

7. Pharmaceutical combination of any one of the claims 1-6, comprising one – eight sdAbs, capable of binding to a same binding site on the first cell-surface molecule, wherein the at least one effector molecule is bound to a single first sdAb of the one – eight sdAbs or wherein the at least one effector molecule is bound to two or more of the sdAbs, if present, and/or wherein each of the at least one effector molecule is bound to a single sdAb separately such that one or more of the sdAbs is/are each bound to a single effector molecule.

8. Pharmaceutical combination of any one of the claims 1-7, wherein the sdAb is a single sdAb or are at least two, preferably two sdAbs, wherein the sdAb(s) can bind to the first cell-surface molecule such as HIVgp41 or which first cell-surface molecule is a tumor-cell surface receptor such as a tumor-cell specific receptor, more preferably a receptor selected from: CD71, CA125, EpCAM(17-1A), CD52, CEA, CD44v6, FAP, EGF-IR, integrin, syndecan-1, vascular integrin alpha-V beta-3, HER2, EGFR, CD20, CD22, Folate receptor 1, CD146, CD56, CD19, CD138, CD27L receptor, prostate specific membrane antigen (PSMA), CanAg, integrin-alphaV, CA6, CD33, mesothelin, Cripto, CD3, CD30, CD239, CD70, CD123, CD352, DLL3, CD25, ephrinA4, MUC-1, Trop2, CEACAM5, CEACAM6, HER3, CD74, PTK7, Notch3, FGF2, C4.4A, FLT3, CD38, FGFR3, CD7, PD-L1, CTLA-4, CD52, PDGFRA, VEGFR1, VEGFR2, c-Met (HGFR), EGFR1, RANKL, ADAMTS5, CD16, CXCR7 (ACKR3), glucocorticoid-induced TNFR-related protein (GITR), most preferably selected from: HER2, c-Met, VEGFR2, CXCR7, CD71 and EGFR1.

9. Pharmaceutical combination of any one of the claims 1-8, wherein the sdAb is a single sdAb or are at least two, preferably two sdAbs, wherein the sdAb(s) is/are selected from: an anti-CD71 sdAb, an anti-HER2 sdAb, an anti-CD20 sdAb, an anti-CA125 sdAb, an anti-EpCAM (17-1A) sdAb, an anti-EGFR sdAb, an anti-CD30 sdAb, an anti-CD33 sdAb, an anti-vascular integrin alpha-v beta-3 sdAb, an anti-CD52 sdAb, an anti-CD22 sdAb, an anti-CEA sdAb, an anti-CD44v6 sdAb, an anti-FAP sdAb, an anti-CD19 sdAb, an anti-CanAg sdAb, an anti-CD56 sdAb, an anti-CD38 sdAb, an anti-CA6 sdAb, an anti-IGF-1R sdAb, an anti-integrin sdAb, an anti-syndecan-1 sdAb, an anti-CD79b, an anti-c-Met sdAb, an anti-EGFR1 sdAb, an anti-VEGFR2 sdAb, an anti-CXCR7 sdAb and an anti-HIVgp41, wherein the sdAb(s) is/are preferably V_{HH}(s), more preferably camelid V_H.

10. Pharmaceutical combination of any one of the claims 1-9, wherein the first conjugate comprises an sdAb that can bind to HER2, CD71, HIVgp41 and/or EGFR, wherein the sdAb is preferably a V_{HH}, more preferably a camelid V_H.

11. Pharmaceutical combination of any one of the claims 1-10, wherein the first conjugate comprises an sdAb for binding to HER2 selected from: sdAb produced by clone 11A4, clone 18C3, clone 22G12, clone Q17 or clone Q17-C-tag; or an sdAb for binding to EGFR and produced by clone anti-EGFR Q86-C-tag; or an sdAb for binding to CD71 and produced by clone anti-CD71 Q52-C-tag; or an sdAb for binding to HIVgp41 and produced by clone anti-HIVgp41 Q8-C-tag; or an sdAb encoded by a cDNA of any one of the SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29 and 31; or any one of the sdAbs with an amino-acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 36-72, wherein optionally the first conjugate further comprises a covalently bound sdAb for binding to albumin, such as any one or more of the sdAbs with an amino-acid sequence of SEQ ID NO: 33, 34 and 35, preferably the sdAb is a V_{HH}, more preferably a camelid V_H.

