

CAMPTOTHECIN CONJUGATES

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to and the benefit of U.S. Application No. 63/321,105, filed on March 17, 2022, and U.S. Application No. 63/407,609, filed on September 16, 2022, the disclosures of which are hereby incorporated by reference in their entirety for all purposes.

REFERENCE TO AN ELECTRONIC SEQUENCE LISTING

[0002] The contents of the electronic sequence listing (761682009440SEQLIST.xml; Size: 1,128,239 bytes; and Date of Creation: March 16, 2023) is herein incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

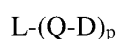
[0003] Antibodies (mAbs) have been investigated for the targeted delivery of cytotoxic agents to tumor cells. While various drug classes have been evaluated for targeted delivery by antibodies, only a few drug classes have proved sufficiently active as antibody drug conjugates, while having a suitable toxicity profile and other pharmacological properties, to warrant clinical development. One drug class receiving interest is the camptothecins.

[0004] The design of Antibody Drug Conjugates (ADCs), by attaching a cytotoxic agent to antibody, typically via a linker, involves consideration of a variety of factors, including the presence of a conjugation handle on the drug for attachment to the linker and linker technology for attaching the drug to an antibody in a conditionally stable manner. The conjugation handle for the parent compound in the class is the C20 hydroxyl functional group in which the linker is attached through a carbonate functional group (e.g., see Walker, M.A. et al. *Bioorganic & Medicinal Chemistry Letters* (2002) 12(2): 217-219. However, carbonate functional groups typically suffer from hydrolytic instability, which cause premature release of free drug into systemic circulation, which can result in reduced ADC potency, insufficient immunologic specificity of the conjugate and increased toxicity. Therefore, there is a need for camptothecin conjugates engineered for control over drug-linker stability to increase the amount of drug delivered to the desired site of action. The present invention addresses those and other needs.

BRIEF SUMMARY OF THE INVENTION

[0005] The invention provides *inter alia*, Camptothecin Conjugates, Camptothecin-Linker Compounds and Camptothecin Compounds methods of preparing and using them, and intermediates thereof. The Camptothecin Conjugates of the present invention are stable in circulation, yet capable of inflicting cell death once free drug is released from a Conjugate in the vicinity or within tumor cells.

[0006] In one embodiment, a Camptothecin Conjugate is provided having a formula:

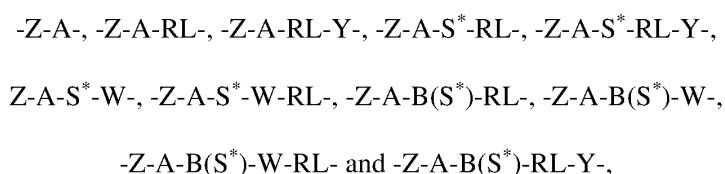


or a salt thereof, wherein

L is a Ligand Unit;

subscript p is an integer of from 1 to 16;

Q is a Linker Unit having a formula selected from the group consisting of:



wherein Z is a Stretcher Unit;

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

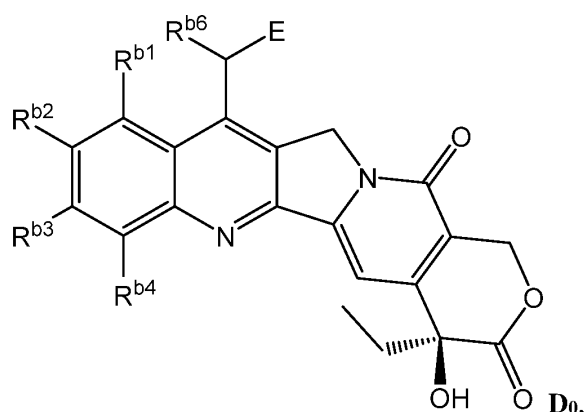
S* is a Partitioning Agent;

RL is a Releasable Linker;

W is an Amino Acid Unit;

Y is a Spacer Unit; and

D is a Drug Unit having a formula of



or a salt thereof; wherein;

E is $-\text{OR}^{\text{b5}}$ or $-\text{NR}^{\text{b5}}\text{R}^{\text{b5'}}$;

R^{b1} is selected from the group consisting of H, halogen, $-\text{CN}$, $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_1\text{-C}_8$ haloalkyl, $\text{C}_2\text{-C}_8$ alkenyl, $\text{C}_2\text{-C}_8$ alkynyl, $\text{C}_6\text{-C}_{12}$ aryl, 5- to 12-membered heteroaryl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, 3- to 10-membered heterocycloalkyl, $(\text{C}_6\text{-C}_{12} \text{ aryl})\text{-C}_2\text{-C}_8$ alkenyl-, $\text{C}_1\text{-C}_8$ hydroxyalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ aminoalkyl-, $\text{C}_1\text{-C}_8$ aminoalkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ alkyl-, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{C}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{O-C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-O-}$, $-\text{COOR}^{\text{a}}$, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; each optionally substituted with $\text{C}_1\text{-C}_3$ alkyl, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, $-\text{C}(\text{O})\text{R}^{\text{a}}$, and $-\text{SR}^{\text{a}}$; or

R^{b1} is combined with R^{b2} , R^{b5} , or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_2\text{-C}_8$ alkynyl, $\text{C}_6\text{-C}_{12}$ aryl, 5- to 12-membered heteroaryl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, 3- to 10-membered heterocycloalkyl, $\text{C}_1\text{-C}_8$ haloalkyl, $\text{C}_1\text{-C}_8$ hydroxyalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{S}(\text{O})_2\text{-}$, $\text{C}_1\text{-C}_8$ aminoalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ aminoalkyl-, $\text{C}_1\text{-C}_8$ aminoalkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ alkyl-, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{O-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{C}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{O-C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-O-}$, $-\text{COOR}^{\text{a}}$, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; each optionally substituted with $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6- membered heterocyclo fused with 6-membered aryl;

R^{b3} is selected from the group consisting of H, halogen, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_1\text{-C}_6$ haloalkyl, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$;

R^{b4} is selected from the group consisting of H or halogen;
each R^{b5} and $R^{b5'}$ are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₆ alkyl-O-C₁-C₆ alkyl-, C₁-C₈ aminoalkyl-, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl-, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, C₁-C₆ hydroxyalkyl-heteroaryl-, phenyl-, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl-, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl-, -OH-, -C₁-C₆ hydroxyalkyl-, -OC₁-C₄ alkyl-, -NH₂-, -NH-C₁-C₄ alkyl-, -N(C₁-C₄ alkyl)₂-, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or
 $R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl-, -OH-, -OC₁-C₄ alkyl-, -NH₂-, -NHC₁-C₄ alkyl-, and -N(C₁-C₄ alkyl)₂;
 R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and
 R^a and $R^{a'}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

[0007] Other embodiments as noted above, are Camptothecin-Linker Compounds useful as intermediates for preparing Camptothecin Conjugates, wherein the Camptothecin-Linker

Compound is comprised of a Camptothecin and a Linker Unit (Q), wherein the Linker Unit is comprised of a Stretcher Unit precursor (Z') capable of forming a covalent bond to a targeting ligand that provides for a Ligand Unit, and a Releasable Linker (RL), which in some aspects of Q not having an Amino Acid Unit is a Glycoside (e.g., Glucuronide) Unit.

[0008] In another aspect, provided herein are methods of treating cancer comprising administering to a subject in need thereof a Camptothecin Conjugate described herein.

[0009] In another aspect, provided herein are kits comprising a Camptothecin Conjugate described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] **FIG. 1A** and **FIG. 1B** show mean tumor volume in a L540cy mouse model over time with administration of one dose of a camptothecin ADC with a Ag4 antibody (**FIG. 1A**) or an h00 antibody (**FIG. 1B**) on day 12.

[0011] **FIG. 2** shows mean tumor volume in EBC-1 mouse models over time with administration of one dose of a glucuronide-based camptothecin ADC with an Ag2 antibody at day 7.

[0012] **FIG. 3** shows mean tumor volume in OV-90 mouse models over time with administration of one dose of a glucuronide-based camptothecin ADC with an Ag3 antibody at day 17.

[0013] **FIG. 4** shows mean tumor volume in 786-O mouse models over time with administration of one dose of a glucuronide-based camptothecin ADC with an Ag5 antibody at day 15.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

[0014] Unless stated otherwise, the following terms and phrases as used herein are intended to have the following meanings. When trade names are used herein, the trade name includes the product formulation, the generic drug, and the active pharmaceutical ingredient(s) of the trade name product, unless otherwise indicated by context.

[0015] The term “antibody” as used herein is used in the broadest sense and specifically covers intact monoclonal antibodies, polyclonal antibodies, monospecific antibodies, multispecific antibodies (e.g., bispecific antibodies), and antibody fragments that exhibit the desired biological activity. The native form of an antibody is a tetramer and consists of two

identical pairs of immunoglobulin chains, each pair having one light chain and one heavy chain. In each pair, the light and heavy chain variable regions (V_L and V_H) are together primarily responsible for binding to an antigen. The light chain and heavy chain variable domains consist of a framework region interrupted by three hypervariable regions, also called “complementarity determining regions” or “CDRs.” The constant regions may be recognized by and interact with the immune system. (see, e.g., Janeway *et al.*, 2001, *Immunol. Biology*, 5th Ed., Garland Publishing, New York). An antibody can be of any type (e.g., IgG, IgE, IgM, IgD, and IgA), class (e.g., IgG₁, IgG₂, IgG₃, IgG₄, IgA₁ and IgA₂) or subclass thereof. The antibody can be derived from any suitable species. In some embodiments, the antibody is of human or murine origin. An antibody can be, for example, human, humanized, or chimeric.

[0016] The term “monoclonal antibody” as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, *i.e.*, the individual antibodies comprising the population are identical except for possible naturally occurring mutations that may be present in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic site. The modifier “monoclonal” indicates the character of the antibody as being obtained from a substantially homogeneous population of antibodies and is not to be construed as requiring production of the antibody by any particular method.

[0017] An “intact antibody” is one which comprises an antigen-binding variable region as well as a light chain constant domain (C_L) and heavy chain constant domains, C_{H1} , C_{H2} , C_{H3} , and C_{H4} , as appropriate for the antibody class. The constant domains may be native sequence constant domains (e.g., human native sequence constant domains) or amino acid sequence variant thereof.

[0018] An “antibody fragment” comprises a portion of an intact antibody, comprising the antigen-binding or variable region thereof. Examples of antibody fragments include Fab, Fab', F(ab')₂, and Fv fragments, diabodies, triabodies, tetrabodies, linear antibodies, single-chain antibody molecules, scFv, scFv-Fc, multispecific antibody fragments formed from antibody fragment(s), a fragment(s) produced by a Fab expression library, or an epitope-binding fragments of any of the above which immunospecifically bind to a target antigen (e.g., a cancer cell antigen, a viral antigen or a microbial antigen).

[0019] An “antigen” is an entity to which an antibody specifically binds.

[0020] The terms “specific binding” and “specifically binds” mean that the antibody or antibody derivative will bind, in a highly selective manner, with its corresponding epitope of a target antigen and not with the multitude of other antigens. Typically, the antibody or antibody derivative binds with an affinity of at least about 1×10^{-7} M, and preferably 10^{-8} M to 10^{-9} M, 10^{-10} M, 10^{-11} M, or 10^{-12} M and binds to the predetermined antigen with an affinity that is at least two-fold greater than its affinity for binding to a non-specific antigen (*e.g.*, BSA, casein) other than the predetermined antigen or a closely related antigen.

[0021] The term “inhibits” or “inhibition of” means to reduce by a measurable amount, or to prevent entirely.

[0022] The term “therapeutically effective amount” refers to an amount of a conjugate effective to treat a disease or disorder in a mammal. In the case of cancer, the therapeutically effective amount of the conjugate may reduce the number of cancer cells; reduce the tumor size; inhibit (*i.e.*, slow to some extent and preferably stop) cancer cell infiltration into peripheral organs; inhibit (*i.e.*, slow to some extent and preferably stop) tumor metastasis; inhibit, to some extent, tumor growth; and/or relieve to some extent one or more of the symptoms associated with the cancer. To the extent the drug may inhibit growth and/or kill existing cancer cells, it may be cytostatic and/or cytotoxic. For cancer therapy, efficacy can, for example, be measured by assessing the time to disease progression (TTP) and/or determining the response rate (RR).

[0023] The term “substantial” or “substantially” refers to a majority, *i.e.* >50% of a population, of a mixture or a sample, preferably more than 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97 %, 98%, or 99% of a population.

[0024] The term “cytotoxic activity” refers to a cell-killing effect of a drug or Camptothecin Conjugate or an intracellular metabolite of a Camptothecin Conjugate. Cytotoxic activity may be expressed as the IC_{50} value, which is the concentration (molar or mass) per unit volume at which half the cells survive.

[0025] The term “cytostatic activity” refers to an anti-proliferative effect of a drug or Camptothecin Conjugate or an intracellular metabolite of a Camptothecin Conjugate.

[0026] The term “cytotoxic agent” as used herein refers to a substance that has cytotoxic activity and causes destruction of cells. The term is intended to include chemotherapeutic agents, and toxins such as small molecule toxins or enzymatically active toxins of bacterial, fungal, plant, or animal origin, including synthetic analogs and derivatives thereof.

[0027] The term “cytostatic agent” as used herein refers to a substance that inhibits a function of cells, including cell growth or multiplication. Cytostatic agents include inhibitors such as protein inhibitors, e.g., enzyme inhibitors. Cytostatic agents have cytostatic activity.

[0028] The terms “cancer” and “cancerous” refer to or describe the physiological condition or disorder in mammals that is typically characterized by unregulated cell growth. A “tumor” comprises one or more cancerous cells.

[0029] An “autoimmune disease” as used herein refers to a disease or disorder arising from and directed against an individual’s own tissues or proteins.

[0030] “Patient” as used herein refers to a subject to whom is administered a Camptothecin Conjugate of the present invention. Patient includes, but are not limited to, a human, rat, mouse, guinea pig, non-human primate, pig, goat, cow, horse, dog, cat, bird, and fowl. Typically, the patient is a rat, mouse, dog, human, or non-human primate, more typically a human.

[0031] The terms “treat” or “treatment,” unless otherwise indicated by context, refer to therapeutic treatment and prophylactic wherein the object is to inhibit or slow down (lessen) an undesired physiological change or disorder, such as the development or spread of cancer. For purposes of this invention, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms, diminishment of extent of disease, stabilized (*i.e.*, not worsening) state of disease, delay or slowing of disease progression, amelioration or palliation of the disease state, and remission (whether partial or total), whether detectable or undetectable. “Treatment” can also mean prolonging survival as compared to expected survival if not receiving treatment. Those in need of treatment include those already with the condition or disorder as well as those prone to have the condition or disorder.

[0032] In the context of cancer, the term “treating” includes any or all of: killing tumor cells; inhibiting growth of tumor cells, cancer cells, or of a tumor; inhibiting replication of tumor cells or cancer cells, lessening of overall tumor burden or decreasing the number of cancerous cells, and ameliorating one or more symptoms associated with the disease.

[0033] In the context of an autoimmune disease, the term “treating” includes any or all of: inhibiting replication of cells associated with an autoimmune disease state including, but not limited to, cells that produce an autoimmune antibody, lessening the autoimmune-antibody burden and ameliorating one or more symptoms of an autoimmune disease.

[0034] “Compound” as the term is used herein, refers to and encompasses the chemical compound itself, either named or represented by structure, and salt form(s) thereof, whether explicitly stated or not, unless context makes clear that such salt forms are to be excluded. The term “compound” further encompasses solvate forms of the compound, in which solvent is noncovalently associated with the compound or is reversibly associated covalently with the compound, as when a carbonyl group of the compound is hydrated to form a gem-diol. Solvate forms include those of the compound itself and its salt form(s) and are inclusive of hemisolvates, monosolvates, disolvates, including hydrates; and when a compound can be associated with two or more solvent molecules, the two or more solvent molecules may be the same or different.

[0035] In some instances, a compound of the invention will include an explicit reference to one or more of the above forms, e.g., salts and solvates, which does not imply any solid state form of the compound; however, this reference is for emphasis only, and is not to be construed as excluding any other of the forms as identified above. Furthermore, when explicit reference to a salt and/or solvate form of a compound or a Ligand Drug Conjugate composition is not made, that omission is not to be construed as excluding the salt and/or solvate form(s) of the compound or Conjugate unless context make clear that such salt and/or solvate forms are to be excluded.

[0036] The phrase “salt thereof” as the phrase is used herein, refers to a salt form of a compound (e.g., a Drug, a Drug Linker compound or a Ligand Drug Conjugate compound). A salt form of a compound is of one or more internal salt forms and/or involves the inclusion of another molecule such as an acetate ion, a succinate ion or other counterion. The counterion in a salt form of a compound is typically an organic or inorganic moiety that stabilizes the charge on the parent compound. A salt form of a compound has one or more than one charged atom in its structure. In instances where multiple charged atoms are part of the salt form, multiple counter ions and/or multiple charged counter ions are present. Hence, a salt form of a compound typically has one or more charged atoms corresponding to those of the non-salt form of the compound and one or more counterions. In some aspects, the non-salt form of a compound contains at least one amino group or other basic moiety, and accordingly in the presence of an acid, an acid addition salt with the basic moiety is obtained. In other aspects, the non-salt form of a compound contains at least one carboxylic acid group or other acidic moiety, and accordingly in the presence of a base, a carboxylate or other anionic moiety is obtained. Exemplary salts include, but are not limited to, sulfate,

trifluoroacetate, citrate, acetate, oxalate, chloride, bromide, iodide, nitrate, bisulfate, phosphate, acid phosphate, isonicotinate, lactate, salicylate, acid citrate, tartrate, oleate, tannate, pantothenate, bitartrate, ascorbate, succinate, maleate, gentisinate, fumarate, gluconate, glucuronate, saccharate, formate, benzoate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, *p*-toluenesulfonate, and pamoate (*i.e.*, 1,1'-methylene-bis-(2-hydroxy-3-naphthoate)) salts.

[0037] A pharmaceutically acceptable salt is a salt form of a compound that is suitable for administration to a subject as described herein and in some aspects includes counteranions or counteranions as described by P. H. Stahl and C. G. Wermuth, editors, *Handbook of Pharmaceutical Salts: Properties, Selection and Use*, Weinheim/Zürich:Wiley-VCH/VHCA, 2002.

[0038] A Linker Unit is a bifunctional moiety that connects a Camptothecin to a Ligand Unit in a Camptothecin Conjugate. The Linker Units of the present invention have several components (e.g., a Stretcher Unit which in some embodiments will have a Basic Unit; a Connector Unit, that can be present or absent; a Parallel Connector Unit, that can also be present or absent; a Releasable Linker; and a Spacer Unit, that can also be present or absent).

[0039] "PEG", "PEG Unit", or "polyethylene glycol" as used herein is an organic moiety comprised of repeating ethylene-oxy subunits and may be polydisperse, monodisperse or discrete (*i.e.*, having discrete number of ethylene-oxy subunits). Polydisperse PEGs are a heterogeneous mixture of sizes and molecular weights whereas monodisperse PEGs are typically purified from heterogeneous mixtures and are therefore provide a single chain length and molecular weight. Preferred PEG Units are discrete PEGs, compounds that are synthesized in stepwise fashion and not via a polymerization process. Discrete PEGs provide a single molecule with defined and specified chain length.

[0040] The PEG Unit provided herein comprises one or multiple polyethylene glycol chains, each comprised of one or more ethyleneoxy subunits, covalently attached to each other. The polyethylene glycol chains can be linked together, for example, in a linear, branched or star shaped configuration. Typically, at least one of the polyethylene glycol chains prior to incorporation into a Camptothecin Conjugate is derivitized at one end with an alkyl moiety substituted with an electrophilic group for covalent attachment to the carbamate nitrogen of a methylene carbamate unit (*i.e.*, represents an instance of R). Typically, the terminal ethyleneoxy subunit in each polyethylene glycol chains not involved in covalent

attachment to the remainder of the Linker Unit is modified with a PEG Capping Unit, typically H or an optionally substituted alkyl such as $-\text{CH}_3$, $-\text{CH}_2\text{CH}_3$, or $-\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$. A preferred PEG Unit has a single polyethylene glycol chain with 4 to 24 $-\text{CH}_2\text{CH}_2\text{O}-$ subunits covalently attached in series and terminated at one end with a PEG Capping Unit.

[0041] “Halogen” as the term is used herein by itself or in combination with another term, unless otherwise stated or implied by context, refers to fluorine, chlorine, bromine, or iodine and is typically $-\text{F}$ or $-\text{Cl}$.

[0042] Unless otherwise indicated, the term “alkyl” by itself or as part of another term refers to a substituted or unsubstituted straight chain or branched, saturated or unsaturated hydrocarbon having the indicated number of carbon atoms (*e.g.*, “ $-\text{C}_1\text{-C}_8$ alkyl” or “ $-\text{C}_1\text{-C}_{10}$ ” alkyl refer to an alkyl group having from 1 to 8 or 1 to 10 carbon atoms, respectively). When the number of carbon atoms is not indicated, the alkyl group has from 1 to 8 carbon atoms. Representative straight chain “ $-\text{C}_1\text{-C}_8$ alkyl” groups include, but are not limited to, -methyl, -ethyl, -n-propyl, -n-butyl, -n-pentyl, -n-hexyl, -n-heptyl and -n-octyl; while branched $-\text{C}_3\text{-C}_8$ alkyls include, but are not limited to, -isopropyl, -*sec*-butyl, -isobutyl, -*tert*-butyl, -isopentyl, and -2-methylbutyl; unsaturated $-\text{C}_2\text{-C}_8$ alkyls include, but are not limited to, -vinyl, -allyl, -1-butenyl, -2-butenyl, -isobutylenyl, -1-pentenyl, -2-pentenyl, -3-methyl-1-butenyl, -2-methyl-2-butenyl, -2,3-dimethyl-2-butenyl, -1-hexyl, -2-hexyl, -3-hexyl, -acetylenyl, -propynyl, -1-butyne, -2-butyne, -1-pentynyl, -2-pentynyl and -3-methyl-1-butyne. Sometimes an alkyl group is unsubstituted. An alkyl group can be substituted with one or more groups. In other aspects, an alkyl group will be saturated.

[0043] Unless otherwise indicated, “alkylene,” by itself or as part of another term, refers to a substituted or unsubstituted saturated, branched or straight chain or cyclic hydrocarbon radical of the stated number of carbon atoms, typically 1-10 carbon atoms, and having two monovalent radical centers derived by the removal of two hydrogen atoms from the same or two different carbon atoms of a parent alkane. Typical alkylene radicals include, but are not limited to: methylene ($-\text{CH}_2-$), 1,2-ethylene ($-\text{CH}_2\text{CH}_2-$), 1,3-propylene ($-\text{CH}_2\text{CH}_2\text{CH}_2-$), 1,4-butylene ($-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$), and the like. In preferred aspects, an alkylene is a branched or straight chain hydrocarbon (*i.e.*, it is not a cyclic hydrocarbon).

[0044] “Alkenyl” as the term is used herein, by itself or as part of another term, unless otherwise stated or implied by context, refers to an organic moiety, substituent, or group that comprises one or more double bond functional groups (*e.g.*, a $-\text{CH}=\text{CH}-$ moiety) or 1, 2, 3, 4,

5, or 6 or more, typically 1, 2, or 3 of such functional groups, more typically one such functional group, and in some aspects may be substituted (i.e., is optionally substituted) with an aryl moiety or group such as phenyl, or may contain non-aromatic linked normal, secondary, tertiary or cyclic carbon atoms, i.e., linear, branched, cyclic or any combination thereof as part of the base moiety unless the alkenyl substituent, moiety or group is a vinyl moiety (e.g., a $-\text{CH}=\text{CH}_2$ moiety). An alkenyl moiety, group or substituent having multiple double bonds may have the double bonds arranged contiguously (i.e., a 1,3-butadienyl moiety) or non-contiguously with one or more intervening saturated carbon atoms or a combination thereof, provided that a cyclic, contiguous arrangement of double bonds do not form a cyclic conjugated system of $4n + 2$ electrons (i.e., is not aromatic).

[0045] An alkenyl moiety, group or substituent contains at least one sp^2 carbon atom in which that carbon atom is divalent and is doubly bonded to another organic moiety or Markush structure to which it is associated, or contains at least two sp^2 carbon atoms in conjugation to each other in which one of the sp^2 carbon atoms is monovalent and is singly bonded to another organic moiety or Markush structure to which it is associated. Typically, when alkenyl is used as a Markush group (i.e., is a substituent) the alkenyl is singly bonded to a Markush formula or another organic moiety with which it is associated through a sp^2 carbon of an alkene functional group of the alkenyl moiety. In some aspects, when an alkenyl moiety is specified, species encompasses those corresponding to any of the optionally substituted alkyl or carbocyclyl, groups moieties or substituents described herein that has one or more *endo* double bonds in which a sp^2 carbon atom thereof is monovalent and monovalent moieties derived from removal of a hydrogen atom from a sp^2 carbon of a parent alkene compound. Such monovalent moieties are exemplified without limitation by vinyl ($-\text{CH}=\text{CH}_2$), allyl, 1-methylvinyl, butenyl, iso-butenyl, 3-methyl-2-butenyl, 1-pentenyl, cyclopentenyl, 1-methyl-cyclopentenyl, 1-hexenyl, 3-hexenyl, and cyclohexenyl. In some aspects, the term alkenyl encompasses those and/or other linear, cyclic and branched chained, all carbon-containing moieties containing at least one double bond functional group in which one of the sp^2 carbon atoms is monovalent.

[0046] The number of carbon atoms in an alkenyl moiety is defined by the number of sp^2 carbon atoms of the alkene functional group(s) that defines it as an alkenyl substituent and the total number of contiguous non-aromatic carbon atoms appended to each of these sp^2 carbons not including any carbon atom of the other moiety or Markush structure for which the alkenyl moiety is a variable group and carbon atoms from any optional substituent to the

alkenyl moiety. That number ranges from 1 to 50 or 1 to 30, typically 1 to 20 or 1 to 12, more typically, 1 to 8, 1 to 6, or 1 to 4 carbon atoms when the double bond functional group is doubly bonded to a Markush structure (e.g. $=CH_2$), or ranges from 2 to 50, typically 2 to 30, 2 to 20, or 2 to 12, more typically 2 to 8, 2 to 6, or 2 to 4 carbon atoms, when the double bond functional group is singly bonded to the Markush structure (e.g., $-CH=CH_2$). For example, C₂-C₈ alkenyl or C₂-C₈ alkenyl means an alkenyl moiety containing 2, 3, 4, 5, 6, 7, or 8 carbon atoms in which at least two are sp² carbon atoms in conjugation with each other with one of these carbon atoms being monovalent, and C₂-C₆ alkenyl or C₂-C₆ alkenyl means an alkenyl moiety containing 2, 3, 4, 5, or 6 carbon atoms in which at least two are sp² carbons that are in conjugation with each other with one of these carbon atoms being monovalent. In some aspects, an alkenyl substituent or group is a C₂-C₆ or C₂-C₄ alkenyl moiety having only two sp² carbons that are in conjugation with each other with one of these carbon atoms being monovalent, and in other aspects that alkenyl moiety is unsubstituted or is substituted with 1 to 4 or more, typically 1 to 3, more typically 1 or 2, independently selected moieties as disclosed herein, including substituents as defined herein for optional substituents, excluding alkyl, arylalkyl, heteroarylalkyl, alkenyl, alkynyl, and any other moiety when the substituted alkenyl would differ by the number of contiguous non-aromatic carbon atoms relative to the unsubstituted alkenyl, wherein the substitution(s) may be at any of the alkenyl moiety's contiguous sp² carbon and sp³ carbon atoms, if any. Typically, an alkenyl substituent is a C₂-C₆ or C₂-C₄ alkenyl moiety having only two sp² carbons that are in conjugation with each other. When the number of carbon atoms is not indicated, an alkenyl moiety has from 2 to 8 carbon atoms.

[0047] "Alkenylene" as the term is used herein, by itself or as part of another term, unless otherwise stated or implied by context, refers to an organic moiety, substituent or group that comprises one or more double bond moieties, as previously described for alkenyl, of the stated number of carbon atoms and has two radical centers derived by the removal of two hydrogen atoms from the same or two different sp² carbon atoms of an alkene functional group or removal of two hydrogen atoms from two separate alkene functional groups in a parent alkene. In some aspects, an alkenylene moiety is that of an alkenyl radical as described herein in which a hydrogen atom has been removed from the same or different sp² carbon atom of a double bond functional group of the alkenyl radical, or from a sp² carbon from a different double bonded moiety to provide a diradical. Typically, alkenylene moieties encompass diradicals containing the structure of $-C=C-$ or $-C=C-X^1-C=C-$ wherein X¹ is

absent or is an optionally substituted saturated alkylene as defined herein, which is typically a C₁-C₆ alkylene, which is more typically unsubstituted. The number of carbon atoms in an alkenylene moiety is defined by the number of sp² carbon atoms of its alkene functional group(s) that defines it as an alkenylene moiety and the total number of contiguous non-aromatic carbon atoms appended to each of its sp² carbons not including any carbon atoms of the other moiety or Markush structure in which the alkenyl moiety is present as a variable group. That number, unless otherwise specified, ranges from 2 to 50 or 2 to 30, typically from 2 to 20 or 2 to 12, more typically from 2 to 8, 2 to 6, or 2 to 4 carbon atoms. For example, C₂-C₈ alkenylene or C₂-C₈ alkenylene means an alkenylene moiety containing 2, 3, 4, 5, 6, 7, or 8 carbon atoms, in which at least two are sp² carbons in which one is divalent or both are monovalent, that are in conjugation with each other and C₂-C₆ alkenylene or C₂-C₆ alkenylene means an alkenyl moiety containing 2, 3, 4, 5, or 6 carbon atoms in which at least two are sp² carbons, in which at least two are sp² carbons in which one is divalent or both are monovalent, that are in conjugation with each other. In some aspects, an alkenylene moiety is a C₂-C₆ or C₂-C₄ alkenylene having two sp² carbons that are in conjugation with each other in which both sp² carbon atoms are monovalent, and in some aspects is unsubstituted. When the number of carbon atoms is not indicated, an alkenylene moiety has from 2 to 8 carbon atoms and is unsubstituted or substituted in the same manner described for an alkenyl moiety.

[0048] “Alkynyl” as the term is used herein, by itself or as part of another term, unless otherwise stated or implied by context, refers to an organic moiety, substituent or group that comprises one or more triple bond functional groups (e.g., a -C≡C- moiety) or 1, 2, 3, 4, 5, or 6 or more, typically 1, 2, or 3 of such functional groups, more typically one such functional group, and in some aspects may be substituted (i.e., is optionally substituted) with an aryl moiety such as phenyl, or by an alkenyl moiety or linked normal, secondary, tertiary or cyclic carbon atoms, i.e., linear, branched, cyclic or any combination thereof unless the alkynyl substituent, moiety or group is -C≡CH). An alkynyl moiety, group or substituent having multiple triple bonds may have the triple bonds arranged contiguously or non-contiguously with one or more intervening saturated or unsaturated carbon atoms or a combination thereof, provided that a cyclic, contiguous arrangement of triple bonds do not form a cyclic conjugated system of 4n + 2 electrons (i.e., is not aromatic).

[0049] An alkynyl moiety, group or substituent contains at least two sp carbon atom in which the carbon atoms are conjugation to each other and in which one of the sp carbon atoms is singly bonded, to another organic moiety or Markush structure to which it is

associated. When alkynyl is used as a Markush group (i.e., is a substituent) the alkynyl is singly bonded to a Markush formula or another organic moiety with which it is associated through a triple-bonded carbon (i.e., a sp carbon) of a terminal alkyne functional group. In some aspects when an alkynyl moiety, group or substituent is specified, species encompasses are any of the optionally substituted alkyl or carbocyclyl, groups moieties or substituents described herein that has one or more *endo* triple bonds and monovalent moieties derived from removal of a hydrogen atom from a sp carbon of a parent alkyne compound. Such monovalent moieties are exemplified without limitation by $\text{-C}\equiv\text{CH}$, and $\text{-C}\equiv\text{C-CH}_3$, and $\text{-C}\equiv\text{C-Ph}$.

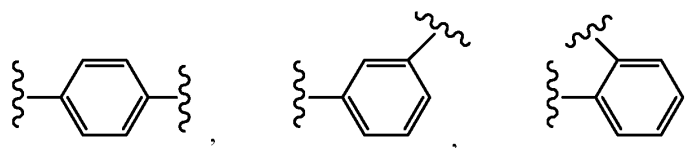
[0050] The number of carbon atoms in an alkynyl substituent is defined by the number of sp carbon atoms of the alkene functional group that defines it as an alkynyl substituent and the total number of contiguous non-aromatic carbon atoms appended to each of these sp carbons not including any carbon atom of the other moiety or Markush structure for which the alkenyl moiety is a variable group. That number can vary ranging from 2 to 50, typically 2 to 30, 2 to 20, or 2 to 12, more typically 2 to 8, 2 to 6, or 2 to 4 carbon atoms, when the triple bond functional group is singly bonded to the Markush structure (e.g., $\text{-CH}\equiv\text{CH}$). For example, C₂-C₈ alkynyl or C₂-C₈ alkynyl means an alkynyl moiety containing 2, 3, 4, 5, 6, 7, or 8 carbon atoms in which at least two are sp carbon atoms in conjugation with each other with one of these carbon atoms being monovalent, and C₂-C₆ alkynyl or C₂-C₆ alkynyl means an alkynyl moiety containing 2, 3, 4, 5, or 6 carbon atoms in which at least two are sp carbons that are in conjugation with each other with one of these carbon atoms being monovalent. In some aspects, an alkynyl substituent or group is a C₂-C₆ or C₂-C₄ alkynyl moiety having two sp carbons that are in conjugation with each other with one of these carbon atoms being monovalent, and in other aspects that alkynyl moiety is unsubstituted. When the number of carbon atoms is not indicated, an alkynyl moiety, group or substituent has from 2 to 8 carbon atoms. An alkynyl moiety may be substituted or unsubstituted in the same manner as described for an alkenyl moiety, except that substitution at the monovalent sp carbon is not permitted.

[0051] The term “Prodrug” as used herein refers to a less biologically active or inactive compound which is transformed within the body into a more biologically active compound via a chemical or biological process (i.e., a chemical reaction or an enzymatic biotransformation). Typically, a biologically active compound is rendered less biologically active (i.e., is converted to a prodrug) by chemically modifying the compound with a prodrug

moiety. In some aspects, the prodrug is a Type II prodrug, which are bioactivated outside cells, e.g., in digestive fluids, or in the body's circulation system, e.g., in blood. Exemplary prodrugs are esters and β -D-glucopyranosides.

[0052] Unless otherwise indicated, "aryl," by itself or as part of another term, means a substituted or unsubstituted monovalent carbocyclic aromatic hydrocarbon radical of the stated number of carbon atoms, typically 6-20 carbon atoms, derived by the removal of one hydrogen atom from a single carbon atom of a parent aromatic ring system. Some aryl groups are represented in the exemplary structures as "Ar". Typical aryl groups include, but are not limited to, radicals derived from benzene, substituted benzene, naphthalene, anthracene, biphenyl, and the like. An exemplary aryl group is a phenyl group.

[0053] Unless otherwise indicated, an "arylene," by itself or as part of another term, is an aryl group as defined above which has two covalent bonds (i.e., it is divalent) and can be in the ortho, meta, or para orientations as shown in the following structures, with phenyl as the exemplary group:



[0054] Unless otherwise indicated, a "C₃-C₈ heterocycle," by itself or as part of another term, refers to a monovalent substituted or unsubstituted aromatic or non-aromatic monocyclic or bicyclic ring system having from 3 to 8 carbon atoms (also referred to as ring members) and one to four heteroatom ring members independently selected from N, O, P or S, and derived by removal of one hydrogen atom from a ring atom of a parent ring system. One or more N, C or S atoms in the heterocycle can be oxidized. The ring that includes the heteroatom can be aromatic or nonaromatic. Heterocycles in which all the ring atoms are involved in aromaticity are referred to as heteroaryls and otherwise are referred to heterocarbocycles.

[0055] Unless otherwise noted, the heterocycle is attached to its pendant group at any heteroatom or carbon atom that results in a stable structure. As such a heteroaryl may be bonded through an aromatic carbon of its aromatic ring system, referred to as a C-linked heteroaryl, or through a non-double-bonded N atom (i.e., not =N-) in its aromatic ring system, which is referred to as an N-linked heteroaryl. Thus, nitrogen-containing heterocycles may be C-linked or N-linked and include pyrrole moieties, such as pyrrol-1-yl

(N-linked) and pyrrol-3-yl (C-linked), and imidazole moieties such as imidazol-1-yl and imidazol-3-yl (both N-linked), and imidazol-2-yl, imidazol-4-yl and imidazol-5-yl moieties (all of which are C-linked).

[0056] Unless otherwise indicated, a “C₃-C₈ heteroaryl,” is an aromatic C₃-C₈ heterocycle in which the subscript denotes the total number of carbons of the cyclic ring system of the heterocycle or the total number of aromatic carbons of the aromatic ring system of the heteroaryl and does not implicate the size of the ring system or the presence or absence of ring fusion. Representative examples of a C₃-C₈ heterocycle include, but are not limited to, pyrrolidinyl, azetidiny, piperidinyl, morpholinyl, tetrahydrofuranyl, tetrahydropyranyl, benzofuranyl, benzothiophene, indolyl, benzopyrazolyl, pyrrolyl, thiophenyl (thiophene), furanyl, thiazolyl, imidazolyl, pyrazolyl, pyrimidinyl, pyridinyl, pyrazinyl, pyridazinyl, isothiazolyl, and isoxazolyl.

[0057] When explicitly given, the size of the ring system of a heterocycle or heteroaryl is indicated by the total number of atoms in the ring. For example, designation as a 5- or 6-membered heteroaryl indicates the total number of aromatic atoms (i.e., 5 or 6) in the heteroaromatic ring system of the heteroaryl but does not imply the number of aromatic heteroatoms or aromatic carbons in that ring system. Fused heteroaryls are explicitly stated or implied by context as such and are typically indicated by the number of aromatic atoms in each aromatic ring that are fused together to make up the fused heteroaromatic ring system. For example, a 5,6-membered heteroaryl is an aromatic 5-membered ring fused to an aromatic 6-membered ring in which one or both rings have aromatic heteroatom(s) or where a heteroatom is shared between the two rings.

[0058] A heterocycle fused to an aryl or heteroaryl such that the heterocycle remains non-aromatic and is part of a larger structure through attachment with the non-aromatic portion of the fused ring system is an example of an optionally substituted heterocycle in which the heterocycle is substituted by ring fusion with the aryl or heteroaryl. Likewise, an aryl or heteroaryl fused to heterocycle or carbocycle that is part of a larger structure through attachment with the aromatic portion of the fused ring system is an example of an optionally substituted aryl or heterocycle in which the aryl or heterocycle is substituted by ring fusion with the heterocycle or carbocycle.

[0059] Unless otherwise indicated, “C₃-C₈ heterocyclo,” by itself or as part of another term, refers to a C₃-C₈ heterocyclic defined above wherein one of the hydrogen atoms of the

heterocycle is replaced with a bond (i.e., it is divalent). Unless otherwise indicated, a “C₃-C₈ heteroarylene,” by itself or as part of another term, refers to a C₃-C₈ heteroaryl group defined above wherein one of the heteroaryl group’s hydrogen atoms is replaced with a bond (i.e., it is divalent).

