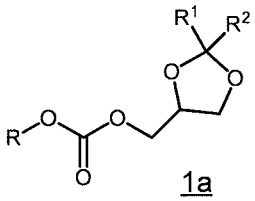
CLAIMS

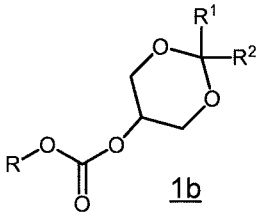
What is claimed is:

1. A stable, synthetic low density lipoprotein (LDL) solid nanoparticle comprising:

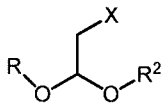
a) a lipophilic anti-cancer agent of the formula **1a**, **1b** or formula **2a**:



1a



1b



2a

wherein:

for formula **1a** or **1b** R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; and R^2 is C_5-C_{22} alkyl; and for formula **2a**: R^2 is C_1-C_{22} alkyl; and X is hydrogen or is selected from the group consisting of Cl, Br and I; and

R is a hydroxyl bearing cancer chemotherapeutic agent (HBCCA) selected from the group consisting of a taxane, abeo-taxane, camptothecin, epothilone, cucurbitacin, quassinoid and an anthracycline;

b) phospholipids (PL); and

c) triglycerides (TG);

wherein the LDL nanoparticle has a mean particle size of 40-80 nm.

2. The LDL nanoparticle of Claim 1, wherein the LDL nanoparticle has a mean size distribution of 60 nm.

3. The LDL nanoparticle of Claim 1, wherein the phospholipids is selected from the group consisting of phosphotidylcholine, phosphotidylethanolamine, symmetric or asymmetric 1,2-diacyl-sn-glycero-3-phosphorylcholines, 1,2-dimyristoyl-sn-glycero-3-phosphorylcholine,1,2-dimyristoyl-sn-glycero-3-phosphorylethanolamine, egg phospholipids, egg phosphatidyl glycerol, dipalmitoylphosphatidylglycerol, egg lecithin, soy lecithin, lecithin (NOS) and mixtures thereof.

4. The LDL nanoparticle of any one of Claims 1 to 3, further comprising cholesterol ester (CE) or cholesterol (C), or mixtures of cholesterol ester and cholesterol.

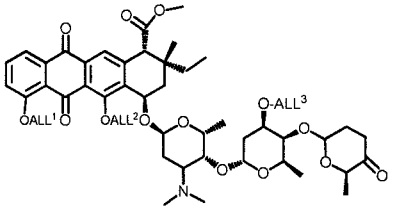
5. The LDL nanoparticle of Claim 4, wherein the cholesterol ester is selected from the group consisting of $C_{16\text{-}22}$ esters of cholesterol, and mixtures thereof; and the triglycerides is selected from the group consisting of soybean oil, triolein, glyceryl tripalmitate and mixtures thereof.

6. The LDL nanoparticle of any one of Claims 1 to 5, further comprising an agent selected from the group consisting of triolein, BHT, ubiquinol, ubiquinol 10, vitamin E, alpha-tocopherol, gamma-tocopherol, lycopene, retinyl derivative and betacarotene, or mixtures thereof.

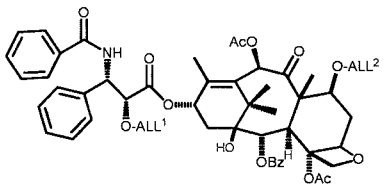
7. The LDL nanoparticle of Claim 6, wherein the anti-cancer agent is selected from the group consisting of a taxane, abeo-taxane, camptothecin, epothilone, cucurbitacin, quassinoid and an anthracycline.

8. The LDL nanoparticle of Claim 6, wherein the anticancer agent is selected from the group consisting of aclarubicin, camptothecin, masoprocol, paclitaxel, pentostatin, amrubicin, cladribine, cytarabine, docetaxel, gemcitabine, elliptinium acetate, epirubicin, etoposide, formestane, fulvestrant, idarubicin, pirarubicin, topotecan, valrubicin and vinblastine.