12. Pharmaceutical combination of any one of the claims 1-11, wherein the effector molecule comprises or consists of at least one of a small molecule such as a drug molecule, a toxin such as a protein toxin, an oligonucleotide such as a BNA, a xeno nucleic acid or an siRNA, an enzyme, a peptide, a protein, or any combination thereof.

13. Pharmaceutical combination of any one of the claims 1-12, wherein the effector molecule is selected from any one or more of a vector, a gene, a cell suicide inducing transgene, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), anti-sense oligonucleotide (ASO, AON), short interfering RNA (siRNA), anti-microRNA (anti-miRNA), DNA aptamer, RNA aptamer, mRNA, mini-circle DNA, peptide nucleic acid (PNA), phosphoramidate morpholino oligomer (PMO), locked nucleic acid (LNA), bridged nucleic acid (BNA), 2'-deoxy-2'-fluoroarabino nucleic acid (FANA), 2'-O-methoxyethyl-RNA (MOE), 3'-fluoro hexitol nucleic acid (FHNA), a plasmid, glycol nucleic acid (GNA) and threose nucleic acid (TNA), or a derivative thereof, more preferably a BNA, for example a BNA for silencing HSP27 protein expression or a BNA for silencing apolipoprotein B expression.

14. Pharmaceutical combination of any one of the claims 1-13, wherein the effector molecule is an oligonucleotide selected from any one or more of a(n): short interfering RNA (siRNA), short hairpin RNA (shRNA), anti-hairpin-shaped microRNA (miRNA), single-stranded RNA, aptamer RNA, double-stranded RNA (dsRNA), anti-microRNA (anti-miRNA, anti-miR), antisense oligonucleotide (ASO), mRNA, DNA, antisense DNA, locked nucleic acid (LNA), bridged nucleic acid (BNA), 2'-O,4'-aminoethylene bridged nucleic Acid (BNA^{NC}), BNA-based siRNA, and BNA-based antisense oligonucleotide (BNA-AON).

15. Pharmaceutical combination of any one of the claims 1-14, wherein the effector molecule is an oligonucleotide selected from any one of an anti-miRNA, a BNA-AON or an siRNA, such as BNA-based siRNA, preferably selected from chemically modified siRNA, metabolically stable siRNA and chemically modified, metabolically stable siRNA.

16. Pharmaceutical combination of any one of the claims 1-15, wherein the effector molecule is an oligonucleotide that capable of silencing a gene, when present in a cell comprising such gene, wherein the gene is any one of genes: apolipoprotein B (apoB), transthyretin (TTR), proprotein convertase subtilisin/kexin type 9 (PCSK9), delta-aminolevulinate synthase 1 (ALAS1), antithrombin 3 (AT3), glycolate oxidase (GO), complement component C5 (CC5), X gene of hepatitis B virus (HBV), S gene of HBV, alpha-1 antitrypsin (AAT) and lactate dehydrogenase (LDH), and/or is capable of targeting an aberrant miRNA when present in a cell comprising such miRNA.

17. Pharmaceutical combination of any one of the claims 1-16, wherein the effector molecule is an oligonucleotide that is capable of targeting an mRNA, when present in a cell comprising such mRNA, wherein the mRNA is involved in expression of any one of proteins: apoB, TTR, PCSK9, ALAS1, AT3, GO, CC5, expression product of X gene of HBV, expression product of S gene of HBV, AAT and LDH, or is capable of antagonizing or restoring an miRNA function such as inhibiting an oncogenic miRNA (onco-miR) or suppression of expression of an onco-miR, when present in a cell comprising such an miRNA.