[0060] Unless otherwise indicated, a “C₃-C₈ carbocycle,” by itself or as part of another term, is a 3-, 4-, 5-, 6-, 7-, or 8-membered monovalent, substituted or unsubstituted, saturated or unsaturated non-aromatic monocyclic or bicyclic carbocyclic ring derived by the removal of one hydrogen atom from a ring atom of a parent ring system. Representative -C₃-C₈ carbocycles include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclopentadienyl, cyclohexyl, cyclohexenyl, 1,3-cyclohexadienyl, 1,4-cyclohexadienyl, cycloheptyl, 1,3-cycloheptadienyl, 1,3,5-cycloheptatrienyl, cyclooctyl, and cyclooctadienyl.

[0061] Unless otherwise indicated, a “C₃-C₈ carbocycle,” by itself or as part of another term, refers to a C₃-C₈ carbocycle group defined above wherein another one of the carbocycle groups’ hydrogen atoms is replaced with a bond (i.e., it is divalent).

[0062] Unless otherwise indicated, the term “heteroalkyl,” by itself or in combination with another term, means, unless otherwise stated, a stable straight or branched chain hydrocarbon, or combinations thereof, fully saturated or containing from 1 to 3 degrees of unsaturation, consisting of the stated number of carbon atoms and from one to ten, preferably one to three, heteroatoms selected from the group consisting of O, N, Si, and S, and wherein the nitrogen and sulfur atoms may optionally be oxidized and the nitrogen heteroatom may optionally be quaternized. The heteroatom(s) O, N and S may be placed at any interior position of the heteroalkyl group or at the position at which the alkyl group is attached to the remainder of the molecule. The heteroatom Si can be placed at any position of the heteroalkyl group, including the position at which the alkyl group is attached to the remainder of the molecule.

[0063] Examples of heteroalkyls include -CH₂-CH₂-O-CH₃, -CH₂-CH₂-NH-CH₃, -CH₂-CH₂-N(CH₃)-CH₃, -CH₂-S-CH₂-CH₃, -CH₂-CH₂-S(O)-CH₃, -NH-CH₂-CH₂-NH-C(O)-CH₂-CH₃, -CH₂-CH₂-S(O)₂-CH₃, -CH=CH-O-CH₃, -Si(CH₃)₃, -CH₂-CH=N-O-CH₃, and -CH=CH-N(CH₃)-CH₃. Up to two heteroatoms may be consecutive, such as, for example, -CH₂-NH-OCH₃ and -CH₂-O-Si(CH₃)₃. Typically, a C₁ to C₄ heteroalkyl or heteroalkylene has 1 to 4 carbon atoms and 1 or 2 heteroatoms and a C₁ to C₃ heteroalkyl or heteroalkylene

has 1 to 3 carbon atoms and 1 or 2 heteroatoms. In some aspects, a heteroalkyl or heteroalkylene is saturated.

[0064] Unless otherwise indicated, the term "heteroalkylene" by itself or in combination with another term means a divalent group derived from heteroalkyl (as discussed above), as exemplified by $-\text{CH}_2-\text{CH}_2-\text{S}-\text{CH}_2-\text{CH}_2-$ and $-\text{CH}_2-\text{S}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-$. For heteroalkylene groups, heteroatoms can also occupy either or both of the chain termini. Still further, for alkylene and heteroalkylene linking groups, no orientation of the linking group is implied.

[0065] Unless otherwise indicated, "aminoalkyl" by itself or in combination with another term means a heteroalkyl wherein an alkyl moiety as defined herein is substituted with an amino, alkylamino, dialkylamino or cycloalkylamino group. Exemplary non-limiting aminoalkyls are $-\text{CH}_2\text{NH}_2$, $-\text{CH}_2\text{CH}_2\text{NH}_2$, $-\text{CH}_2\text{CH}_2\text{NHCH}_3$, and $-\text{CH}_2\text{CH}_2\text{N}(\text{CH}_3)_2$ and further includes branched species such as $-\text{CH}(\text{CH}_3)\text{NH}_2$ and $-\text{C}(\text{CH}_3)\text{CH}_2\text{NH}_2$ in the (R)- or (S)- configuration. Alternatively, an aminoalkyl is an alkyl moiety, group, or substituent as defined herein wherein a sp^3 carbon other than the radical carbon has been replaced with an amino or alkylamino moiety wherein its sp^3 nitrogen replaces the sp^3 carbon of the alkyl provided that at least one sp^3 carbon remains. When referring to an aminoalkyl moiety as a substituent to a larger structure or another moiety the aminoalkyl is covalently attached to the structure or moiety through the carbon radical of the alkyl moiety of the aminoalkyl.

[0066] "Hydroxyalkyl" as the term is used herein by itself or in combination with another term, unless otherwise stated or implied by context, refers to an alkyl moiety, group, or substituent having a hydroxyl radical in place of one or more hydrogen atoms. In some aspects, one or two hydrogen atoms are replaced with a hydroxyl substituent in a hydroxyalkyl group. A hydroxyalkyl is typically denoted by the number of contiguous carbon atoms of its alkyl or alkylene moiety. Thus, a C_1 hydroxyalkyl is exemplified without limitation by $-\text{CH}_2\text{OH}$, and a C_2 hydroxyalkyl is exemplified without limitation by $-\text{CH}_2\text{CH}_2\text{OH}$ or $-\text{CH}_2(\text{OH})\text{CH}_3$.

[0067] "Haloalkyl" as the term is used herein by itself or in combination with another term, unless otherwise stated or implied by context, refers to an alkyl moiety, group, or substituent having a halogen in place of one or more hydrogen atoms. In some aspects, one or two hydrogen atoms are replaced with a halogen in a haloalkyl group. A haloalkyl is typically denoted by the number of contiguous carbon atoms of its alkyl or alkylene moiety. Thus, a C_1 haloalkyl is exemplified without limitation by $-\text{CH}_2\text{F}$, $-\text{CH}_2\text{Cl}$, $-\text{CH}_2\text{Br}$, or $-\text{CH}_2\text{I}$, and a

C₂ haloalkyl is exemplified without limitation by –CH₂CH₂F, –CH₂CH₂Cl, –CH₂CH₂Br, –CH₂CH₂I, –CH(F)CH₃, –CH(Cl)CH₃, –CH(Br)CH₃, or –CH(I)CH₃. In some embodiments, the term “haloalkyl” refers to an alkyl moiety, group, or substituent having halogens in place of two or more hydrogen atoms. For example, a C₁ haloalkyl is also exemplified without limitation by –CHF₂, –CHCl₂, –CHBr₂, or –CHI₂, and a C₂ haloalkyl is exemplified without limitation by –CH₂CHF₂, –CH₂CHCl₂, –CH₂CHBr₂, –CH₂CHI₂, –CF₂CH₃, –CCl₂CH₃, –CBr₂CH₃, or –CI₂CH₃. In some embodiments, the term “haloalkyl” refers to an alkyl moiety, group, or substituent having halogens in place of all hydrogen atoms. In some embodiments, the term “haloalkyl” encompasses fully halogenated alkyl moieties, groups, or substituents. For example, a C₁ haloalkyl is also exemplified without limitation by –CF₃, –CCl₃, –CBr₃, or –CI₃.

[0068] Unless otherwise indicated “alkylamino” and “cycloalkylamino” by itself or in combination with another term means an alkyl or cycloalkyl radical, as described herein, wherein the radical carbon of the alkyl or cycloalkyl radical has been replaced with a nitrogen radical, provided that at least one sp³ carbon remains. In those instances where the alkylamino is substituted at its nitrogen with another alkyl moiety the resulting substituted radical is sometimes referred to as a dialkylamino moiety, group, or substituent wherein the alkyl moieties substituting nitrogen are independently selected.

[0069] Exemplary and non-limiting amino, alkylamino, and dialkylamino substituents, include those having the structure of –N(R')₂, wherein R' in these examples are independently selected from hydrogen or C₁₋₆ alkyl, typically hydrogen or methyl, whereas in cycloalkyl amines, which are included in heterocycloalkyls, both R' together with the nitrogen to which they are attached define a heterocyclic ring. When both R' are hydrogen or alkyl, the moiety is sometimes described as a primary amino group and a tertiary amine group, respectively. When one R' is hydrogen and the other is alkyl, then the moiety is sometimes described as a secondary amino group. Primary and secondary alkylamino moieties are more reactive as nucleophiles towards carbonyl-containing electrophilic centers whereas tertiary amines are more basic.

[0070] “Substituted alkyl” and “substituted aryl” mean alkyl and aryl, respectively, in which one or more hydrogen atoms, typically one, are each independently replaced with a substituent. Typical substituents include, but are not limited to a –X, –R', –OH, –OR', –SR', –N(R')₂, –N(R')₃, =NR', –CX₃, –CN, –NO₂, –NR'C(=O)R', –C(=O)R', –C(=O)N(R')₂, –S(=O)₂R', –S(=O)₂NR', –S(=O)R', –OP(=O)(OR')₂, –P(=O)(OR')₂, –PO₃[–], PO₃H₂, –C(=O)R', –

$C(=S)R'$, $-CO_2R'$, $-CO_2^-$, $-C(=S)OR'$, $-C(=O)SR'$, $-C(=S)SR'$, $-C(=O)N(R')_2$, $-C(=S)N(R')_2$, and $-C(=NR)N(R')_2$, where each X is independently selected from the group consisting of a halogen: -F, -Cl, -Br, and -I; and wherein each R' is independently selected from the group consisting of -H, $-C_1$ - C_{20} alkyl, $-C_6$ - C_{20} aryl, $-C_3$ - C_{14} heterocycle, a protecting group, and a prodrug moiety.

[0071] More typically substituents are selected from the group consisting of $-X$, $-R'$, $-OH$, $-OR'$, $-SR'$, $-N(R')_2$, $-N(R')_3$, $=NR'$, $-NR'C(=O)R'$, $-C(=O)R'$, $-C(=O)N(R')_2$, $-S(=O)_2R'$, $-S(=O)_2NR'$, $-S(=O)R'$, $-C(=O)R'$, $-C(=S)R'$, $-C(=O)N(R')_2$, $-C(=S)N(R')_2$, and $-C(=NR)N(R')_2$, wherein each X is independently selected from the group consisting of -F and -Cl, or are selected from the group consisting of $-X$, $-R'$, $-OH$, $-OR'$, $-N(R')_2$, $-N(R')_3$, $-NR'C(=O)R'$, $-C(=O)N(R')_2$, $-S(=O)_2R'$, $-S(=O)_2NR'$, $-S(=O)R'$, $-C(=O)R'$, $-C(=O)N(R')_2$, $-C(=NR)N(R')_2$, a protecting group, and a prodrug moiety, wherein each X is -F; and wherein each R' is independently selected from the group consisting of hydrogen, $-C_1$ - C_{20} alkyl, $-C_6$ - C_{20} aryl, $-C_3$ - C_{14} heterocycle, a protecting group, and a prodrug moiety.

[0072] In some aspects, an alkyl substituent is selected from the group consisting $-N(R')_2$, $-N(R')_3$ and $-C(=NR)N(R')_2$, wherein R' is selected from the group consisting of hydrogen and $-C_1$ - C_{20} alkyl. In other aspects, alkyl is substituted with a series of ethyleneoxy moieties to define a PEG Unit. Alkylene, carbocycle, carbocyclo, arylene, heteroalkyl, heteroalkylene, heterocycle, heterocyclo, heteroaryl, and heteroarylene groups as described above may also be similarly substituted.

[0073] “Protecting group” as used herein, means a moiety that prevents or reduces the ability of the atom or functional group to which it is linked from participating in unwanted reactions. Typical protecting groups for atoms or functional groups are given in Greene (1999), “PROTECTIVE GROUPS IN ORGANIC SYNTHESIS, 3RD ED.”, Wiley Interscience. Protecting groups for heteroatoms such as oxygen, sulfur and nitrogen are used in some instances to minimize or avoid unwanted their reactions with electrophilic compounds. In other instances, the protecting group is used to reduce or eliminate the nucleophilicity and/or basicity of the unprotected heteroatom. Non-limiting examples of protected oxygen are given by $-OR^{PR}$, wherein R^{PR} is a protecting group for hydroxyl, wherein hydroxyl is typically protected as an ester (e.g. acetate, propionate, or benzoate). Other protecting groups for hydroxyl avoid interfering with the nucleophilicity of organometallic reagents or other highly basic reagents, where hydroxyl is typically protected as an ether, including alkyl or

heterocycloalkyl ethers, (e.g., methyl or tetrahydropyranyl ethers), alkoxymethyl ethers (e.g., methoxymethyl or ethoxymethyl ethers), optionally substituted aryl ethers, and silyl ethers (e.g., trimethylsilyl (TMS), triethylsilyl (TES), tert-butyldiphenylsilyl (TBDPS), tert-butyldimethylsilyl (TBS/TBDMS), triisopropylsilyl (TIPS), and [2-(trimethylsilyl)ethoxy]-methylsilyl (SEM)). Nitrogen protecting groups include those for primary or secondary amines as in -NHR^{PR} or $\text{-N(R}^{\text{PR}}\text{)}_2$, wherein at least one of R^{PR} is a nitrogen atom protecting group or both R^{PR} together comprise a protecting group.

[0074] A protecting group is suitable when it is capable of preventing or avoiding unwanted side-reactions or premature loss of the protecting group under reaction conditions required to effect desired chemical transformation elsewhere in the molecule and during purification of the newly formed molecule when desired, and can be removed under conditions that do not adversely affect the structure or stereochemical integrity of that newly formed molecule. By way of example and not limitation, a suitable protecting group may include those previously described for protecting functional groups. A suitable protecting group is sometimes a protecting group used in peptide coupling reactions.

[0075] “Electron withdrawing group” as used herein means a functional group or electronegative atom that draws electron density away from an atom to which it is bonded either inductively and/or through resonance, whichever is more dominant (i.e., a functional group or atom may be electron withdrawing inductively but may overall be electron donating through resonance) and tends to stabilize anions or electron-rich moieties. The electron withdrawing effect is typically transmitted inductively, albeit in attenuated form, to other atoms attached to the bonded atom that has been made electron deficient by the electron withdrawing group (EWG), thus affecting the electrophilicity of a more remote reactive center. Exemplary electron withdrawing groups include, but are not limited to -C(=O) , -CN , -NO_2 , -CX_3 , -X , $\text{-C(=O)OR}'$, $\text{-C(=O)N(R}^{\text{'}}\text{)}_2$, $\text{-C(=O)R}'$, -C(=O)X , $\text{-S(=O)}_2\text{R}'$, $\text{-S(=O)}_2\text{OR}'$, $\text{-S(=O)}_2\text{NHR}'$, $\text{-S(=O)}_2\text{N(R}^{\text{'}}\text{)}_2$, $\text{-P(=O)(OR}^{\text{'}}\text{)}_2$, $\text{-P(=O)(CH}_3\text{)NHR}'$, -NO , $\text{-N(R}^{\text{'}}\text{)}_3^+$, wherein X is -F , -Br , -Cl , or -I , and R' in some aspects is, at each occurrence, independently selected from the group consisting of hydrogen and C_{1-6} alkyl, and certain O-linked moieties as described herein such as acyloxy.

[0076] Exemplary EWGs can also include aryl groups (e.g., phenyl) depending on substitution and certain heteroaryl groups (e.g., pyridine). Thus, the term “electron withdrawing groups” also includes aryls or heteroaryls that are further substituted with electron withdrawing groups. Typically, electron withdrawing groups on aryls or heteroaryls

are -C(=O), -CN, -NO₂, -CX₃, and -X, wherein X independently selected is halogen, typically -F or -Cl. Depending on their substituents, an alkyl moiety may also be an electron withdrawing group.

[0077] “Succinimide moiety” as used herein, refers to an organic moiety comprised of a succinimide ring system, which is present in one type of Stretcher Unit (Z) that is typically further comprised of an alkylene-containing moiety bonded to the imide nitrogen of that ring system. A succinimide moiety typically results from Michael addition of a sulfhydryl group of a Ligand Unit to the maleimide ring system of a Stretcher Unit precursor (Z'). A succinimide moiety is therefore comprised of a thio-substituted succinimide ring system and when present in a Camptothecin Conjugate has its imide nitrogen substituted with the remainder of the Linker Unit of the Camptothecin Conjugate and is optionally substituted with substituent(s) that were present on the maleimide ring system of Z'.

[0078] “Acid-amide moiety,” as used herein refers to succinic acid having an amide substituent that results from the thio-substituted succinimide ring system of a succinimide moiety having undergone breakage of one of its carbonyl-nitrogen bonds by hydrolysis. Hydrolysis resulting in a succinic acid-amide moiety provides a Linker Unit less likely to suffer premature loss of the Ligand Unit to which it is bonded through elimination of the antibody-thio substituent. Hydrolysis of the succinimide ring system of the thio-substituted succinimide moiety is expected to provide regiochemical isomers of acid-amide moieties that are due to differences in reactivity of the two carbonyl carbons of the succinimide ring system attributable at least in part to any substituent present in the maleimide ring system of the Stretcher Unit precursor and to the thio substituent introduced by the targeting ligand.

[0079] In many instances, the assembly of the conjugates, linkers and components described herein will refer to reactive groups. A “reactive group” or RG is a group that contains a reactive site (RS) capable of forming a bond with either the components of the Linker unit (i.e., A, W, Y) or the Camptothecin D. RS is the reactive site within a Reactive Group (RG). Non-limiting examples of reactive groups include sulfhydryl groups to form disulfide bonds or thioether bonds; aldehyde, ketone, or hydrazine groups to form hydrazone bonds; carboxylic or amino groups to form peptide bonds; carboxylic or hydroxy groups to form ester bonds; sulfonic acids to form sulfonamide bonds; alcohols to form carbamate bonds; and amines to form sulfonamide bonds or carbamate bonds.

[0080] The following table is illustrative of Reactive Groups, Reactive Sites, and exemplary functional groups that can form after reaction of the reactive site. The table is not limiting. One of skill in the art will appreciate that the noted R' and R'' portions in the table are effectively any organic moiety (e.g., an alkyl group, aryl group, heteroaryl group, or substituted alkyl, aryl, or heteroaryl, group) which is compatible with the bond formation provided in converting RG to one of the Exemplary Functional Groups. It will also be appreciated that, as applied to the embodiments of the present invention, R' may represent one or more components of the self-stabilizing linker or optional secondary linker, as the case may be, and R'' may represent one or more components of the optional secondary linker, Camptothecin, stabilizing unit, or detection unit, as the case may be.

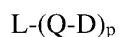
RG	RS	Exemplary Functional Groups
1) R'-SH	-S-	R'-S-R'', R'-S-S-R''
2) R'-C(=O)OH	-C(=O)-	R'-C(=O)NH-R''
3) R'-C(=O)ONHS	-C(=O)-	R'-C(=O)NH-R''
4) R'S(=O) ₂ -OH	-S(=O) ₂ -	R'S(=O) ₂ NH-R''
5) R'-CH ₂ -X (X is Br, I, Cl)	-CH ₂ -	R'-CH ₂ -S-R''
6) R'-NH ₂	-N-	R'-NHC(=O)R''

Embodiments

[0081] A number of embodiments of the invention are described below, which are not meant to limit the invention in any way, are followed by a more detailed discussion of the components that make up the conjugates. One of skill in the art will understand that each of the conjugates identified and any of the selected embodiments thereof is meant to include the full scope of each component and linker.

Camptothecin Conjugates

[0082] In one embodiment, provided herein are camptothecin conjugates having a formula:



or a salt thereof, wherein

L is a Ligand Unit;

the subscript p is an integer of from 1 to 16;

Q is a Linker Unit having a formula selected from the group consisting of:

-Z-A-, -Z-A-RL-, -Z-A-RL-Y-, Z-A-S^{*}-W-, -Z-A-S^{*}-RL-, -Z-A-B(S^{*})-RL-,
-Z-A-S^{*}-W-RL-, -Z-A-S^{*}-RL-Y-, and -Z-A-B(S^{*})-RL-Y-;

wherein Z is a Stretcher Unit,

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

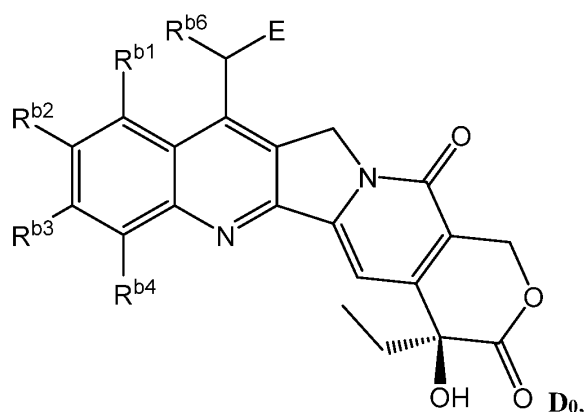
is a Partitioning Agent;

W is a Peptide Unit;

RL is a Releasable Unit;

Y is a Spacer Unit; and

[0083] D is a Drug Unit having a formula of



or a salt thereof; wherein

E is -OR^{b5} or -NR^{b5}R^{b5'};

R^{b1} is selected from the group consisting of H, halogen, -CN, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with R^a, -OR^a, -NR^aR^{a'}, -C(O)R^a, and -SR^a; or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;

each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₆ alkyl-O-C₁-C₆ alkyl-, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, C₁-C₆ hydroxyalkyl-, heteroaryl-, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, C₁-C₆ hydroxyalkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo,

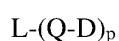
phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and $R^{a'}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

[0084] Also provided herein are camptothecin conjugates having a formula:



or a salt thereof, wherein

L is a Ligand Unit;

the subscript p is an integer of from 1 to 16;

Q is a Linker Unit having a formula selected from the group consisting of:

-Z-A-, -Z-A-RL-, -Z-A-RL-Y-, Z-A-S*-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-,
-Z-A-S*-W-RL-, -Z-A-S*-RL-Y-, and -Z-A-B(S*)-RL-Y-;

wherein Z is a Stretcher Unit,

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

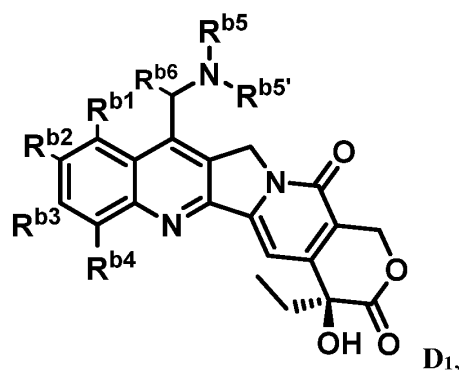
is a Partitioning Agent;

W is a Peptide Unit;

RL is a Releasable Unit;

Y is a Spacer Unit; and

D is a Drug Unit having a formula of



or a salt thereof; wherein

R^{b1} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b1} is combined with R^{b2} , R^{b5} , or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;

each R^{b5} and $R^{b5'}$ are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄

hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, and heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂; R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and R^a and R^{a'} are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

[0085] Also provided herein are Camptothecin Conjugates comprising a Drug Unit corresponding to Formula D₁ or any variation thereof, wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

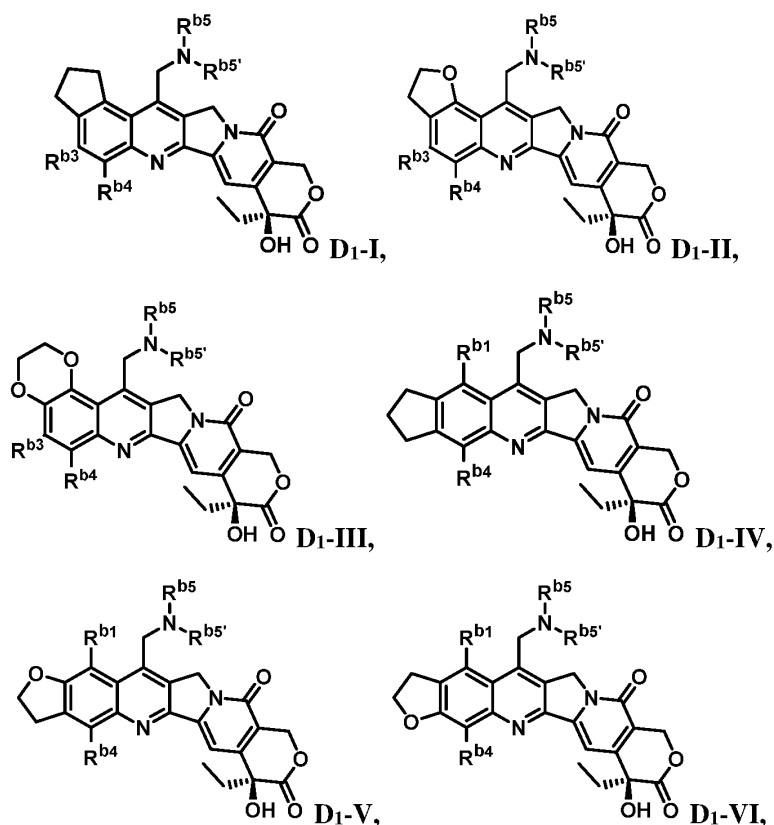
[0086] In some embodiments of Formula D₀, E is -NR^{b5}R^{b5'}. In some embodiments of Formula D₀, E is -OR^{b5}. In some embodiments, E is -OR^{b5}, R^{b1} is H, R^{b2} and R^{b3} combine

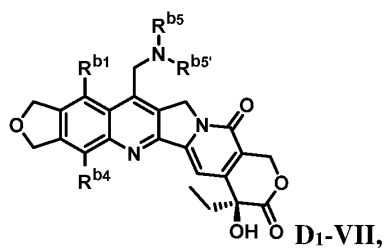
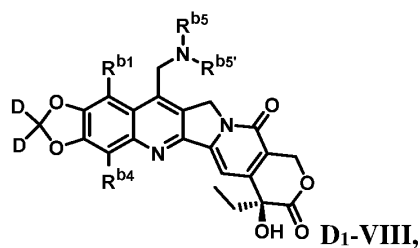
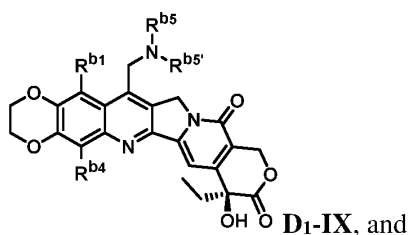
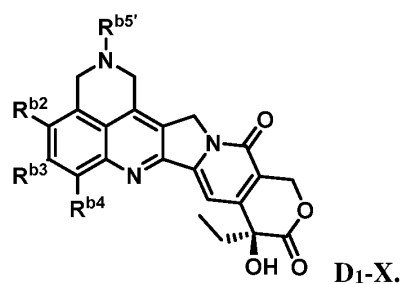
together with the intervening atoms to form 5-membered heterocycle, and each of R^{b4} , R^{b5} , and R^{b6} are H.

[0087] In some embodiments, at least one of R^{b1} , R^{b2} , R^{b3} , and R^{b4} is halogen. In some embodiments, at least one of R^{b1} , R^{b2} , R^{b3} , and R^{b4} is C_1 - C_6 alkyl. In some embodiments, at least one of R^{b1} , R^{b2} , R^{b3} , and R^{b4} is $-OR^a$, and R^a is H or C_1 - C_6 alkyl. In some embodiments, R^{b5} and $R^{b5'}$ are each H.

[0088] In some embodiments, the site of covalent attachment of D to the linker (e.g., secondary linker) of the drug linker moiety is indicated by the dagger in formula **D1a** or **D1b** or any variation thereof (e.g., **D1a-I** through **D1a-X**, **D1b-I** through **D1b-X**, etc.). It is also contemplated that D may be covalently attached to the linker (e.g., secondary linker) of the drug linker moiety at any site in D that is compatible with attachment to the linker (e.g., secondary linker) (e.g., at any OH, NH_2 , NHR , NR_2 , SH, etc.), whether or not said site is marked by a dagger in any of the formulae herein. In some embodiments, D is connected to the remainder of a Drug-Linker moiety through a OH or NH_2 group of R^{b5} .

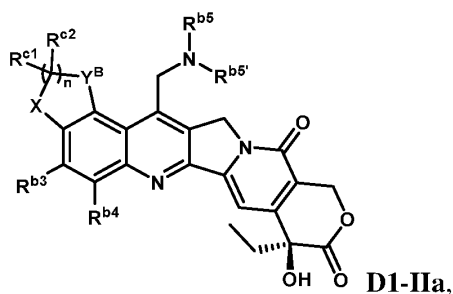
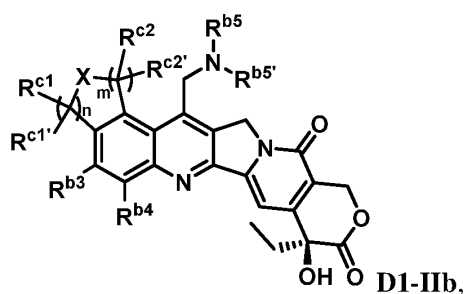
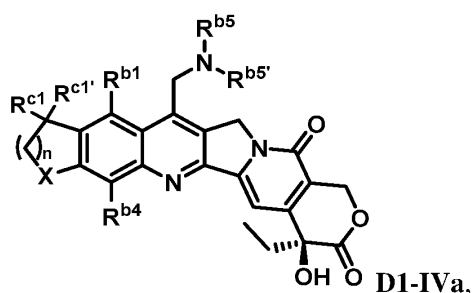
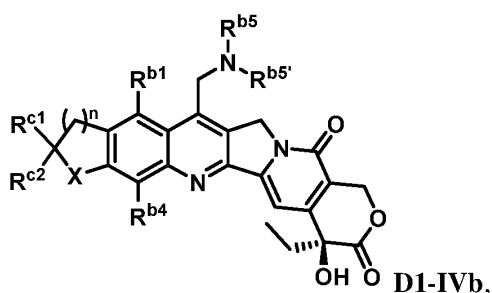
[0089] In some embodiments, D has a formula selected from the group consisting of

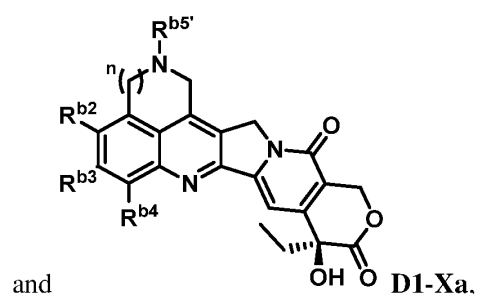




[0090] For any of formulas **D1-I** through **D1-X** and variations thereof, the variables may be defined according to formula **D0** or any variation thereof, or they may be defined according to formula **D1** or any variation thereof. In some embodiments, D has a structure corresponding to any of formulas **D1-I** through **D1-X** and variations thereof, wherein the nitrogen atom to which $R^{b5'}$ is bound is replaced by an oxygen atom and $R^{b5'}$ is absent.

[0091] In some embodiments, D has a formula selected from the group consisting of





wherein

X and Y^B are each independently O, S, S(O)₂, CR^xR^{x'}, or NR^x;

R^x and R^{x'} are each independently selected from the group consisting of H, OH, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ aminoalkyl-C(O)-, C₁-C₆ alkyl-C(O)-, C₁-C₆ hydroxyalkyl-C(O)-, C₁-C₆ alkyl-NH-C(O)-, or C₁-C₆ alkyl-S(O)₂-; and

m and n are each 1 or 2;

each R^{c1}, R^{c1'}, R^{c2}, and R^{c2'} is independently

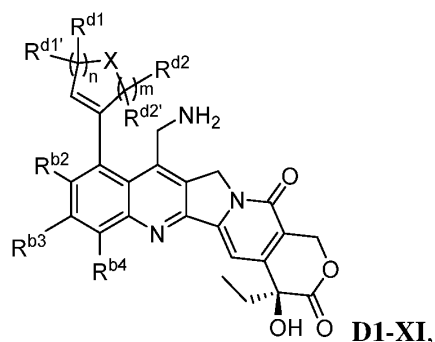
- (i) selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, -OR^a, -NR^aR^{a'}, and -SR^a, C₁-C₆ alkyl-C(O)-, C₁-C₆ alkyl-NR^a-C(O)-, and C₁-C₆ alkyl-S(O)₂-; or
- (ii) taken together with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; or
- (iii) taken together with R^{x'} and the intervening atoms to form a 3 to 6-membered carbocyclo or heterocyclo;

when m and n are both present, the sum of m + n is 2 or 3; and

the remaining variables are as defined for **D1**.

[0092] In some embodiments, D has a structure corresponding to any of formulas **D1-IIa**, **D1-IIb**, **D1-IVa**, or **D1-IVb**, wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent.

[0093] In some embodiments, D has a formula selected from the group consisting of

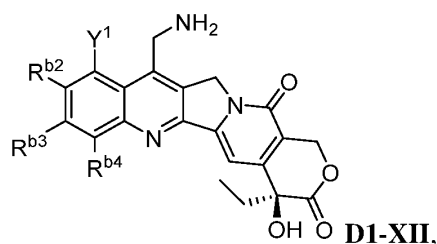


wherein

R^{d1} , $R^{d1'}$, R^{d2} , and $R^{d2'}$ are each independently selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a, C₁-C₆ alkyl-C(O)-, C₁-C₆ alkyl-NR^a-C(O)-, and C₁-C₆ alkyl-S(O)₂-; and

the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

In some embodiments, D has a formula selected from the group consisting of

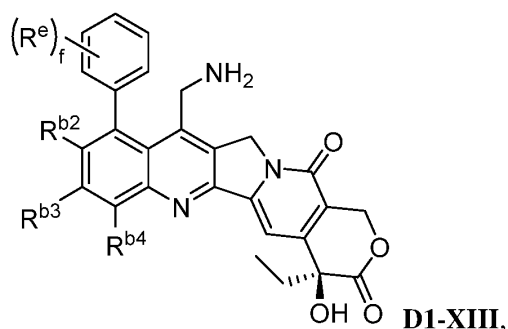


wherein

Y¹ is a 5- or 6-membered heteroaryl, optionally substituted with halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, or C₁-C₆ alkyl-S(O)₂-; and

the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

[0094] In some embodiments, D has a formula selected from the group consisting of

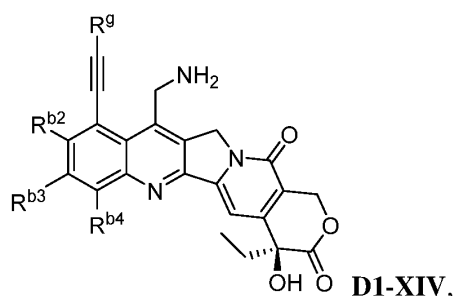


wherein

each R^e is independently selected from the group consisting of halogen, -OH, -NH₂, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkyl-S(O)₂-, and C₁-C₆ alkyl-NR^a-C(O)-; f is 0, 1, 2, 3, 4, or 5; and

the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

[0095] In some embodiments, D has a formula selected from the group consisting of



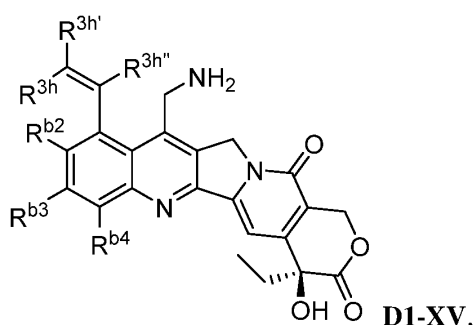
wherein

R^g is H, C₁-C₆ alkyl, or 3 to 8-membered heterocyclyl; and

the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

In some embodiments, R^g is C₁-C₆ alkyl.

[0096] In some embodiments, D has a formula selected from the group consisting of



wherein

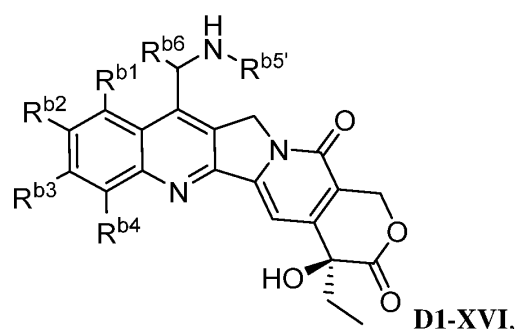
R^{3h} , $R^{3h'}$, and $R^{3h''}$ are each independently selected from the group consisting of H,

C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, -C(O)-C₁-C₆ alkyl, -C(O)O-C₁-C₆ alkyl, -C(O)NH-C₁-C₆ alkyl, C₆-C₁₀ aryl, -C₆-C₁₀ aryl-C₁-C₆ alkyl, and -C₆-C₁₀ aryl-C₁-C₆ alkoxy;

each optionally substituted with, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a; and

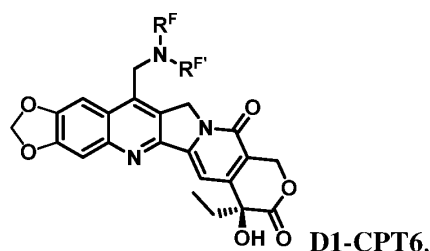
the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

[0097] In some embodiments, D has a formula selected from the group consisting of



wherein the variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, and **D1-Xa**.

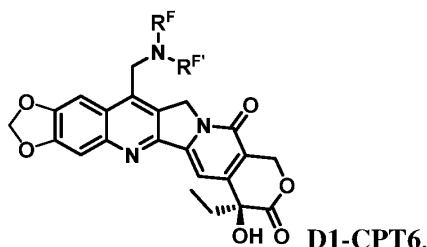
[0098] In some embodiments, D incorporates the structure of a camptothecin having a structure of



or a pharmaceutically acceptable salt thereof, wherein each R^F and $R^{F'}$ is independently selected from the group consisting of -H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, and heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl, NH₂-SO₂-C₁-C₈ alkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl, or R^F and $R^{F'}$ are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; wherein the cycloalkyl, heterocycloalkyl, phenyl and heteroaryl portions of R^F and $R^{F'}$ are substituted

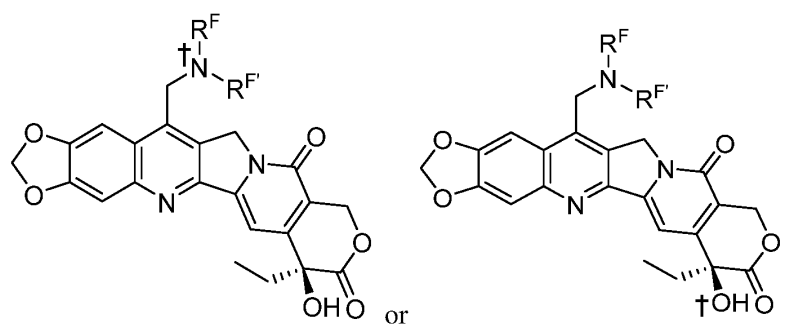
with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂.

[0099] In some embodiments, D incorporates the structure of a camptothecin having a structure of



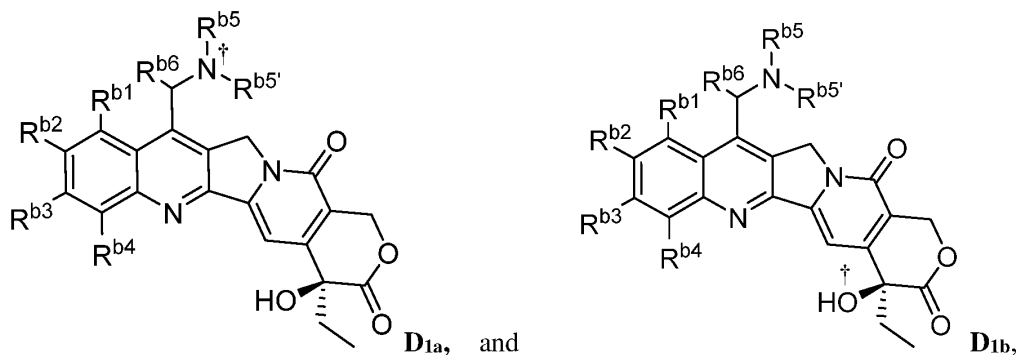
or a pharmaceutically acceptable salt thereof, wherein each R^F and R^{F'} is independently selected from the group consisting of -H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₆-O-C₁-C₆ alkyl, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, heteroaryl-C₁-C₆ hydroxyalkyl, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, and heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl, NH₂-SO₂-C₁-C₈ alkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl, or R^F and R^{F'} are combined with the nitrogen atom to which each is attached to form a 5-, 6-, or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; wherein the cycloalkyl, heterocycloalkyl, phenyl, and heteroaryl portions of R^F and R^{F'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂.