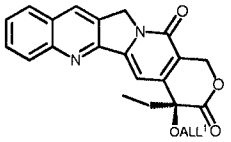
9. The LDL nanoparticle of Claim 6, wherein the pro-drug of the anti-cancer agent is an acid labile lipophilic molecular conjugates (ALLMC) selected from the group consisting of:



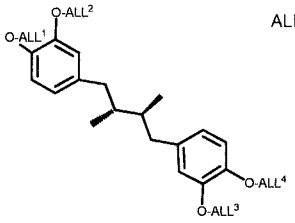
ALLMC of aclarubicin



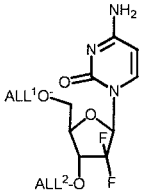
ALLMC of paclitaxel



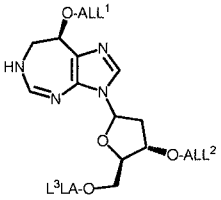
ALLMC of camptothecin



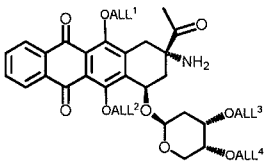
ALLMC of masoprocol



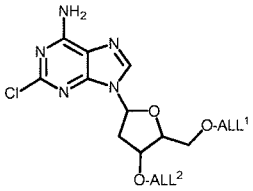
ALLMC of gemcitabine



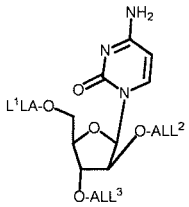
ALLMC of pentostatin



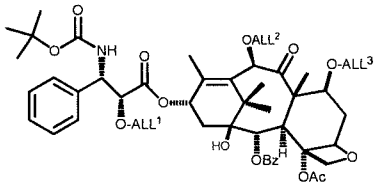
ALLMC of amrubicin



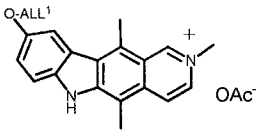
ALLMC of cladribine



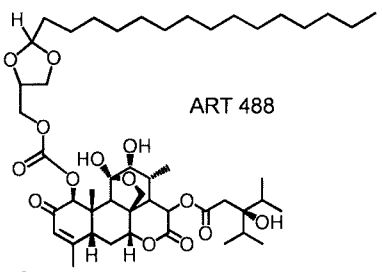
ALLMC of cytarabine



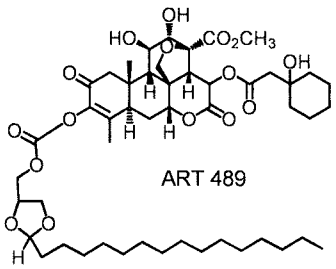
ALLMC of docetaxel



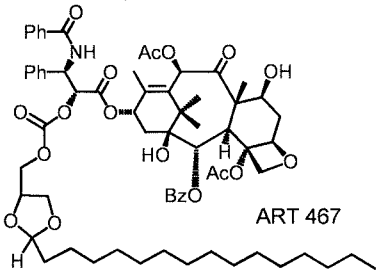
ALLMC of elliptinium acetate



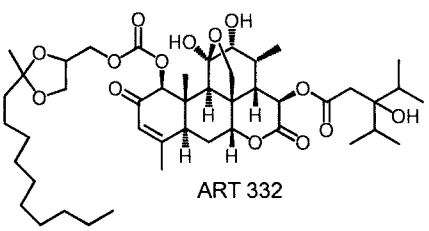
ART 488



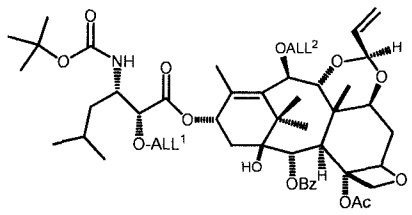
ART 489



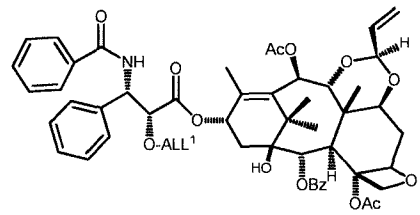
ART 467



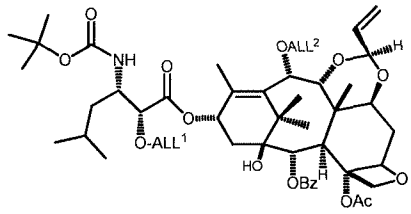
ART 332



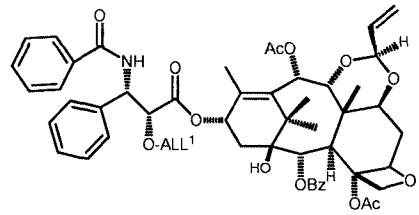
ALLMC of a 10-beta-taxane analog (19a)