18. Pharmaceutical combination of any one of the claims 1-17, wherein the effector molecule comprises or, when dependent on any one of the claims 1-11, consists of at least one proteinaceous molecule, preferably selected from any one or more of a peptide, a protein, an enzyme and a protein toxin.

19. Pharmaceutical combination of any one of the claims 1-18, wherein the effector molecule comprises or, when dependent on any one of the claims 1-11, consists of at least one of: urease and Cre-recombinase, a proteinaceous toxin, a ribosome-inactivating protein, a protein toxin, a bacterial toxin, a plant toxin, more preferably selected from any one or more of a viral toxin such as apoptin; a bacterial toxin such as Shiga toxin, Shiga-like toxin, Pseudomonas aeruginosa exotoxin (PE) or exotoxin A of PE, full-length or truncated diphtheria toxin (DT), cholera toxin; a fungal toxin such as alpha-sarcin; a plant toxin including ribosome-inactivating proteins and the A chain of type 2 ribosome-inactivating proteins such as dianthin *e.g.* dianthin-30 or dianthin-32, saporin *e.g.* saporin-S3 or saporin-S6, bouganin or de-immunized derivative debouganin of bouganin, shiga-like toxin A, pokeweed antiviral protein, ricin, ricin A chain, modeccin, modeccin A chain, abrin, abrin A chain, volkensin, volkensin A chain, viscumin, viscumin A chain; or an animal or human toxin such as frog RNase, or granzyme B or human angiogenin, or any toxic fragment or toxic derivative thereof; preferably the protein toxin is dianthin and/or saporin.

20. Pharmaceutical combination of any one of the claims 1-19, wherein the effector molecule comprises or, when dependent on any one of the claims 1-11, consists of at least one payload.

21. Pharmaceutical combination of any one of the claims 1-20, wherein the effector molecule comprises or, when dependent on any one of the claims 1-11, consists of at least one of: a toxin targeting ribosomes, a toxin targeting elongation factors, a toxin targeting tubulin, a toxin targeting DNA and a toxin targeting RNA, more preferably any one or more of emtansine, pasudotox, maytansinoid derivative

DM1, maytansinoid derivative DM4, monomethyl auristatin E (MMAE, vedotin), monomethyl auristatin F (MMAF, mafodotin), a Calicheamicin, N-Acetyl-γ-calicheamicin, a pyrrolobenzodiazepine (PBD) dimer, a benzodiazepine, a CC-1065 analogue, a duocarmycin, Doxorubicin, paclitaxel, docetaxel, cisplatin, cyclophosphamide, etoposide, docetaxel, 5-fluorouracyl (5-FU), mitoxantrone, a tubulysin, an indolinobenzodiazepine, AZ13599185, a cryptophycin, rhizoxin, methotrexate, an anthracycline, a camptothecin analogue, SN-38, DX-8951f, exatecan mesylate, truncated form of *Pseudomonas aeruginosa* exotoxin (PE38), a Duocarmycin derivative, an amanitin, α-amanitin, a spliceostatin, a thailanstatin, ozogamicin, tesirine, Amberstatin269 and soravtansine, or a derivative thereof.

22. Pharmaceutical combination of any one of the claims 1-21, wherein the first conjugate comprises or consists of an antibody-drug conjugate (ADC), such as an ADCs comprising at least one sdAb and a toxin derived from any one of ADCs: gemtuzumab ozogamicin, brentuximab vedotin, trastuzumab emtansine, inotuzumab ozogamicin, moxetumomab pasudotox and polatuzumab vedotin.

23. Pharmaceutical combination of any one of the claims 1-22, wherein the saponin comprises an aglycone core structure selected from:

2alpha-hydroxy oleanolic acid;
16alpha-hydroxy oleanolic acid;
hederagenin (23-hydroxy oleanolic acid);
16alpha,23-dihydroxy oleanolic acid;
gypsogenin;
quillaic acid;
protoaescigenin-21(2-methylbut-2-enoate)-22-acetate;
23-oxo-barringtogenol C-21,22-bis(2-methylbut-2-enoate);
23-oxo-barringtogenol C-21(2-methylbut-2-enoate)-16,22-diacetate;
digitogenin;
3,16,28-trihydroxy oleanan-12-en; and
gypsogenic acid,

preferably, the saponin comprises an aglycone core structure selected from quillaic acid and gypsogenin, more preferably the saponin comprises an aglycone core structure quillaic acid.