[0100] In some embodiments, D has a formula of



wherein the dagger represents the point of covalent attachment of D to the linker (e.g., secondary linker) of the drug linker moiety. In some embodiments, the dagger denotes attachment of the linker directly to the daggered nitrogen (e.g., by replacement of the R^{b5} moiety). In other embodiments, the dagger denotes attached of the linker to a suitable atom (e.g., a nitrogen or oxygen atom) of the R^{b5} moiety. In some embodiments, R^F is selected from the group consisting of C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-N-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl, NH₂-SO₂-C₁-C₈ alkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl. In some embodiments, R^F is -H. In some embodiments, R^F is methyl. In some embodiments, R^F and R^{F'} are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl. In some embodiments, R^F is selected from the group consisting of C₁-C₆ alkyl-O-C₁-C₆ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-N-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl, NH₂-SO₂-C₁-C₈ alkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl. In some embodiments, R^F is -H. In some embodiments, R^F is methyl. In some embodiments, R^F and R^{F'} are combined with the nitrogen atom to which each is attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ hydroxyalkyl-, and C₁-C₈ aminoalkyl.

[0101] In some embodiments, D is a Drug Unit having a formula selected from the group consisting of



or a salt thereof, wherein the dagger indicates the site of covalent attachment of D to Q and the remaining variables are as defined for **D1**. In some embodiments, the remaining variables are as defined for **D0**. In some embodiments of Formula **D1a**, the dagger denotes attachment of the linker directly to the daggered nitrogen (e.g., by replacement of the R^{b5} moiety). In other embodiments of Formula **D1a**, the dagger denotes attached of the linker to a suitable atom (e.g., a nitrogen or oxygen atom) of the R^{b5} moiety.

[0102] In some embodiments of Formula **D1a** or Formula **D1b**, R^{b1} , R^{b2} , R^{b3} , and R^{b4} are each hydrogen.

[0103] In some embodiments of Formula **D1a** or Formula **D1b**, R^{b1} , R^{b2} , and R^{b4} are hydrogen, and R^{b3} is halogen. In some embodiments, R^{b3} is fluoro.

[0104] In some embodiments of Formula **D1a** or Formula **D1b**, R^{b2} , R^{b3} , and R^{b4} are hydrogen, and R^{b1} is halogen. In some embodiments, R^{b1} is fluoro.

[0105] In some embodiments of Formula **D1a** or Formula **D1b**, R^{b2} and R^{b4} are hydrogen, and R^{b1} and R^{b3} are both halogen. In some embodiments, R^{b1} and R^{b3} are both fluoro.

[0106] In some embodiments of Formula **D1a** or Formula **D1b**, R^{b1} is hydrogen, and R^{b2} , R^{b3} and R^{b4} are each halogen. In some embodiments, R^{b2} , R^{b3} , and R^{b4} are each fluoro.

[0107] In some embodiments of Formula **D1a** or Formula **D1b**, R^{b1} , R^{b3} , and R^{b4} are hydrogen, and R^{b2} is C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, halogen, $-OR^a$ or $-SR^a$. In some embodiments, R^{b2} is C_1 - C_6 alkyl or halogen. In some embodiments, R^{b2} is C_1 - C_6 alkyl. In some embodiments, R^{b2} is methyl. In some embodiments, R^{b2} is C_1 - C_6 alkoxy. In some embodiments, R^{b2} is methoxy. In some embodiments, R^{b2} is halogen. In some embodiments, R^{b2} is fluoro. In some embodiments, R^{b2} is chloro. In some embodiments, R^{b2} is bromo. In

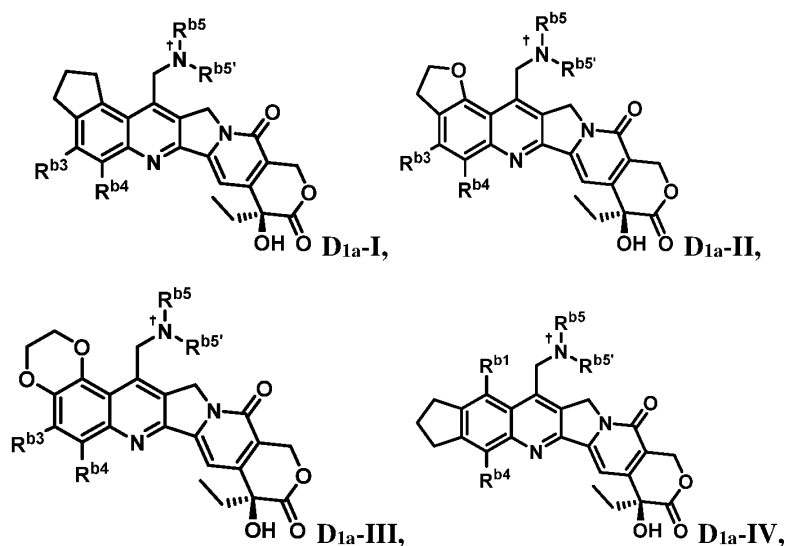
some embodiments, R^{b2} is C_1 - C_6 haloalkyl. In some embodiments, R^{b2} is trifluoromethyl. In some embodiments, R^{b2} is C_1 - C_6 haloalkylthio. In some embodiments, R^{b2} is trifluoromethylthio. In some embodiments, R^{b2} is hydroxyl.

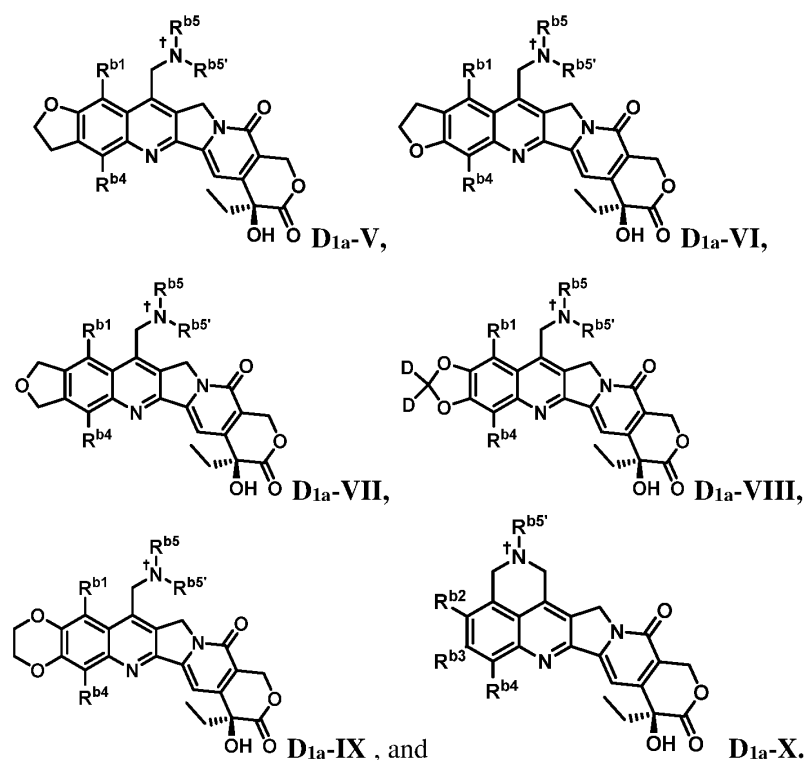
[0108] In some embodiments of Formula **D1a** or Formula **D1b**, R^{b1} and R^{b4} are hydrogen, R^{b2} is C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, halogen, $-OR^a$, or $-SR^a$; and R^{b3} is C_1 - C_6 alkyl or halogen. In some embodiments, R^{b2} is C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halogen or hydroxy, and R^{b3} is C_1 - C_6 alkyl or halogen. In some embodiments, R^{b2} is C_1 - C_6 alkyl. In some embodiments, R^{b2} is methyl. In some embodiments, R^{b2} is C_1 - C_6 alkoxy. In some embodiments, R^{b2} is halogen. In some embodiments, R^{b2} is fluoro. In some embodiments, R^{b2} is methoxy. In some embodiments, R^{b2} is hydroxyl. In some embodiments, R^{b3} is C_1 - C_6 alkyl. In some embodiments, R^{b3} is methyl. In some embodiments, R^{b3} is halogen. In some embodiments, R^{b3} is fluoro. In some embodiments, R^{b2} is C_1 - C_6 alkyl and R^{b3} is halogen. In some embodiments, R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, R^{b2} is C_1 - C_6 alkoxy and R^{b3} is halogen. In some embodiments, R^{b2} is methoxy and R^{b3} is fluoro. In some embodiments, R^{b2} and R^{b3} are halogen. In some embodiments, R^{b2} and R^{b3} are both fluoro. In some embodiments, R^{b2} is halogen and R^{b3} is C_1 - C_6 alkyl. In some embodiments, R^{b2} is fluoro and R^{b3} is methyl. In some embodiments, R^{b2} is hydroxyl and R^{b3} is halogen. In some embodiments, R^{b2} is hydroxyl and R^{b3} is fluoro.

[0109] In some embodiments of Formula **D1a** or Formula **D1b**, R^{b2} is C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, halogen, $-OR^a$ or $-SR^a$; both R^{b1} and R^{b3} are independently selected from the group consisting of C_1 - C_6 alkyl, halogen, C_2 - C_6 alkenyl, $(C_6-C_{12}$ aryl)- C_2 - C_6 alkenyl- optionally substituted with $-OR^a$, and $-OR^a$; and R^{b4} is hydrogen. In some embodiments, R^{b2} is C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, halogen, $-OR^a$, or $-SR^a$; both R^{b1} and R^{b3} are independently selected from the group consisting of C_1 - C_6 alkyl, halogen, C_2 - C_6 alkenyl, $(C_6-C_{12}$ aryl)- C_2 - C_6 alkenyl-, each optionally substituted with $-OR^a$, and $-OR^a$; and R^{b4} is hydrogen. In some embodiments, R^{b1} is C_1 - C_6 alkyl. In some embodiments, R^{b1} is methyl. In some embodiments, R^{b1} is halogen. In some embodiments, R^{b1} is fluoro. In some embodiments, R^{b1} is chloro. In some embodiments, R^{b1} is bromo. In some embodiments, R^{b1} is $(C_6-C_{12}$ aryl)- C_2 - C_6 alkenyl-, optionally substituted with $-OR^a$. In some embodiments, R^{b1} is 4-methoxystyryl. In some embodiments, R^{b1} is C_2 - C_6 alkenyl. In some embodiments, R^{b1} is vinyl. In some embodiments, R^{b1} is 1-methylvinyl. In some embodiments, R^{b1} is 1-methylvinyl. In some embodiments, R^{b2} is C_1 - C_6 alkyl. In some embodiments, R^{b2} is methyl. In some embodiments, R^{b2} is C_1 - C_6 alkoxy. In some embodiments, R^{b2} is methoxy.

In some embodiments, R^{b2} is hydroxyl. In some embodiments, R^{b3} is C_1 - C_6 alkyl. In some embodiments, R^{b3} is methyl. In some embodiments, R^{b3} is ethyl. In some embodiments, R^{b3} is C_1 - C_6 alkoxy. In some embodiments, R^{b3} is methoxy. In some embodiments, R^{b3} is halogen. In some embodiments, R^{b3} is fluoro. In some embodiments, R^{b3} is chloro. In some embodiments, R^{b3} is bromo. In some embodiments, R^{b2} is C_1 - C_6 alkyl and R^{b1} and R^{b3} are halogen. In some embodiments, R^{b2} is methyl and R^{b1} and R^{b3} are both fluoro. In some embodiments, R^{b2} is methyl, R^{b1} is fluoro and R^{b3} is bromo. In some embodiments, R^{b2} is methyl, R^{b1} is bromo and R^{b3} is fluoro. In some embodiments, R^{b2} is methyl, R^{b1} is chloro and R^{b3} is fluoro. In some embodiments, R^{b2} is methyl, R^{b1} is fluoro and R^{b3} is chloro. In some embodiments, R^{b2} is C_1 - C_6 alkoxy and R^{b1} and R^{b3} is halogen. In some embodiments, R^{b2} is methoxy and R^{b1} and R^{b3} are both fluoro. In some embodiments, R^{b2} is methoxy, R^{b1} is bromo and R^{b3} is fluoro. In some embodiments, R^{b2} is methoxy, R^{b1} is fluoro and R^{b3} is bromo. In some embodiments, R^{b2} is hydroxyl and R^{b1} and R^{b3} are halogen. In some embodiments, R^{b2} is hydroxyl and R^{b1} and R^{b3} are both fluoro. In some embodiments, R^{b1} is halogen and R^{b2} and R^{b3} are both C_1 - C_6 alkyl. In some embodiments, R^{b1} is fluoro and R^{b2} and R^{b3} are both methyl. In some embodiments, R^{b1} is fluoro, R^{b2} is methyl and R^{b3} is ethyl. In some embodiments, R^{b1} and R^{b2} are both C_1 - C_6 alkyl and R^{b3} is halogen. In some embodiments, R^{b1} and R^{b2} are both methyl and R^{b3} is fluoro.

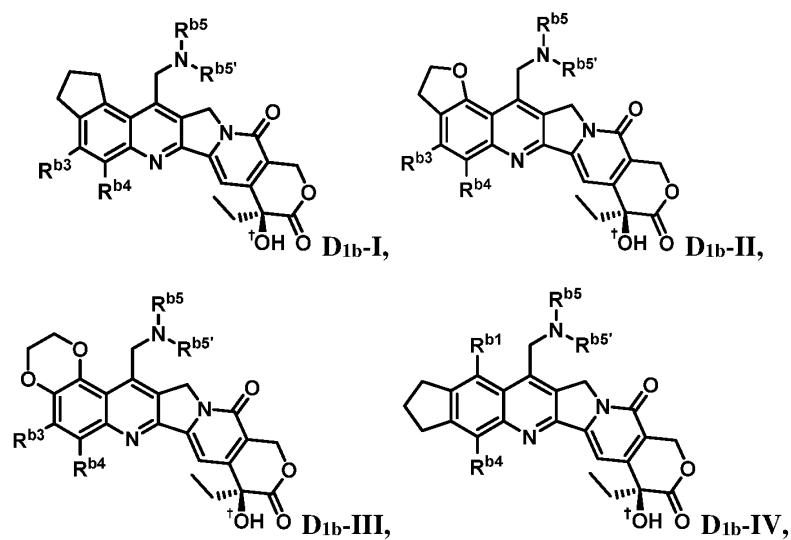
[0110] In some embodiments, D has a formula selected from the group consisting of

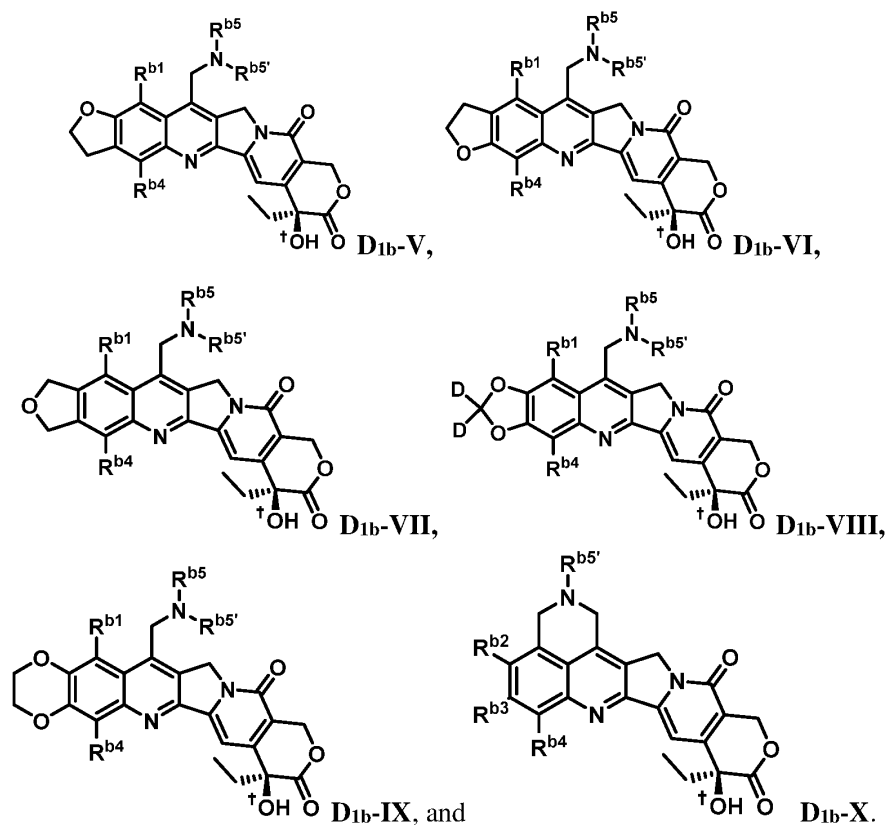




[0111] For any of formulas **D1a-I** through **D1a-X** or any variation thereof, the variables may be defined according to formula **D0** or any variation thereof, or they may be defined according to formula **D1** or any variation thereof.

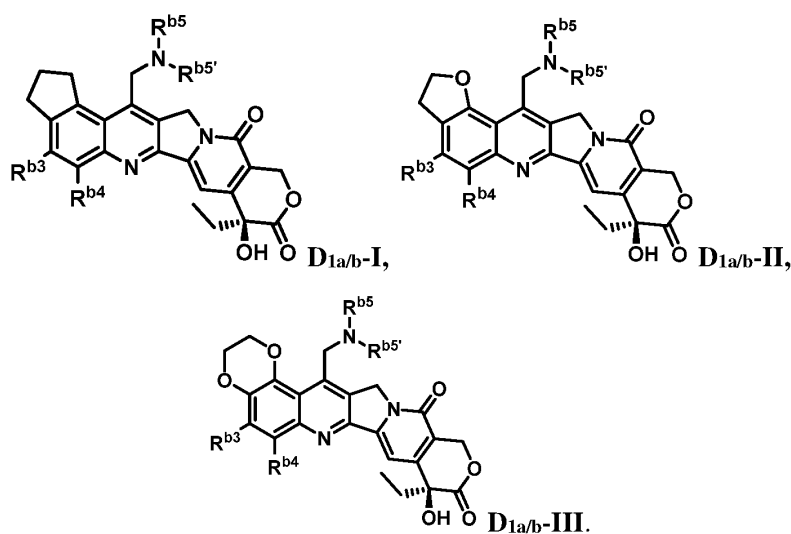
[0112] In some embodiments, D has a formula selected from the group consisting of



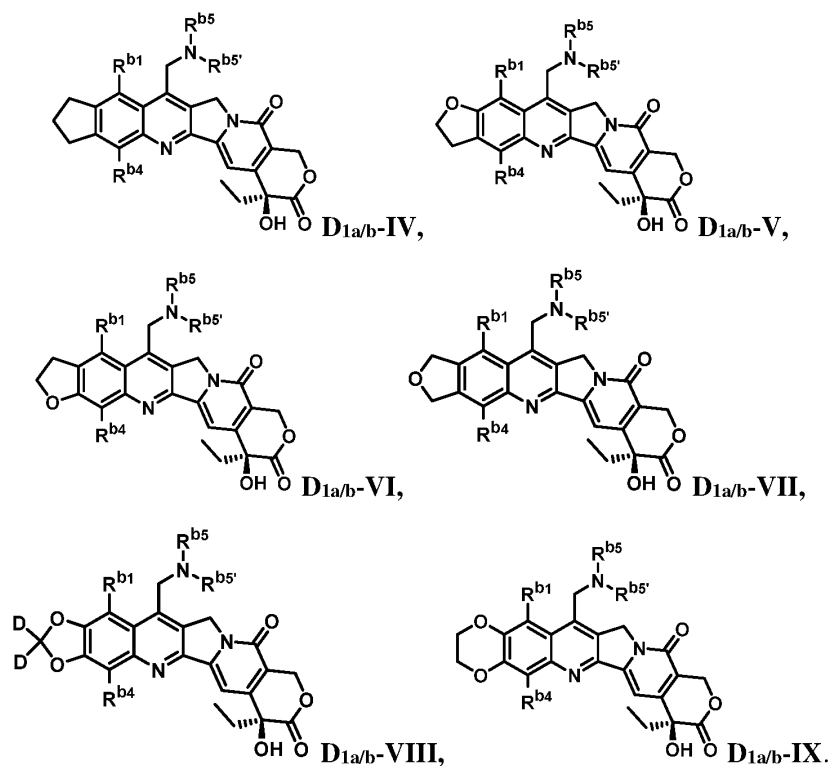


[0113] For any of formulas **D1b-I** through **D1b-X** or any variation thereof, the variables may be defined according to formula **D0** or any variation thereof, or they may be defined according to formula **D1** or any variation thereof. In some embodiments, D has a structure corresponding to any of formulas **D1b-I** through **D1b-IX** and variations thereof, wherein the nitrogen atom to which $R^{b5'}$ is bound is replaced by an oxygen atom and $R^{b5'}$ is absent.

[0114] In some embodiments of Formula **D1a** or Formula **D1b**, R^{b1} is combined with R^{b2} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo ring. In some embodiments, the drug has the structure of Formula **D1a/b-I**, Formula **D1a/b-II**, or Formula **D1a/b-III** as follows:



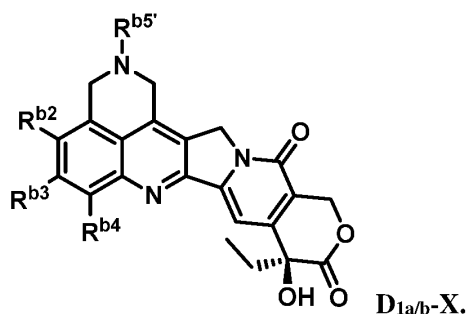
[0115] In some embodiments of Formula **D1a** or Formula **D1b**, R^{b2} is combined with R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo ring; wherein one or more hydrogens are optionally replaced with deuterium. In some embodiments, the drug has the structure of Formula **D1a/b-IV**, **D1a/b-V**, **D1a/b-VI**, **D1a/b-VII**, **D1a/b-VIII** or **D1a/b-IX** as follows:



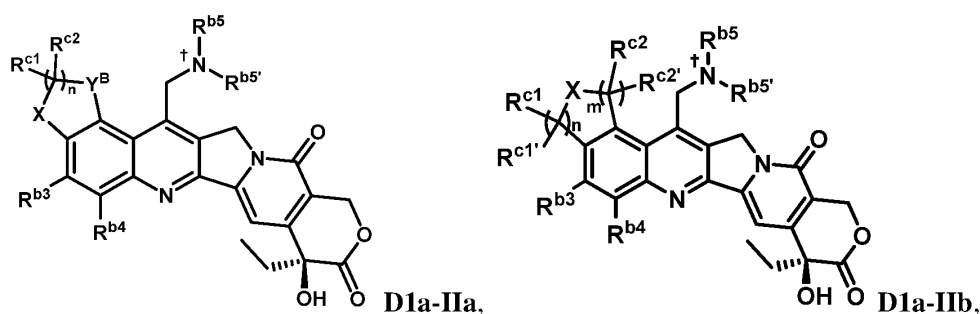
[0116] For any of formulas **D_{1a/b-I}** through **D_{1/ba-IX}** or any variation thereof, the variables may be defined according to formula **D₀** or any variation thereof, or they may be defined according to formula **D₁** or any variation thereof. In some embodiments, D has a structure corresponding to any of formulas **D_{1a/b-I}** through **D_{1a/b-X}** and variations thereof, wherein the nitrogen atom to which $R^{b5'}$ is bound is replaced by an oxygen atom and $R^{b5'}$ is absent.

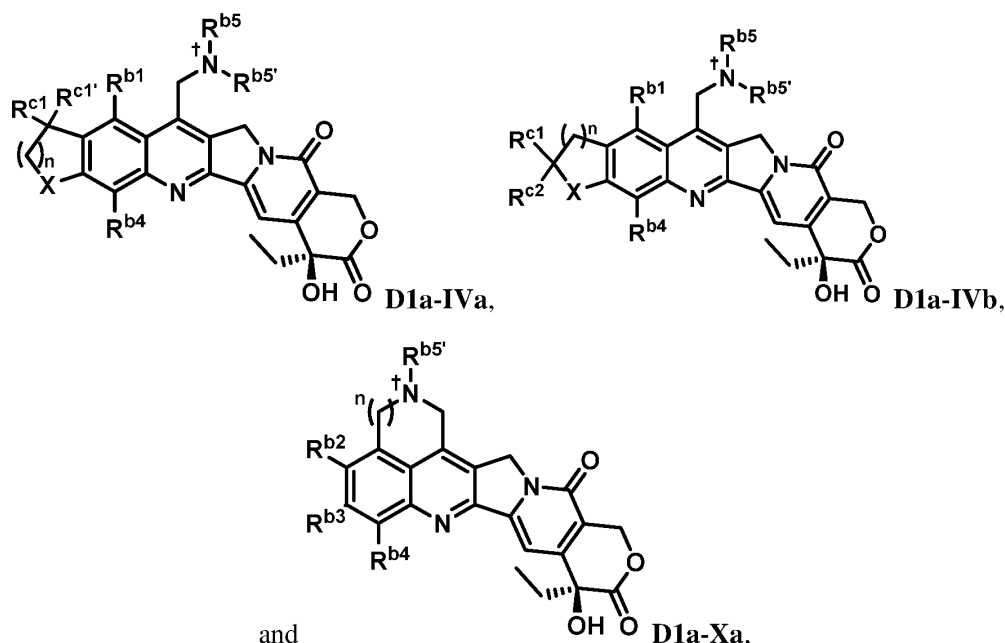
[0117] In some embodiments of Formula **D₁**, R^{b5} and $R^{b5'}$ are both H. In some embodiments, R^{b5} is C₁-C₆ alkyl (e.g., methyl, ethyl) and $R^{b5'}$ is H.

[0118] In some embodiments of Formula **D_{1a}** or Formula **D_{1b}**, R^{b1} is combined with R^{b5} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo ring. In some embodiments, the drug has the structure of Formula **D_{1a/b-X}** as follows:



[0119] In some embodiments, D has a formula selected from the group consisting of





wherein

X and Y^B are each independently O, S, S(O)₂, CR^xR^{x'}, or NR^x;

R^x and R^{x'} are each independently selected from the group consisting of H, OH, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ aminoalkyl-C(O)-, C₁-C₆ alkyl-C(O)-, C₁-C₆ hydroxyalkyl-C(O)-, C₁-C₆ alkyl-NH-C(O)-, or C₁-C₆ alkyl-S(O)₂-; and

m and n are each 1 or 2;

each R^{c1}, R^{c1'}, R^{c2}, and R^{c2'} is independently

- (i) selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, -OR^a, -NR^aR^{a'}, and -SR^a, C₁-C₆ alkyl-C(O)-, C₁-C₆ alkyl-NR^a-C(O)-, and C₁-C₆ alkyl-S(O)₂-; or
- (ii) taken together with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocycle or heterocycle; or
- (iii) taken together with R^{x'} and the intervening atoms to form a 3- to 6-membered carbocycle or heterocycle; or

any two of R^{c1}, R^{c1'}, R^{c2}, and R^{c2'} are taken together to form a 3- to 6-membered carbocycle or heterocycle, and the remaining two of R^{c1}, R^{c1'}, R^{c2}, and R^{c2'} are independently selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a, -C(O)-C₁-C₆ alkyl, -C(O)NR^a-C₁-C₆ alkyl, and -S(O)₂-C₁-C₆ alkyl;

when m and n are both present, the sum of m + n is 2 or 3; and

the remaining variables are as defined for **D1a** and **D1b**.

[0120] In some embodiments, D has the formula **D1a-IIa**, wherein X is O. In some embodiments, D has the formula **D1a-IIa**, wherein X is S. In some embodiments, D has the formula **D1a-IIa**, wherein X is $CR^xR^{x'}$. In some embodiments, D has the formula **D1a-IIa**, wherein Y^B is O. In some embodiments, D has the formula **D1a-IIa**, wherein Y^B is S. In some embodiments, D has the formula **D1a-IIa**, wherein Y^B is $CR^xR^{x'}$. In some embodiments, D has the formula **D1a-IIa**, wherein X is O and Y^B is $CR^xR^{x'}$. In some embodiments, D has the formula **D1a-IIa**, wherein X is O and Y^B is $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1a-IIa**, wherein X is $CR^xR^{x'}$ and Y^B is O. In some embodiments, D has the formula **D1a-IIa**, wherein X is $CR^xR^{x'}$ and Y^B is O, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1a-IIa**, wherein X is S and Y^B is $CR^xR^{x'}$. In some embodiments, D has the formula **D1a-IIa**, wherein X is S and Y^B is $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1a-IIa**, wherein X is $CR^xR^{x'}$ and Y^B is S. In some embodiments, D has the formula **D1a-IIa**, wherein X is $CR^xR^{x'}$ and Y^B is S, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1a-IIa**, wherein X and Y^B are both $CR^xR^{x'}$. In some embodiments, D has the formula **D1a-IIa**, wherein X and Y^B are both $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1a-IIa**, wherein X and Y^B are both $CR^xR^{x'}$, and R^{b3} is halo. In some embodiments, D has the formula **D1a-IIa**, wherein X and Y^B are both $CR^xR^{x'}$, R^x and $R^{x'}$ are both H, and R^{b3} is fluoro. In some embodiments, D has the formula **D1a-IIa**, wherein X and Y^B are both $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, n is 1 or 2. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, R^{b5} is H. In some embodiments, $R^{b5'}$ is H. In some embodiments, R^{b5} and $R^{b5'}$ are both H.

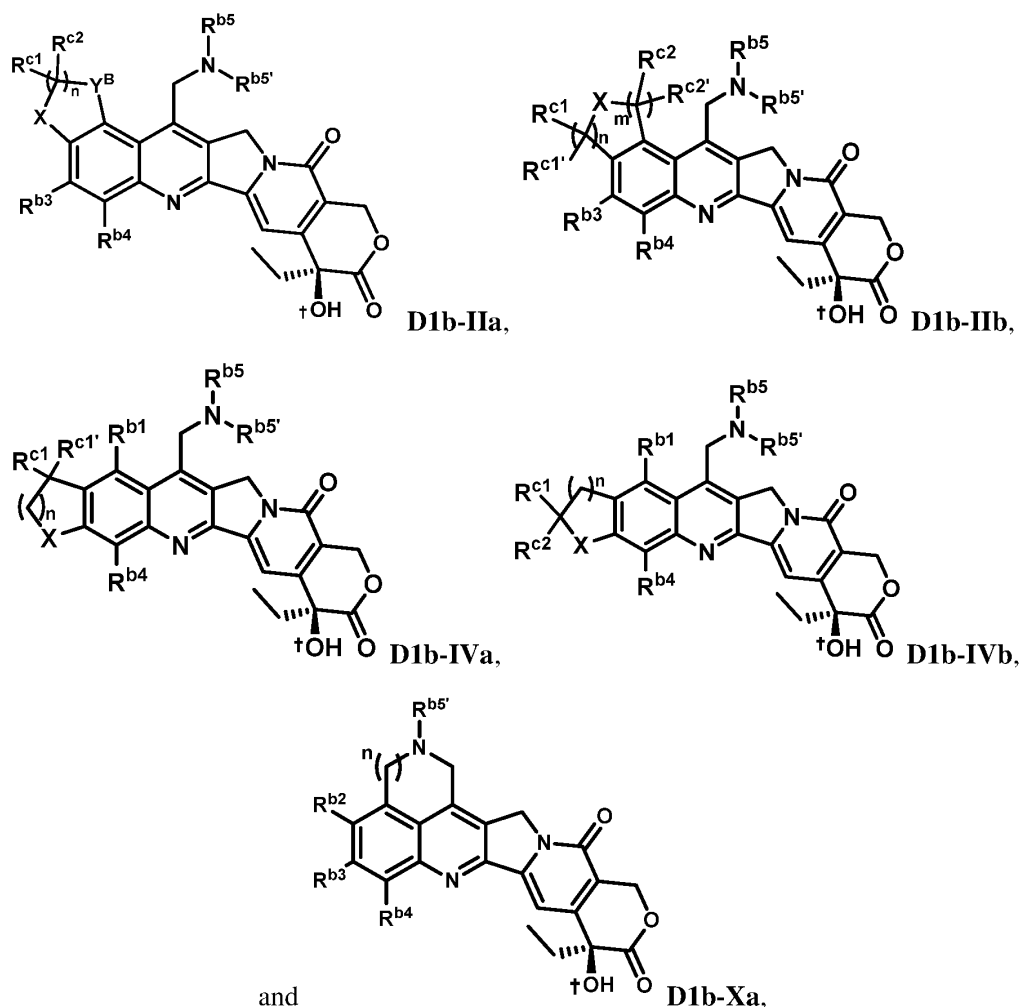
[0121] In some embodiments, D has the formula **D1a-IIb**, wherein X is O. In some embodiments, D has the formula **D1a-IIb**, wherein X is $CR^xR^{x'}$. In some embodiments, D has the formula **D1a-IIb**, wherein X is $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1a-IIb**, wherein X is $CR^xR^{x'}$, and R^{b3} is halo. In some embodiments, D has the formula **D1a-IIb**, wherein X is $CR^xR^{x'}$, R^x and $R^{x'}$ are both H, and R^{b3} is halo. In some embodiments, D has the formula **D1a-IIb**, wherein X is $CR^xR^{x'}$, R^x and $R^{x'}$ are both H, and R^{b3} is fluoro. In some embodiments, n is 1. In some embodiments, m is 1. In some embodiments, n and m are both 1. In some embodiments, R^{b5} is H. In some embodiments, $R^{b5'}$ is H. In some embodiments, R^{b5} and $R^{b5'}$ are both H.

[0122] In some embodiments, D has the formula **D1a-IVa**, wherein X is O. In some embodiments, D has the formula **D1a-IVa**, wherein X is S. In some embodiments, D has the formula **D1a-IVa**, wherein X is CR^xR^{x'}. In some embodiments, D has the formula **D1a-IVa**, wherein X is CR^xR^{x'}, wherein R^x and R^{x'} are both H. In some embodiments, D has the formula **D1a-IVa**, wherein X is CR^xR^{x'} and R^{b1} is halo. In some embodiments, D has the formula **D1a-IVa**, wherein X is CR^xR^{x'}, R^x and R^{x'} are both H, and R^{b1} is halo. In some embodiments, D has the formula **D1a-IVa**, wherein X is CR^xR^{x'}, R^x and R^{x'} are both H, and R^{b1} is fluoro. In some embodiments, D has the formula **D1a-IVa**, wherein X is O and R^{c1} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-IVa**, wherein X is O and R^{c1} is methyl. In some embodiments, n is 1. In some embodiments, n and m are both 1. In some embodiments, R^{b5} is H. In some embodiments, R^{b5'} is H. In some embodiments, R^{b5} and R^{b5'} are both H.

[0123] In some embodiments, D has the formula **D1a-IVb**, wherein X is O. In some embodiments, D has the formula **D1a-IVb**, wherein X is S. In some embodiments, D has the formula **D1a-IVb**, wherein X is CR^xR^{x'}. In some embodiments, D has the formula **D1a-IVb**, wherein X is CR^xR^{x'}, wherein R^x and R^{x'} are both H. In some embodiments, D has the formula **D1a-IVb**, wherein X is CR^xR^{x'} and R^{b1} is halo. In some embodiments, D has the formula **D1a-IVb**, wherein X is CR^xR^{x'}, R^x and R^{x'} are both H, and R^{b1} is halo. In some embodiments, D has the formula **D1a-IVb**, wherein X is CR^xR^{x'}, R^x and R^{x'} are both H, and R^{b1} is fluoro. In some embodiments, D has the formula **D1a-IVb**, wherein X is O and R^{c1} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-IVb**, wherein X is O and R^{c1} is methyl. In some embodiments, n is 1. In some embodiments, n and m are both 1. In some embodiments, R^{b5} is H. In some embodiments, R^{b5'} is H. In some embodiments, R^{b5} and R^{b5'} are both H.

[0124] In some embodiments, D has the formula **D1a-Xa**, wherein n is 1 or 2. In some embodiments, D has the formula **D1a-Xa**, wherein n is 1. In some embodiments, D has the formula **D1a-Xa**, wherein n is 2. In some embodiments, D has the formula **D1a-Xa**, wherein R^{b5'} is H. In some embodiments, D has the formula **D1a-Xa**, wherein n is 1 and R^{b5'} is H. In some embodiments, R^{b2} is OH. In some embodiments, R^{b3} is halo. In some embodiments, R^{b3} is fluoro. In some embodiments, R^{b2} is OH and R^{b3} is fluoro.

[0125] In some embodiments, D has a formula selected from the group consisting of



wherein the variables are as defined for **D1a**, **D1b**, **D1a-IIa**, **D1a-IIb**, **D1a-IVa**, **D1a-IVb**, and **D1a-Xa**. In some embodiments, D has a structure corresponding to any of formulas **D1a**, **D1b**, **D1a-IIa**, **D1a-IIb**, **D1a-IVa**, and **D1a-IVb** and variations thereof, wherein the nitrogen atom to which $R^{b5'}$ is bound is replaced by an oxygen atom and $R^{b5'}$ is absent.

[0126] In some embodiments, D has the formula **D1b-IIa**, wherein X is O. In some embodiments, D has the formula **D1b-IIa**, wherein X is S. In some embodiments, D has the formula **D1b-IIa**, wherein X is $CR^xR^{x'}$. In some embodiments, D has the formula **D1b-IIa**, wherein Y^B is O. In some embodiments, D has the formula **D1b-IIa**, wherein Y^B is S. In some embodiments, D has the formula **D1b-IIa**, wherein Y^B is $CR^xR^{x'}$. In some embodiments, D has the formula **D1b-IIa**, wherein X is O and Y^B is $CR^xR^{x'}$. In some embodiments, D has the formula **D1b-IIa**, wherein X is O and Y^B is $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1b-IIa**, wherein X is $CR^xR^{x'}$ and Y^B is O. In some embodiments, D has the formula **D1b-IIa**, wherein X is $CR^xR^{x'}$ and Y^B is

O, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1b-IIa**, wherein X is S and Y^B is $CR^xR^{x'}$. In some embodiments, D has the formula **D1b-IIa**, wherein X is S and Y^B is $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1b-IIa**, wherein X is $CR^xR^{x'}$ and Y^B is S. In some embodiments, D has the formula **D1b-IIa**, wherein X is $CR^xR^{x'}$ and Y^B is S, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1b-IIa**, wherein X and Y^B are both $CR^xR^{x'}$. In some embodiments, D has the formula **D1b-IIa**, wherein X and Y^B are both $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1b-IIa**, wherein X and Y^B are both $CR^xR^{x'}$, and R^{b3} is halo. In some embodiments, D has the formula **D1b-IIa**, wherein X and Y^B are both $CR^xR^{x'}$, R^x and $R^{x'}$ are both H, and R^{b3} is halo. In some embodiments, D has the formula **D1b-IIa**, wherein X and Y^B are both $CR^xR^{x'}$, R^x and $R^{x'}$ are both H, and R^{b3} is fluoro. In some embodiments, D has the formula **D1b-IIa**, wherein X and Y^B are both $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, n is 1 or 2. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, R^{b5} is H. In some embodiments, $R^{b5'}$ is H. In some embodiments, R^{b5} and $R^{b5'}$ are both H.