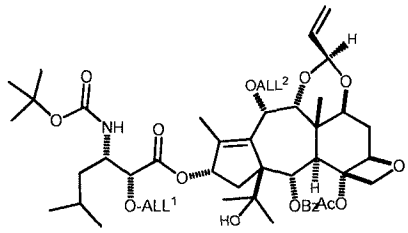
ALLMC of a 10-beta taxane analog (19b)



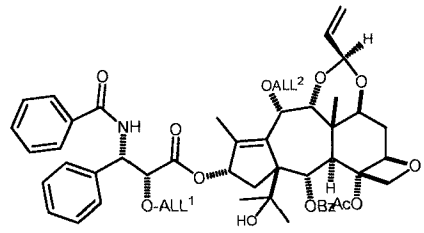
ALLMC of a 10-alpha taxane analog (19c)



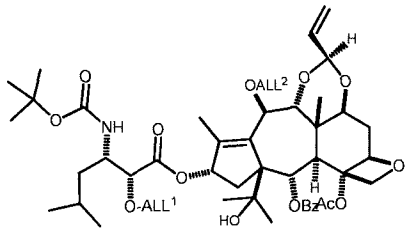
ALLMC of a 10-alpha analog (19d)



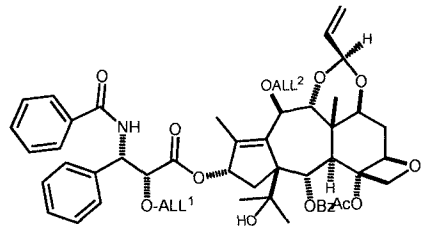
ALLMC of a 10-alpha abeo-taxane analog (19e)



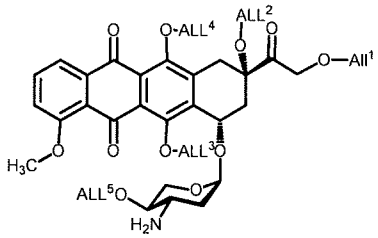
ALLMC of a 10-alpha abeo-taxane analog (19f)



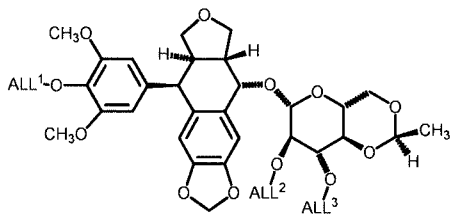
ALLMC of a 10-beta abeo-taxane analog (19g)



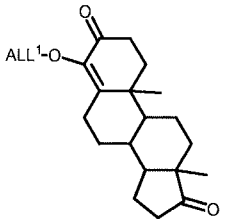
ALLMC of a 10-beta abeo-taxane analog (19h)



