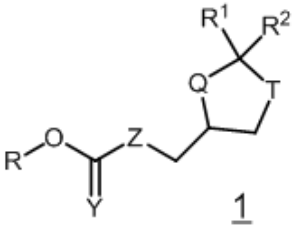
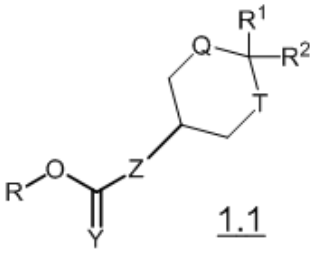
What is claimed is:

1. An acid labile lipophilic molecular conjugate (ALLMC) of the formula **1**, **1.1**:



1



1.1

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent;

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;

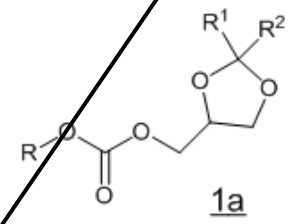
Z is O;

Q is O; and T is O;

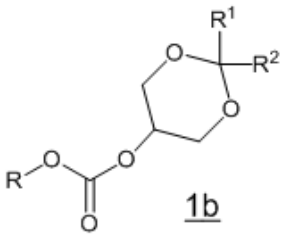
and their isolated enantiomers, diastereoisomers or mixtures thereof;

or a pharmaceutically acceptable salt thereof.

2. The acid labile lipophilic molecular conjugate of Claim 1 comprising the formula **1a**, or **1b**:



1a



1b

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent (HBCCA);

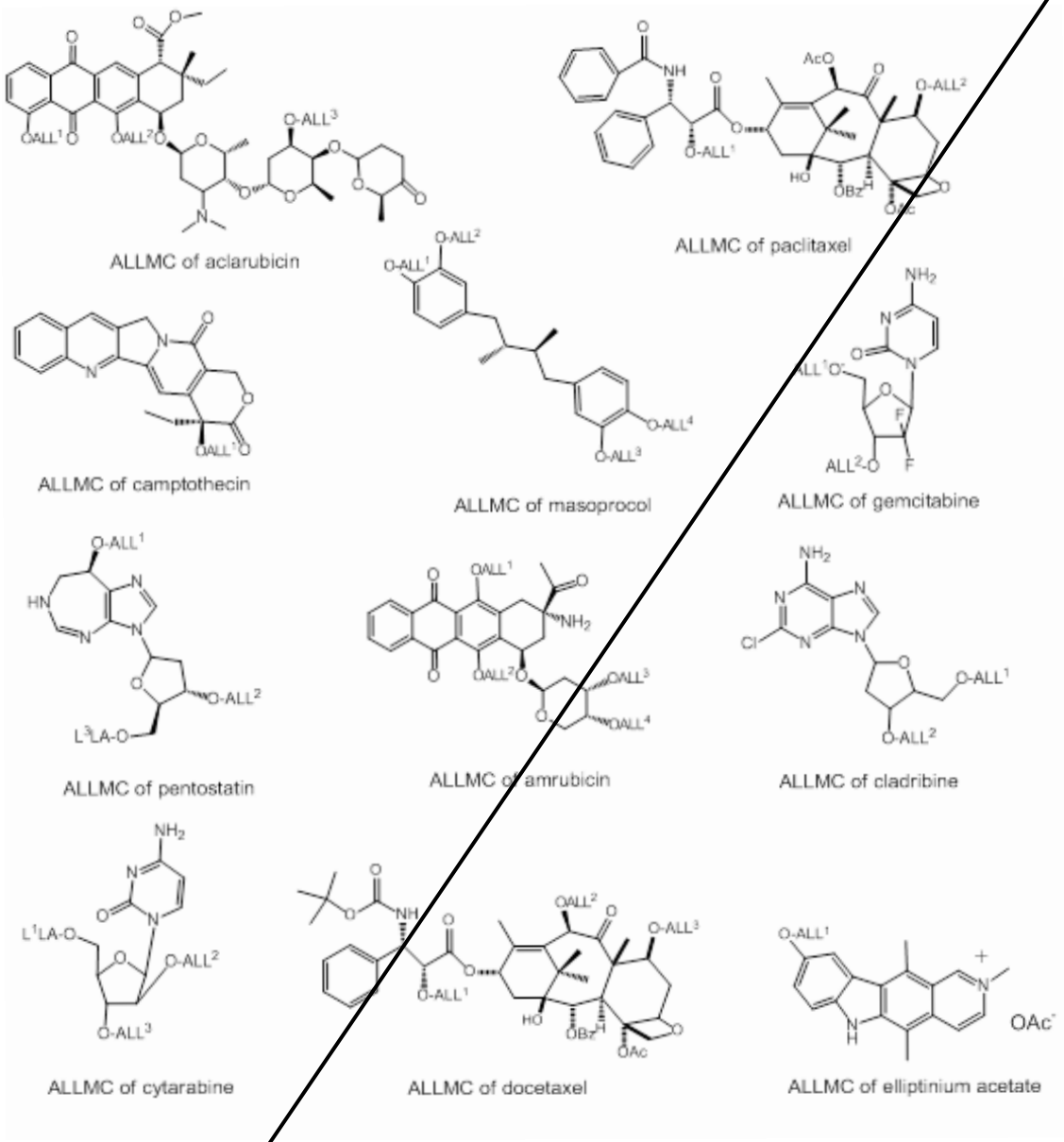
R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; and