[0127] In some embodiments, D has the formula **D1b-IIb**, wherein X is O. In some embodiments, D has the formula **D1b-IIb**, wherein X is $CR^xR^{x'}$. In some embodiments, D has the formula **D1b-IIb**, wherein X is $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1b-IIb**, wherein X is $CR^xR^{x'}$, and R^{b3} is halo. In some embodiments, D has the formula **D1b-IIb**, wherein X is $CR^xR^{x'}$, R^x and $R^{x'}$ are both H, and R^{b3} is halo. In some embodiments, D has the formula **D1b-IIb**, wherein X is $CR^xR^{x'}$, R^x and $R^{x'}$ are both H, and R^{b3} is fluoro. In some embodiments, n is 1. In some embodiments, m is 1. In some embodiments, n and m are both 1. In some embodiments, R^{b5} is H. In some embodiments, $R^{b5'}$ is H. In some embodiments, R^{b5} and $R^{b5'}$ are both H.

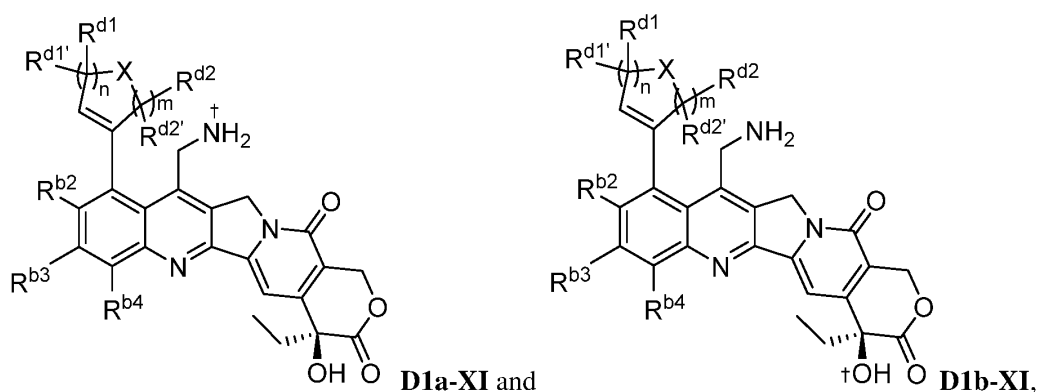
[0128] In some embodiments, D has the formula **D1b-IVa**, wherein X is O. In some embodiments, D has the formula **D1b-IVa**, wherein X is S. In some embodiments, D has the formula **D1b-IVa**, wherein X is $CR^xR^{x'}$. In some embodiments, D has the formula **D1b-IVa**, wherein X is $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1b-IVa**, wherein X is $CR^xR^{x'}$ and R^{b1} is halo. In some embodiments, D has the formula **D1b-IVa**, wherein X is $CR^xR^{x'}$, R^x and $R^{x'}$ are both H, and R^{b1} is halo. In some embodiments, D has the formula **D1b-IVa**, wherein X is $CR^xR^{x'}$, R^x and $R^{x'}$ are both H, and R^{b1} is fluoro. In some embodiments, D has the formula **D1b-IVa**, wherein X is O and R^{c1} is C_1 - C_6 alkyl. In some embodiments, D has the formula **D1b-IVa**, wherein X is O and R^{c1} is

methyl. In some embodiments, n is 1. In some embodiments, n and m are both 1. In some embodiments, R^{b5} is H. In some embodiments, $R^{b5'}$ is H. In some embodiments, R^{b5} and $R^{b5'}$ are both H.

[0129] In some embodiments, D has the formula **D1b-IVb**, wherein X is O. In some embodiments, D has the formula **D1b-IVb**, wherein X is S. In some embodiments, D has the formula **D1b-IVb**, wherein X is $CR^xR^{x'}$. In some embodiments, D has the formula **D1b-IVb**, wherein X is $CR^xR^{x'}$, wherein R^x and $R^{x'}$ are both H. In some embodiments, D has the formula **D1b-IVb**, wherein X is $CR^xR^{x'}$ and R^{b1} is halo. In some embodiments, D has the formula **D1b-IVb**, wherein X is $CR^xR^{x'}$, R^x and $R^{x'}$ are both H, and R^{b1} is halo. In some embodiments, D has the formula **D1b-IVb**, wherein X is $CR^xR^{x'}$, R^x and $R^{x'}$ are both H, and R^{b1} is fluoro. In some embodiments, D has the formula **D1b-IVb**, wherein X is O and R^{c1} is C_1 - C_6 alkyl. In some embodiments, D has the formula **D1b-IVb**, wherein X is O and R^{c1} is methyl. In some embodiments, n is 1. In some embodiments, n and m are both 1. In some embodiments, R^{b5} is H. In some embodiments, $R^{b5'}$ is H. In some embodiments, R^{b5} and $R^{b5'}$ are both H.

[0130] In some embodiments, D has the formula **D1b-Xa**, wherein n is 1 or 2. In some embodiments, D has the formula **D1b-Xa**, wherein n is 1. In some embodiments, D has the formula **D1b-Xa**, wherein n is 2. In some embodiments, D has the formula **D1b-Xa**, wherein $R^{b5'}$ is H. In some embodiments, D has the formula **D1b-Xa**, wherein n is 1 and $R^{b5'}$ is H. In some embodiments, R^{b2} is OH. In some embodiments, R^{b3} is halo. In some embodiments, R^{b3} is fluoro. In some embodiments, R^{b2} is OH and R^{b3} is fluoro.

[0131] In some embodiments, D has a formula selected from the group consisting of



R^{d1} , $R^{d1'}$, R^{d2} , and $R^{d2'}$ are each independently selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a, -C(O)-C₁-C₆ alkyl, -C(O)NR^a-C₁-C₆ alkyl, and -S(O)₂-C₁-C₆ alkyl; and

the remaining variables are as defined for **D1a** and **D1b**. In some embodiments, D has a structure corresponding to any of formulas **D1a-XI** and **D1b-XI** and variations thereof, wherein the NH₂ group is replaced by an OH group.

[0132] In some embodiments, D has the formula **D1a-XI**, wherein R^{b2} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, and -SR^a, wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XI**, wherein R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, and -SR^a, wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XI**, wherein X is O, S, S(O)₂, CR^xR^{x'}, or NR^x; wherein R^x and R^{x'} are each independently selected from the group consisting of H, OH, C₁-C₆ alkyl, -C(O)-C₁-C₆ alkyl, -C(O)NH-C₁-C₆ alkyl, and -S(O)₂-C₁-C₆ alkyl.

[0133] In some embodiments, D has the formula **D1a-XI**, wherein R^{b2} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XI**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1a-XI**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1a-XI**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XI**, wherein R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XI**, wherein n is 1 or 2. In some embodiments, D has the formula **D1a-XI**, wherein n is 1. In some embodiments, D has the formula **D1a-XI**, wherein n is 2. In some embodiments, D has the formula **D1a-XI**, wherein m is 1 or 2. In some embodiments, D has the formula **D1a-XI**, wherein m is 1. In some embodiments, D has the formula **D1a-XI**, wherein m is 2. In some embodiments, D has the formula **D1a-XI**, wherein n and m are both 1. In some embodiments, D has the formula **D1a-XI**, wherein n is 1 and m is 2. In some embodiments, D has the formula **D1a-XI**, wherein n is 2 and m is 1. In some embodiments, D has the formula **D1a-XI**, wherein X is O. In some embodiments, D has the formula **D1a-XI**, wherein X is CR^xR^{x'}. In some embodiments, D has the formula **D1a-XI**, wherein X is CR^xR^{x'}, and R^x and R^{x'} are both H. In some embodiments, D has the formula **D1a-XI**, wherein X is NR^x. In some embodiments, D has the formula **D1a-XI**, wherein X is NR^x, wherein R^x is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XI**, wherein X is NR^x, wherein R^x is methyl.

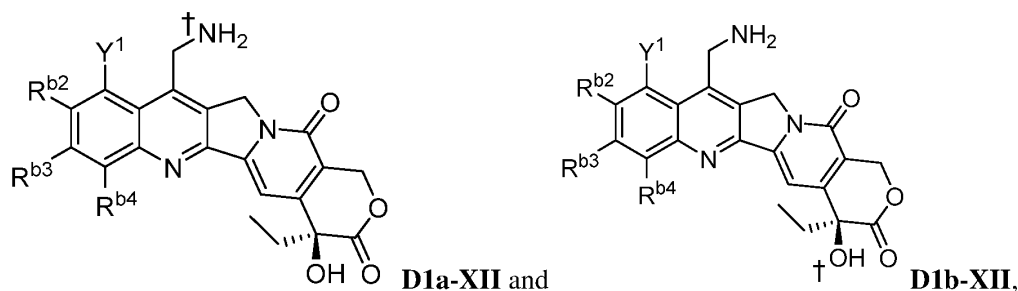
In some embodiments, D has the formula **D1a-XI**, wherein X is NR^x , wherein R^x is methyl. In some embodiments, D has the formula **D1a-XI**, wherein X is S. In some embodiments, D has the formula **D1a-XI**, wherein X is S(O)_2 . In some embodiments, D has the formula **D1a-XI**, wherein X is $-\text{S(O)}_2\text{-C}_1\text{-C}_6$ alkyl. In some embodiments, D has the formula **D1a-XI**, wherein X is $-\text{S(O)}_2\text{-CH}_3$.

[0134] In some embodiments, D has the formula **D1b-XI**, wherein R^{b2} is selected from the group consisting of H, halogen, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $-\text{OR}^a$, $-\text{NHR}^a$, and $-\text{SR}^a$, wherein each R^a is independently selected from the group consisting of H, $\text{C}_1\text{-C}_6$ alkyl, and $\text{C}_1\text{-C}_6$ haloalkyl. In some embodiments, D has the formula **D1b-XI**, wherein R^{b3} is selected from the group consisting of H, halogen, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $-\text{OR}^a$, $-\text{NHR}^a$, and $-\text{SR}^a$, wherein each R^a is independently selected from the group consisting of H, $\text{C}_1\text{-C}_6$ alkyl, and $\text{C}_1\text{-C}_6$ haloalkyl. In some embodiments, D has the formula **D1b-XI**, wherein X is O, S, S(O)_2 , $\text{CR}^x\text{R}^{x'}$, or NR^x ; wherein R^x and $\text{R}^{x'}$ are each independently selected from the group consisting of H, OH, $\text{C}_1\text{-C}_6$ alkyl, $-\text{C(O)-C}_1\text{-C}_6$ alkyl, $-\text{C(O)NH-C}_1\text{-C}_6$ alkyl, and $-\text{S(O)}_2\text{-C}_1\text{-C}_6$ alkyl.

[0135] In some embodiments, D has the formula **D1b-XI**, wherein R^{b2} is $\text{C}_1\text{-C}_6$ alkyl. In some embodiments, D has the formula **D1b-XI**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1b-XI**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1b-XI**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XI**, wherein R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XI**, wherein n is 1 or 2. In some embodiments, D has the formula **D1b-XI**, wherein n is 1. In some embodiments, D has the formula **D1b-XI**, wherein n is 2. In some embodiments, D has the formula **D1b-XI**, wherein m is 1 or 2. In some embodiments, D has the formula **D1b-XI**, wherein m is 1. In some embodiments, D has the formula **D1b-XI**, wherein m is 2. In some embodiments, D has the formula **D1b-XI**, wherein n and m are both 1. In some embodiments, D has the formula **D1b-XI**, wherein n is 1 and m is 2. In some embodiments, D has the formula **D1b-XI**, wherein n is 2 and m is 1. In some embodiments, D has the formula **D1b-XI**, wherein X is O. In some embodiments, D has the formula **D1b-XI**, wherein X is $\text{CR}^x\text{R}^{x'}$. In some embodiments, D has the formula **D1b-XI**, wherein X is $\text{CR}^x\text{R}^{x'}$, and R^x and $\text{R}^{x'}$ are both H. In some embodiments, D has the formula **D1b-XI**, wherein X is NR^x . In some embodiments, D has the formula **D1b-XI**, wherein X is NR^x , wherein R^x is $\text{C}_1\text{-C}_6$ alkyl. In some embodiments, D has the formula **D1b-XI**, wherein X is NR^x , wherein R^x is methyl. In some embodiments, D has the formula **D1b-XI**, wherein X is

NR^x, wherein R^x is methyl. In some embodiments, D has the formula **D1b-XI**, wherein X is S. In some embodiments, D has the formula **D1b-XI**, wherein X is S(O)₂. In some embodiments, D has the formula **D1b-XI**, wherein X is –S(O)₂-C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XI**, wherein X is –S(O)₂-CH₃.

[0136] In some embodiments, D has a formula selected from the group consisting of



wherein

Y¹ is a 5- or 6-membered heteroaryl, optionally substituted with halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, or C₁-C₆ alkyl-S(O)₂-; and the remaining variables are as defined for **D1a** and **D1b**. In some embodiments, D has a structure corresponding to any of formulas **D1a-XII** and **D1b-XII** and variations thereof, wherein the NH₂ group is replaced by an OH group.

[0137] In some embodiments, D has the formula **D1a-XII**, wherein R^{b2} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, and -SR^a, wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XII**, wherein R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, and -SR^a, wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl.

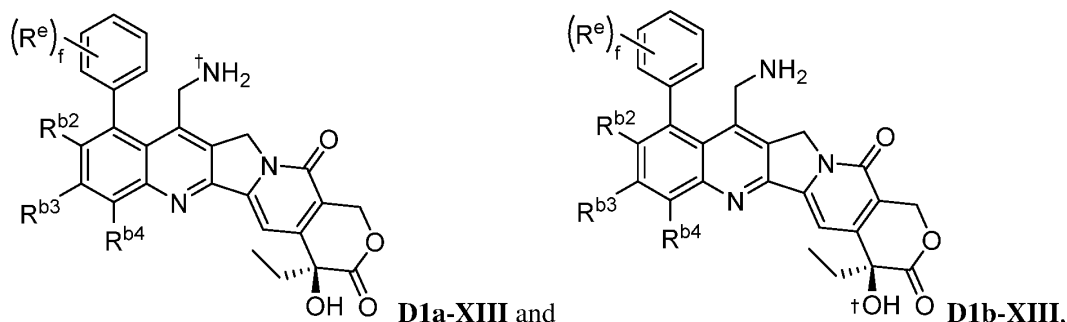
[0138] In some embodiments, D has the formula **D1a-XII**, wherein R^{b2} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XII**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1a-XII**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1a-XII**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XI**, wherein R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XII**, wherein Y¹ is a 5-membered heteroaryl optionally substituted with C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, or –S(O)₂-C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XII**, wherein Y¹ is an unsubstituted 5-membered heteroaryl. In some embodiments, D has the

formula **D1a-XII**, wherein Y^1 is an unsubstituted thiophene. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is an unsubstituted thiophene; and R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is a 5-membered heteroaryl, substituted with C_1 - C_6 alkyl, C_1 - C_6 hydroxyalkyl, or $-S(O)_2$ - C_1 - C_6 alkyl. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is a thiophene, substituted with C_1 - C_6 alkyl, C_1 - C_6 hydroxyalkyl, or $-S(O)_2$ - C_1 - C_6 alkyl. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is a thiophene, substituted with C_1 - C_6 hydroxyalkyl. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is a thiophene, substituted with hydroxyethyl. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is a thiophene, substituted with hydroxyethyl; and R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is a furan. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is an unsubstituted furan. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is a pyrrole. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is a substituted pyrrole. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is a pyrrole substituted by $-S(O)_2$ - C_1 - C_6 alkyl. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is a pyrrole substituted by $-S(O)_2$ - CH_3 . In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is a pyridine. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is an unsubstituted pyridine. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is an isoxazole. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is an unsubstituted isoxazole. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is an isoxazole substituted by one or more C_1 - C_6 alkyl. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is an isoxazole substituted by one or more methyl. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is an isoxazole substituted by one methyl group. In some embodiments, D has the formula **D1a-XII**, wherein Y^1 is an isoxazole substituted by two methyl groups.

[0139] In some embodiments, D has the formula **D1b-XII**, wherein R^{b2} is selected from the group consisting of H, halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, $-OR^a$, $-NHR^a$, and $-SR^a$, wherein each R^a is independently selected from the group consisting of H, C_1 - C_6 alkyl, and C_1 - C_6 haloalkyl. In some embodiments, D has the formula **D1b-XII**, wherein R^{b3} is selected from the group consisting of H, halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, $-OR^a$, $-NHR^a$, and $-SR^a$, wherein each R^a is independently selected from the group consisting of H, C_1 - C_6 alkyl, and C_1 - C_6 haloalkyl.

[0140] In some embodiments, D has the formula **D1b-XII**, wherein R^{b2} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XII**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1b-XII**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1b-XII**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XI**, wherein R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a 5-membered heteroaryl optionally substituted with C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, or -S(O)₂-C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is an unsubstituted 5-membered heteroaryl. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is an unsubstituted thiophene. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is an unsubstituted thiophene; and R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a 5-membered heteroaryl, substituted with C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, or -S(O)₂-C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a thiophene, substituted with C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, or -S(O)₂-C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a thiophene, substituted with C₁-C₆ hydroxyalkyl. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a thiophene, substituted with hydroxyethyl. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a thiophene, substituted with hydroxyethyl; and R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a furan. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is an unsubstituted furan. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a pyrrole. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a substituted pyrrole. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a pyrrole substituted by -S(O)₂-C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a pyrrole substituted by -S(O)₂-CH₃. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is a pyridine. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is an unsubstituted pyridine. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is an isoxazole. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is an unsubstituted isoxazole. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is an isoxazole substituted by one or more C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is an isoxazole substituted by one or more methyl. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is an isoxazole substituted by one methyl group. In some embodiments, D has the formula **D1b-XII**, wherein Y¹ is an isoxazole substituted by two methyl groups.

[0141] In some embodiments, D has a formula selected from the group consisting of



wherein

each R^e is independently selected from the group consisting of halogen, -OH, -NH₂, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, -S(O)₂-C₁-C₆ alkyl, and -C(O)NH-C₁-C₆ alkyl;

f is 0, 1, 2, 3, 4, or 5; and

the remaining variables are as defined for **D1a** and **D1b**. In some embodiments, D has a structure corresponding to any of formulas **D1a-XIII** and **D1b-XIII** and variations thereof, wherein the NH₂ group is replaced by an OH group.

[0142] In some embodiments, D has the formula **D1a-XIII**, wherein R^{b2} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, and -SR^a, wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XIII**, wherein R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, and -SR^a, wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XIII**, wherein R^e is selected from the group consisting of halogen, -OH, -NH₂, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, -S(O)₂-C₁-C₆ alkyl, and -C(O)NH-C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XIII**, wherein f is 0, 1, 2, 3, 4, or 5. In some embodiments, D has the formula **D1a-XIII**, wherein f is 0. In some embodiments, D has the formula **D1a-XIII**, wherein f is 1. In some embodiments, D has the formula **D1a-XIII**, wherein f is 2. In some embodiments, D has the formula **D1a-XIII**, wherein f is 3. In some embodiments, D has the formula **D1a-XIII**, wherein f is 4. In some embodiments, D has the formula **D1a-XIII**, wherein f is 5.

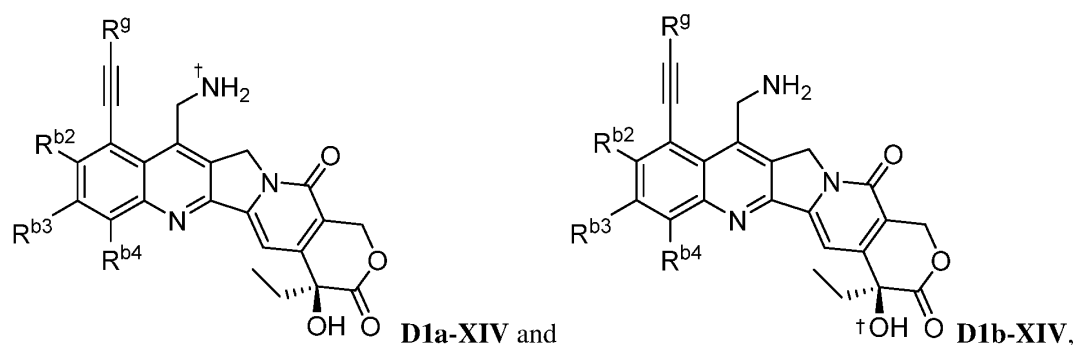
[0143] In some embodiments, D has the formula **D1a-XIII**, wherein R^{b2} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XIII**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1a-XIII**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1a-XIII**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1a-**

XIII, wherein R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XIII**, wherein R^e is -OH. In some embodiments, D has the formula **D1a-XIII**, wherein R^e is -OH and f is 1. In some embodiments, D has the formula **D1a-XIII**, wherein R^e is halo. In some embodiments, D has the formula **D1a-XIII**, wherein R^e is fluoro. In some embodiments, D has the formula **D1a-XIII**, wherein R^e is -NH₂. In some embodiments, D has the formula **D1a-XIII**, wherein R^e is -C(O)NH-C₁-C₆ alkyl.

[0144] In some embodiments, D has the formula **D1b-XIII**, wherein R^{b2} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, and -SR^a, wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1b-XIII**, wherein R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, and -SR^a, wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1b-XIII**, wherein R^e is selected from the group consisting of halogen, -OH, -NH₂, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, -S(O)₂-C₁-C₆ alkyl, and -C(O)NH-C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XIII**, wherein f is 0, 1, 2, 3, 4, or 5. In some embodiments, D has the formula **D1b-XIII**, wherein f is 0. In some embodiments, D has the formula **D1b-XIII**, wherein f is 1. In some embodiments, D has the formula **D1b-XIII**, wherein f is 2. In some embodiments, D has the formula **D1b-XIII**, wherein f is 3. In some embodiments, D has the formula **D1b-XIII**, wherein f is 4. In some embodiments, D has the formula **D1b-XIII**, wherein f is 5.

[0145] In some embodiments, D has the formula **D1b-XIII**, wherein R^{b2} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XIII**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1b-XIII**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1b-XIII**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XIII**, wherein R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XIII**, wherein R^e is -OH. In some embodiments, D has the formula **D1b-XIII**, wherein R^e is -OH and f is 1. In some embodiments, D has the formula **D1b-XIII**, wherein R^e is halo. In some embodiments, D has the formula **D1b-XIII**, wherein R^e is fluoro. In some embodiments, D has the formula **D1b-XIII**, wherein R^e is -NH₂. In some embodiments, D has the formula **D1b-XIII**, wherein R^e is -C(O)NH-C₁-C₆ alkyl.

[0146] In some embodiments, D has a formula selected from the group consisting of



wherein

R^g is H, C₁-C₆ alkyl, or 3 to 8-membered heterocyclyl; and

the remaining variables are as defined for **D1a** and **D1b**. In some embodiments, R^g is C₁-C₆ alkyl. In some embodiments, D has a structure corresponding to any of formulas **D1a-XIV** and **D1b-XIV** and variations thereof, wherein the NH₂ group is replaced by an OH group.

[0147] In some embodiments, D has the formula **D1a-XIV**, wherein R^{b2} is H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XIV**, wherein R^{b3} is H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XIV**, wherein R^g is H, C₁-C₆ alkyl, or 3- to 8-membered heterocyclyl.

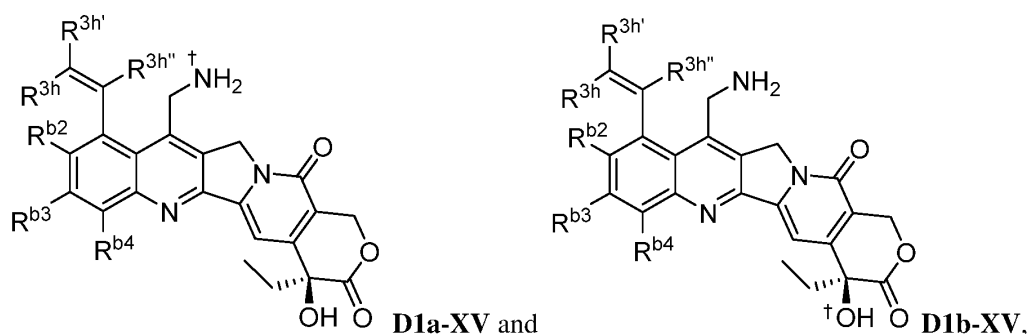
[0148] In some embodiments, D has the formula **D1a-XIV**, wherein R^{b2} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XIV**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1a-XIV**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1a-XIV**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XIV**, wherein R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XIV**, wherein R^g is H. In some embodiments, D has the formula **D1a-XIV**, wherein R^g is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XIV**, wherein R^g is 3- to 8-membered heterocyclyl. In some embodiments, D has the formula **D1a-XIV**, wherein R^g is H, R^{b2} is methyl, and R^{b3} is fluoro.

[0149] In some embodiments, D has the formula **D1b-XIV**, wherein R^{b2} is H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1b-XIV**, wherein R^{b3} is H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group

consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1b -XIV**, wherein R^g is H, C₁-C₆ alkyl, or 3- to 8-membered heterocyclyl.

[0150] In some embodiments, D has the formula **D1b -XIV**, wherein R^{b2} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1b -XIV**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1b -XIV**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1b -XIV**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1b -XIV**, wherein R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1b -XIV**, wherein R^g is H. In some embodiments, D has the formula **D1b -XIV**, wherein R^g is C₁-C₆ alkyl. In some embodiments, D has the formula **D1b -XIV**, wherein R^g is 3- to 8-membered heterocyclyl. In some embodiments, D has the formula **D1b -XIV**, wherein R^g is H, R^{b2} is methyl, and R^{b3} is fluoro.

[0151] In some embodiments, D has a formula selected from the group consisting of



wherein

R^{3h}, R^{3h'}, and R^{3h''} are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, -C(O)-C₁-C₆ alkyl, -C(O)O-C₁-C₆ alkyl, -C(O)NH-C₁-C₆ alkyl, C₆-C₁₀ aryl, -C₆-C₁₀ aryl-C₁-C₆ alkyl, and -C₆-C₁₀ aryl-C₁-C₆ alkoxy; each optionally substituted with, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a; and the remaining variables are as defined for **D1a** and **D1b**. In some embodiments, D has a structure corresponding to any of formulas **D1a-XV** and **D1b-XV** and variations thereof, wherein the NH₂ group is replaced by an OH group.

[0152] In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} is H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XV**, wherein R^{b3} is H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -

NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl.

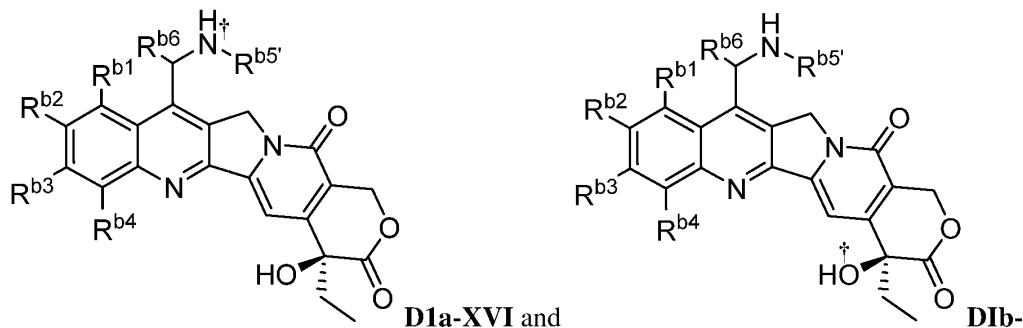
[0153] In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} is -OH. In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} is halo. In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} is fluoro. In some embodiments, D has the formula **D1a-XV**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1a-XV**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} is H and R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} and R^{b3} are both fluoro. In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} is -OH and R^{b3} is H. In some embodiments, D has the formula **D1a-XV**, wherein R^{3h}, R^{3h'}, and R^{3h''} are each H. In some embodiments, D has the formula **D1a-XV**, wherein R^{3h} and R^{3h'} are both H and R^{3h''} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XV**, wherein R^{3h} and R^{3h'} are both H and R^{3h''} is methyl. In some embodiments, D has the formula **D1a-XV**, wherein R^{3h} and R^{3h'} are both C₁-C₆ alkyl and R^{3h''} is H. In some embodiments, D has the formula **D1a-XV**, wherein R^{3h} and R^{3h'} are both methyl and R^{3h''} is H. In some embodiments, D has the formula **D1a-XV**, wherein R^{3h} is H, and R^{3h'} and R^{3h''} are both methyl. In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} is methyl, R^{b3} is fluoro, and R^{3h}, R^{3h'}, and R^{3h''} are each H. In some embodiments, D has the formula **D1a-XV**, wherein R^{b2} is methyl, R^{b3} is fluoro, R^{3h} and R^{3h'} are both H, and R^{3h''} is methyl. In some embodiments, D has the formula **D1a-XV**, wherein R^{3h} and R^{3h''} are both H, and R^{3h'} is -C₆-C₁₀ aryl-C₁-C₆ alkoxy.

[0154] In some embodiments, D has the formula **D1b-XV**, wherein R^{b2} is H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1b-XV**, wherein R^{b3} is H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl.

[0155] In some embodiments, D has the formula **D1b-XV**, wherein R^{b2} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XV**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1b-XV**, wherein R^{b2} is -OH. In some embodiments, D has the formula **D1b-XV**, wherein R^{b2} is halo. In some embodiments, D has the formula **D1b-**

XV, wherein R^{b2} is fluoro. In some embodiments, D has the formula **D1b-XV**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1b-XV**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XV**, wherein R^{b2} is methyl and R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XV**, wherein R^{b2} is H and R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XV**, wherein R^{b2} and R^{b3} are both fluoro. In some embodiments, D has the formula **D1b-XV**, wherein R^{b2} is -OH and R^{b3} is H. In some embodiments, D has the formula **D1b-XV**, wherein R^{3h} , $R^{3h'}$, and $R^{3h''}$ are each H. In some embodiments, D has the formula **D1b-XV**, wherein R^{3h} and $R^{3h'}$ are both H and $R^{3h''}$ is C_1 - C_6 alkyl. In some embodiments, D has the formula **D1b-XV**, wherein R^{3h} and $R^{3h'}$ are both H and $R^{3h''}$ is methyl. In some embodiments, D has the formula **D1b-XV**, wherein R^{3h} and $R^{3h'}$ are both C_1 - C_6 alkyl and $R^{3h''}$ is H. In some embodiments, D has the formula **D1b-XV**, wherein R^{3h} and $R^{3h'}$ are both methyl and $R^{3h''}$ is H. In some embodiments, D has the formula **D1b-XV**, wherein R^{3h} is H, and $R^{3h'}$ and $R^{3h''}$ are both methyl. In some embodiments, D has the formula **D1b-XV**, wherein R^{b2} is methyl, R^{b3} is fluoro, and R^{3h} , $R^{3h'}$, and $R^{3h''}$ are each H. In some embodiments, D has the formula **D1b-XV**, wherein R^{b2} is methyl, R^{b3} is fluoro, R^{3h} and $R^{3h'}$ are both H, and $R^{3h''}$ is methyl. In some embodiments, D has the formula **D1b-XV**, wherein R^{3h} and $R^{3h''}$ are both H, and $R^{3h'}$ is - C_6 - C_{10} aryl- C_1 - C_6 alkoxy.

[0156] In some embodiments, D has a formula selected from the group consisting of



XVI,

wherein the variables are as defined for **D1a** and **D1b**. In some embodiments, D has a structure corresponding to any of formulas **D1a-XVI** and **D1b-XVI** and variations thereof, wherein the nitrogen atom to which $R^{b5'}$ is bound is replaced by an oxygen atom and $R^{b5'}$ is absent.

[0157] In some embodiments, D has the formula **D1a-XVI**, wherein R^{b1} is H, halogen, -OH, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_1 - C_6 alkoxy, C_1 - C_6 haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C_1 - C_6

alkyl, and C₁-C₆ haloalkyl. In some embodiments, R^{b1} is H, halogen, -CN, -OH, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is H, halogen, -OH, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b3} is H, halogen, -OH, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} and R^{b3} are taken together to form a methylenedioxy moiety. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b6} is H or is taken together with R^{b1} to form a carbocyclo or heterocyclo. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b5'} is H, -C(O)-C₁-C₆ alkyl, or -C(O)-C₁-C₆ alkylamino.

[0158] In some embodiments, D has the formula **D1a-XVI**, wherein R^{b1} is halo. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b1} is fluoro. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b1} is bromo. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b1} is chloro. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b1} is -CN. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b1} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b1} is methyl.

[0159] In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is halo. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is chloro. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is bromo. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is fluoro. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is C₁-C₆ alkoxy. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is methoxy. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is C₁-C₆ hydroxyalkyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is trihalomethyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is trifluoromethyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is C₂-C₆ alkenyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is -OH. In some embodiments, D has

the formula **D1a-XVI**, wherein R^{b2} is $-SR^a$. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is $-SR^a$, wherein R^a is C_1-C_6 alkyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is $-SR^a$, wherein R^a is methyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is $-SR^a$, wherein R^a is C_1-C_6 haloalkyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is $-SR^a$, wherein R^a is trihalomethyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} is $-SR^a$, wherein R^a is trifluoromethyl.

[0160] In some embodiments, D has the formula **D1a-XVI**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b3} is chloro. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b3} is bromo. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b3} is C_1-C_6 alkyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b3} is methyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b3} is ethyl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b3} is C_1-C_6 alkoxy. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b3} is methoxy.

[0161] In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} and R^{b3} are taken together with their intervening atoms to form 5-membered heterocyclo fused with 6-membered aryl. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b2} and R^{b3} are taken together with their intervening atoms to form 2,3-dihydrobenzofuranyl.

[0162] In some embodiments, D has the formula **D1a-XVI**, wherein R^{b1} and R^{b6} are taken together with their intervening atoms to form a carbocyclo. In some embodiments, D has the formula **D1a-XVI**, wherein R^{b1} and R^{b6} are taken together with their intervening atoms to form a 6-membered cycloalkyl.

[0163] In some embodiments, D has the formula **D1a-XVI**, wherein $R^{b5'}$ is H. In some embodiments, D has the formula **D1a-XVI**, wherein $R^{b5'}$ is H. In some embodiments, D has the formula **D1a-XVI**, wherein $R^{b5'}$ is $-C(O)-C_1-C_6$ alkyl. In some embodiments, D has the formula **D1a-XVI**, wherein $R^{b5'}$ is $-C(O)-C_1-C_6$ alkylamino. In some embodiments, D has the formula **D1a-XVI**, wherein $R^{b5'}$ is 3- to 10- membered heteroaryl substituted with C_1-C_6 hydroxyalkyl. In some embodiments, D has the formula **D1a-XVI**, wherein $R^{b5'}$ is 5- to 6- membered heteroaryl substituted with C_1-C_6 hydroxyalkyl. In some embodiments, D has the formula **D1a-XVI**, wherein $R^{b5'}$ is pyridinyl substituted with $-CH_2OH$.

[0164] In some embodiments, D has the formula **D1b-XVI**, wherein R^{b1} is H, halogen, -OH, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, R^{b1} is H, halogen, -CN, -OH, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is H, halogen, -OH, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b3} is H, halogen, -OH, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, -OR^a, -NHR^a, or -SR^a; wherein each R^a is independently selected from the group consisting of H, C₁-C₆ alkyl, and C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} and R^{b3} are taken together to form a methylenedioxy moiety. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b6} is H or is taken together with R^{b1} to form a carbocyclo or heterocyclo. In some embodiments, D has the formula **D1b-XVI**, wherein $R^{b5'}$ is H, -C(O)-C₁-C₆ alkyl, or -C(O)-C₁-C₆ alkylamino.

[0165] In some embodiments, D has the formula **D1b-XVI**, wherein R^{b1} is halo. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b1} is fluoro. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b1} is bromo. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b1} is chloro. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b1} is -CN. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b1} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b1} is methyl.

[0166] In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is C₁-C₆ alkyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is methyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is halo. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is chloro. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is bromo. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is fluoro. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is C₁-C₆ alkoxy. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is methoxy. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is C₁-C₆ haloalkyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is C₁-C₆ hydroxyalkyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is trihalomethyl. In some

embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is trifluoromethyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is C_2 - C_6 alkenyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is -OH. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is -SR^a. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is -SR^a, wherein R^a is C_1 - C_6 alkyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is -SR^a, wherein R^a is methyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is -SR^a, wherein R^a is C_1 - C_6 haloalkyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is -SR^a, wherein R^a is trihalomethyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} is -SR^a, wherein R^a is trifluoromethyl.

[0167] In some embodiments, D has the formula **D1b-XVI**, wherein R^{b3} is halo. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b3} is chloro. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b3} is bromo. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b3} is fluoro. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b3} is C_1 - C_6 alkyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b3} is methyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b3} is ethyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b3} is C_1 - C_6 alkoxy. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b3} is methoxy.

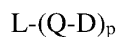
[0168] In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} and R^{b3} are taken together with their intervening atoms to form a 5-membered heterocycle fused with 6-membered heteroaryl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b2} and R^{b3} are taken together with their intervening atoms to form 2,3-dihydrobenzofuranyl.

[0169] In some embodiments, D has the formula **D1b-XVI**, wherein R^{b1} and R^{b6} are taken together with their intervening atoms to form a carbocycle. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b1} and R^{b6} are taken together with their intervening atoms to form a 6-membered cycloalkyl.

[0170] In some embodiments, D has the formula **D1b-XVI**, wherein $R^{b5'}$ is H. In some embodiments, D has the formula **D1b-XVI**, wherein $R^{b5'}$ is H. In some embodiments, D has the formula **D1b-XVI**, wherein $R^{b5'}$ is -C(O)- C_1 - C_6 alkyl. In some embodiments, D has the formula **D1b-XVI**, wherein $R^{b5'}$ is -C(O)- C_1 - C_6 alkylamino. In some embodiments, D has the formula **D1b-XVI**, wherein $R^{b5'}$ is 3- to 10- membered heteroaryl substituted with C_1 - C_6 hydroxyalkyl. In some embodiments, D has the formula **D1b-XVI**, wherein $R^{b5'}$ is 5- to 6-

membered heteroaryl substituted with C₁-C₆ hydroxyalkyl. In some embodiments, D has the formula **D1b-XVI**, wherein R^{b5'} is pyridinyl substituted with -CH₂OH.