24. Pharmaceutical combination of any one of the claims 1-23, wherein the saponin optionally comprises a first saccharide chain bound to the C_3 atom or the C_{28} atom of the aglycone core structure of the saponin, preferably bound to the C_3 atom, and/or wherein the saponin optionally comprises a second saccharide chain bound to the C_{28} atom of the aglycone core structure of the saponin.

25. Pharmaceutical combination of claim 24, wherein

- the saponin comprises the first saccharide chain selected from:

GlcA-,
Glc-,

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-,
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-,
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-,
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-,
Xyl-(1→4)-Rha-(1→2)-Gal-(1→2)-Fuc-(1→2)-GlcA-, and
Xyl-(1→4)-Fuc-(1→2)-Gal-(1→2)-Fuc-(1→2)-GlcA

and/or

- the saponin comprises the second saccharide chain selected from:

Glc-,
Gal-,
Rha-(1→2)-[Xyl-(1→4)]-Rha-,
Rha-(1→2)-[Ara-(1→3)-Xyl-(1→4)]-Rha-,
Ara-,
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-,
Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R3-(→4)]-3-OAc-Fuc- wherein R3 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-),
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-,
Api-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R4-(→4)]-Fuc- wherein R4 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)-[R5-(→4)]-Fuc- wherein R5 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-,
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-,
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-,
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)-[R6-(→4)]-Fuc- wherein R6 is 5-O-[5-O-Rha-(1→2)-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)-[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/Xyl-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R8-(→4)]-Fuc- wherein R8 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)-[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),
Xyl-(1→3)-Xyl-(1→4)-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-(→3)]-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-(→3)]-Fuc- wherein R12 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-.

26. Pharmaceutical combination of any one of the claims 1-25, wherein the saponin in the second conjugate comprises the first saccharide chain and comprises the second saccharide chain of claim 24 or 25, wherein the first saccharide chain comprises more than one saccharide moiety and the second saccharide chain comprises more than one saccharide moiety, and wherein the aglycone core structure is quillaic acid or gypsogenin, wherein one, two or three, preferably one or two, of:

i. an aldehyde group in the aglycone core structure has been derivatised,
ii. a carboxyl group of a glucuronic acid moiety in the first saccharide chain has been derivatised, and
iii. at least one acetoxy (Me(CO)O-) group in the second saccharide chain has been derivatised.

27. Pharmaceutical combination of any one of the claims 1-26, wherein the saponin in the second conjugate comprises:

i. an aglycone core structure comprising an aldehyde group which has been derivatised by:
- reduction to an alcohol;
- transformation into a hydrazone bond through reaction with N-ε-maleimidocaproic acid hydrazide (EMCH) wherein the maleimide group of the EMCH is optionally derivatised by formation of a thioether bond with mercaptoethanol;
- transformation into a hydrazone bond through reaction with N-[ß-maleimidopropionic acid] hydrazide (BMPH) wherein the maleimide group of the BMPH is optionally derivatised by formation of a thioether bond with mercaptoethanol; or
- transformation into a hydrazone bond through reaction with N-[κ-maleimidoundecanoic acid] hydrazide (KMUH) wherein the maleimide group of the KMUH is optionally derivatised by formation of a thioether bond with mercaptoethanol;
ii. a first saccharide chain comprising a carboxyl group, preferably a carboxyl group of a glucuronic acid moiety, which has been derivatised by transformation into an amide bond through reaction with 2-amino-2-methyl-1,3-propanediol (AMPD) or *N*-(2-aminoethyl)maleimide (AEM);
iii. a second saccharide chain comprising an acetoxy group (Me(CO)O-) which has been derivatised by transformation into a hydroxyl group (HO-) by deacetylation; or
iv. any combination of two or three derivatisations i., ii. and/or iii., preferably any combination of two derivatisations i., ii. and/or iii.