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

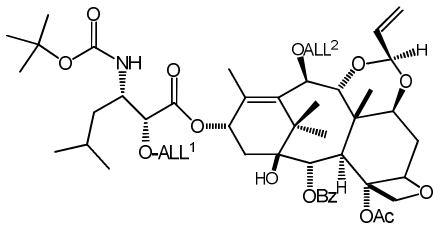
3. The acid labile lipophilic molecular conjugate of Claim 1, wherein the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of taxanes, abeo-taxanes, camptothecins, epothilones, cucurbitacins, quassinoids, anthracyclines, and their analogs and derivatives.

4. The acid labile lipophilic molecular conjugate of Claim 1, wherein the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of aclarubicin, camptothecin, masoprocol, paclitaxel, pentostatin, amrubicin, cladribine, cytarabine, docetaxel, elliptinium acetate, epirubicin, etoposide, formestane, fulvestrant, gemcitabine, idarubicin, pirarubicin, topotecan, valrubicin and vinblastine.

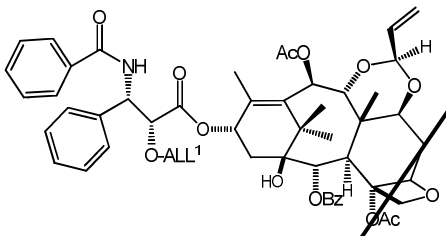
5. The acid labile lipophilic molecular conjugate of Claim 1, wherein the conjugate is selected from the following compounds:



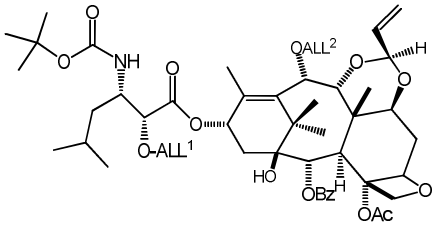
ART 489; ART 488; ART 467; ART 332



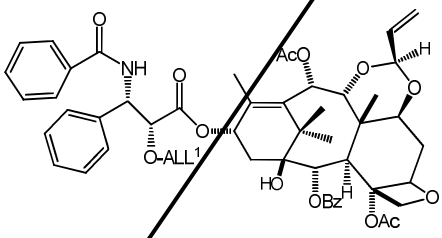
ALLMC of a 10-beta-taxane analog (19a)



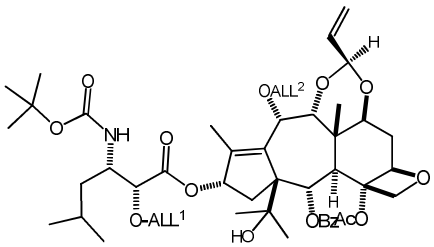
ALLMC of a 10-beta taxane analog (19b)