[0171] In another embodiment, a Camptothecin Conjugate is provided having a formula:

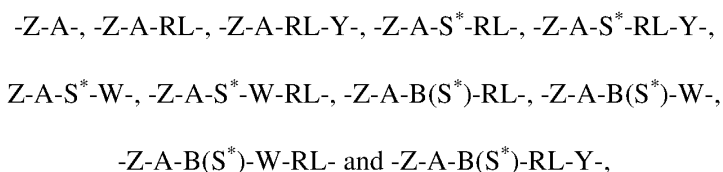


or a salt thereof, wherein

L is a Ligand Unit;

subscript p is an integer of from 1 to 16;

Q is a Linker Unit having a formula selected from the group consisting of:



wherein Z is a Stretcher Unit;

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

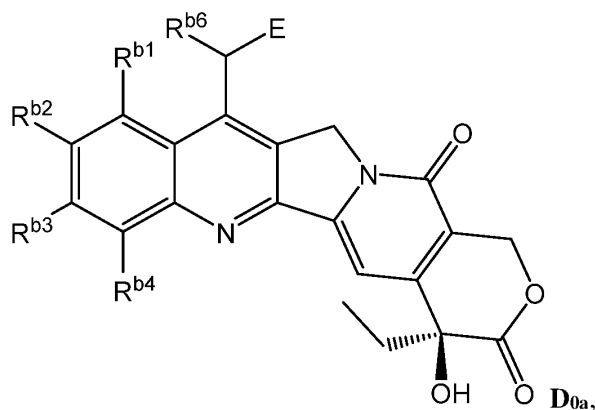
S* is a Partitioning Agent;

RL is a Releasable Linker;

W is an Amino Acid Unit;

Y is a Spacer Unit; and

D is a Drug Unit having a formula of



or a salt thereof; wherein;

E is -OR^{b5} or -NR^{b5}R^{b5'};

R^{b1} is selected from the group consisting of H, halogen, -CN, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with C₁-C₃ alkyl, -OR^a, -NR^aR^{a'}, -C(O)R^a, and -SR^a; or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b3} is combined with R^{b2} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo or a 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b4} is selected from the group consisting of H and halogen;

each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₆ alkyl-O-C₁-C₆ alkyl-, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ hydroxyalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, heteroaryl-C₁-C₆ hydroxyalkyl, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈

aminoalkyl-, C₁-C₆ alkoxy-C(O)-N-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂; R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and R^a and R^{a'} are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

wherein a) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, R^{b5} is H and R^{b5'} is C₁-C₆ alkyl-O-C₁-C₆ alkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl;

b) when E is NH₂, R^{b1} is selected from the group consisting of -CN, 5- to 12-membered heteroaryl with at least one annular N, 3- to 10-membered heterocycloalkyl with at least one annular N, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with C₁-C₃ alkyl, -OR^a, -NR^aR^{a'}, -C(O)R^a, and -SR^a., or R^{b1} is combined with R^{b2} and the intervening atoms to form a 5-, 6-, or 7-membered heterocyclo

with at least one annular N, or 5- or 6-membered heterocyclo fused with 6-membered aryl; R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

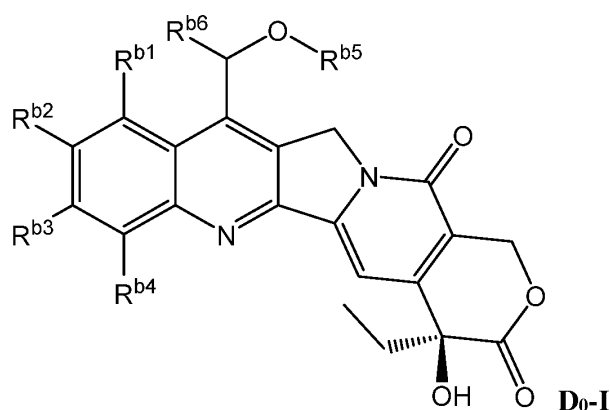
R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered heterocyclo with at least one annular N, or R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl;

c) when R^{b2} is -OH or methyl and R^{b3} is F, then R^{b1} does not come together with R^{b5} or R^{b5'} and the intervening atoms to form a ring; and

d) D is not selected from the group consisting of (S)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-14-((4-(2-aminoethyl)piperazin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-14-((4-aminopiperidin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, and *tert*-butyl (S)-(1-((7-ethyl-7-hydroxy-8,11-dioxo-7,8,11,13-tetrahydro-10H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-14-yl)methyl)piperidin-4-yl)carbamate

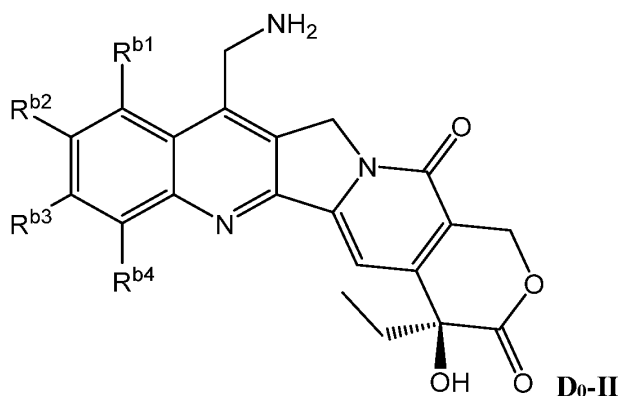
wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

[0172] In some embodiments, D has the formula of **D₀-I**



or a salt thereof; wherein R^{b1} - R^{b6} are each defined as for D_0 .

[0173] In some embodiments, D has the formula of **D₀-II**



or a salt thereof; wherein;

R^{b1} is selected from the group consisting of -CN, 5- to 12-membered heteroaryl with at least one annular N, 3- to 10-membered heterocycloalkyl with at least one annular N,

C_1 - C_8 hydroxyalkyl, C_1 - C_8 alkyl- $C(O)$ - C_1 - C_8 aminoalkyl-, C_1 - C_8 aminoalkyl- $C(O)$ - C_1 - C_8 alkyl-, C_1 - C_8 alkyl- NR^a - $C(O)$ -, C_1 - C_8 alkyl- $C(O)$ -, C_1 - C_8 alkyl- $OC(O)$ -, C_6 - C_{12} aryl- $C(O)$ -, C_6 - C_{12} aryl- $O-C(O)-NR^a$ -, C_6 - C_{12} aryl- $NR^a-C(O)-O$ -, $-COOR^a$, $-NR^aR^{a'}$, and $-SR^a$; each optionally substituted with C_1 - C_3 alkyl, $-OR^a$, $-NR^aR^{a'}$, $-C(O)R^a$, and $-SR^a$; or

R^{b1} is combined with R^{b2} and the intervening atoms to form a 5-, 6-, or 7-membered heterocyclo with at least one annular N, or 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b2} is selected from the group consisting of H, halogen, C_1 - C_8 alkyl, C_2 - C_8 alkynyl, C_6 - C_{12} aryl, 5- to 12-membered heteroaryl, C_3 - C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl,

C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with -OR^a-, -NR^aR^{a'}-, and -SR^a-, or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered heterocycle with at least one annular N, or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocycle fused with 6-membered aryl;

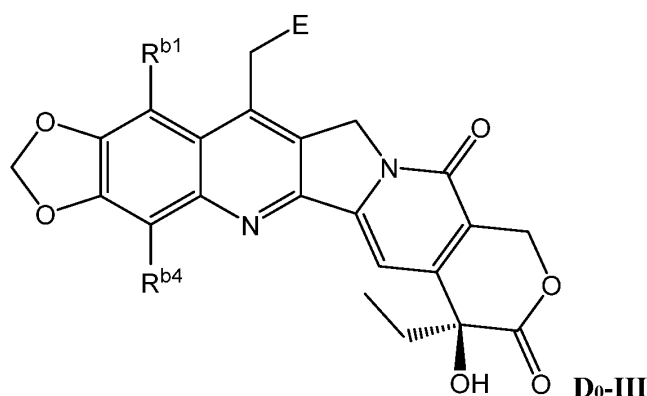
R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a-, -NR^aR^{a'}-, and -SR^a-,

R^{b4} is selected from the group consisting of H or halogen; and

R^a and R^{a'} are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

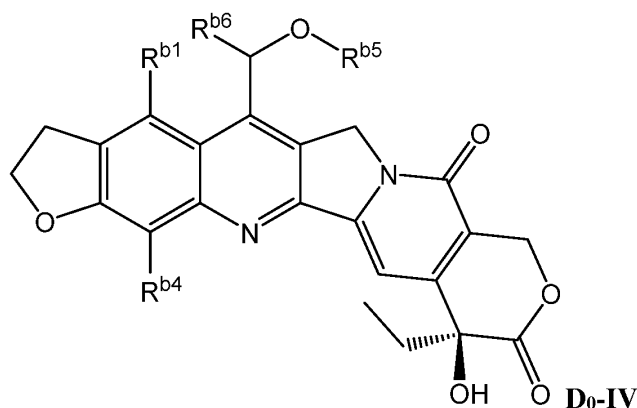
wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

[0174] In some embodiments, D has the formula of **D₀-III**



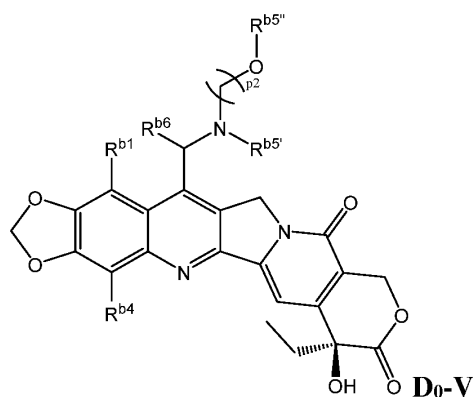
or a salt thereof; wherein R^{b1}, R^{b4}, and R^{b6} are each defined as for D_{0a}.

[0175] In some embodiments, D has the formula of **D₀-IV**



or a salt thereof; wherein R^{b1} , R^{b4} , R^{b5} , R^{b6} are each defined as for **D_{0a}**. In some embodiments, R^{b1} , R^{b4} , R^{b5} , and R^{b6} are each H.

[0176] In some embodiments, D has the formula of **D_{0-V}**



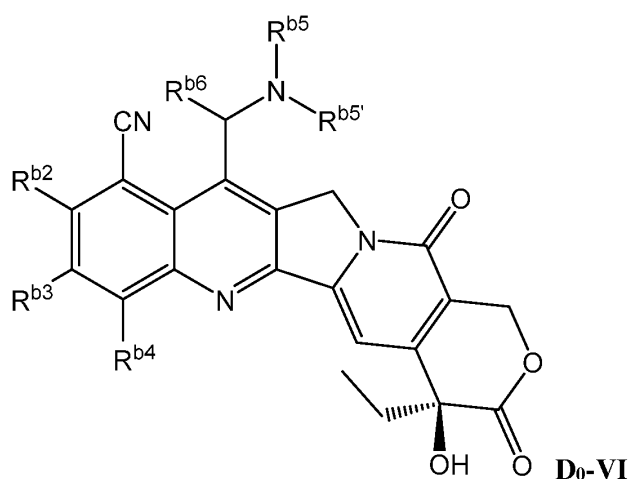
or a salt thereof; wherein:

p_2 is 2 to 6;

$R^{b5'}$ is selected from the group consisting of H, C_1 - C_6 alkyl and C_1 - C_6 haloalkyl; and

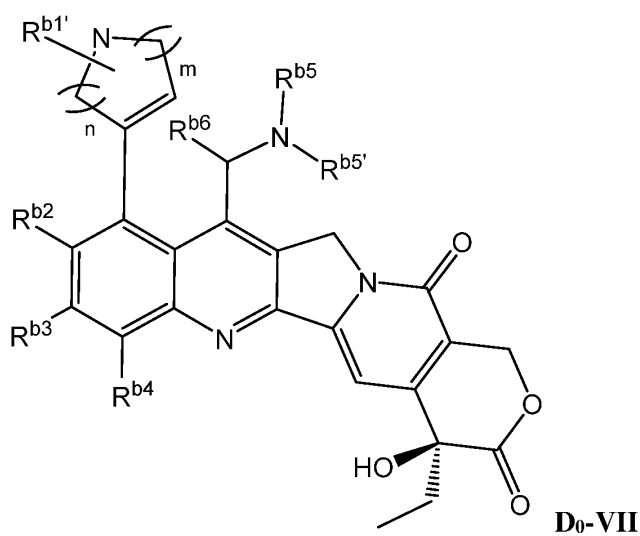
R^{b1} , R^{b4} , $R^{b5'}$, R^{b6} are each defined as for **D_{0a}**. In some embodiments, p_2 is 2, $R^{b5'}$ is methyl, and R^{b1} , R^{b4} , $R^{b5'}$, R^{b6} are each H.

[0177] In some embodiments, D has the formula of **D_{0-VI}**



or a salt thereof; wherein R^{b2} , R^{b3} , R^{b4} , R^{b5} , $R^{b5'}$, and R^{b6} are each defined as for **D_{0a}**. In some embodiments, R^{b2} is methyl, R^{b3} is F, and R^{b5} , $R^{b5'}$, and R^{b6} are each H.

[0178] In some embodiments, D has the formula of **D₀-VII**



or a salt thereof; wherein;

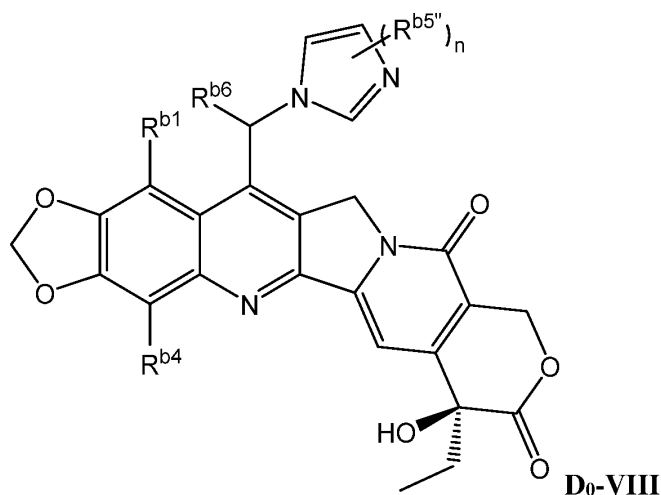
m and n are each 1 or 2, and when m and n are both present, $m + n$ is 2 or 3;

$R^{b1'}$ is C_1 - C_3 alkyl or $-C(O)R^a$; and

R^{b2} , R^{b3} , R^{b4} , R^{b5} , $R^{b5'}$, and R^{b6} are each defined as for **D_{0a}**.

In some embodiments, m is 1, n is 2, $R^{b1'}$ is methyl, and R^{b2} , R^{b3} , R^{b4} , R^{b5} , $R^{b5'}$, R^{b6} are each H. In some embodiments, m is 1, n is 2, $R^{b1'}$ is $C(O)CH_3$, and R^{b2} , R^{b3} , R^{b4} , R^{b5} , $R^{b5'}$, and R^{b6} are each H.

[0179] In some embodiments, D has the formula of **D₀-VIII**



or a salt thereof; wherein:

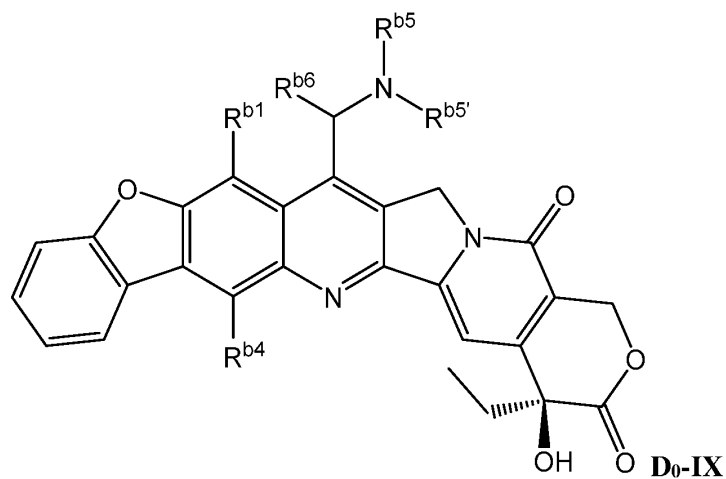
n is 1, 2 or 3;

$R^{b5''}$ is $-C_1-C_6$ hydroxyalkyl; and

R^{b1} , R^{b4} , and R^{b6} are each defined as for **D_{0a}**.

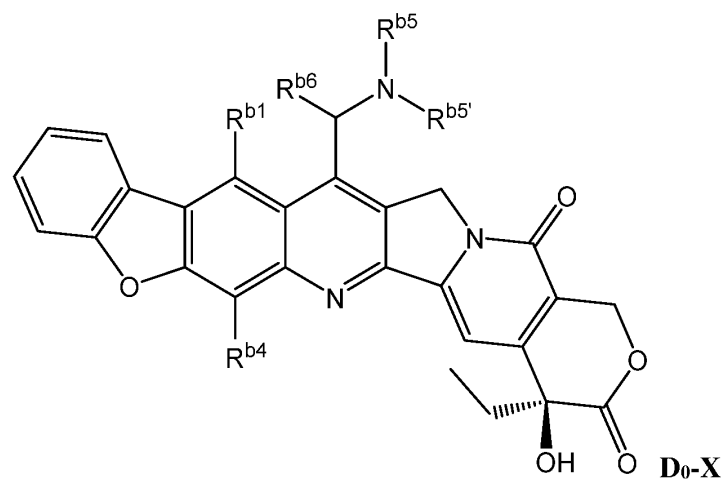
In some embodiments, n is 1, $R^{b5''}$ is $-CH_2OH$, and R^{b1} , R^{b4} , and R^{b6} are each H.

[0180] In some embodiments, D has the formula of **D₀-IX**



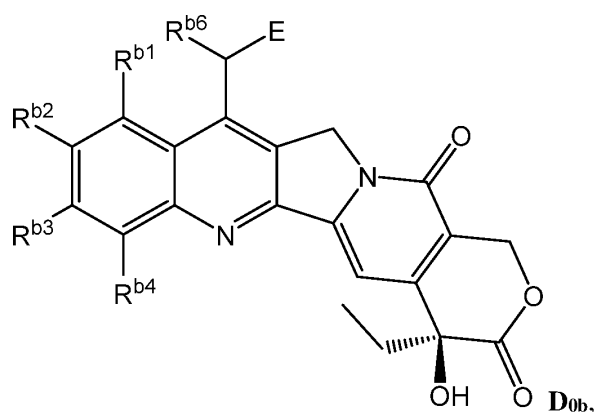
or a salt thereof; wherein R^{b1} , R^{b4} , R^{b5} , $R^{b5'}$, and R^{b6} are each defined as for **D_{0a}**. In some embodiments, R^{b1} , R^{b4} , R^{b5} , $R^{b5'}$, and R^{b6} are each H.

[0181] In some embodiments, D has the formula of **D_{0-X}**



or a salt thereof; wherein R^{b1} , R^{b4} , R^{b5} , $R^{b5'}$, and R^{b6} are each defined as for **D_{0a}**. In some embodiments, R^{b1} , R^{b4} , R^{b5} , $R^{b5'}$, and R^{b6} are each H.

[0182] In some embodiments, D₀ has a formula of **D_{0b}**



or a salt thereof; wherein;

E is $-\text{OR}^{\text{b5}}$ or $-\text{NR}^{\text{b5}}\text{R}^{\text{b5'}}$;

R^{b1} is selected from the group consisting of H, halogen, $-\text{CN}$, $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_1\text{-C}_8$ haloalkyl, $\text{C}_2\text{-C}_8$ alkenyl, $\text{C}_2\text{-C}_8$ alkynyl, $\text{C}_6\text{-C}_{12}$ aryl, 5- to 12-membered heteroaryl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, 3- to 10-membered heterocycloalkyl, $(\text{C}_6\text{-C}_{12} \text{ aryl})\text{-C}_2\text{-C}_8$ alkenyl-, $\text{C}_1\text{-C}_8$ hydroxyalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ aminoalkyl-, $\text{C}_1\text{-C}_8$ aminoalkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ alkyl-, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{C}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{O-C}(\text{O})\text{-NR}^{\text{a}}$ -, $\text{C}_6\text{-C}_{12}$ aryl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-O-}$, $-\text{COOR}^{\text{a}}$, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; each optionally substituted with $\text{C}_1\text{-C}_3$ alkyl, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, $-\text{C}(\text{O})\text{R}^{\text{a}}$, and $-\text{SR}^{\text{a}}$; or

R^{b1} is combined with R^{b2} , R^{b5} , or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_2\text{-C}_8$ alkynyl, $\text{C}_6\text{-C}_{12}$ aryl, 5- to 12-membered heteroaryl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, 3- to 10-membered heterocycloalkyl, $\text{C}_1\text{-C}_8$ haloalkyl, $\text{C}_1\text{-C}_8$ hydroxyalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{S}(\text{O})_2\text{-}$, $\text{C}_1\text{-C}_8$ aminoalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ aminoalkyl-, $\text{C}_1\text{-C}_8$ aminoalkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ alkyl-, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-NR}^{\text{a}}$ -, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{O-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-NR}^{\text{a}}$ -, $\text{C}_6\text{-C}_{12}$ aryl- $\text{C}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{O-C}(\text{O})\text{-NR}^{\text{a}}$ -, $\text{C}_6\text{-C}_{12}$ aryl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-O-}$, $-\text{COOR}^{\text{a}}$, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; each optionally substituted with $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b3} is selected from the group consisting of H, halogen, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_1\text{-C}_6$ haloalkyl, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$;

R^{b4} is selected from the group consisting of H or halogen;
 each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ aminoalkyl-, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl-, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, C₁-C₆ hydroxyalkyl-heteroaryl-, phenyl-, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl-, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl-, -OH-, -C₁-C₆ hydroxyalkyl-, -OC₁-C₄ alkyl-, -NH₂-, -NH-C₁-C₄ alkyl-, -N(C₁-C₄ alkyl)₂-, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl-; or

R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl-, -OH-, -OC₁-C₄ alkyl-, -NH₂-, -NHC₁-C₄ alkyl-, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and R^{a'} are each independently selected from the group consisting of H, C₁-C₆ alkyl-, C₁-C₆ haloalkyl-, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

wherein a) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane and E is -NR^{b5}R^{b5'}, then each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl-, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl-, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-

C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocycle or heterocycle; wherein the cycloalkyl, carbocycle, heterocycloalkyl, heterocycle, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

b) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, E is not -OH;

c) when R^{b2} is methyl and R^{b3} is F, then R^{b1} does not come together with R^{b6} and the intervening atoms to form a ring, and

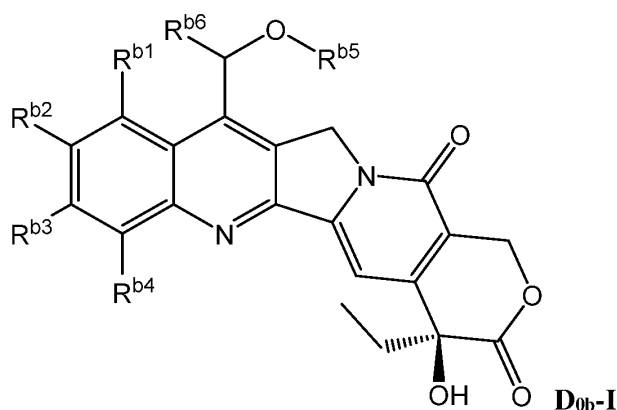
d) D is not selected from the group consisting of (*S*)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(7*H*)-dione, and (*S*)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(7*H*)-dione..

[0183] In some embodiments, E is -NR^{b5}R^{b5'}. In some embodiments, E is -OR^{b5}.

[0184] In some embodiments, when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane and E is -NR^{b5}R^{b5'}, then each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀

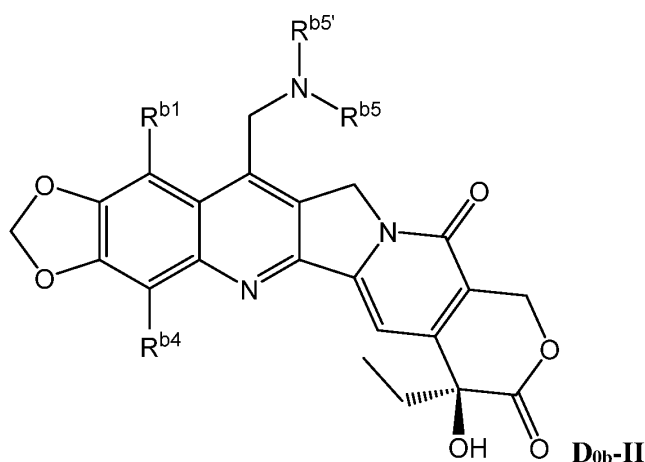
heterocycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heteroaryl having 0 to 3 substituents independently selected from the group consisting of halogen, C_1 - C_4 alkyl, -OH, - C_1 - C_6 hydroxyalkyl, - OC_1 - C_4 alkyl, - NH_2 , - NH - C_1 - C_4 alkyl, - $N(C_1$ - C_4 alkyl) $_2$, C_1 - C_6 alkoxy- $C(O)$ - NH -, C_1 - C_6 alkoxy- $C(O)$ - C_1 - C_8 aminoalkyl-, and C_1 - C_8 aminoalkyl.

[0185] In some embodiments, D has the formula of **D_{0b}-I**



or a salt thereof; R^{b1} - R^{b6} are each defined as for D_{0b} ; and wherein when R^{b2} is combined with R^{b3} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle, the heterocycle has no more than one O.

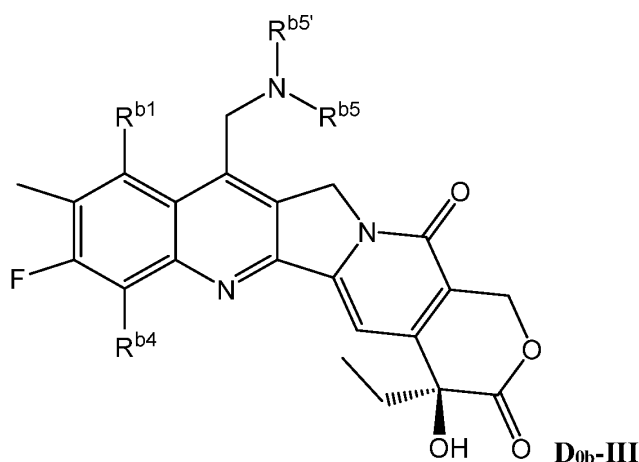
[0186] In some embodiments, D has the formula of **D_{0b}-II**



or a salt thereof; wherein;

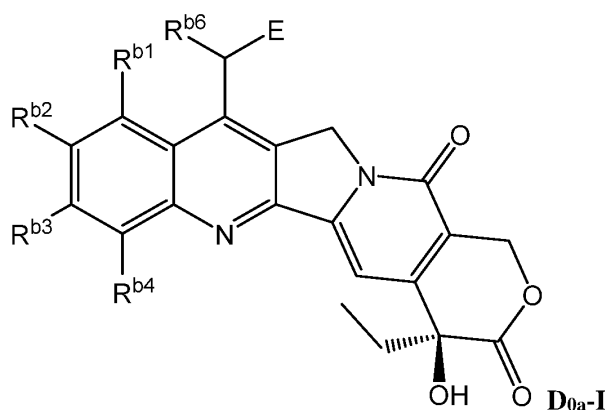
R^{b5} is H and $R^{b5'}$ is selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or $R^{b5'}$ is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂; and R^{b1} and R^{b4} are each defined as for D_{0b}, provided that

[0187] In some embodiments, D has the formula of **D_{0b}-III**



or a salt thereof; wherein R^{b1} , R^{b4} , R^{b5} , and $R^{b5'}$ are each defined as for **D_{0b}**.

[0188] In some embodiments, D has the formula of **D_{0a}-I**



or a salt thereof; wherein;

E is $-OR^{b5}$ or $-NR^{b5}R^{b5'}$;

R^{b1} is selected from the group consisting of H, halogen, $-CN$, C_1 - C_8 alkyl, C_1 - C_8 haloalkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, C_6 - C_{12} aryl, 5- to 12-membered heteroaryl, C_3 - C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, $(C_6$ - C_{12} aryl)- C_2 - C_8 alkenyl-, C_1 - C_8 hydroxyalkyl, C_1 - C_8 alkyl- $C(O)$ - C_1 - C_8 aminoalkyl-, C_1 - C_8 aminoalkyl- $C(O)$ - C_1 - C_8 alkyl-, C_1 - C_8 alkyl- NR^a - $C(O)$ -, C_1 - C_8 alkyl- $C(O)$ -, C_1 - C_8 alkyl- $OC(O)$ -, C_6 - C_{12} aryl- $C(O)$ -, C_6 - C_{12} aryl- $O-C(O)$ - NR^a -, C_6 - C_{12} aryl- NR^a - $C(O)$ - O -, $-COOR^a$, $-OR^a$, $-NR^aR^{a'}$, and $-SR^a$; each optionally substituted with C_1 - C_3 alkyl, $-OR^a$, $-NR^aR^{a'}$, $-C(O)R^a$, and $-SR^a$; or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; ,or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b3} is combined with R^{b2} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo or a 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b4} is selected from the group consisting of H and halogen;

each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-O-C₁-C₈ alkyl, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ hydroxyalkyl-C(O)-, , C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, heteroaryl-C₁-C₆ hydroxyalkyl, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄

hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and R^{a'} are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

wherein a) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, and E is -NR^{b5}R^{b5'}, then each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, phenyl-C(O)-, and phenyl-SO₂-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

b) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, E is not -OH;

c) when E is NH₂, R^{b1} is selected from the group consisting of -CN, 5- to 12-membered heteroaryl with at least one annular N, 3- to 10-membered heterocycloalkyl with at least one annular N, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with C₁-C₃ alkyl, -OR^a-, -NR^aR^{a'}-, -C(O)R^a-, and -SR^a-, or R^{b1} is combined with R^{b2} and the intervening atoms to form a 5-, 6-, or 7-membered heterocyclo with at least one annular N, or 5- or 6-membered heterocyclo fused with 6-membered aryl; R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with -OR^a-, -NR^aR^{a'}-, and -SR^a-, or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered heterocyclo with at least one annular N, or R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl; and

d) when R^{b2} is -OH or methyl and R^{b3} is F, then R^{b1} does not come together with R^{b5}, R^{b5'} or R^{b6} and the intervening atoms to form a ring; and

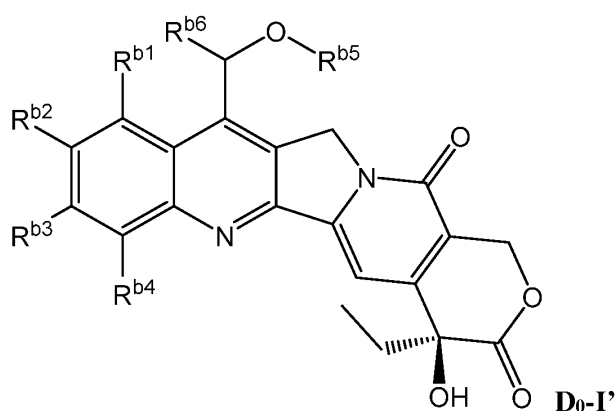
e) D is not selected from the group consisting of (S)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-14-((4-(2-aminoethyl)piperazin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-14-((4-aminopiperidin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, and *tert*-

butyl (*S*)-(1-((7-ethyl-7-hydroxy-8,11-dioxo-7,8,11,13-tetrahydro-10*H*-[1,3]dioxolo[4,5-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-14-yl)methyl)piperidin-4-yl)carbamate.

wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

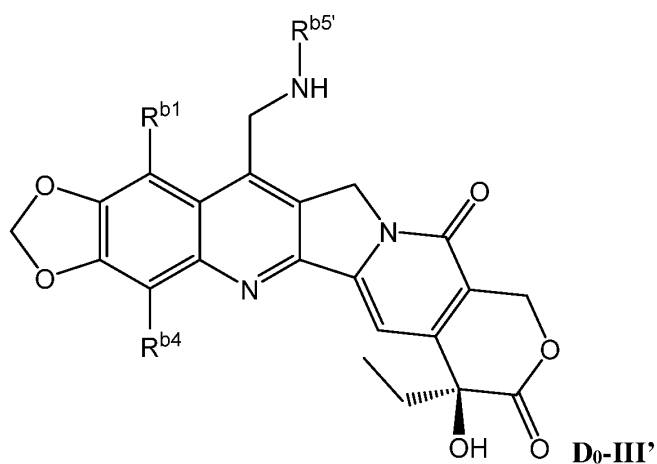
[0189] In some embodiments, E is $-NR^{b5}R^{b5'}$. In some embodiments, E is $-OR^{b5}$.

[0190] In some embodiments, D has the formula of **D₀-I'**



or a salt thereof; R^{b1} - R^{b6} are each defined as for **D_{0a}-I**; and wherein when R^{b2} is combined with R^{b3} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle, the heterocycle has no more than one O.

[0191] In some embodiments, D has the formula of **D₀-III'**

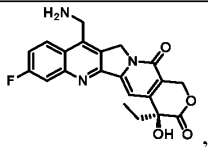
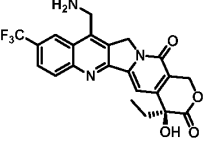
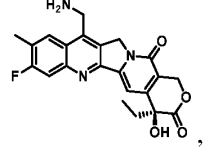
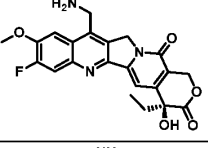
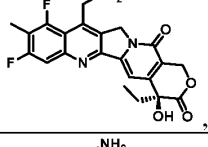
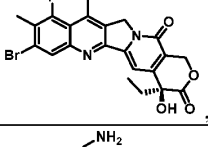
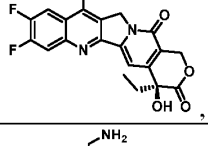
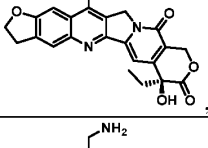
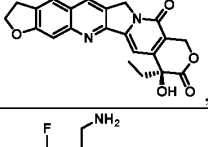
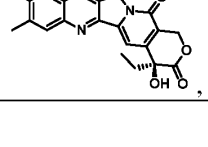


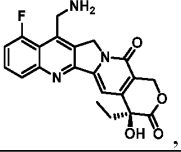
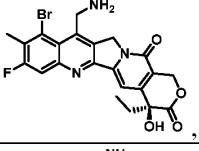
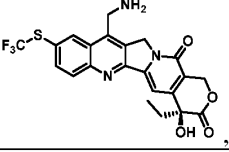
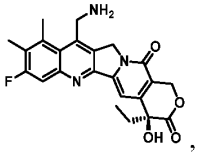
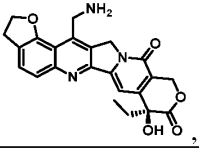
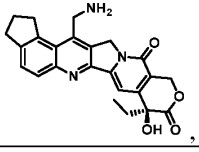
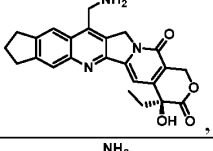
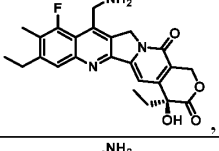
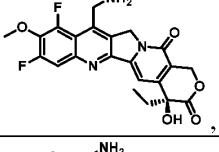
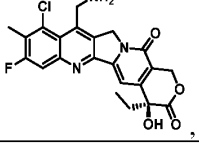
or a salt thereof; wherein each R^{b1} - R^{b4} , $R^{b5'}$ and R^{b6} are each defined as **D_{0a}-I**.