28. Pharmaceutical combination of any one of the claims 1-27, wherein the saponin is selected from: *Quillaja* bark saponin, dipsacoside 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, 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, or a stereoisomer thereof, and/or a combination thereof, preferably the saponin is any one or more of QS-21, SO1861, SA1641 and GE1741, more preferably QS-21 or SO1861, most preferably SO1861.

29. Pharmaceutical combination of any one of the claims 1-28, wherein the saponin is selected from: SO1861, SA1657, GE1741, SA1641, QS-21, QS-21A, QS-21 A-api, QS-21 A-xyl, QS-21B, QS-21 B-api, QS-21 B-xyl, QS-7-xyl, QS-7-api, QS-17-api, QS-17-xyl, QS1861, QS1862, Quillajasaponin, Saponinum album, QS-18, Quil-A, Gyp1, gypsoside A, AG1, AG2, SO1542, SO1584, SO1658, SO1674, SO1832, SO1862, SO1904, or a stereoisomer thereof and/or any combinations thereof, preferably the saponin is SO1861 and/or GE1741 and/or SA1641 and/or QS-21, more preferably the saponin is SO1861 or QS21.

30. Pharmaceutical combination of any one of the claims 1-29, wherein the second conjugate comprises a binding molecule for binding to the second cell-surface molecule which binding molecule is any one or more of: a ligand, such as a proteinaceous ligand, for binding to the second cell-surface molecule such as EGF or a cytokine, or an immunoglobulin or at least one binding fragment or binding domain of said immunoglobulin capable of binding to the second cell-surface molecule, wherein the immunoglobulin is preferably any one or more of an antibody such as a monoclonal antibody, preferably a human antibody, an IgG, a molecule comprising or consisting of a sdAb, at least one V_{HH} domain or at least one V_H domain, a variable heavy chain new antigen receptor (V_{NAR}) domain, a Fab, an scFv, an Fv, a dAb, an F(ab)2, a Fcab fragment.

31. Pharmaceutical combination of any one of the claims 1-30, wherein the second conjugate comprises a binding molecule for binding to the second cell-surface molecule, wherein the second cell-surface molecule is a cell-surface receptor present on an aberrant cell such as a tumor cell, an auto-immune cell, an infected cell such as a virally infected cell.

32. Pharmaceutical combination of any one of the claims 1-31, wherein the second conjugate comprises a binding molecule for binding to the second cell-surface molecule or an antibody or a binding fragment or binding domain thereof, or a sdAb, or a receptor ligand, wherein preferably the second cell-surface receptor is HIVgp41 or a tumor-cell surface receptor or a tumor-cell specific receptor, or a cell-surface receptor selected from: CD71, CA125, EpCAM(17-1A), CD52, CEA, CD44v6, FAP, EGF-IR, integrin, syndecan-1, vascular integrin alpha-V beta-3, HER2, EGFR, CD20, CD22, Folate receptor 1, CD146, CD56, CD19, CD138, CD27L receptor, prostate specific membrane antigen (PSMA), CanAg, integrin-alphaV, CA6, CD33, mesothelin, Cripto, CD3, CD30, CD239, CD70, CD123, CD352, DLL3, CD25, ephrinA4, MUC-1, Trop2, CEACAM5, CEACAM6, HER3, CD74, PTK7, Notch3, FGF2, C4.4A, FLT3, CD38, FGFR3, CD7, PD-L1, CTLA-4, CD52, PDGFRA, VEGFR1, VEGFR2, c-Met (HGFR), EGFR1, RANKL, ADAMTS5, CD16, CXCR7 (ACKR3), glucocorticoid-induced TNFR-related protein (GITR), most preferably selected from: HER2, c-Met, VEGFR2, CXCR7, CD71, EGFR and EGFR1.