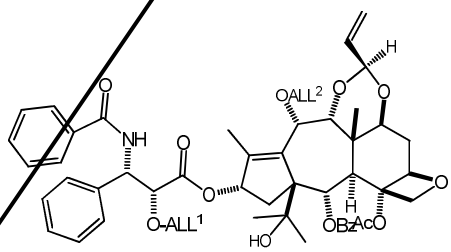
ALLMC of a 10-alpha taxane analog (19c)



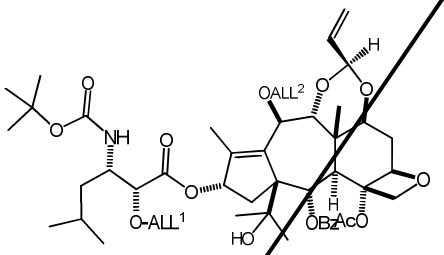
ALLMC of a 10-alpha analog (19d)



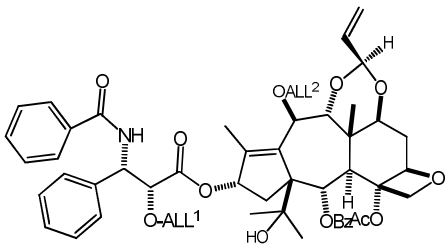
ALLMC of a 10-alpha abeo-taxane analog (19e)



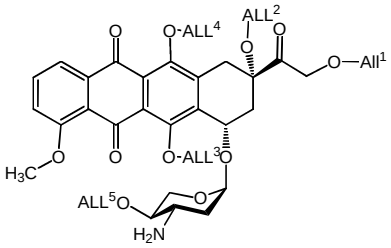
ALLMC of a 10-alpha abeo-taxane analog (19f)



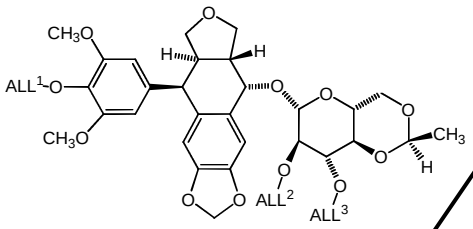
ALLMC of a 10-beta abeo-taxane analog (19g)



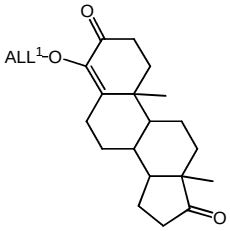
ALLMC of a 10-beta abeo-taxane analog (19h)



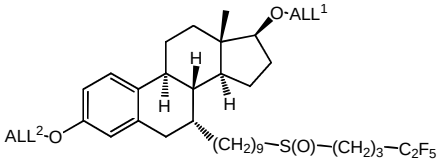
ALLMC of epirubicin



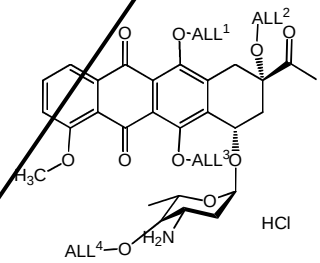
ALLMC of etoposide



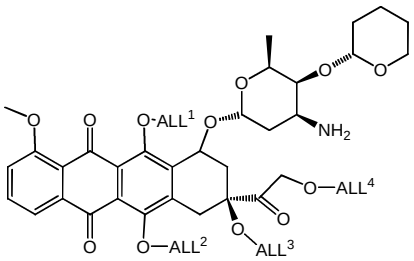
ALLMC of formestane



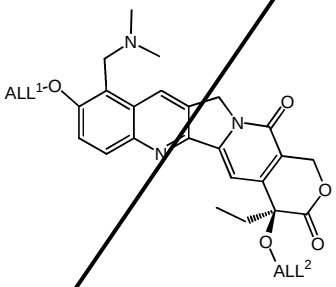
ALLMC of fulvestrant



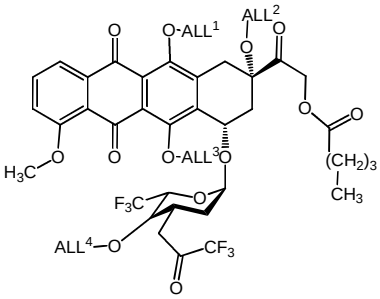
ALLMC of idarubicin



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, provided that at least one of –ALL^1, -ALL^2, -ALL^3 and –ALL^4 is an acid labile lipophilic group.