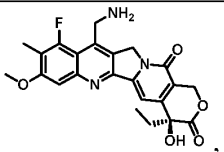
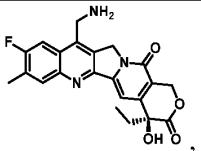
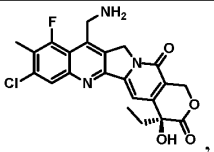
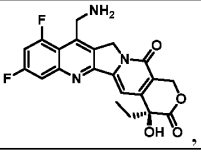
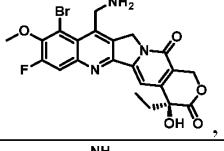
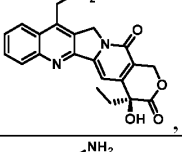
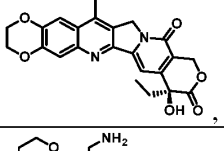
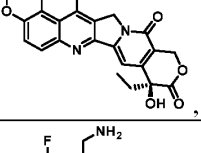
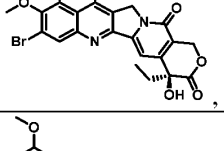
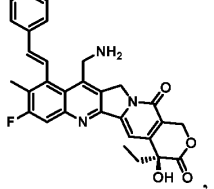
[0192] In some embodiments, D is a compound of Table I or a salt thereof selected from the group consisting of:

Table I

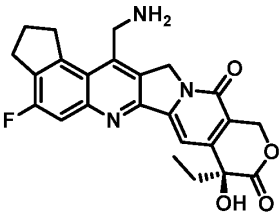
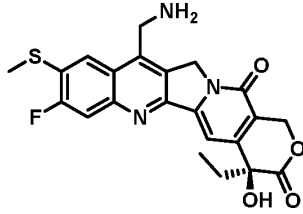
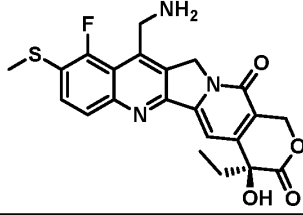
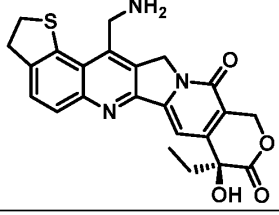
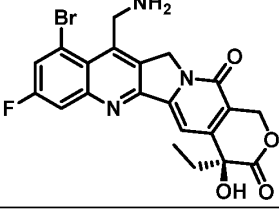
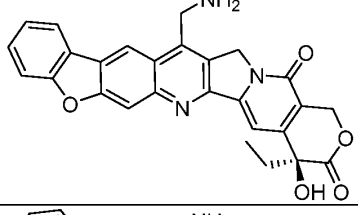
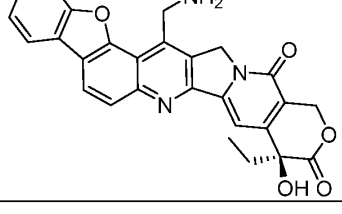
Compound No.	STRUCTURE
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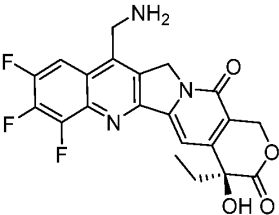
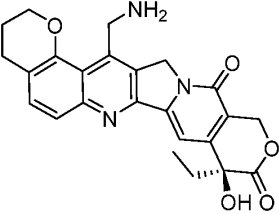
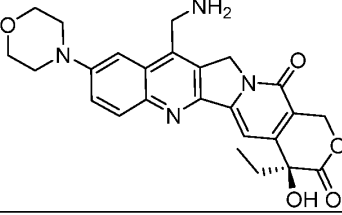
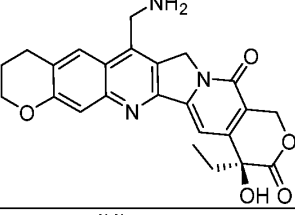
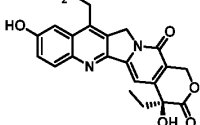
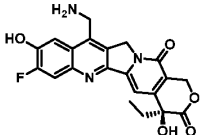
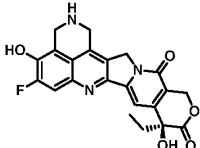
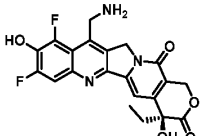
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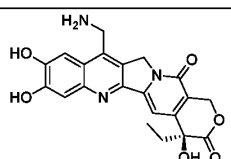
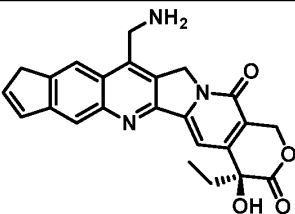
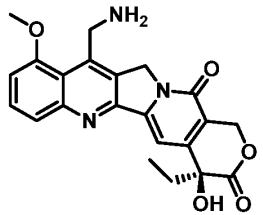
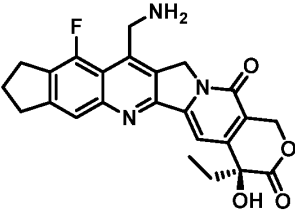
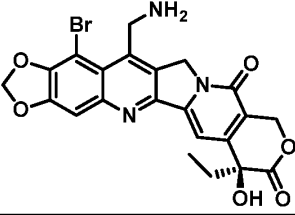
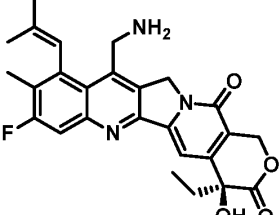
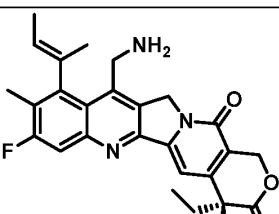
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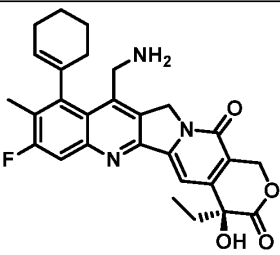
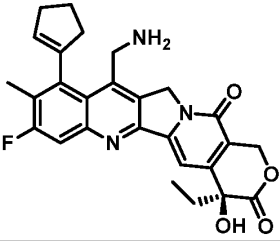
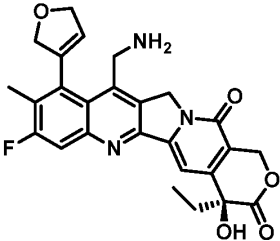
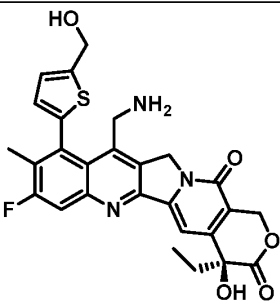
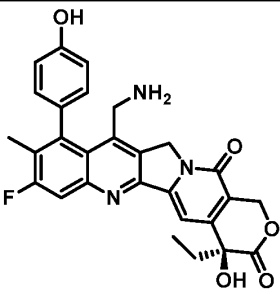
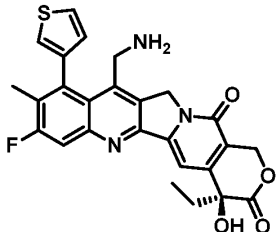
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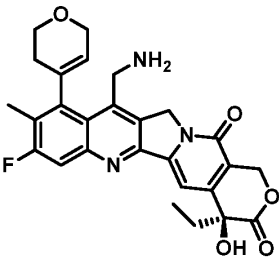
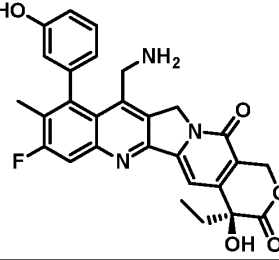
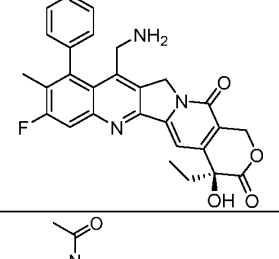
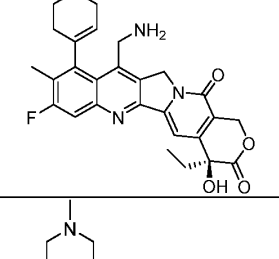
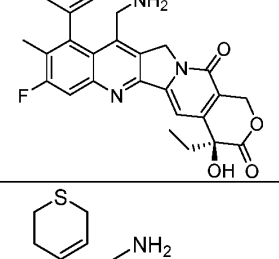
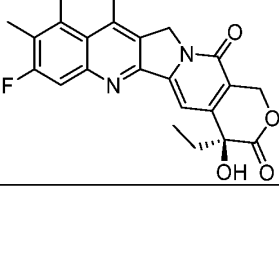
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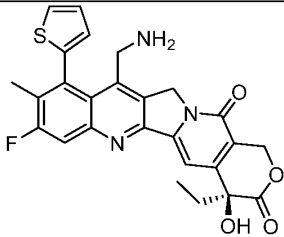
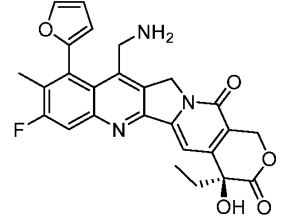
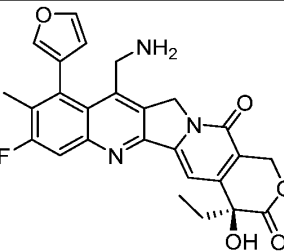
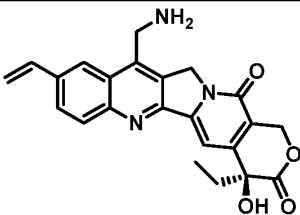
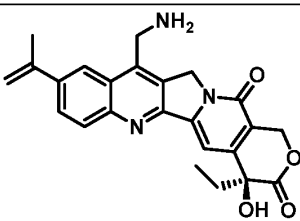
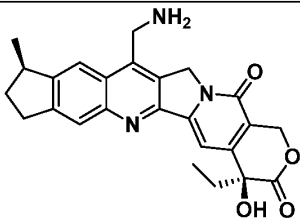
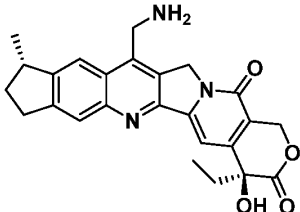
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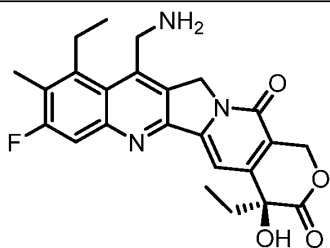
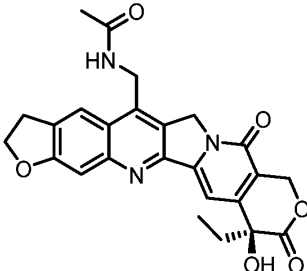
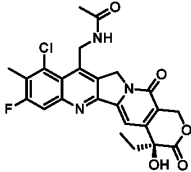
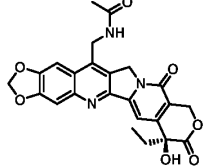
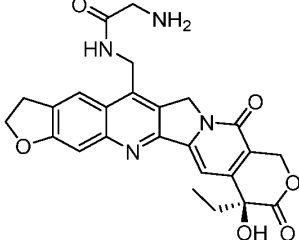
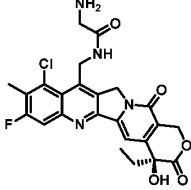
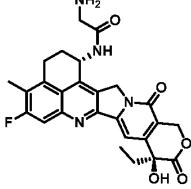
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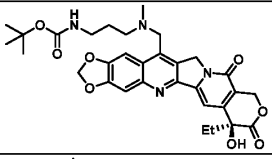
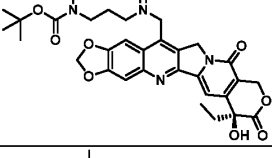
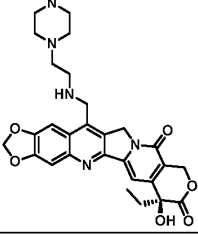
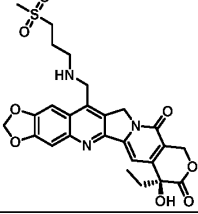
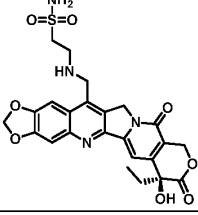
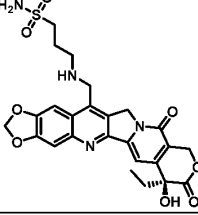
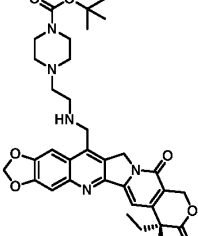
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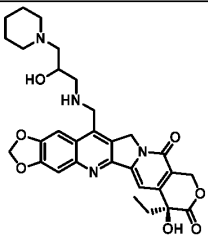
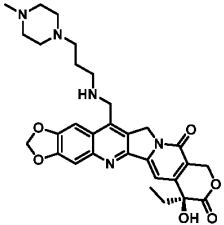
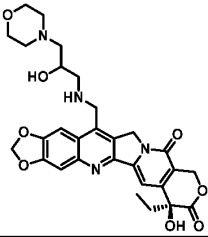
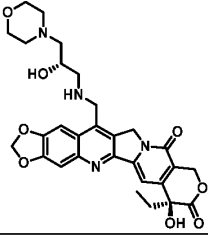
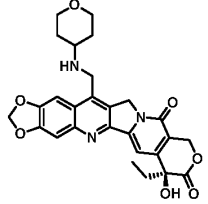
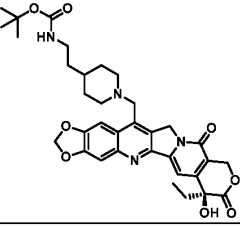
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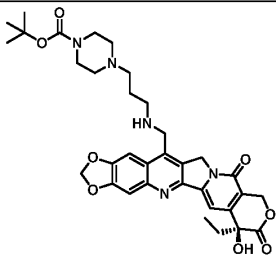
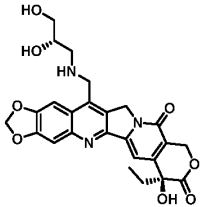
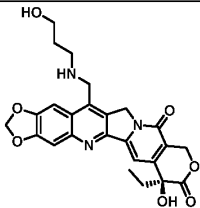
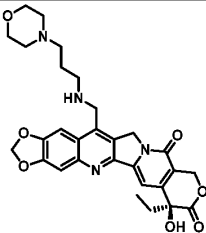
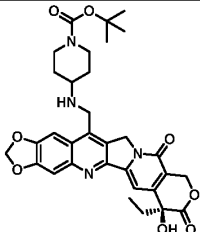
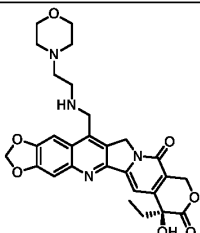
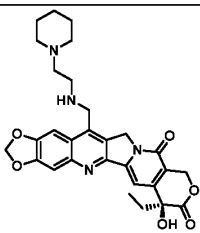
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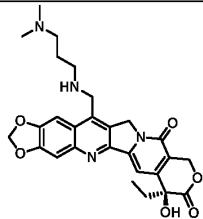
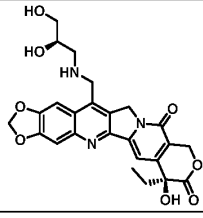
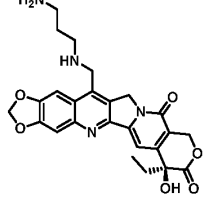
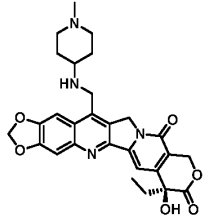
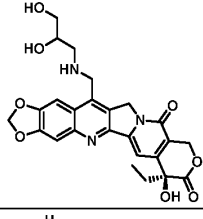
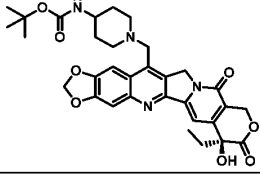
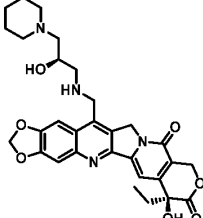
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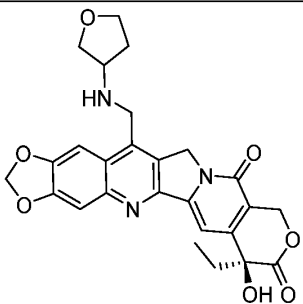
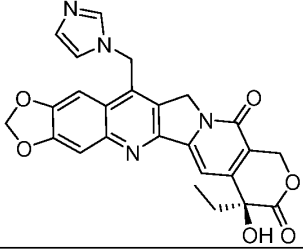
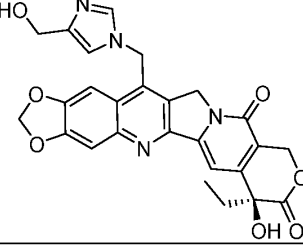
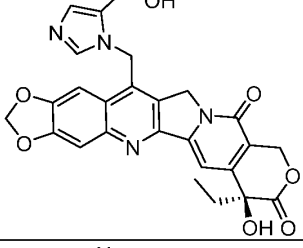
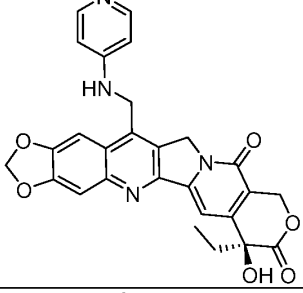
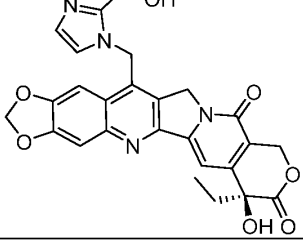
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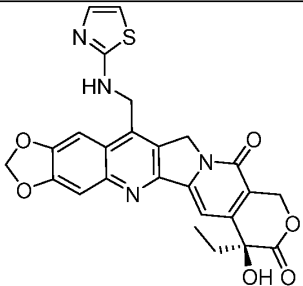
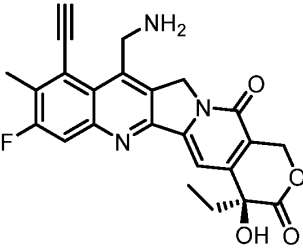
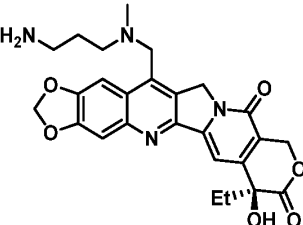
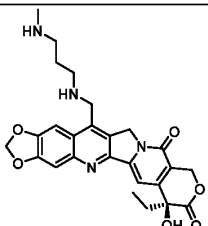
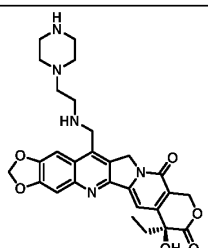
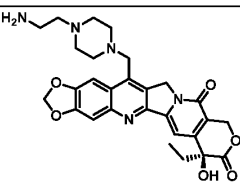
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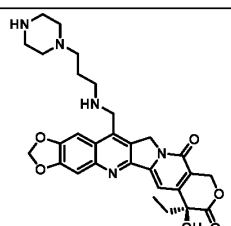
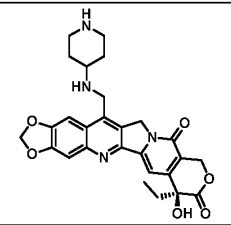
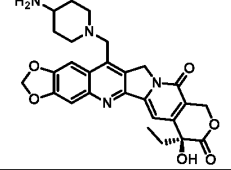
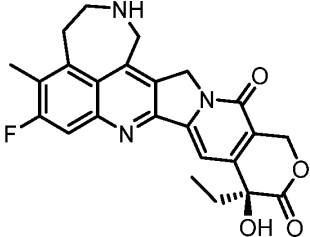
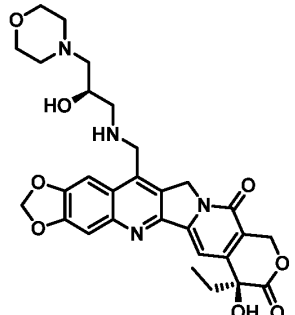
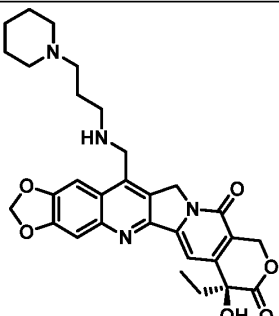
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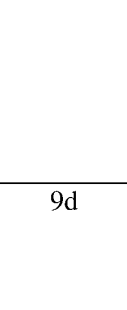
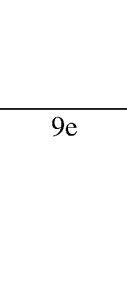
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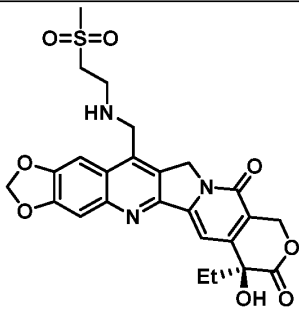
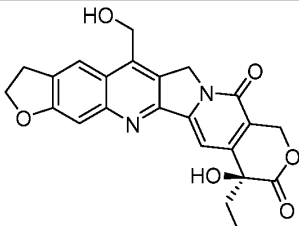
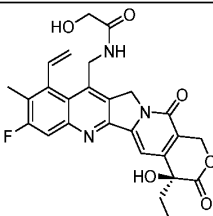
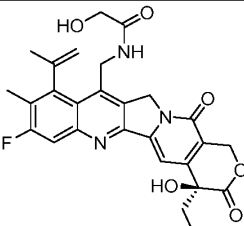
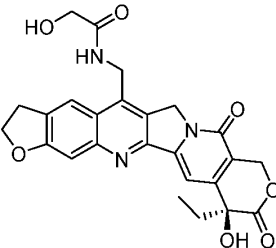
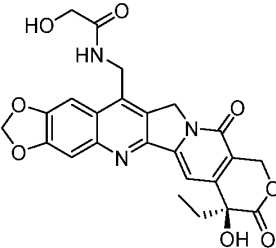
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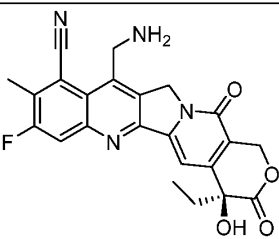
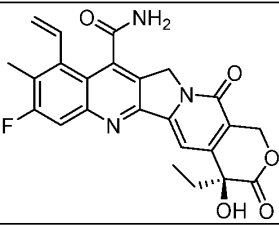
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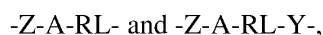
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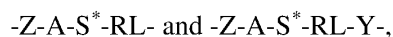
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[0193] In one group of embodiments, Q has a formula selected from the group consisting of:



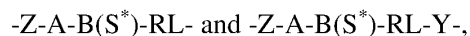
wherein RL is a Releasable Linker that is a Glycoside (e.g., Glucuronide) Unit and the groups Z, A and Y have the meanings provided above and in any one of the embodiments specifically recited herein.

[0194] In one group of embodiments, Q has a formula selected from the group consisting of:



wherein RL is a Releasable Linker that is a Glycoside (e.g., Glucuronide) Unit and the groups Z, A, S* and Y have the meanings provided above and in any one of the embodiments specifically recited herein.

[0195] In one group of embodiments, Q has a formula selected from the group consisting of:



wherein RL is a Releasable Linker that is a Glycoside (e.g., Glucuronide) Unit and the groups Z, A, S*, B and Y have the meanings provided above and in any one of the embodiments specifically recited herein.

[0196] In another group of embodiments, Q has a formula selected from the group consisting of:

-Z-A- or -Z-A-RL- ,

wherein RL is a Releasable Linker that is other than a Glycoside (e.g., Glucuronide) Unit and the groups Z and A have the meanings provided above and in any one of the embodiments specifically recited herein.

[0197] In another group of embodiments, Q has a formula selected from the group consisting of:

-Z-A-S^{*}-RL- and -Z-A-B(S^{*})-RL-,

wherein RL is a Releasable Linker that is other than a Glycoside (e.g., Glucuronide) Unit and the groups Z, A, S^{*} and B have the meanings provided above and in any one of the embodiments specifically recited herein.

[0198] In another group of embodiments, Q has a formula selected from the group consisting of:

-Z-A-S^{*}-W- and -Z-A-B(S^{*})-W-,

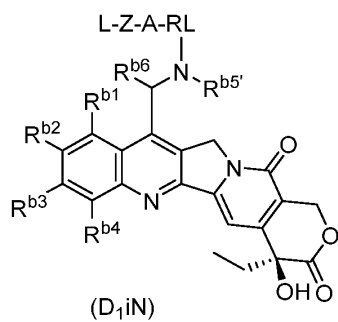
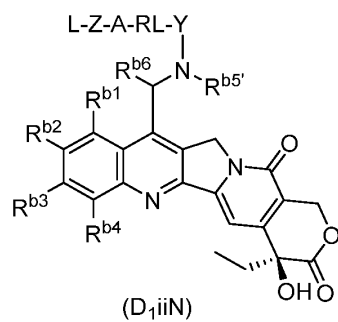
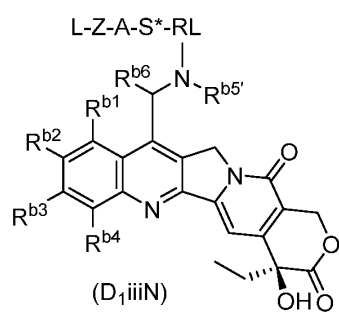
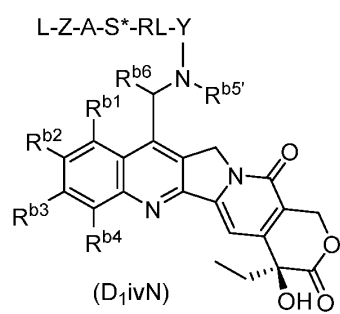
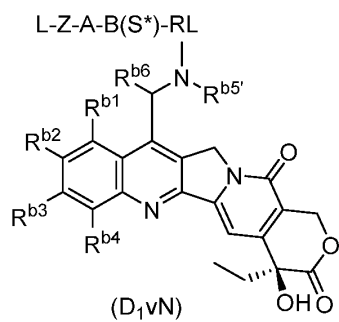
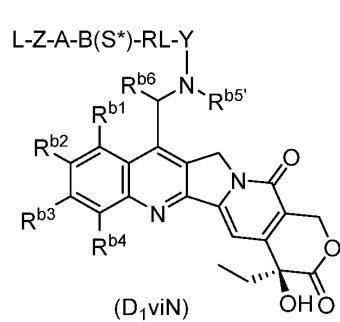
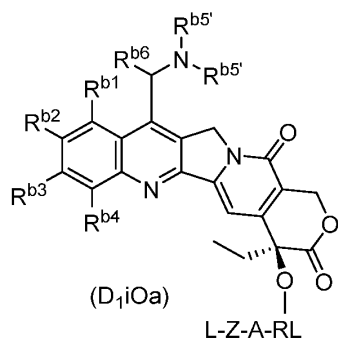
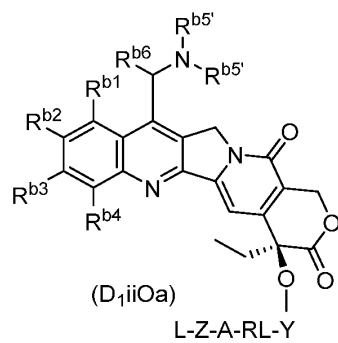
wherein the groups Z, A, S^{*}, B and W have the meanings provided above and in any one of the embodiments specifically recited herein.

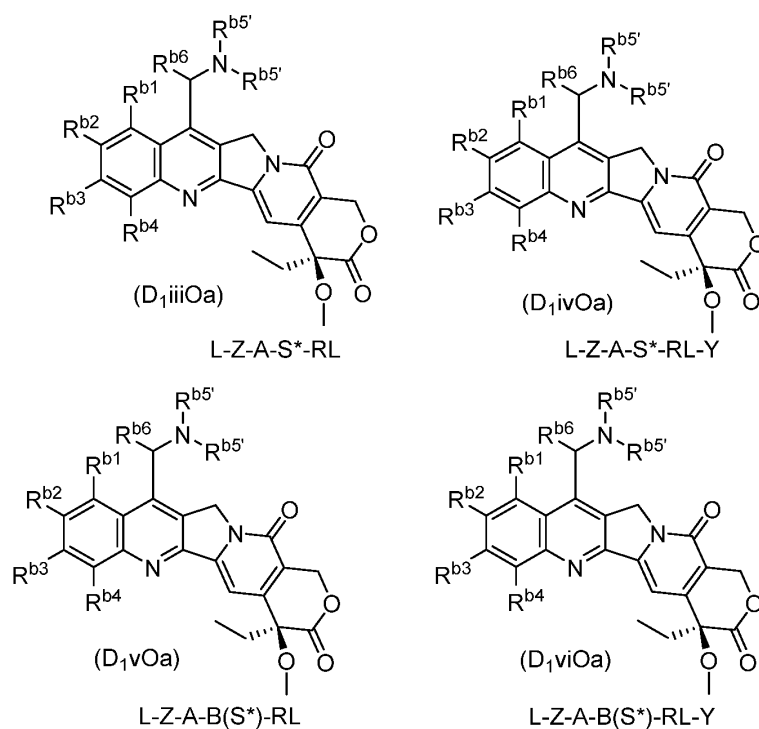
[0199] In another group of embodiments, Q has a formula selected from the group consisting of:

-Z-A-S^{*}-W-RL- and -Z-A-B(S^{*})-W-RL-,

wherein RL is a Releasable Linker that is other than a Glycoside (e.g., Glucuronide) Unit and the groups Z, A, S^{*}, B and W have the meanings provided above and in any one of the embodiments specifically recited herein.

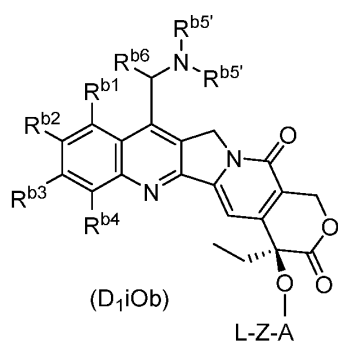
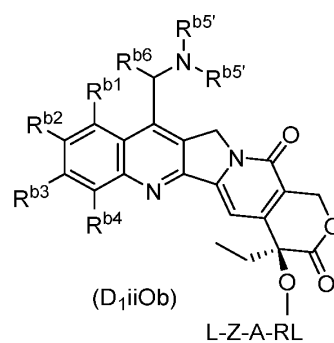
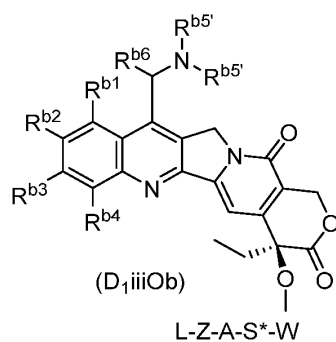
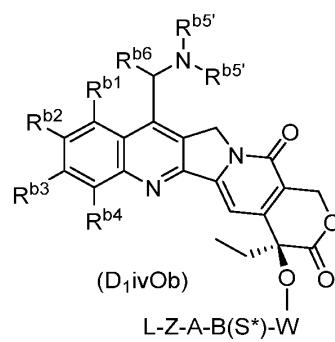
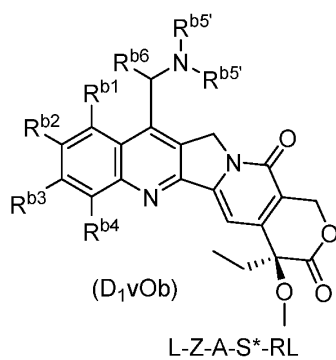
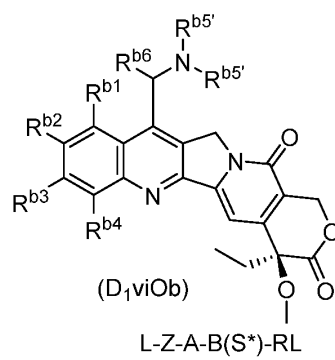
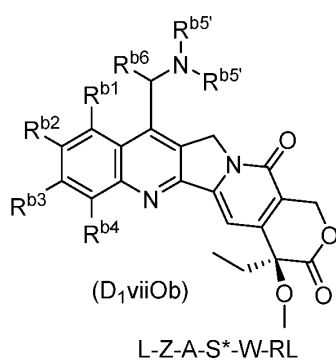
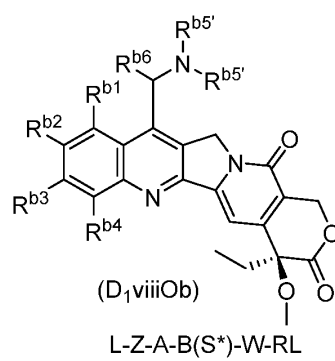
[0200] In one group of embodiments, the Camptothecin Conjugates in which Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S^{*}-RL-, -Z-A-S^{*}-RL-Y-, -Z-A-B(S^{*})-RL- or -Z-A-B(S^{*})-RL-Y- and are comprised of a Drug Unit having formula **D₁** are represented by formulae of:





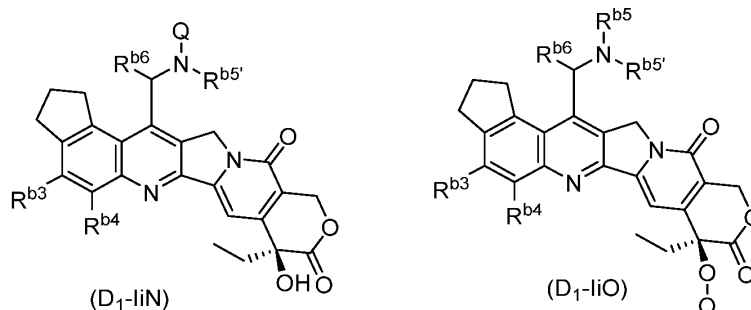
respectively, wherein RL is any one of the Releasable Linkers disclosed herein, preferably RL is a Glycoside (e.g., Glucuronide) Unit, and the groups L, Z, A, S*, B and Y have the meanings provided above and in any one of the embodiments specifically recited herein. Also provided herein are Camptothecin Conjugates corresponding to any of formulas D_{1i}N, D_{1ii}N, D_{1iii}N, D_{1iv}N, D_{1v}N, or D_{1vi}N wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0201] In other embodiments the Camptothecin Conjugates in which Q has the formula of -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL- and -Z-A-B(S*)-W-RL- and are comprised of a Drug Unit having formula D₁ are represented by formulae of:



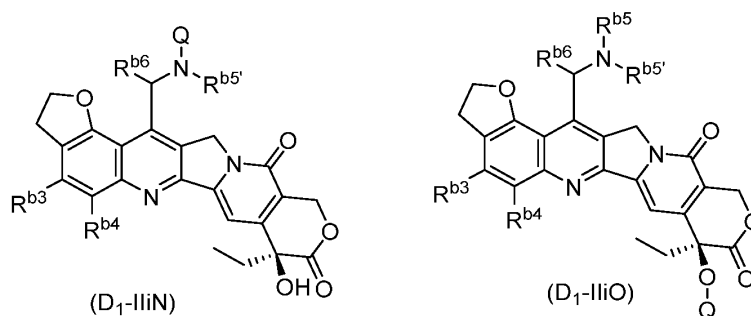
respectively, wherein RL is a Releasable Linker that is other than a Glycoside (e.g., Glucuronide) Unit and the groups L, Z, A, S*, B and W have the meanings provided above and in any one of the embodiments specifically recited herein.

[0202] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-I are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D₁**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁IiN wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

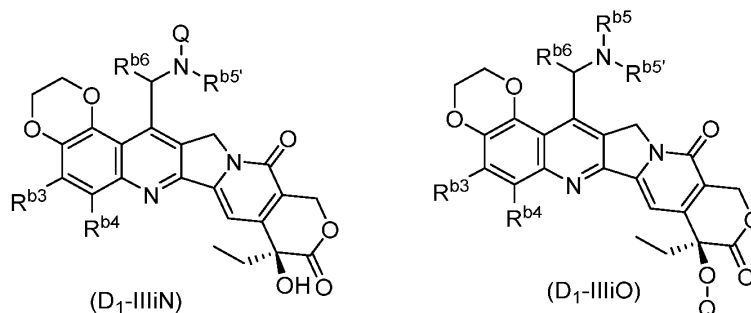
[0203] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-II are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D₁**, **D1-IIa**, **D1-IIb**,

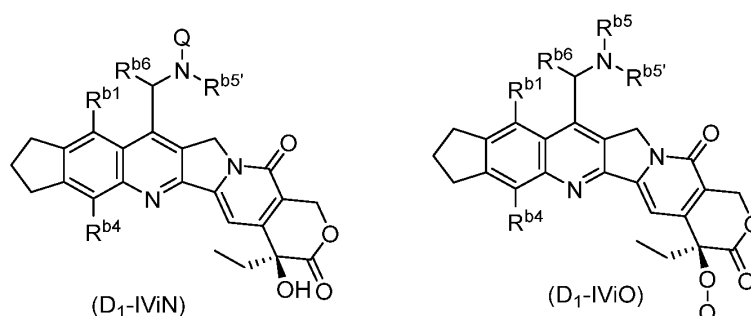
D1-IVa, D1-IVb, D1-Xa, D1-XI, D1-XII, D1-XIII, D1-XIV, D1-XV, and D1-XVI. Also provided herein are Camptothecin Conjugates corresponding to formula D₁₁IIIN wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0204] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-III are represented by the formulae of:



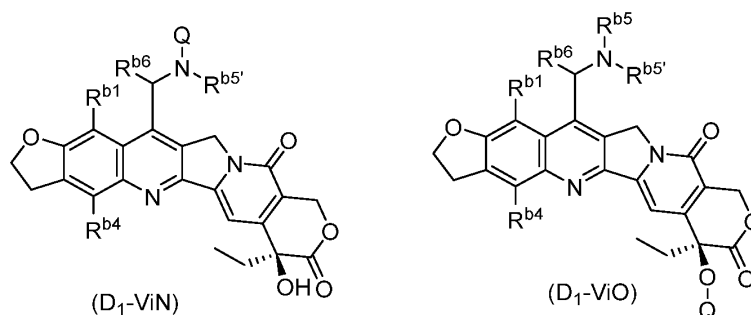
respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1, D1-IIa, D1-IIb, D1-IVa, D1-IVb, D1-Xa, D1-XI, D1-XII, D1-XIII, D1-XIV, D1-XV, and D1-XVI.** Also provided herein are Camptothecin Conjugates corresponding to formula D₁IIIiN wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0205] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-IV are represented by the formulae of:



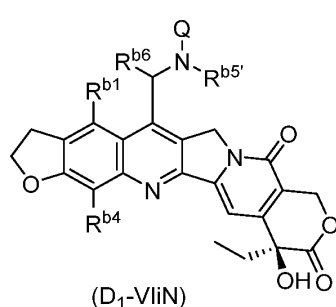
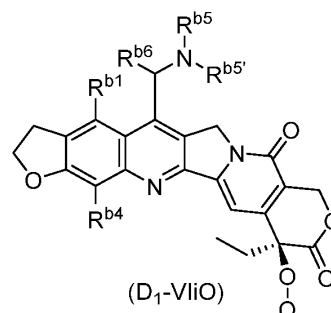
respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁IViN wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0206] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-V are represented by the formulae of:



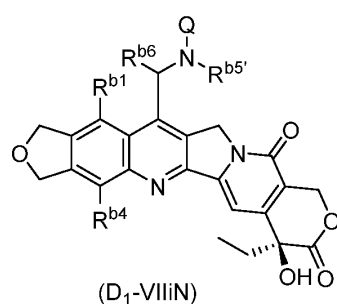
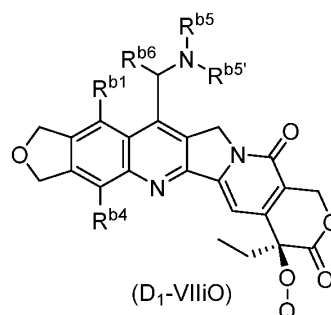
respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁ViN wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0207] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-VI are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D₁**, **D₁-IIa**, **D₁-IIb**, **D₁-IVa**, **D₁-IVb**, **D₁-Xa**, **D₁-XI**, **D₁-XII**, **D₁-XIII**, **D₁-XIV**, **D₁-XV**, and **D₁-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁VIIiN wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

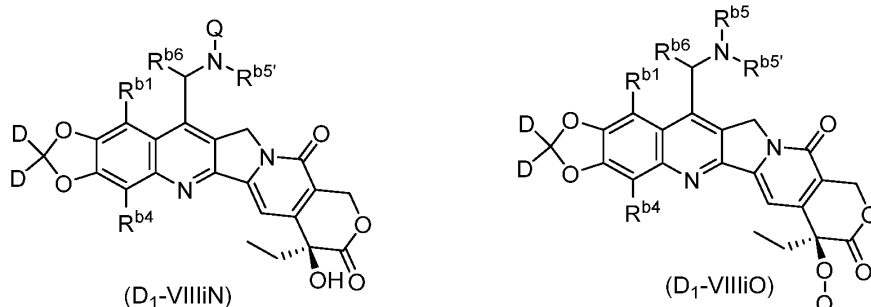
[0208] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D₁-VII are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D₁**, **D₁-IIa**, **D₁-IIb**, **D₁-IVa**, **D₁-IVb**, **D₁-Xa**, **D₁-XI**, **D₁-XII**, **D₁-XIII**, **D₁-XIV**, **D₁-XV**, and **D₁-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁VIIIiN wherein the

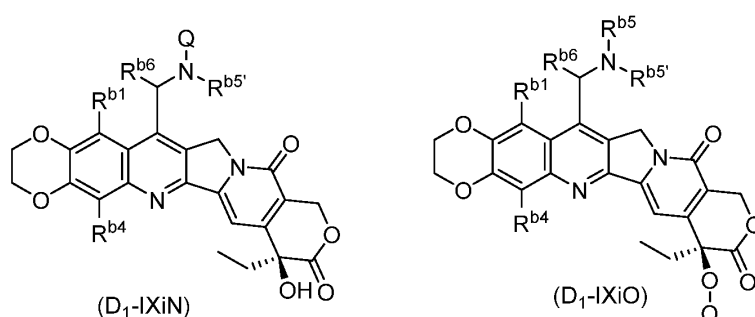
nitrogen atom to which $R^{b5'}$ is bound is replaced by an oxygen atom and $R^{b5'}$ is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0209] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-VIII are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D1-VIIIiN wherein the nitrogen atom to which $R^{b5'}$ is bound is replaced by an oxygen atom and $R^{b5'}$ is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

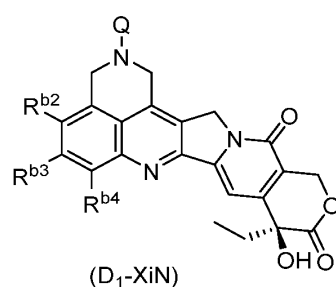
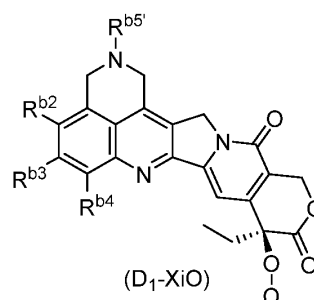
[0210] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-IX are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**.

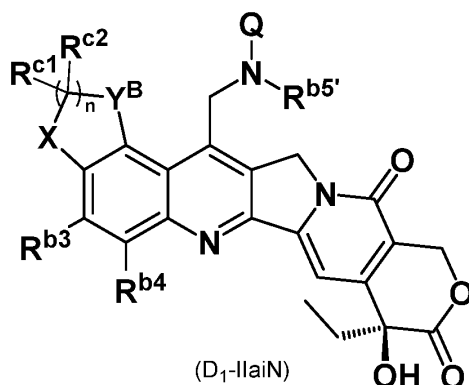
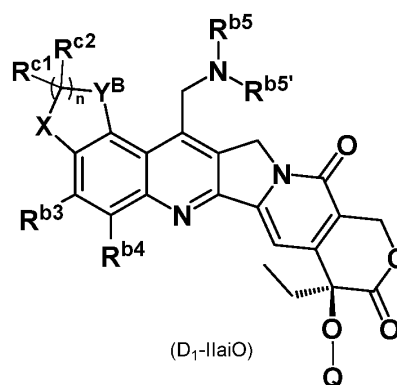
Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁IXiN wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0211] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-X are represented by the formulae of:



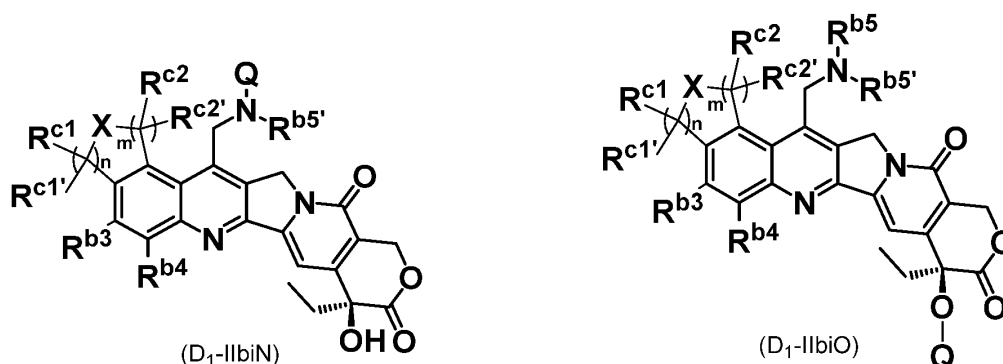
respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**.

