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(54) Title: SAPONIN DERIVATIVES WITH IMPROVED THERAPEUTIC WINDOW

(57) Abstract: The invention relates to a saponin derivative based on a saponin comprising a triterpene aglycone and a first saccharide chain and/or a second saccharide chain, and comprising: an aglycone core structure comprising an aldehyde group which has been derivatised; and/or the first saccharide chain wherein the first saccharide chain comprises a carboxyl group, which has been derivatised; and/or the second saccharide chain wherein the second saccharide chain comprises at least one acetoxy group which has been derivatised. The invention also relates to a first pharmaceutical composition comprising the saponin derivative of the invention. In addition, the invention relates to a pharmaceutical combination comprising the first pharmaceutical composition of the invention and a second pharmaceutical composition comprising any one or more of an antibody-toxin conjugate, a receptor-ligand – toxin conjugate, an antibody-drug conjugate, a receptor-ligand – drug conjugate, an antibody-oligonucleotide conjugate or a receptor-ligand – oligonucleotide conjugate. The invention also relates to the first pharmaceutical composition or the pharmaceutical combination of the invention, for use as a medicament, or use in the treatment or prophylaxis of a cancer, an infectious disease, viral infection, hypercholesterolemia, primary hyperoxaluria, haemophilia A, haemophilia B, alpha-1 antitrypsin related liver disease, acute hepatic porphyria, transthyretin-mediated amyloidosis, or an auto-immune disease. Furthermore, the invention relates to an in vitro or ex vivo method for transferring a molecule from outside a cell to inside said cell, comprising contacting said cell with the molecule and with a saponin derivative of the invention.

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