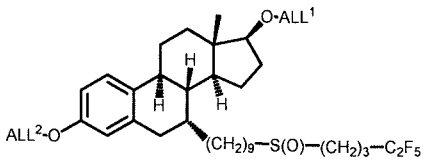
ALLMC of epirubicin



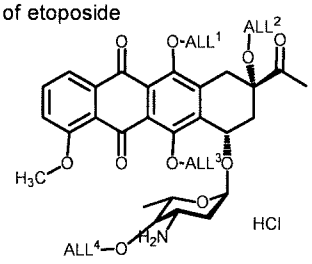
ALLMC of etoposide



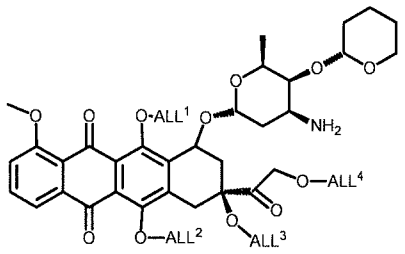
ALLMC of formestane



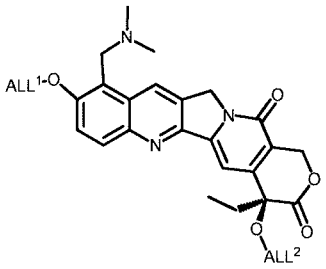
ALLMC of fulvestrant



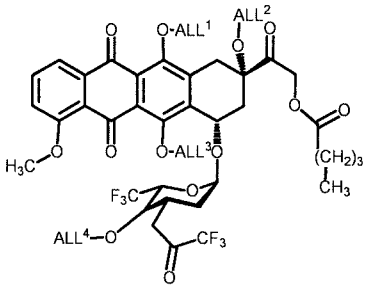
ALLMC of idarubicin



ALLMC of pirarubicin

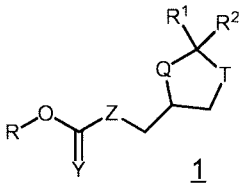


ALLMC of topotecan

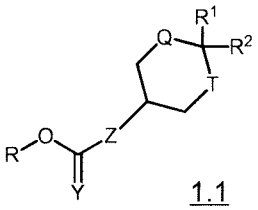


ALLMC of valrubicin

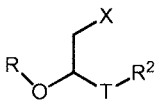
wherein -ALL^1, -ALL^2, -ALL^3 and -ALL^4 are each independently hydrogen or an acid labile lipophilic group of the formula:



1



1.1



2

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent;

for formula **1** or **1.1**:

R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl;

R^2 is C_5-C_{22} alkyl;

Y is selected from O, NR' or S wherein R' is hydrogen or C_1-C_6 alkyl;

Z is O or S;

Q is O or S; and T is O or S;

for formula **2**:

R^2 is a C_1-C_{22} alkyl;

T is O or S; and

X is a hydrogen or a leaving group selected from the group consisting of mesylates, sulfonates and Cl, Br and I;

and their isolated enantiomers, diastereoisomers or mixtures thereof;

10. The LDL nanoparticle of any one of Claims 1 to 9, wherein the lipophilic anti-cancer agent has a logP greater than 4.0, greater than 6.0 or greater than 8.0.

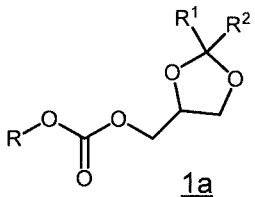
11. The LDL nanoparticle of Claim 4, wherein the weight ratio of PL:TG:CE:C ranges from 73:12:2:1 to 78:12:2:1; optionally further comprising an additive selected from the group consisting of triolein, BHT, ubiquinol, ubiquinol 10, vitamin E, alpha-tocopherol, gamma-tocopherol, lycopene, retinyl derivative and betacarotene, or mixtures thereof.

12. The LDL nanoparticle of Claim 11, wherein the weight ratio of PL:TG:CE:C is 77:10:2:1.

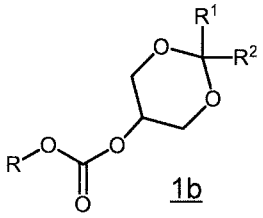
13. The LDL nanoparticle of any one of Claims 1 to 12, further comprising a poloxamer that are nonionic triblock copolymers composed of a central hydrophobic chain of polyoxypropylene (poly(propylene oxide)) flanked by two hydrophilic chains of polyoxyethylene (poly(ethylene oxide)), or mixtures thereof.