33. Pharmaceutical combination of any one of the claims 1-32, wherein the second conjugate comprises a binding molecule for binding to the second cell-surface molecule which is an immunoglobulin selected from, preferably a sdAb derived from or based on: an anti-CD71 antibody such as IgG type OKT-9, an anti-HER2 antibody such as trastuzumab (Herceptin), pertuzumab, an anti-CD20 antibody such as rituximab, ofatumumab, tositumomab, obinutuzumab ibritumomab, an anti-CA125 antibody such as oregovomab, an anti-EpCAM (17-1A) antibody such as edrecolomab, an anti-EGFR antibody such as cetuximab, matuzumab, panitumumab, nimotuzumab, an anti-CD30 antibody such as brentuximab, an anti-CD33 antibody such as gemtuzumab, huMy9-6, an anti-vascular integrin alpha-v beta-3 antibody such as etaracizumab, an anti-CD52 antibody such as alemtuzumab, an anti-CD22 antibody such as epratuzumab, pinatuzumab, binding fragment (Fv) of anti-CD22 antibody moxetumomab, humanized monoclonal antibody inotuzumab, an anti-CEA antibody such as labetuzumab, an anti-CD44v6 antibody such as bivatuzumab, an anti-FAP antibody such as sibrotuzumab, an anti-CD19 antibody such as huB4, an anti-CanAg antibody such as huC242, an anti-CD56 antibody such as huN901, an anti-CD38 antibody such as daratumumab, OKT-10 anti-CD38 monoclonal antibody, an anti-CA6 antibody such as DS6, an anti-IGF-1R antibody such as cixutumumab, 3B7, an anti-integrin antibody such as CNTO 95, an anti-syndecan-1 antibody such as B-B4, an anti-CD79b such as polatuzumab, an anti-HIVgp41 antibody, preferably any one of an anti-HIVgp41 antibody, an anti-CD71 antibody, an anti-HER2 antibody and an anti-EGFR antibody, more preferably any one of: trastuzumab, pertuzumab, cetuximab, matuzumab, an anti-CD71 antibody, OKT-9, most preferably trastuzumab, cetuximab, the anti-CD71 antibody OKT-9.

34. Pharmaceutical combination of any one of the claims 1-33, wherein the second conjugate comprises the saponin which is covalently bound via a thio-ether bond to a sulfhydryl group in the binding molecule, the covalent bonding via linker N-ε-maleimidocaproic acid hydrazide (EMCH) that is covalently bound to an aldehyde group in position C_{23} of the aglycone core structure of the saponin and that is covalently bound to the sulfhydryl group in the binding molecule, such as a sulfhydryl group of a cysteine.

35. Pharmaceutical combination of any one of the claims 1-34, wherein the second conjugate comprises the saponin which is a bidesmosidic triterpene saponin belonging to the type of a 12,13-dehydrooleanane with optionally an aldehyde function in position C_{23} of the aglycone core structure of the saponin, and comprising a glucuronic acid unit in a first saccharide chain at the C_3beta-OH group of the aglycone core structure of the saponin, wherein the saponin is covalently bound to an amino-acid residue of the binding molecule via the carboxyl group of the glucuronic acid unit in the first saccharide chain, preferably via at least one linker, wherein the amino-acid residue preferably is selected from cysteine and lysine.

36. Pharmaceutical combination of claim 35, wherein the second conjugate comprises the saponin which comprises a glucuronic acid unit in the first saccharide chain at the C_3beta-OH group of the aglycone core structure of the at least one saponin, which glucuronic acid unit is covalently bound to a

linker, which linker is preferably covalently bound via an amide bond to an amine group in the binding molecule, such as an amine group of a lysine or an N-terminus of the binding molecule, preferably the glucuronic acid unit is covalently bound linker 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (HATU).

37. Pharmaceutical combination of any one of the claims 1-36, wherein the second conjugate comprises more than one covalently bound saponin, preferably 2, 3, 4, 5, 6, 8, 10, 16, 32, 64, 128 or 1-100, or any number therein between, such as 7, 9, 12 saponins.