6. A pharmaceutical composition comprising: a) a therapeutically effective amount of a compound of Claims 1, in the form of a single diastereoisomer; and b) a pharmaceutically acceptable excipient.

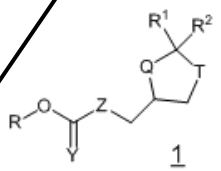
7. A pharmaceutical composition for the treatment of cancer in a patient in need of such treatment comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable excipient.

8. The pharmaceutical composition of Claim 7, wherein the cancer is selected from the group consisting of leukemia, neuroblastoma, glioblastoma, cervical, colorectal, pancreatic, renal and melanoma.

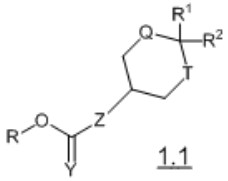
9. The pharmaceutical composition of Claim 7, wherein the cancer is selected from the group consisting of lung cancer, breast cancer, prostate cancer, ovarian cancer and head and neck cancer.

10. The pharmaceutical composition of Claim 7, wherein the pharmaceutical composition provides at least a 10% to 50% diminished degree of resistant expressed by the cancer cells when compared with the non-conjugated hydroxyl bearing cancer chemotherapeutic agent.

11. A pharmaceutical composition for reducing or eliminating the side effects of chemotherapy associated with the administration of a cancer chemotherapeutic agent to a patient, comprising a therapeutically effective amount of an acid labile lipophilic molecular conjugate of the formula **1**, or **1.1**:



1



1.1

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent;

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 O;

Z is O; and

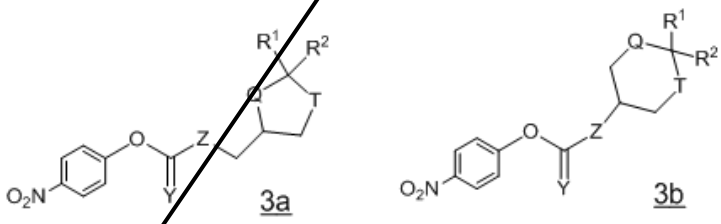
Q is O; and T is O;

and their isolated enantiomers, diastereoisomers or mixtures thereof.

12. The pharmaceutical composition of Claim 11, wherein the pharmaceutical composition provides a higher concentration of the cancer chemotherapeutic agent in a cancer cell of the patient.

13. The pharmaceutical composition of Claim 12, wherein the pharmaceutical composition delivers a higher concentration of the cancer chemotherapeutic agent in the cancer cell, when compared to the administration of a non-conjugated cancer chemotherapeutic agent to the patient, by at least 5%, 10%, 20% or at least 50%.

14. A compound of the formula **3a** or **3b**:



wherein:

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 selected from O or S; and

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

15. The compound of Claim 14, wherein:

R^1 is hydrogen or C_1-C_4 alkyl;

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

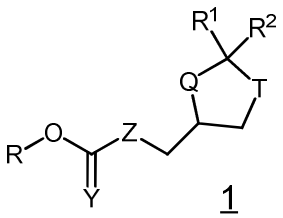
Y is O or S;

Z is O; and

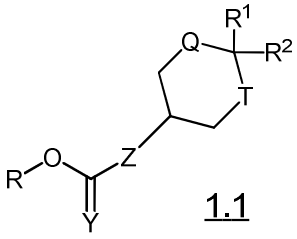
Q is O; and T is O.