[0212] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-IIa are represented by the formulae of:



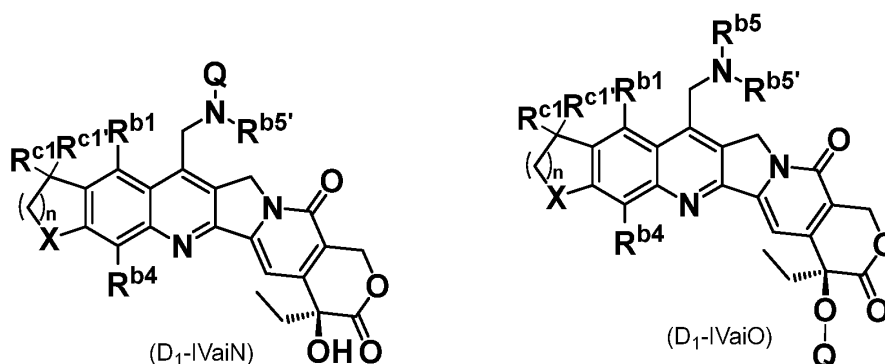
respectively, wherein Q has the formula of $-Z-A-RL-$, $-Z-A-RL-Y-$, $-Z-A-S^*-RL-$, $-Z-A-S^*-RL-Y-$, $-Z-A-B(S^*)-RL-$, $-Z-A-B(S^*)-RL-Y-$, $-Z-A-$, $-Z-A-RL-$, $-Z-A-S^*-W-$, $-Z-A-B(S^*)-W-$, $-Z-A-S^*-RL-$, $-Z-A-B(S^*)-RL-$, $-Z-A-S^*-W-RL-$, or $-Z-A-B(S^*)-W-RL-$; the groups L, Z, A, S^* , B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁-IIaiN wherein the nitrogen atom to which $R^{b5'}$ is bound is replaced by an oxygen atom and $R^{b5'}$ is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0213] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-IIb are represented by the formulae of:



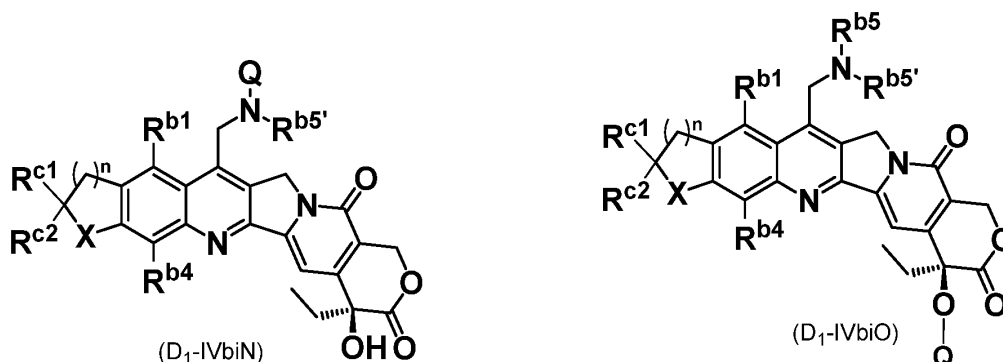
respectively, wherein Q has the formula of $-Z-A-RL-$, $-Z-A-RL-Y-$, $-Z-A-S^*-RL-$, $-Z-A-S^*-RL-Y-$, $-Z-A-B(S^*)-RL-$, $-Z-A-B(S^*)-RL-Y-$, $-Z-A-$, $-Z-A-RL-$, $-Z-A-S^*-W-$, $-Z-A-B(S^*)-W-$, $-Z-A-S^*-RL-$, $-Z-A-B(S^*)-RL-$, $-Z-A-S^*-W-RL-$, or $-Z-A-B(S^*)-W-RL-$; the groups L, Z, A, S^* , B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁-IIbiN wherein the nitrogen atom to which $R^{b5'}$ is bound is replaced by an oxygen atom and $R^{b5'}$ is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0214] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-IVa are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D1-IVaiN wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

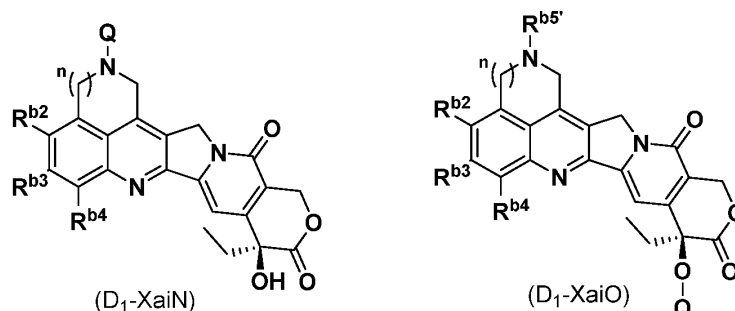
[0215] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-IVb are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**,

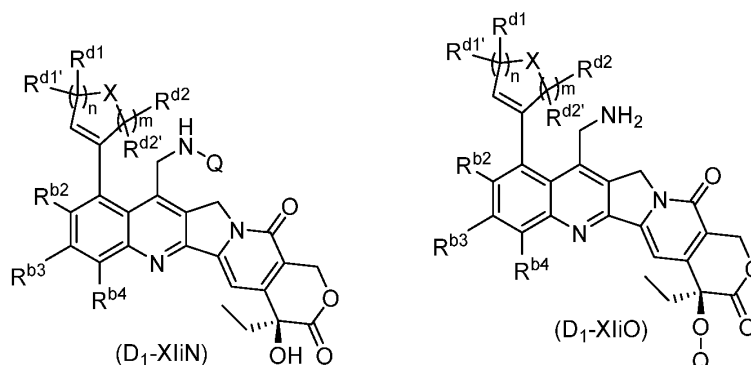
D1-IVa, D1-IVb, D1-Xa, D1-XI, D1-XII, D1-XIII, D1-XIV, D1-XV, and D1-XVI. Also provided herein are Camptothecin Conjugates corresponding to formula D1-IVbIN wherein the nitrogen atom to which R^{b5'} is bound is replaced by an oxygen atom and R^{b5'} is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0216] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-Xa are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1, D1-IIa, D1-IIb, D1-IVa, D1-IVb, D1-Xa, D1-XI, D1-XII, D1-XIII, D1-XIV, D1-XV, and D1-XVI.**

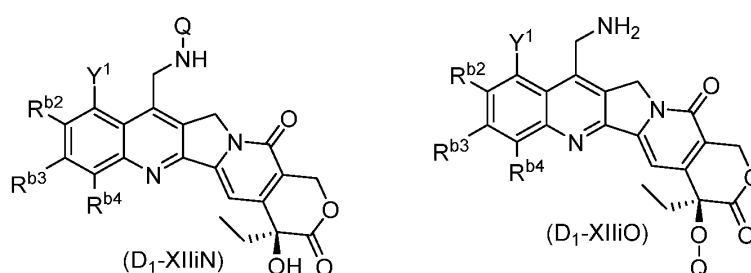
[0217] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-XI are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1, D1-IIa, D1-IIb, D1-IVa, D1-IVb, D1-Xa, D1-XI, D1-XII, D1-XIII, D1-XIV, D1-XV, and D1-XVI.**

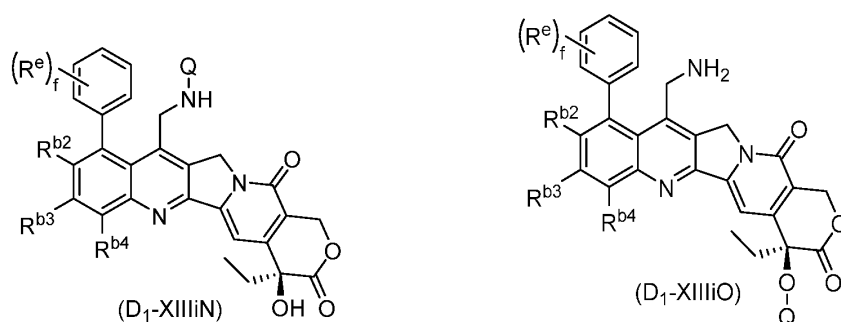
Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁-XIIiN wherein the nitrogen atom to which Q is bound is replaced by an oxygen atom and the hydrogen substituting the aforementioned nitrogen atom is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0218] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D₁-XII are represented by the formulae of:



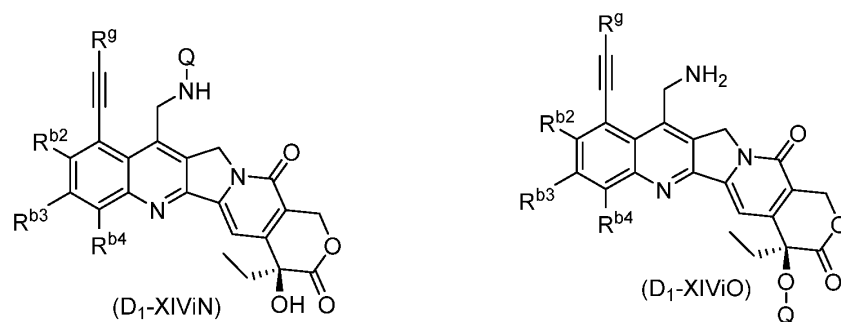
respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁-XIIiN wherein the nitrogen atom to which Q is bound is replaced by an oxygen atom and the hydrogen substituting the aforementioned nitrogen atom is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0219] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D₁-XIII are represented by the formulae of:



respectively, wherein Q has the formula of $-Z-A-RL-$, $-Z-A-RL-Y-$, $-Z-A-S^*-RL-$, $-Z-A-S^*-RL-Y-$, $-Z-A-B(S^*)-RL-$, $-Z-A-B(S^*)-RL-Y-$, $-Z-A-$, $-Z-A-RL-$, $-Z-A-S^*-W-$, $-Z-A-B(S^*)-W-$, $-Z-A-S^*-RL-$, $-Z-A-B(S^*)-RL-$, $-Z-A-S^*-W-RL-$, or $-Z-A-B(S^*)-W-RL-$; the groups L, Z, A, S^* , B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula $D_1-XIIIiN$ wherein the nitrogen atom to which Q is bound is replaced by an oxygen atom and the hydrogen substituting the aforementioned nitrogen atom is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

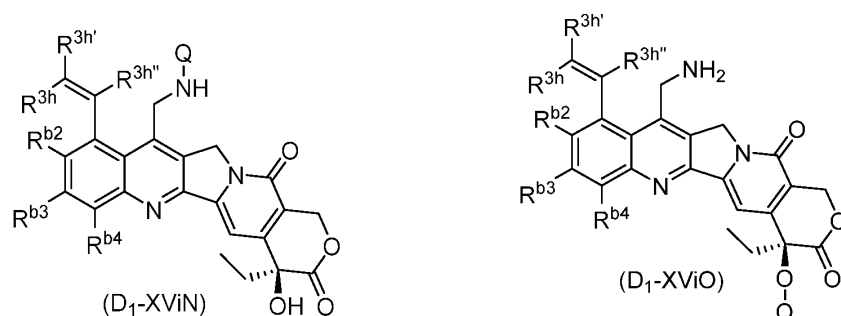
[0220] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D_1-XIV are represented by the formulae of:



respectively, wherein Q has the formula of $-Z-A-RL-$, $-Z-A-RL-Y-$, $-Z-A-S^*-RL-$, $-Z-A-S^*-RL-Y-$, $-Z-A-B(S^*)-RL-$, $-Z-A-B(S^*)-RL-Y-$, $-Z-A-$, $-Z-A-RL-$, $-Z-A-S^*-W-$, $-Z-A-B(S^*)-W-$, $-Z-A-S^*-RL-$, $-Z-A-B(S^*)-RL-$, $-Z-A-S^*-W-RL-$, or $-Z-A-B(S^*)-W-RL-$; the groups L, Z, A, S^* , B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula $D_1-XIViN$ wherein

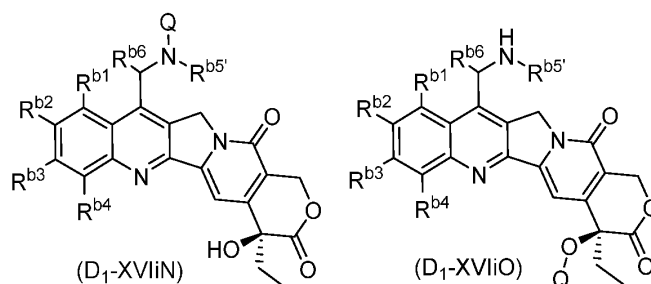
the nitrogen atom to which Q is bound is replaced by an oxygen atom and the hydrogen substituting the aforementioned nitrogen atom is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0221] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-XV are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D₁**, **D₁-IIa**, **D₁-IIb**, **D₁-IVa**, **D₁-IVb**, **D₁-Xa**, **D₁-XI**, **D₁-XII**, **D₁-XIII**, **D₁-XIV**, **D₁-XV**, and **D₁-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁-XViN wherein the nitrogen atom to which Q is bound is replaced by an oxygen atom and the hydrogen substituting the aforementioned nitrogen atom is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

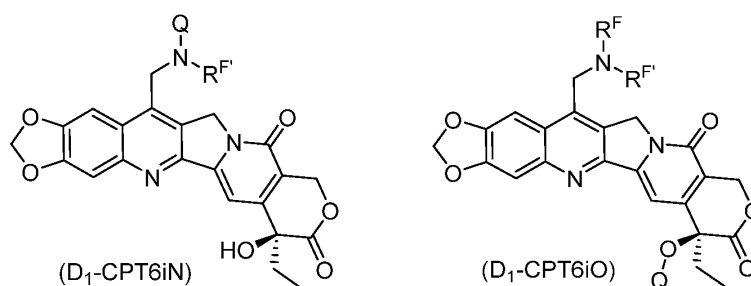
[0222] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D1-XVI are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-

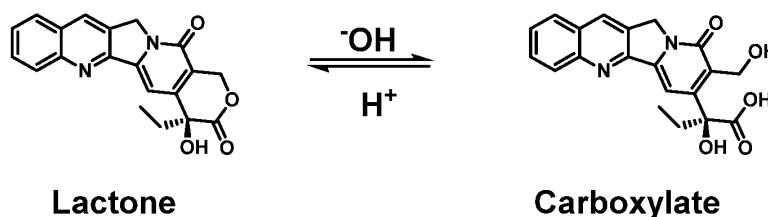
W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, and **D1-XVI**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁-XVIIiN wherein the nitrogen atom to which Q is bound is replaced by an oxygen atom and the hydrogen substituting the aforementioned nitrogen atom is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0223] In another group of embodiments, the Camptothecin Conjugates comprised of a Drug Unit having formula D₁-CPT6 are represented by the formulae of:



respectively, wherein Q has the formula of -Z-A-RL-, -Z-A-RL-Y-, -Z-A-S*-RL-, -Z-A-S*-RL-Y-, -Z-A-B(S*)-RL-, -Z-A-B(S*)-RL-Y-, -Z-A-, -Z-A-RL-, -Z-A-S*-W-, -Z-A-B(S*)-W-, -Z-A-S*-RL-, -Z-A-B(S*)-RL-, -Z-A-S*-W-RL-, or -Z-A-B(S*)-W-RL-; the groups L, Z, A, S*, B, RL, and Y have the meanings provided above and in any one of the embodiments specifically recited herein; and the remaining variables are as defined for **D1**, **D1-IIa**, **D1-IIb**, **D1-IVa**, **D1-IVb**, **D1-Xa**, **D1-XI**, **D1-XII**, **D1-XIII**, **D1-XIV**, **D1-XV**, **D1-XVI**, and **D1-CPT6**. Also provided herein are Camptothecin Conjugates corresponding to formula D₁-CPT6iN wherein the nitrogen atom to which Q is bound is replaced by an oxygen atom and the hydrogen substituting the aforementioned nitrogen atom is absent, such that Q is attached to the Drug Unit via an oxygen atom of the Drug Unit.

[0224] Camptothecin molecules are known to undergo a pH dependent, reversible hydrolysis between a ring closed lactone form and a ring open carboxylate.



Without being bound by theory, it is believed that at acidic pH, the lactone form is favored while at physiologic pH the predominant form is the ring opened carboxylate. In biological systems camptothecin free drugs or drug-linkers, or conjugates thereof, may exist in either the lactone or carboxylate forms. Camptothecin-based antibody drug conjugates (ADC) have demonstrated activity to target cells regardless of the state of the lactone of the bound drug. Without being bound by theory, this effect is believed to be due to ADC processing in acidic intracellular vesicles, which favor equilibrium to the active closed-lactone form of camptothecin (Lau, U. Y. et al. *Mol. Pharmaceutics* 2018, 15, 9, 4063–4072).

[0225] It is to be understood that the Drug Units herein, as well as Drug-Linkers and conjugates thereof, can undergo equilibrium between the lactone and carboxylate forms. As such, for any of the lactone structures described herein, the carboxylate form is also to be understood to be within the scope of the present disclosure. All carboxylate forms of camptothecin structures depicted in the lactone form, including genericized formulae, are understood to be included herein in the same context as the lactone forms, as though each lactone structure was specifically and individually included in the carboxylate form.

Camptothecin-Linker Compounds

[0226] In some embodiments, when preparing the Camptothecin Conjugates, it will be desirable to synthesize the full drug-linker combination prior to conjugation to a targeting agent. In such embodiments, Camptothecin-Linker Compounds as described herein, are intermediate compounds. In those embodiments, the Stretcher Unit in a Camptothecin-Linker compound is not yet covalently attached to the Ligand Unit (i.e., is a Stretcher Unit precursor, Z'), and therefore has a functional group for conjugation to a targeting ligand. In one embodiment, a Camptothecin-Linker compound is comprised of a Camptothecin compound (shown herein as formulae **D1**, **D1a**, **D1b**, or any subformula thereof), and a Linker Unit (Q) comprising a Glycoside (e.g., Glucuronide) Unit as a Releasable Linker (RL) through which the Ligand Unit is connected to the Camptothecin.

[0227] In another embodiment, a Camptothecin-Linker Compound comprises a Camptothecin compound of formulae **D1**, **D1a**, **D1b**, or any subformula thereof, and a Linker

Unit (Q) comprising a Releasable Linker (RL) that is other than a Glycoside (e.g., Glucuronide) Unit through which the Ligand Unit is connected to the conjugated Camptothecin compound. Thus, in either embodiment the Linker Unit comprises, in addition to RL, a Stretcher Unit precursor (Z') comprising a functional group for conjugation to a targeting agent that is the precursor to the Ligand Unit and thus is capable of (directly or indirectly) connecting the RL to the Ligand Unit. In some of those embodiments a Parallel Connector Unit (B) when it is desired to add a Partitioning Agent (S^{*}) as a side chain appendage. In any one of those embodiments, a Connector Unit (A) is present when it is desirable to add more distance between the Stretcher Unit and RL.

[0228] In one group of embodiments, a Camptothecin-Linker compound is comprised of a Camptothecin compound having formula **D1**, **D1a**, **D1b**, or any subformula thereof, and a Linker Unit (Q), wherein Q comprises a Releasable Linker (RL) that is a Glycoside (e.g., Glucuronide) Unit, directly attached to a Stretcher Unit precursor (Z') or indirectly to Z' through attachment to intervening component(s) of the Camptothecin-Linker compound's Linker Unit (i.e., A, S^{*} and/or B(S^{*})), wherein Z' is comprised of a functional group capable of forming a covalent bond to a targeting agent.

[0229] In another group of embodiments, a Camptothecin-Linker Compound is comprised of a Camptothecin having formula **D1**, **D1a**, **D1b**, or any subformula thereof, and a Linker Unit (Q), wherein Q comprises a Releasable Linker (RL) that is other than a Glycoside (e.g., Glucuronide) Unit (RL), directly attached to a Stretcher Unit precursor (Z') or indirectly to Z' through attachment to intervening component(s) of the Camptothecin-Linker Compound's Linker Unit (i.e., A, S^{*} and/or B(S^{*})), wherein Z' is comprised of a functional group capable of forming a covalent bond to a targeting agent.

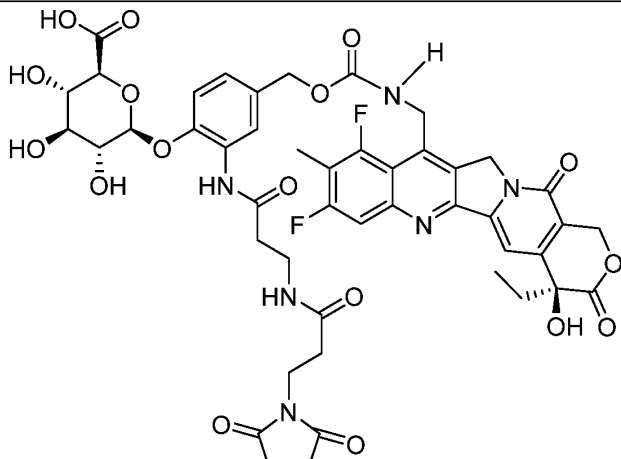
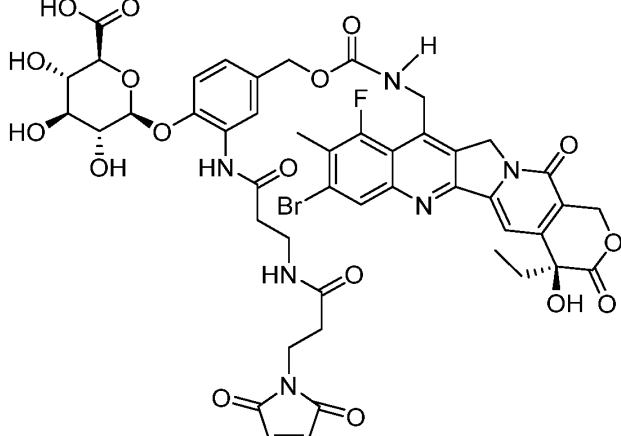
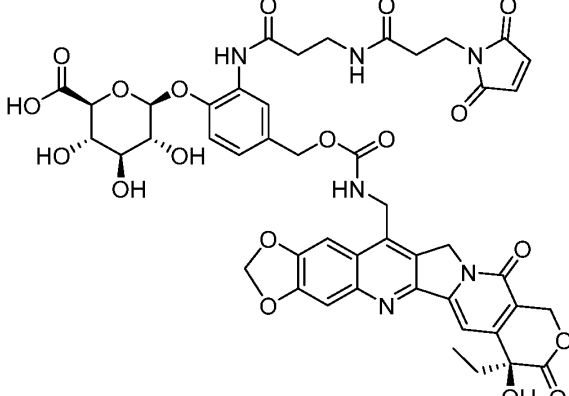
[0230] In the context of the Camptothecin Conjugates and/or the Camptothecin-Linker Compounds – the assembly is best described in terms of its component groups. While some procedures are also described herein, the order of assembly and the general conditions to prepare the Conjugates and Compounds will be well understood by one of skill in the art.

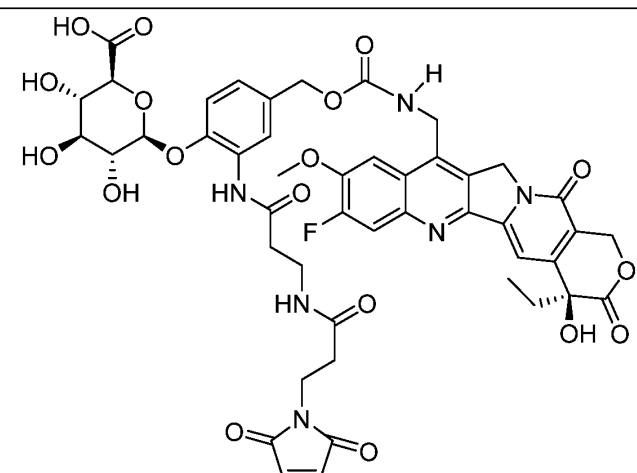
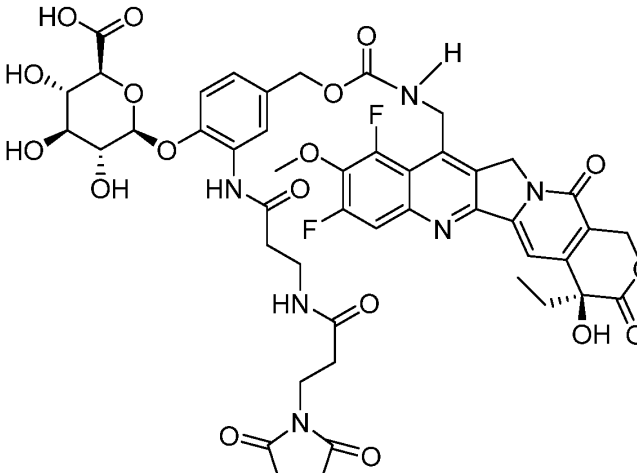
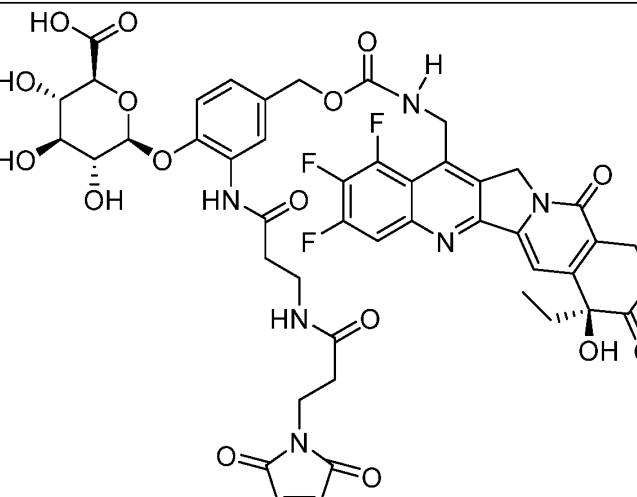
[0231] In some embodiments, provided herein is a Camptothecin-Linker compound, wherein the compound is selected from the group consisting of the compounds in Table II. In some embodiments, provided herein is a Camptothecin Conjugate, wherein the Conjugate comprises a Ligand attached to a succinimide moiety or a succinic acid-amide moiety of a

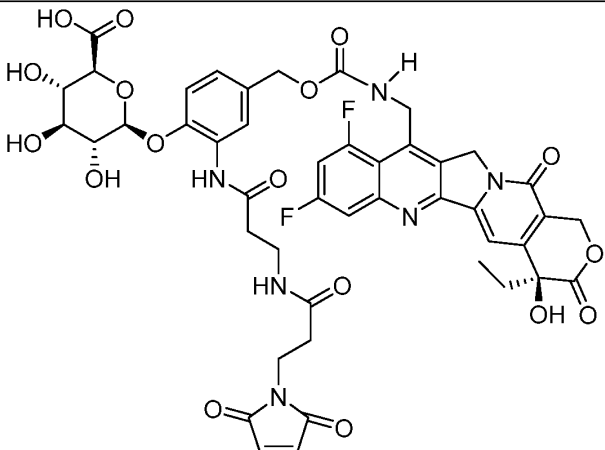
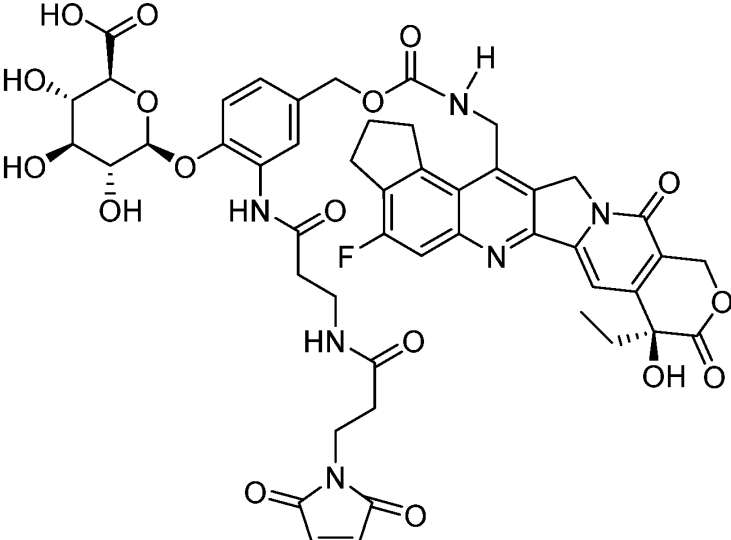
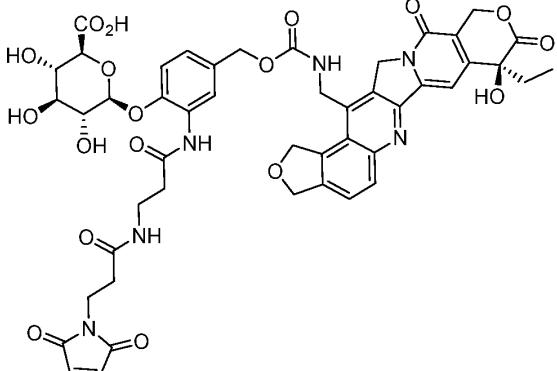
Drug-Linker moiety, wherein the Drug-Linker moiety comprises a compound of Table II, wherein the maleimide moiety is replaced by the succinimide or succinic acid-amide moiety.

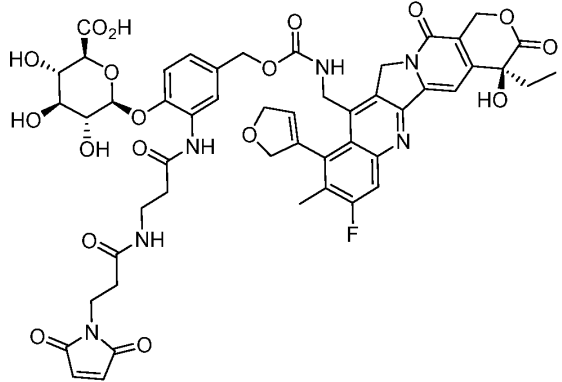
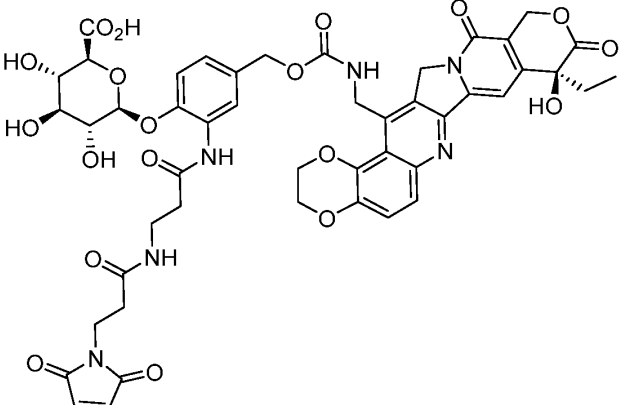
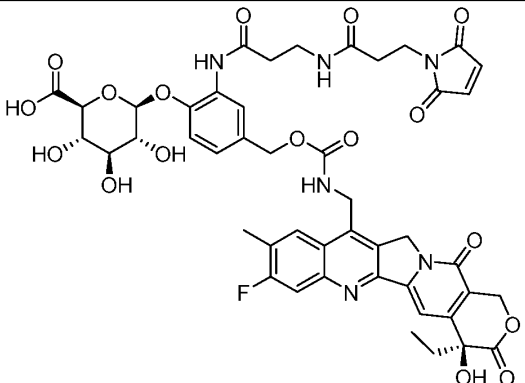
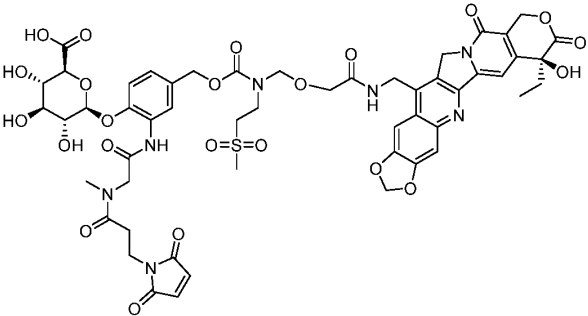
Table II

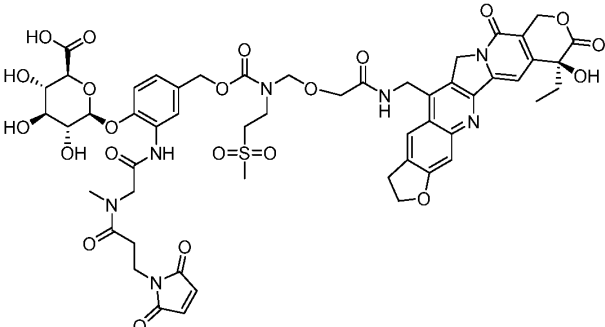
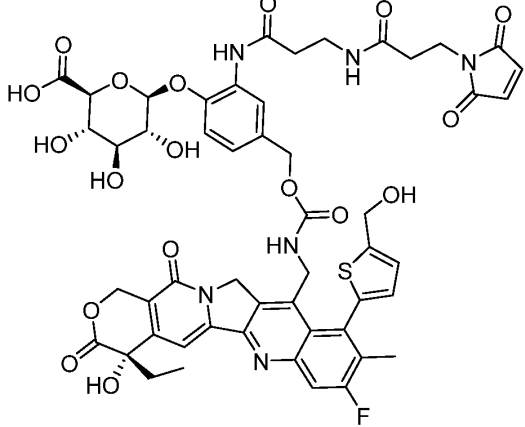
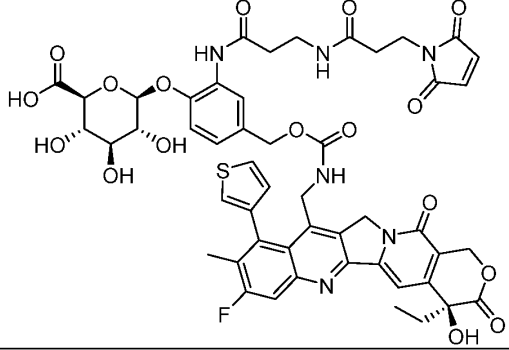
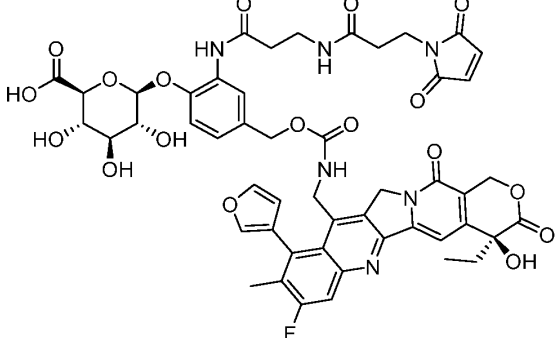
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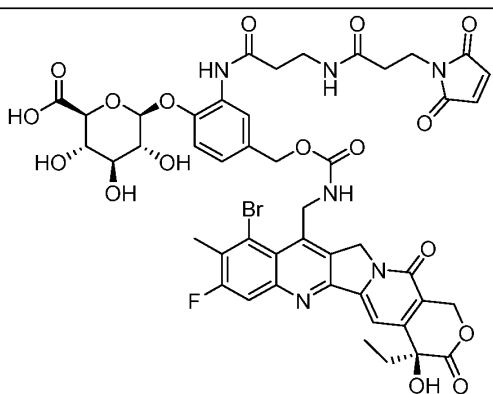
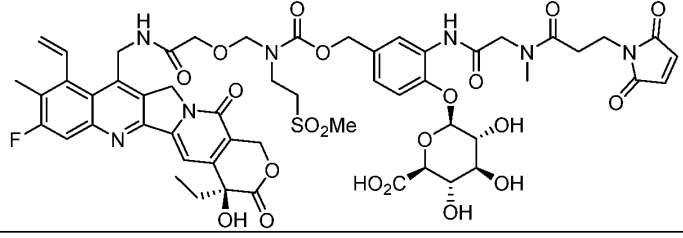
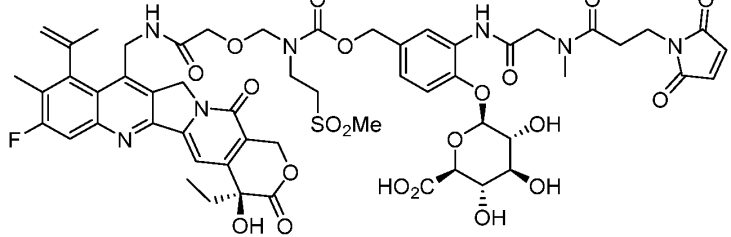
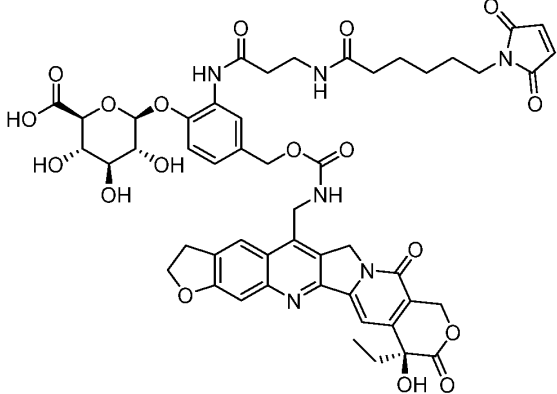
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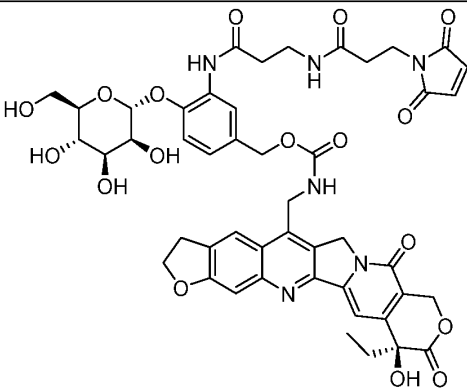
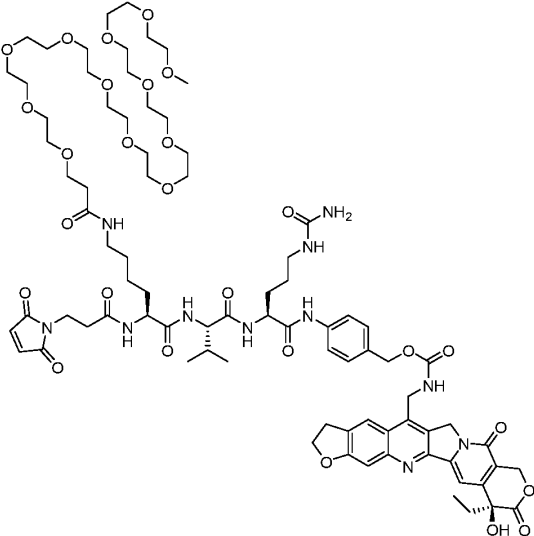
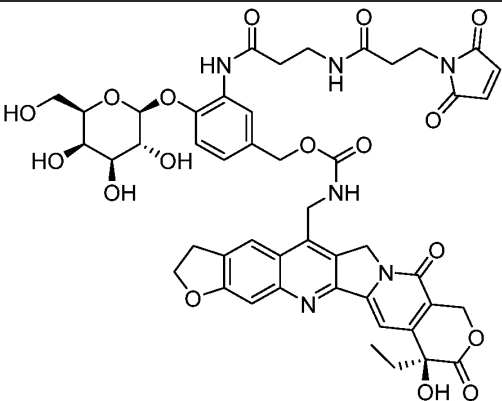
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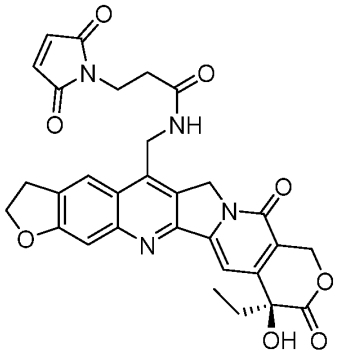
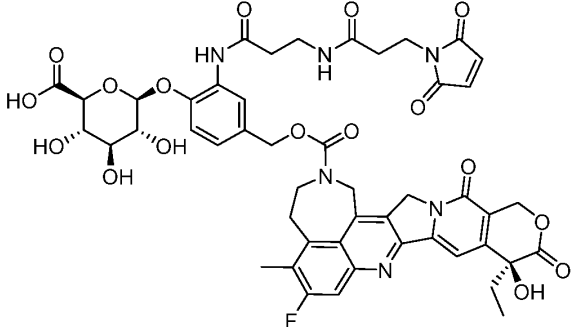
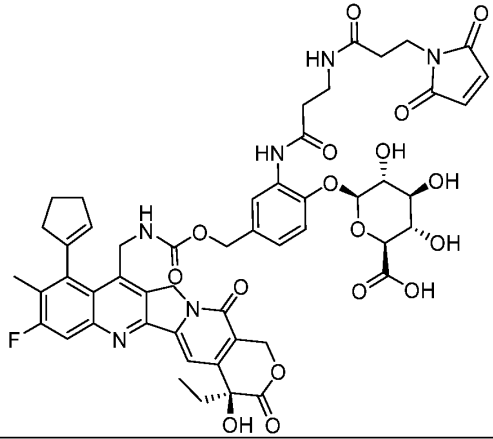
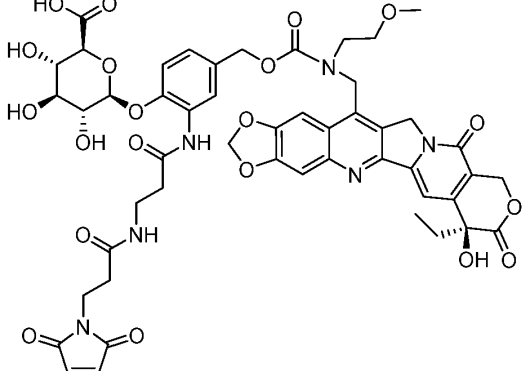
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4q	
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4y	
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4aa	

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4ad	
4ae	

Component groups**Ligand Units:**

[0232] In some embodiments of the invention, a Ligand Unit is present. The Ligand Unit (L-) is a targeting agent that specifically binds to a target moiety. In one group of embodiments, the Ligand Unit specifically and selectively binds to a cell component (a Cell Binding Agent) or to another target molecule of interest. The Ligand Unit acts to target and present the camptothecin (such as one of formula **D1**, **D1a**, **D1b**, or any subformula thereof) to the particular target cell population with which the Ligand Unit interacts due to the presence of its targeted component or molecule and allows for subsequent release of free drug within (i.e., intracellularly) or within the vicinity of the target cells (i.e., extracellularly). Ligand Units, L, include, but are not limited to, proteins, polypeptides, and peptides. Suitable Ligand Units include, for example, antibodies, e.g., full-length antibodies and antigen binding fragments thereof, interferons, lymphokines, hormones, growth factors, colony-stimulating factors, vitamins, nutrient-transport molecules (such as, but not limited to, transferrin), or any other cell binding molecule or substance. In some embodiments, the Ligand Unit (L) is from an antibody or a non-antibody protein targeting agent.