14. A process for preparing a stable, synthetic low density lipoprotein (LDL) solid nanoparticle comprising:

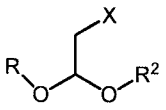
a) a lipophilic anti-cancer agent of the formula **1a**, **1b** or formula **2a**:



1a



1b



2a

wherein:

for formula **1a** or **1b** R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; and R^2 is C_5-C_{22} alkyl; and for formula **2a**: R^2 is C_1-C_{22} alkyl; and X is hydrogen or is selected from the group consisting of Cl, Br and I; and

R is a hydroxyl bearing cancer chemotherapeutic agent (HBCCA) selected from the group consisting of a taxane, abeo-taxane, camptothecin, epothilone, cucurbitacin, quassinoid and an anthracycline;

b) phospholipids (PL); and

c) triglycerides (TG);

the process comprising:

1) combining the lipophilic anti-cancer agent, phospholipids and triglycerides to form a mixture;

2) homogenizing the mixture by dissolution in a volatile solvent;

3) removing the solvent;

4) forming a coarse emulsion by blending of the mixture in a buffer to form an emulsion mixture;

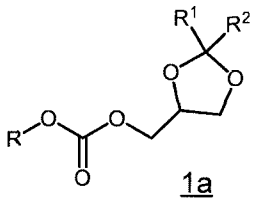
5) microfluidizing the emulsion mixture in a microfluidizer apparatus for a sufficient amount of time to produce a particle preparation of 100 nm or less; and

6) sterilizing the nanoparticle preparation through a 0.22 micron filter to obtain the synthetic LDL nanoparticles with a mean particle size range of 40 nm to 80 nm.

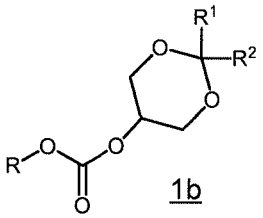
15. The process of Claim 14, wherein the synthetic low density lipoprotein (LDL) nanoparticle mixture wherein the phospholipids is selected from the group consisting of phosphotidylcholine, phosphotidylethanolamine, symmetric or asymmetric 1,2-diacyl-sn-glycero-3-phosphorylcholines, 1,2-dimyristoyl-sn-glycero-3-phosphorylcholine,1,2-dimyristoyl-sn-glycero-3-phosphorylethanolamine, egg phospholipids, egg phosphatidyl glycerol, dipalmitoylphosphatidylglycerol, egg lecithin, soy lecithin, lecithin (NOS) and mixtures thereof.

16. The process of Claim 14 or 15, wherein the LDL nanoparticle further comprises cholesterol (C) or cholesterol ester (CE) selected from the group consisting of C_{16-22} esters of cholesterol, cholesterol and mixtures thereof; and the triglycerides is selected from the group consisting of soybean oil, triolein, glyceryl tripalmitate and mixtures thereof; or mixtures of cholesterol and cholesterol esters.

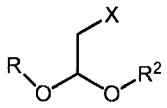
17. A stable, synthetic low density lipoprotein (LDL) solid nanoparticle comprising: a) a lipophilic anti-cancer agent of the formula **1a**, **1b** or formula **2a**:



1a



1b



2a

wherein:

for formula **1a** or **1b:** R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; and R^2 is C_5-C_{22} alkyl; and for formula **2a**: R^2 is C_1-C_{22} alkyl; and X is hydrogen or is selected from the group consisting of Cl, Br and I; and

R is a hydroxyl bearing cancer chemotherapeutic agent (HBCCA) selected from the group consisting of a taxane, abeo-taxane, camptothecin, epothilone, cucurbitacin, quassinoid and an anthracycline;

b) phospholipids (PL); and

c) triglycerides (TG) prepared by the process comprising:

1) combining the lipophilic anti-cancer agent, phospholipids and triglycerides to form a mixture;

2) homogenizing the mixture by dissolution in a volatile solvent;

3) removing the solvent;

4) forming a coarse emulsion by blending of the mixture in a buffer to form an emulsion mixture;

5) microfluidizing the emulsion mixture in a microfluidizer apparatus for a sufficient amount of time to produce a particle preparation of 100 nm or less; and

6) sterilizing the nanoparticle preparation through a 0.22 micron filter to obtain the synthetic LDL nanoparticles with a mean particle size range of 40 nm to 80 nm.

18. The use of a stable, synthetic low density lipoprotein (LDL) nanoparticle of any one of Claims 1 to 14, and Claim 17 in the manufacture of a medicament for the treatment of cancer in a patient in need of such treatment.

19. The use of Claim 18, wherein the cancer is selected from the group consisting of leukemia, neuroblastoma, glioblastoma, cervical, colorectal, pancreatic, renal melanoma, lung, breast, prostate, ovarian and head and neck.