What is claimed is:

1. An acid labile lipophilic molecular conjugate (ALLMC) of the formula **1**, **1.1**:



1



1.1

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent;

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

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

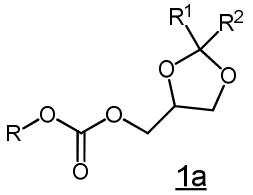
Y is selected from O, or S;

Z is O;

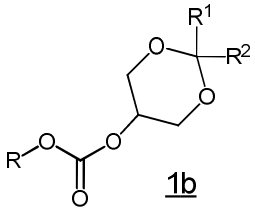
Q is O; and T is O;

wherein the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of taxanes, abeo-taxanes, camptothecins, epothilones, cucurbitacins, quassinoids, anthracyclines, aclarubicin, masoprocol, paclitaxel, pentostatin, amrubicin, cladribine, cytarabine, docetaxel, elliptinium acetate, epirubicin, etoposide, formestane, fulvestrant, gemcitabine, idarubicin, pirarubicin, topotecan, valrubicin and vinblastine and their isolated enantiomers, diastereoisomers or mixtures thereof;
or a pharmaceutically acceptable salt thereof.

2. The acid labile lipophilic molecular conjugate of Claim 1 comprising the formula **1a**, or **1b**:



1a



1b

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent (HBCCA);

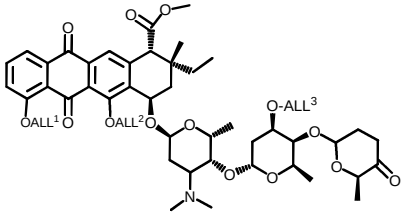
R^1 is hydrogen, C_1-C_4 alkyl or C_5-C_{22} alkyl; and

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

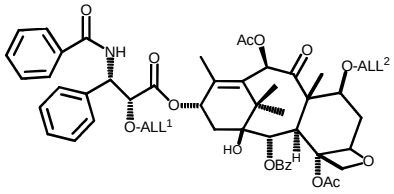
3. The acid labile lipophilic molecular conjugate of Claim 1, wherein the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of taxanes, abeo-taxanes, camptothecins, epothilones, cucurbitacins, quassinoids, anthracyclines, and their analogs and derivatives.

4. The acid labile lipophilic molecular conjugate of Claim 1, wherein the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of aclarubicin, camptothecin, masoprocol, paclitaxel, pentostatin, amrubicin, cladribine, cytarabine, docetaxel, elliptinium acetate, epirubicin, etoposide, formestane, fulvestrant, gemcitabine, idarubicin, pirarubicin, topotecan, valrubicin and vinblastine.

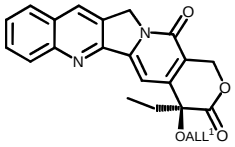
5. The acid labile lipophilic molecular conjugate of Claim 1, wherein the conjugate is selected from the following compounds:



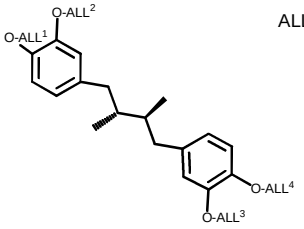
ALLMC of aclarubicin



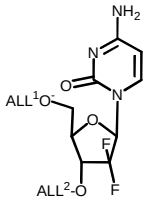
ALLMC of paclitaxel



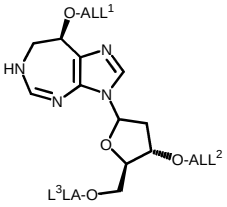
ALLMC of camptothecin



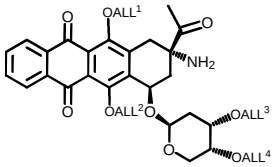
ALLMC of masoprocol



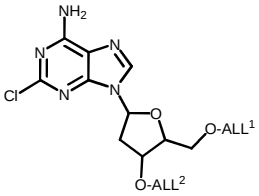
ALLMC of gemcitabine



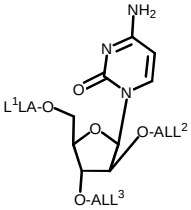
ALLMC of pentostatin



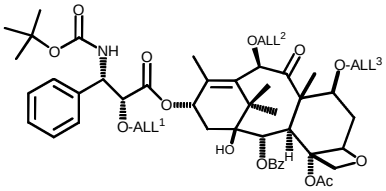
ALLMC of amrubicin



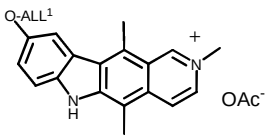
ALLMC of cladribine



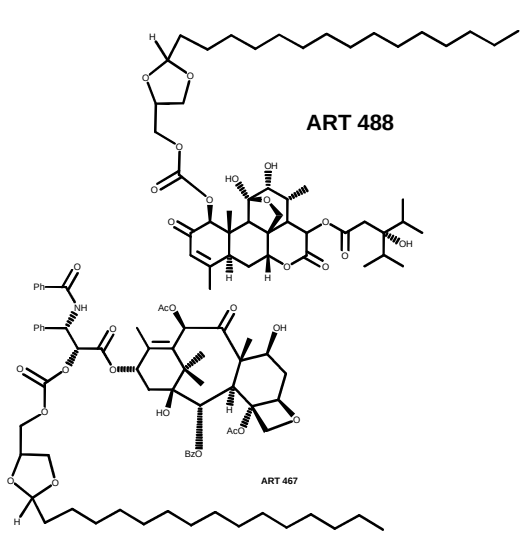
ALLMC of cytarabine



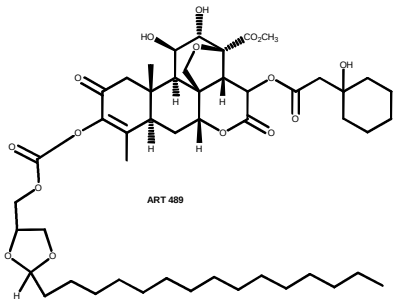
ALLMC of docetaxel



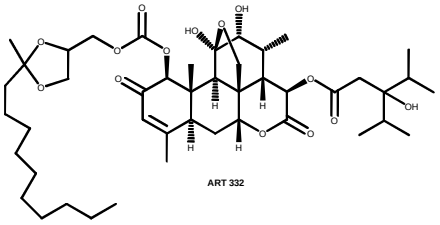
ALLMC of elliptinium acetate



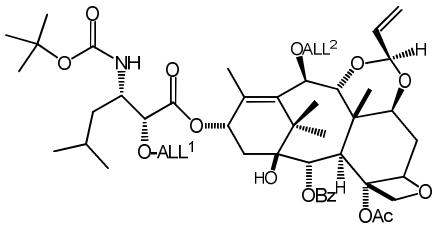
ART 488



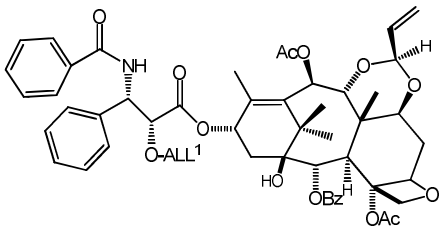
ART 489



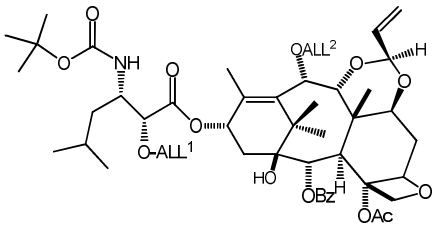
ART 332



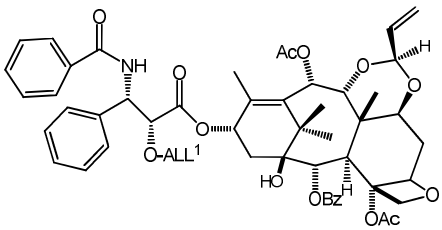
ALLMC of a 10-beta-taxane analog (19a)



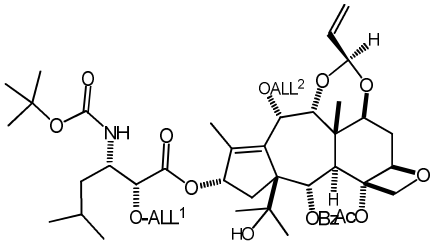
ALLMC of a 10-beta taxane analog (19b)