38. Pharmaceutical combination of claim 37, wherein the more than one covalently bound saponin are covalently bound directly to an amino-acid residue of the binding molecule, preferably to a cysteine and/or to a lysine, and/or are covalently bound via at least one linker and/or via at least one cleavable linker.

39. Pharmaceutical combination of claim 37, wherein the more than one covalently bound saponin are part of a covalent saponin conjugate comprising at least one oligomeric molecule or polymeric molecule and with the more than one saponin covalently bound thereto, wherein the covalent saponin conjugate is covalently bound to the binding molecule

40. Pharmaceutical combination of claim 39, wherein 1-8 of the covalent saponin conjugates are bound to the binding molecule, more preferably 2-4 of the covalent saponin conjugates, wherein the at least one covalent saponin conjugate is optionally based on a dendron, wherein optionally 1-32 saponin(s), preferably 2, 3, 4, 5, 6, 8, 10, 16, 32, or any number therein between, such as 7, 9, 12 saponins, are covalently bound to the oligomeric molecule or to the polymeric molecule of the at least one covalent saponin conjugate, either directly or via a linker.

41. Pharmaceutical combination of any one of the claims 1-40, wherein the saponin is covalently bound to the binding molecule via a cleavable linker.

42. Pharmaceutical combination of claim 41, wherein the cleavable linker is subject to cleavage under acidic conditions, reductive conditions, enzymatic conditions and/or light-induced conditions, and preferably the cleavable linker comprises a cleavable bond selected from a hydrazone bond and a hydrazide bond subject to cleavage under acidic conditions, and/or a bond susceptible to proteolysis, for example proteolysis by Cathepsin B, and/or a bond susceptible for cleavage under reductive conditions such as a disulfide bond.

43. Pharmaceutical combination of claim 41 or 42, wherein the cleavable linker is subject to cleavage *in vivo* under acidic conditions as for example 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.

44. Pharmaceutical combination of claim 40 or any one of claims 41-43 when dependent on claim 39, wherein the oligomeric molecule or the polymeric molecule of the covalent saponin conjugate is covalently bound to the binding molecule, preferably to an amino-acid residue of the binding molecule.

45. Pharmaceutical combination of claim 44, wherein the saponin is covalently bound to the oligomeric molecule or to the polymeric molecule of the covalent saponin conjugate via a cleavable linker according to any one of the claims 41-43.

46. Pharmaceutical combination of claim 44 or 45, wherein the saponin is covalently bound to the oligomeric molecule or to the polymeric molecule of the covalent saponin conjugate via any one or more of an imine bond, a hydrazone bond, a hydrazide bond, an oxime bond, a 1,3-dioxolane bond, a disulfide bond, a thio-ether bond, an amide bond, a peptide bond or an ester bond, preferably via a linker.

47. Pharmaceutical combination of any one of the claims 44-46, wherein the saponin comprises an aglycone core structure comprising an aldehyde function in position C_{23} and the saponin comprising optionally a glucuronic acid function in a first saccharide chain at the C_3beta-OH group of aglycone core structure of the saponin, which aldehyde function is involved in the covalent bonding to the oligomeric molecule or to the polymeric molecule of the covalent saponin conjugate, and/or, if present, the glucuronic acid function is involved in the covalent bonding to the oligomeric molecule or to the polymeric molecule of the covalent saponin conjugate, the bonding of the saponin either via a direct covalent bond, or via a linker.

48. Pharmaceutical combination of claim 47, wherein the aldehyde function in position C_{23} of aglycone core structure of the saponin is covalently bound to linker EMCH, which EMCH is covalently bound via a thio-ether bond to a sulfhydryl group in the oligomeric molecule or in the polymeric molecule of the covalent saponin conjugate, such as a sulfhydryl group of a cysteine.

49. Pharmaceutical combination of claim 47 or 48, wherein the glucuronic acid function in the first saccharide chain at the C_3beta-OH group of the aglycone core structure of the saponin is covalently bound to linker HATU, which HATU is covalently bound via an amide bond to an amine group in the oligomeric molecule or in the polymeric molecule of the covalent saponin conjugate, such as an amine group of a lysine or an N-terminus of a protein.