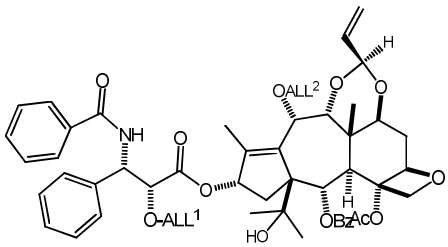
ALLMC of a 10-alpha taxane analog (19c)



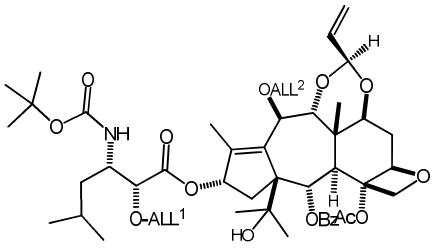
ALLMC of a 10-alpha analog (19d)



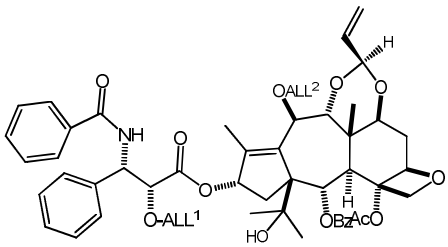
ALLMC of a 10-alpha abeo-taxane analog (19e)



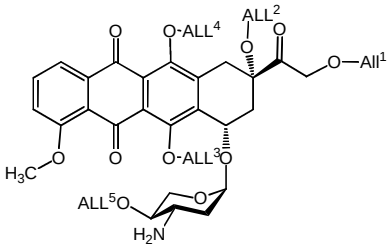
ALLMC of a 10-alpha abeo-taxane analog (19f)



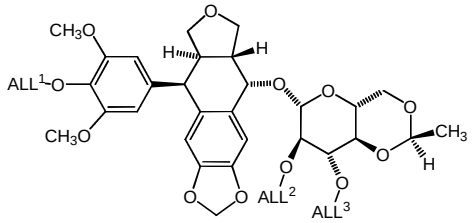
ALLMC of a 10-beta abeo-taxane analog (19g)



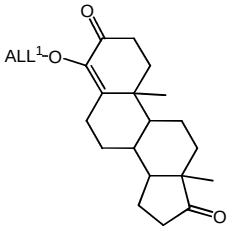
ALLMC of a 10-beta abeo-taxane analog (19h)



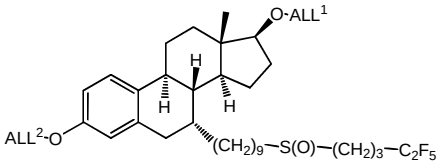
ALLMC of epirubicin



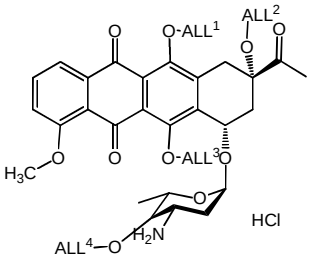
ALLMC of etoposide



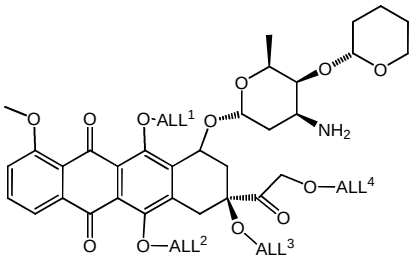
ALLMC of formestane



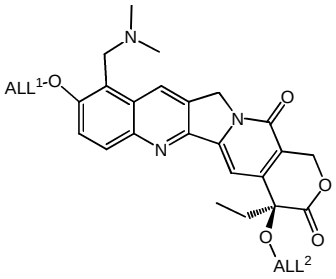
ALLMC of fulvestrant



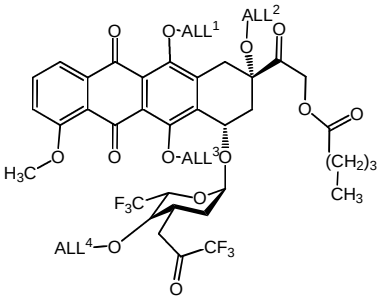
ALLMC of idarubicin



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, provided that at least one of –ALL^1, -ALL^2, -ALL^3 and –ALL^4 is an acid labile lipophilic group.