50. Pharmaceutical combination of any one of the claims 44-49, wherein the polymeric molecule or the oligomeric molecule of the covalent saponin conjugate is bound to the binding molecule, preferably to an amino-acid residue of the binding molecule, involving a click chemistry group on the polymeric molecule or the oligomeric molecule of the covalent saponin conjugate, the click chemistry group preferably selected from a tetrazine, an azide, an alkene or an alkyne, or a cyclic derivative of these groups, more preferably the click chemistry group is an azide.

51. Pharmaceutical combination of any one of the claims 44-50, wherein the polymeric molecule or the oligomeric molecule of the covalent saponin conjugate comprises a polymeric structure and/or an oligomeric structure selected from: a linear polymer, a branched polymer and/or a cyclic polymer, an oligomer, a dendrimer, a dendron, a dendronized polymer, a dendronized oligomer, a DNA, a polypeptide, a poly-lysine, a poly-ethylene glycol, an oligo-ethylene glycol (OEG), such as OEG_3, OEG_4 and OEG_5, or an assembly of these polymeric structures and/or oligomeric structures which assembly is preferably built up by covalent cross-linking, preferably the polymeric molecule or the oligomeric molecule of the covalent saponin conjugate is a dendron such as a poly-amidoamine (PAMAM) dendrimer.

52. Pharmaceutical combination of any one of the claims 1-51, for use as a medicament.

53. Use of the pharmaceutical combination of any one of the claims 1-51, in the manufacture of a medicament for treatment or the prophylaxis of a cancer, an auto-immune disease such as rheumatoid arthritis, an enzyme deficiency, a gene defect, a disease relating to a gene defect, an amyloidosis, a disease related to an enzyme deficiency, an infection such as a viral infection, hypercholesterolemia, primary hyperoxaluria, haemophilia A, haemophilia B, alpha-1 antitrypsin related liver disease, acute hepatic porphyria, transthyretin-mediated amyloidosis.

54. Pharmaceutical combination for use of claim 52 or use of the pharmaceutical combination of claim 53, wherein the saponin is SO1861 or QS-21, or wherein the saponin is SO1861 or QS-21.

55. Pharmaceutical combination for use of claim 53 or 54 or the use of the pharmaceutical combination of claim 53 or 54, wherein:

- said use is in the treatment or prevention of cancer in a human subject; and/or
- said use is in the treatment or prophylaxis of cancer in a patient in need thereof, wherein the first and the second cell-surface molecules are the same or a different tumor-cell surface molecules, preferably (a) tumor cell-specific surface molecule(s), and wherein the sdAb and the binding molecule of the second conjugate bind to the tumor-cell surface molecules, preferably tumor cell-specific surface molecules; and/or
- the pharmaceutical combination, preferably a therapeutically effective amount of the pharmaceutical combination, is to be administered to a patient in need thereof, preferably a human patient.

56. *In vitro* or *ex vivo* method for transferring the first conjugate of any one of the claims 1-51 from outside a cell to inside said cell, preferably to the cytosol of said cell, comprising the steps of:

a) providing a cell which expresses the first cell-surface molecule according to any one of the claims 1-51 on its surface, and optionally expresses the second cell-surface molecule according to any one of the claims 1-51 on its surface, said cell preferably selected from a liver cell, an aberrant cell such as a virally infected cell, an auto-immune cell and a tumor cell;

b) providing the first conjugate of any one of the claims 1-51 for transferring into the cell provided in step a);

c) providing the saponin of any one of the claims 1-51, or, when the cell provided in step a) expresses the second cell-surface molecule according to any one of the claims 1-51 on its surface, providing the second conjugate of any one of the claims 1-51;

d) contacting the cell of step a) *in vitro* or *ex vivo* with the first conjugate of step b) and any one or more of the saponin, and the conjugate of step c),

therewith establishing the transfer of the first conjugate from outside the cell into said cell, preferably into the cytosol of said cell.