6. A pharmaceutical composition comprising: a) a therapeutically effective amount of a compound of Claim 1, in the form of a single diastereoisomer; and b) a pharmaceutically acceptable excipient.

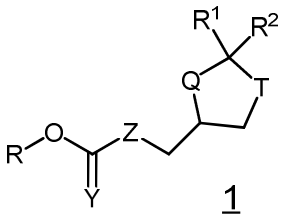
7. A pharmaceutical composition for use in the treatment of cancer in a patient in need of such treatment comprising a therapeutically effective amount of a compound of Claim 1 and a pharmaceutically acceptable excipient.

8. The pharmaceutical composition of Claim 7, wherein the cancer is selected from the group consisting of leukemia, neuroblastoma, glioblastoma, cervical, colorectal, pancreatic, renal and melanoma.

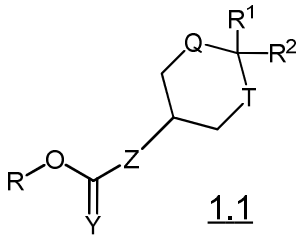
9. The pharmaceutical composition of Claim 7, wherein the cancer is selected from the group consisting of lung cancer, breast cancer, prostate cancer, ovarian cancer and head and neck cancer.

10. The pharmaceutical composition of Claim 7, wherein the pharmaceutical composition provides at least a 10% to 50% diminished degree of resistant expressed by the cancer cells when compared with the non-conjugated hydroxyl bearing cancer chemotherapeutic agent.

11. A pharmaceutical composition for use in reducing or eliminating the side effects of chemotherapy associated with the administration of a cancer chemotherapeutic agent to a patient, comprising a therapeutically effective amount of an acid labile lipophilic molecular conjugate of the formula **1**, or **1.1**:



1



1.1

wherein:

R is a hydroxyl bearing cancer chemotherapeutic agent;

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 O;

Z is O; and

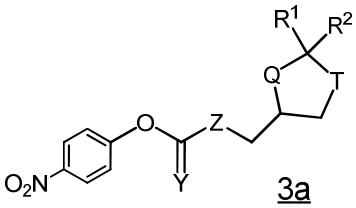
Q is O; and T is O;

wherein the hydroxyl bearing cancer chemotherapeutic agent is selected from the group consisting of taxanes, abeo-taxanes, camptothecins, epothilones, cucurbitacins, quassinoids, anthracyclines, aclarubicin, masoprocol, paclitaxel, pentostatin, amrubicin, cladribine, cytarabine, docetaxel, elliptinium acetate, epirubicin, etoposide, formestane, fulvestrant, gemcitabine, idarubicin, pirarubicin, topotecan, valrubicin and vinblastine and their isolated enantiomers, diastereoisomers or mixtures thereof.

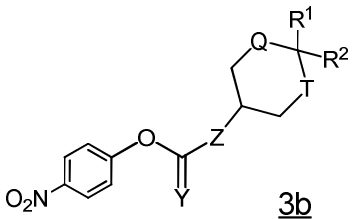
12. The pharmaceutical composition of Claim 11, wherein the pharmaceutical composition provides a higher concentration of the cancer chemotherapeutic agent in a cancer cell of the patient.

13. The pharmaceutical composition of Claim 11, wherein the pharmaceutical composition delivers a higher concentration of the cancer chemotherapeutic agent in the cancer cell, when compared to the administration of a non-conjugated cancer chemotherapeutic agent to the patient, by at least 5%, 10%, 20% or at least 50%.

14. A compound of the formula **3a** or **3b**:



3a



3b

wherein:

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 selected from O or S; and

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

15. The compound of Claim 14, wherein:

R^1 is hydrogen or C_1-C_4 alkyl;

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

Y is O or S;

Z is O; and

Q is O; and T is O.