[0233] In one group of embodiments a Ligand Unit is bonded to Q (a Linker Unit) which comprises a Glucuronide Releasable Linker. As noted above, still other linking components can be present in the conjugates described herein to serve the purpose of providing additional space between the Camptothecin drug compound and the Ligand Unit (e.g., a Stretcher Unit and optionally a Connector Unit, A), or providing attributes to the composition to increase solubility (e.g., a Partitioning Agent, S^{*}). In some of those embodiments, the Ligand Unit is bonded to Z of the Linker Unit via a heteroatom of the Ligand Unit. Heteroatoms that may be present on a Ligand Unit for that bonding include sulfur (in one embodiment, from a sulfhydryl group of a targeting ligand), oxygen (in one embodiment, from a carboxyl or hydroxyl group of a targeting ligand) and nitrogen, optionally substituted (in one embodiment, from a primary or secondary amine functional group of a targeting ligand or in another embodiment from an optionally substituted amide nitrogen). Those heteroatoms can be present on the targeting ligand in the ligand's natural state, for example in a naturally occurring antibody, or can be introduced into the targeting ligand via chemical modification or biological engineering.

[0234] In one embodiment, a targeting agent that is a precursor to a Ligand Unit has a sulfhydryl functional group so that the Ligand Unit is bonded to the Linker Unit via the sulfur atom of the sulfhydryl functional group.

[0235] In another embodiment, a targeting agent that is a precursor to Ligand Unit has one or more lysine residues that are capable of reacting with activated esters (such esters include, but are not limited to, *N*-hydroxysuccinimide, pentafluorophenyl, and *p*-nitrophenyl esters) of a Stretcher Unit precursor of a Camptothecin-Linker Compound intermediate and thus provides an amide bond consisting of the nitrogen atom of the Ligand Unit and the C=O group of the Linker Unit's Stretcher Unit.

[0236] In yet another aspect, a targeting agent that is a precursor to Ligand Unit has one or more lysine residues capable of chemical modification to introduce one or more sulfhydryl groups. In those embodiments, the Ligand Unit is covalently attached to the Linker Unit via the sulfhydryl functional group's sulfur atom. The reagents that can be used to modify lysines in that manner include, but are not limited to, *N*-succinimidyl *S*-acetylthioacetate (SATA) and 2-Iminothiolane hydrochloride (Traut's Reagent).

[0237] In another embodiment, a targeting agent that is a precursor to a Ligand Unit has one or more carbohydrate groups capable of modification to provide one or more sulfhydryl functional groups. The chemically modified Ligand Unit in a Camptothecin Conjugate is bonded to a Linker Unit component (e.g., a Stretcher Unit) via the sulfur atom of the sulfhydryl functional group.

[0238] In yet another embodiment, a targeting agent that is a precursor to a Ligand Unit has one or more carbohydrate groups that can be oxidized to provide an aldehyde (-CHO) functional group (*see, e.g.,* Laguzza, *et al.*, 1989, *J. Med. Chem.* 32(3):548-55). In these embodiments, the corresponding aldehyde interacts with a reactive site on a Stretcher Unit precursor to form a bond between the Stretcher Unit and the Ligand Unit. Reactive sites on a Stretcher Unit precursor that capable of interacting with a reactive carbonyl-containing functional group on a targeting Ligand Unit include, but are not limited to, hydrazine and hydroxylamine. Other protocols for the modification of proteins for the attachment of Linker Units (Q) or related species are described in Coligan *et al.*, *Current Protocols in Protein Science*, vol. 2, John Wiley & Sons (2002) (incorporated herein by reference).

[0239] In some aspects, a targeting agent that is a precursor to a Ligand Unit is capable of forming a bond by interacting with a reactive functional group on a Stretcher Unit

precursor (Z') to form a covalent bond between the Stretcher Unit (Z) and the Ligand Unit, which corresponds in structure to the targeting agent. The functional group of Z' having that capability for interacting with a targeting agent will depend on the nature of the targeting agent that will correspond in structure to the Ligand Unit. In some embodiments, the reactive group is a maleimide that is present on a Stretcher Unit prior to its attachment to form a Ligand Unit (i.e., a maleimide moiety of a Stretcher Unit precursor). Covalent attachment of a Ligand Unit to a Stretcher Unit is accomplished through a sulfhydryl functional group of a targeting agent that is a precursor to a Ligand Unit interacting with the maleimide functional group of Z' to form a thio-substituted succinimide. The sulfhydryl functional group can be present on the targeting agent in the targeting agent's natural state, for example, in a naturally occurring residue, or can be introduced into the targeting agent via chemical modification or by biological engineering.

[0240] In still another embodiment, the Ligand Unit is from an antibody and the sulfhydryl group is generated by reduction of an interchain disulfide of the antibody. Accordingly, in some embodiments, the Linker Unit is conjugated to a cysteine residue from reduced interchain disulfide(s).

[0241] In yet another embodiment, the Ligand Unit is from an antibody and the sulfhydryl functional group is chemically introduced into the antibody, for example, by introduction of a cysteine residue. Accordingly, in some embodiments, the Linker Unit (with or without an attached Camptothecin) is conjugated to a Ligand Unit through an introduced cysteine residue of a Ligand Unit.

[0242] It has been observed for bioconjugates that the site of drug conjugation can affect a number of parameters including ease of conjugation, drug-linker stability, effects on biophysical properties of the resulting bioconjugates, and *in vitro* cytotoxicity. With respect to drug-linker stability, the site of conjugation of a drug-linker moiety to a Ligand Unit can affect the ability of the conjugated drug-linker moiety to undergo an elimination reaction, in some instances, to cause premature release of free drug. Sites for conjugation on a targeting agent include, for example, a reduced interchain disulfide as well as selected cysteine residues at engineered sites. In some embodiments conjugation methods to form Camptothecin Conjugates as described herein use thiol residues at genetically engineered sites that are less susceptible to the elimination reaction (e.g., positions 239 according to the EU index as set forth in Kabat) in comparison to conjugation methods that use thiol residues from a reduced disulfide bond. In other embodiments conjugation methods to form

Camptothecin Conjugates as described herein use thiol residues resulting from interchain disulfide bond reduction.

[0243] In some embodiments, a Camptothecin Conjugate comprises a non-immunoreactive protein, polypeptide, or peptide as its Ligand Unit. Accordingly, in some embodiments, the Ligand Unit is from a non-immunoreactive protein, polypeptide, or peptide. Examples include, but are not limited to, transferrin, epidermal growth factors (“EGF”), bombesin, gastrin, gastrin-releasing peptide, platelet-derived growth factor, IL-2, IL-6, transforming growth factors (“TGF”), such as TGF- α and TGF- β , vaccinia growth factor (“VGF”), insulin and insulin-like growth factors I and II, somatostatin, lectins and apoprotein from low density lipoprotein.

[0244] Particularly preferred Ligand Units are from antibodies. Accordingly, in any one of the embodiments described herein, the Ligand Unit is from an antibody. Useful polyclonal antibodies are heterogeneous populations of antibody molecules derived from the sera of immunized animals. Useful monoclonal antibodies are homogeneous populations of antibodies to a particular antigenic determinant (*e.g.*, a cancer cell antigen, a viral antigen, a microbial antigen, a protein, a peptide, a carbohydrate, a chemical, nucleic acid, or fragments thereof). A monoclonal antibody (mAb) to an antigen-of-interest in some embodiments is prepared by using any technique known in the art, which provides for production of antibody molecules by continuous cell lines in culture.

[0245] Useful monoclonal antibodies include, but are not limited to, human monoclonal antibodies, humanized monoclonal antibodies, or chimeric human-mouse (or other species) monoclonal antibodies. The antibodies include full-length antibodies and antigen binding fragments thereof. Human monoclonal antibodies can be made by any of numerous techniques known in the art (*e.g.*, Teng *et al.*, 1983, *Proc. Natl. Acad. Sci. USA.* 80:7308-7312; Kozbor *et al.*, 1983, *Immunology Today* 4:72-79; and Olsson *et al.*, 1982, *Meth. Enzymol.* 92:3-16).

[0246] An antibody useful for practicing the invention is an intact antibody or a functionally active fragment, derivative or analog of an antibody, wherein the antibody or fragment thereof is capable of immunospecific binding to target cells (*e.g.*, cancer cell antigens, viral antigens, or microbial antigens) or other antibodies that are bound to tumor cells or matrix. In this regard, “functionally active” means that the fragment, derivative or analog is able to immunospecifically bind to target cells. To determine which CDR

sequences bind the antigen, synthetic peptides containing the CDR sequences in some embodiments are used in binding assays with the antigen by a binding assay method known in the art (e.g., the Biacore™ assay) (See, e.g., Kabat *et al.*, 1991, *Sequences of Proteins of Immunological Interest*, Fifth Edition, National Institute of Health, Bethesda, Md; Kabat E *et al.*, 1980, *J. Immunology* 125(3):961-969).

[0247] Other useful antibodies include fragments of antibodies such as, but not limited to, F(ab')₂ fragments, Fab fragments, Fvs, single chain antibodies, diabodies, triabodies, tetrabodies, scFv, scFv-FV, or any other molecule with the same specificity as the antibody.

[0248] Additionally, recombinant antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which in some embodiments are made using standard recombinant DNA techniques, are useful antibodies. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as for example, those having a variable region derived from a murine monoclonal and human immunoglobulin constant regions. (See, e.g., U.S. Patent No. 4,816,567; and U.S. Patent No. 4,816,397, which are incorporated herein by reference in their entirety.) Humanized antibodies are antibody molecules from non-human species having one or more complementarity determining regions (CDRs) from the non-human species and a framework region from a human immunoglobulin molecule. (See, e.g., U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety.) Such chimeric and humanized monoclonal antibodies in some embodiments are produced by recombinant DNA techniques known in the art, for example using methods described in International Publication No. WO 87/02671; European Patent Publication No. 0 184 187; European Patent Publication No. 0 171 496; European Patent Publication No. 0 173 494; International Publication No. WO 86/01533; U.S. Patent No. 4,816,567; Berter *et al.*, *Science* (1988) 240: 1041-1043; Liu *et al.*, *Proc. Nat'l. Acad. Sci. USA* (1987) 84: 3439-3443; Liu *et al.*, *J. Immunol.* (1987) 139: 3521-3526; Sun *et al.*, *Proc. Natl. Acad. Sci. USA* (1987) 84: 214-218; Nishimura *et al.*, *Cancer. Res.* (1987) 47: 999-1005; Wood *et al.*, *Nature* (1985) 314: 446-449; Shaw *et al.*, *J. Natl. Cancer Inst.* (1988) 80: 1553-1559; Morrison, *Science* (1985) 229: 1202-1207; Oi *et al.*, *BioTechniques* (1986) 4: 214-221; U.S. Patent No. 5,225,539; Jones *et al.*, *Nature* (1986) 321: 552-525; Verhoeyan *et al.*, *Science* (1988) 239: 1534-1536; and Beidler *et al.*, *J. Immunol.* (1988) 141: 4053-4060; each of which is incorporated herein by reference in its entirety.

[0249] Completely human antibodies in some instances (e.g., when immunogenicity to a non-human or chimeric antibody may occur) are more desirable and in some embodiments are produced using transgenic mice that are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which are capable of expressing human heavy and light chain genes.

[0250] Antibodies include analogs and derivatives that are either modified, *i.e.*, by the covalent attachment of any type of molecule as long as such covalent attachment permits the antibody to retain its antigen binding immunospecificity. For example, but not by way of limitation, derivatives and analogs of the antibodies include those that have been further modified, *e.g.*, by glycosylation, acetylation, PEGylation, phosphorylation, amidation, derivitization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular antibody unit or other protein, etc. In some embodiments one or more of those numerous chemical modifications are carried out by known techniques including, but not limited to, specific chemical cleavage, acetylation, formylation, metabolic synthesis in the presence of tunicamycin, etc. In other embodiments, an analog or derivative of an antibody contains one or more unnatural amino acids, which is sometimes in combination with one or more of the above-described chemical modifications.

[0251] In some embodiments the antibody has one or more modifications (*e.g.*, substitutions, deletions or additions) in amino acid residues that interact with Fc receptors. Those include modifications in amino acid residues identified as involved in the interaction between the anti-Fc domain and the FcRn receptor (*see, e.g.*, International Publication No. WO 97/34631, which is incorporated herein by reference in its entirety).

[0252] In some embodiments, antibodies immunospecific for a cancer cell antigen are obtained commercially or produced by a method known to one of skill in the art such as, recombinant expression techniques. The nucleotide sequence encoding antibodies immunospecific for a cancer cell antigen is sometimes obtained, *e.g.*, from the GenBank database or a database like it, the literature publications, or by routine cloning and sequencing.

[0253] In a specific embodiment, a known antibody for the treatment of cancer is used.

[0254] In another specific embodiment, an antibody for the treatment of an autoimmune disease is used in accordance with the compositions and methods of the invention.

[0255] In certain embodiments, useful antibodies bind to a receptor or a receptor complex expressed on an activated lymphocyte. That receptor or receptor complex, in some embodiments, is an immunoglobulin gene superfamily member, a TNF receptor superfamily member, an integrin, a cytokine receptor, a chemokine receptor, a major histocompatibility protein, a lectin, or a complement control protein.

[0256] In some embodiments, the antibody that is incorporated into a Camptothecin Conjugate will specifically bind CD19, CD30, CD33, CD70 or LIV-1.

[0257] Exemplary antigens are provided below. Exemplary antibodies that bind the indicated antigen are shown in parentheses.

[0258] In some embodiments, the antigen is a tumor-associated antigen. In some embodiments, the tumor-associated antigen is a transmembrane protein. For example, the following antigens are transmembrane proteins: ANTXR1, BAFF-R, CA9 (exemplary antibodies include girentuximab), CD147 (exemplary antibodies include gavilimomab and metuzumab), CD19, CD20 (exemplary antibodies include divozilimab and ibritumomab tiuxetan), CD274 also known as PD-L1 (exemplary antibodies include adebrelimab, atezolizumab, garivulimab, durvalumab, and avelumab), CD30 (exemplary antibodies include iratumumab and brentuximab), CD33 (exemplary antibodies include lintuzumab), CD352, CD45 (exemplary antibodies include apamistamab), CD47 (exemplary antibodies include letaplimab and magrolimab), CLPTM1L, DPP4, EGFR, ERVMER34-1, FASL, FSHR, FZD5, FZD8, GUCY2C (exemplary antibodies include indusatumab), IFNAR1 (exemplary antibodies include faralimomab), IFNAR2, LMP2, MLANA, SIT1, TLR2/4/1 (exemplary antibodies include tomaralimab), TM4SF5, TMEM132A, TMEM40, UPK1B, VEGF, and VEGFR2 (exemplary antibodies include gentuximab).

[0259] In some embodiments, the tumor-associated antigen is a transmembrane transport protein. For example, the following antigens are transmembrane transport proteins: ASCT2 (exemplary antibodies include idactamab), MFSD13A, Mincle, NOX1, SLC10A2, SLC12A2, SLC17A2, SLC38A1, SLC39A5, SLC39A6 also known as LIV1 (exemplary antibodies include ladiratuzumab), SLC44A4, SLC6A15, SLC6A6, SLC7A11, and SLC7A5.

[0260] In some embodiments, the tumor-associated antigen is a transmembrane or membrane-associated glycoprotein. For example, the following antigens are transmembrane or membrane-associated glycoproteins: CA-125, CA19-9, CAMPATH-1 (exemplary antibodies include alemtuzumab), carcinoembryonic antigen (exemplary antibodies include

arcitumomab, cergutuzumab, amunaleukin, and labetuzumab), CD112, CD155, CD24, CD247, CD37 (exemplary antibodies include lilotomab), CD38 (exemplary antibodies include felzartamab), CD3D, CD3E (exemplary antibodies include foralumab and teplizumab), CD3G, CD96, CDCP1, CDH17, CDH3, CDH6, CEACAM1, CEACAM6, CLDN1, CLDN16, CLDN18.1 (exemplary antibodies include zolbetuximab), CLDN18.2 (exemplary antibodies include zolbetuximab), CLDN19, CLDN2, CLEC12A (exemplary antibodies include tepoditamab), DPEP1, DPEP3, DSG2, endosialin (exemplary antibodies include ontuxizumab), ENPP1, EPCAM (exemplary antibodies include adecatumumab), FN, FN1, Gp100, GPA33, gpNMB (exemplary antibodies include glembatumumab), ICAM1, L1CAM, LAMP1, MELTF also known as CD228, NCAM1, Nectin-4 (exemplary antibodies include enfortumab), PDPN, PMSA, PROM1, PSCA, PSMA, Siglecs 1-16, SIRPa, SIRPg, TACSTD2, TAG-72, Tenascin, Tissue Factor also known as TF (exemplary antibodies include tisotumab), and ULBP1/2/3/4/5/6.

[0261] In some embodiments, the tumor-associated antigen is a transmembrane or membrane-associated receptor kinase. For example, the following antigens are transmembrane or membrane-associated receptor kinases: ALK, Axl (exemplary antibodies include tilvestamab), BMPR2, DCLK1, DDR1, EPHA receptors, EPHA2, ERBB2 also known as HER2 (exemplary antibodies include trastuzumab, bevacizumab, pertuzumab, and margetuximab), ERBB3, FLT3, PDGFR-B (exemplary antibodies include rinucumab), PTK7 (exemplary antibodies include cofetuzumab), RET, ROR1 (exemplary antibodies include cirmtuzumab), ROR2, ROS1, and Tie3.

[0262] In some embodiments, the tumor-associated antigen is a membrane-associated or membrane-localized protein. For example, the following antigens are membrane-associated or membrane-localized proteins: ALPP, ALPPL2, ANXA1, FOLR1 (exemplary antibodies include farletuzumab), IL13Ra2, IL1RAP (exemplary antibodies include nidanilimab), NT5E, OX40, Ras mutant, RGS5, RhoC, SLAMF7 (exemplary antibodies include elotuzumab), and VSIR.

[0263] In some embodiments, the tumor-associated antigen is a transmembrane G-protein coupled receptor (GPCR). For example, the following antigens are GPCRs: CALCR, CD97, GPR87, and KISS1R.

[0264] In some embodiments, the tumor-associated antigen is cell-surface-associated or a cell-surface receptor. For example, the following antigens are cell-surface-associated and/or

cell-surface receptors: B7-DC, BCMA, CD137, CD 244, CD3 (exemplary antibodies include orelizumab and visilizumab), CD48, CD5 (exemplary antibodies include zolimomab aritox), CD70 (exemplary antibodies include cusatuzumab and vorsetuzumab), CD74 (exemplary antibodies include milatuzumab), CD79A, CD-262 (exemplary antibodies include tigatuzumab), DR4 (exemplary antibodies include mapatumumab), FAS, FGFR1, FGFR2 (exemplary antibodies include aprutumab), FGFR3 (exemplary antibodies include vofatamab), FGFR4, GTR (exemplary antibodies include ragifilimab), Gpc3 (exemplary antibodies include ragifilimab), HAVCR2, HLA-E, HLA-F, HLA-G, LAG-3 (exemplary antibodies include encelimumab), LY6G6D, LY9, MICA, MICB, MSLN, MUC1, MUC5AC, NY-ESO-1, OY-TES1, PVRIG, Sialyl-Thomsen-Nouveau Antigen, Sperm protein 17, TNFRSF12, and uPAR.

[0265] In some embodiments, the tumor-associated antigen is a chemokine receptor or cytokine receptor. For example, the following antigens are chemokine receptors or cytokine receptors: CD115 (exemplary antibodies include axatilimab, cabiralizumab, and emactuzumab), CD123, CXCR 4 (exemplary antibodies include ulocuplumab), IL-21R, and IL-5R (exemplary antibodies include benralizumab).

[0266] In some embodiments, the tumor-associated antigen is a co-stimulatory, surface-expressed protein. For example, the following antigens are co-stimulatory, surface-expressed proteins: B7-H3 (exemplary antibodies include enoblituzumab and omburtamab), B7-H4, B7-H6, and B7-H7.

[0267] In some embodiments, the tumor-associated antigen is a transcription factor or a DNA-binding protein. For example, the following antigens are transcription factors: ETV6-AML, MYCN, PAX3, PAX5, and WT1. The following protein is a DNA-binding protein: BORIS.

[0268] In some embodiments, the tumor-associated antigen is an integral membrane protein. For example, the following antigens are integral membrane proteins: SLITRK6 (exemplary antibodies include sirtratumab), UPK2, and UPK3B.

[0269] In some embodiments, the tumor-associated antigen is an integrin. For example, the following antigens are integrin antigens: alpha v beta 6, ITGAV (exemplary antibodies include abituzumab), ITGB6, and ITGB8.

[0270] In some embodiments, the tumor-associated antigen is a glycolipid. For example, the following are glycolipid antigens: FucGM1, GD2 (exemplary antibodies include

dinutuximab), GD3 (exemplary antibodies include mitumomab), GloboH, GM2, and GM3 (exemplary antibodies include racotumomab).

[0271] In some embodiments, the tumor-associated antigen is a cell-surface hormone receptor. For example, the following antigens are cell-surface hormone receptors: AMHR2 and androgen receptor.

[0272] In some embodiments, the tumor-associated antigen is a transmembrane or membrane-associated protease. For example, the following antigens are transmembrane or membrane-associated proteases: ADAM12, ADAM9, TMPRSS11D, and metalloproteinase.

[0273] In some embodiments, the tumor-associated antigen is aberrantly expressed in individuals with cancer. For example, the following antigens may be aberrantly expressed in individuals with cancer: AFP, AGR2, AKAP-4, ARTN, BCR-ABL, C5 complement, CCNB1, CSPG4, CYP1B1, De2-7 EGFR, EGF, Fas-related antigen 1, FBP, G250, GAGE, HAS3, HPV E6 E7, hTERT, IDO1, LCK, Legumain, LYPD1, MAD-CT-1, MAD-CT-2, MAGEA3, MAGEA4, MAGEC2, MerTk, ML-IAP, NA17, NY-BR-1, p53, p53 mutant, PAP, PLAVI, polysialic acid, PR1, PSA, Sarcoma translocation breakpoints, SART3, sLe, SSX2, Survivin, Tn, TRAIL, TRAIL1, TRP-2, and XAGE1.

[0274] In some embodiments, the antigen is an immune-cell-associated antigen. In some embodiments, the immune-cell-associated antigen is a transmembrane protein. For example, the following antigens are transmembrane proteins: BAFF-R, CD163, CD19, CD20 (exemplary antibodies include rituximab, ocrelizumab, divozilimab; ibritumomab tiuxetan), CD25 (exemplary antibodies include basiliximab), CD274 also known as PD-L1 (exemplary antibodies include avelumab, atezolizumab, garivulimab, durvalumab, and avelumab), CD30 (exemplary antibodies include iratumumab and brentuximab), CD33 (exemplary antibodies include lintuzumab), CD352, CD45 (exemplary antibodies include apamistamab), CD47 (exemplary antibodies include letaplimab and magrolimab), CTLA4 (exemplary antibodies include ipilimumab), FASL, IFNAR1 (exemplary antibodies include faralimomab), IFNAR2, LAYN, LILRB2, LILRB4, PD-1 (exemplary antibodies include ipilimumab, nivolumab, pembrolizumab, balstilimab, budigalimab, geptanolimab, toripalimab, and pidilizumabsf), SIT1, and TLR2/4/1 (exemplary antibodies include tomaralimab).

[0275] In some embodiments, the immune-cell-associated antigen is a transmembrane transport protein. For example, Mincle is a transmembrane transport protein.

[0276] In some embodiments, the immune-cell-associated antigen is a transmembrane or membrane-associated glycoprotein. For example, the following antigens are transmembrane or membrane-associated glycoproteins: CD112, CD155, CD24, CD247, CD28, CD30L, CD37 (exemplary antibodies include lilotomab), CD38 (exemplary antibodies include felzartamab), CD3D, CD3E (exemplary antibodies include foralumab and teplizumab), CD3G, CD44, CLEC12A (exemplary antibodies include tepoditamab), DCIR, DCSIGN, Dectin 1, Dectin 2, ICAM1, LAMP1, Siglecs 1-16, SIRPa, SIRPg, and ULBP1/2/3/4/5/6.

[0277] In some embodiments, the immune-cell-associated antigen is a transmembrane or membrane-associated receptor kinase. For example, the following antigens are transmembrane or membrane-associated receptor kinases: Axl (exemplary antibodies include tilvestamab) and FLT3.

[0278] In some embodiments, the immune-cell-associated antigen is a membrane-associated or membrane-localized protein. For example, the following antigens are membrane-associated or membrane-localized proteins: CD83, IL1RAP (exemplary antibodies include nidanilimab), OX40, SLAMF7 (exemplary antibodies include clotuzumab), and VSIR.

[0279] In some embodiments, the immune-cell-associated antigen is a transmembrane G-protein coupled receptor (GPCR). For example, the following antigens are GPCRs: CCR4 (exemplary antibodies include mogamulizumab-kpkc), CCR8, and CD97.

[0280] In some embodiments, the immune-cell-associated antigen is cell-surface-associated or a cell-surface receptor. For example, the following antigens are cell-surface-associated and/or cell-surface receptors: B7-DC, BCMA, CD137, CD2 (exemplary antibodies include sipilizumab), CD 244, CD27 (exemplary antibodies include varlilumab), CD278 (exemplary antibodies include feladilimab and vopratelimab), CD3 (exemplary antibodies include otelixizumab and visilizumab), CD40 (exemplary antibodies include dacetuzumab and lucatumumab), CD48, CD5 (exemplary antibodies include zolimomab aritox), CD70 (exemplary antibodies include cusatuzumab and vorsetuzumab), CD74 (exemplary antibodies include milatuzumab), CD79A, CD-262 (exemplary antibodies include tigatuzumab), DR4 (exemplary antibodies include mapatumumab), GITR (exemplary antibodies include ragifilimab), HAVCR2, HLA-DR, HLA-E, HLA-F, HLA-G, LAG-3 (exemplary antibodies include encelimab), MICA, MICB, MRC1, PVRIG, Sialyl-Thomsen-Nouveau Antigen, TIGIT (exemplary antibodies include etigilimab), Trem2, and uPAR.

[0281] In some embodiments, the immune-cell-associated antigen is a chemokine receptor or cytokine receptor. For example, the following antigens are chemokine receptors or cytokine receptors: CD115 (exemplary antibodies include axatilimab, cabiralizumab, and emactuzumab), CD123, CXCR4 (exemplary antibodies include ulocuplumab), IL-21R, and IL-5R (exemplary antibodies include benralizumab).

[0282] In some embodiments, the immune-cell-associated antigen is a co-stimulatory, surface-expressed protein. For example, the following antigens are co-stimulatory, surface-expressed proteins: B7-H 3 (exemplary antibodies include enoblituzumab and omburtamab), B7-H4, B7-H6, and B7-H7.

[0283] In some embodiments, the immune-cell-associated antigen is a peripheral membrane protein. For example, the following antigens are peripheral membrane proteins: B7-1 (exemplary antibodies include galiximab) and B7-2.

[0284] In some embodiments, the immune-cell-associated antigen is aberrantly expressed in individuals with cancer. For example, the following antigens may be aberrantly expressed in individuals with cancer: C5 complement, IDO1, LCK, MerTk, and Tyrol.

[0285] In some embodiments, the antigen is a stromal-cell-associated antigen. In some embodiments, the stromal-cell-associated antigen is a transmembrane or membrane-associated protein. For example, the following antigens are transmembrane or membrane-associated proteins: FAP (exemplary antibodies include sibrotuzumab), IFNAR1 (exemplary antibodies include faralimomab), and IFNAR2.

[0286] In some embodiments, the antigen is CD30. In some embodiments, the antibody is an antibody or antigen-binding fragment that binds to CD30, such as described in International Patent Publication No. WO 02/43661. In some embodiments, the anti-CD30 antibody is cAC10, which is described in International Patent Publication No. WO 02/43661. cAC10 is also known as brentuximab. In some embodiments, the anti-CD30 antibody comprises the CDRs of cAC10. In some embodiments, the CDRs are as defined by the Kabat numbering scheme. In some embodiments, the CDRs are as defined by the Chothia numbering scheme. In some embodiments, the CDRs are as defined by the IMGT numbering scheme. In some embodiments, the CDRs are as defined by the AbM numbering scheme. In some embodiments, the anti-CD30 antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1, 2, 3, 4, 5, and 6, respectively. In some embodiments, the anti-CD30 antibody comprises a heavy

chain variable region comprising an amino acid sequence that is at least 95%, at least 96%, at least 97%, at last 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at last 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 8. In some embodiments, the anti-CD30 antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 9 or SEQ ID NO: 10 and a light chain comprising the amino acid sequence of SEQ ID NO: 11.

[0287] In some embodiments, the antigen is CD70. In some embodiments, the antibody is an antibody or antigen-binding fragment that binds to CD70, such as described in International Patent Publication No. WO 2006/113909. In some embodiments, the antibody is a h1F6 anti-CD70 antibody, which is described in International Patent Publication No. WO 2006/113909. h1F6 is also known as vorsetuzumab. In some embodiments, the anti-CD70 antibody comprises a heavy chain variable region comprising the three CDRs of SEQ ID NO:12 and a light chain variable region comprising the three CDRs of SEQ ID NO:13. In some embodiments, the CDRs are as defined by the Kabat numbering scheme. In some embodiments, the CDRs are as defined by the Chothia numbering scheme. In some embodiments, the CDRs are as defined by the IMGT numbering scheme. In some embodiments, the CDRs are as defined by the AbM numbering scheme. In some embodiments, the anti-CD70 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 95%, at least 96%, at least 97%, at last 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 12 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at last 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 13. In some embodiments, the anti-CD30 antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 14 and a light chain comprising the amino acid sequence of SEQ ID NO: 15.

[0288] In some embodiments, the antigen is interleukin-1 receptor accessory protein (IL1RAP). IL1RAP is a co-receptor of the IL1 receptor (IL1R1) and is required for interleukin-1 (IL1) signaling. IL1 has been implicated in the resistance to certain chemotherapy regimens. IL1RAP is overexpressed in various solid tumors, both on cancer cells and in the tumor microenvironment, but has low expression on normal cells. IL1RAP is also overexpressed in hematopoietic stem and progenitor cells, making it a candidate to target for chronic myeloid leukemia (CML). IL1RAP has also been shown to be overexpressed in

acute myeloid leukemia (AML). Antibody binding to IL1RAP could block signal transduction from IL-1 and IL-33 into cells and allow NK-cells to recognize tumor cells and subsequent killing by antibody dependent cellular cytotoxicity (ADCC).

[0289] In some embodiments, the antigen is ASCT2. ASCT2 is also known as SLC1A5. ASCT2 is a ubiquitously expressed, broad-specificity, sodium-dependent neutral amino acid exchanger. ASCT2 is involved in glutamine transport. ASCT2 is overexpressed in different cancers and is closely related to poor prognosis. Downregulating ASCT2 has been shown to suppress intracellular glutamine levels and downstream glutamine metabolism, including glutathione production. Due to its high expression in many cancers, ASCT2 is a potential therapeutic target. These effects attenuated growth and proliferation, increased apoptosis and autophagy, and increased oxidative stress and mTORC1 pathway suppression in head and neck squamous cell carcinoma (HNSCC). Additionally, silencing ASCT2 improved the response to cetuximab in HNSCC.

[0290] In some embodiments, an antibody-drug conjugate provided herein binds to TROP2. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 16, 17, 18, 19, 20, and 21, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 22 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 23. In some embodiments, the antibody of the antibody drug conjugate is sacituzumab. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 24, 25, 26, 27, 28, and 29, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 30 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 31. In some embodiments, the antibody of the antibody drug conjugate is datopotamab.

[0291] In some embodiments, an antibody-drug conjugate provided herein binds to MICA. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 32, 33, 34, 35, 36, and 37, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 38 and a light chain variable region

comprising the amino acid sequence of SEQ ID NO: 39. In some embodiments, the antibody of the antibody drug conjugate is h1D5v11 hIgG1K. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 40, 41, 42, 43, 44, and 45, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 46 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 47. In some embodiments, the antibody of the antibody drug conjugate is MICA.36 hIgG1K G236A. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 48, 49, 50, 51, 52, and 53, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 54 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 55. In some embodiments, the antibody of the antibody drug conjugate is h3F9 H1L3 hIgG1K. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 56, 57, 58, 59, 60, and 61, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 62 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 63. In some embodiments, the antibody of the antibody drug conjugate is CM33322 Ab28 hIgG1K.

[0292] In some embodiments, an antibody-drug conjugate provided herein binds to CD24. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 64, 65, 66, 67, 68, and 69, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 70 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 71. In some embodiments, the antibody of the antibody drug conjugate is SWA11.

[0293] In some embodiments, an antibody-drug conjugate provided herein binds to ITGav. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 72, 73, 74, 75, 76, and 77, respectively. In some embodiments,

the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 78 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 79. In some embodiments, the antibody of the antibody drug conjugate is intetumumab. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 80, 81, 82, 83, 84, and 85, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 86 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 87. In some embodiments, the antibody of the antibody drug conjugate is abituzumab.

[0294] In some embodiments, an antibody-drug conjugate provided herein binds to gpA33. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 88, 89, 90, 91, 92, and 93, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 94 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 95.

[0295] In some embodiments, an antibody-drug conjugate provided herein binds to IL1Rap. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 96, 97, 98, 99, 100, and 101, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 102 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 103. In some embodiments, the antibody of the antibody drug conjugate is nidanimab.

[0296] In some embodiments, an antibody-drug conjugate provided herein binds to EpCAM. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 104, 105, 106, 107, 108, and 109, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 110 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 111. In some embodiments, the antibody of the antibody drug conjugate is adcatumumab. In some embodiments, the

antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 112, 113, 114, 115, 116, and 117, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 118 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 119. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 118 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 1182. In some embodiments, the antibody of the antibody drug conjugate is Ep157305. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 120, 121, 122, 123, 124, and 125, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 126 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 127. In some embodiments, the antibody of the antibody drug conjugate is Ep3-171. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 128, 129, 130, 131, 132, and 133, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 134 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 135. In some embodiments, the antibody of the antibody drug conjugate is Ep3622w94. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 136, 137, 138, 139, 140, and 141, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 142 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 143. In some embodiments, the antibody of the antibody drug conjugate is EpING1. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 144, 145, 146, 147, 148, and 149, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 150 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 151. In some

embodiments, the antibody of the antibody drug conjugate is EpAb2-6. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 104, 105, 1181, 107, 108, and 109, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1 comprising the amino acid sequence of SEQ ID NO: 1181.

[0297] In some embodiments, an antibody-drug conjugate provided herein binds to CD352. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 152, 153, 154, 155, 156, and 157, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 158 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 159. In some embodiments, the antibody of the antibody drug conjugate is h20F3.

[0298] In some embodiments, an antibody-drug conjugate provided herein binds to CS1. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 160, 161, 162, 163, 164, and 165, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 166 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 167. In some embodiments, the antibody of the antibody drug conjugate is elotuzumab.

[0299] In some embodiments, an antibody-drug conjugate provided herein binds to CD38. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 168, 169, 170, 171, 172, and 173, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 174 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 175. In some embodiments, the antibody of the antibody drug conjugate is daratumumab.

[0300] In some embodiments, an antibody-drug conjugate provided herein binds to CD25. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-

H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 176, 177, 178, 179, 180, and 181, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 182 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 183. In some embodiments, the antibody of the antibody drug conjugate is daclizumab.

[0301] In some embodiments, an antibody-drug conjugate provided herein binds to ADAM9. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 184, 185, 186, 187, 188, and 189, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 190 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 191. In some embodiments, the antibody of the antibody drug conjugate is chMAbA9-A. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 192, 193, 194, 195, 196, and 197, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 198 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 199. In some embodiments, the antibody of the antibody drug conjugate is hMAbA9-A. In some embodiments, an antibody-drug conjugate provided herein binds to ADAM9. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1183, 185, 186, 187, 188, and 189, respectively. In some embodiments, an antibody-drug conjugate provided herein binds to ADAM9. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1 comprising the amino acid sequences of SEQ ID NO: 1183. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1184, 193, 194, 1185, 196, and 197, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1 comprising the amino acid sequences of SEQ ID NO: 1184. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-L1 comprising the amino acid sequences of SEQ ID NO: 1185.

[0302] In some embodiments, an antibody-drug conjugate provided herein binds to CD59. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 200, 201, 202, 203, 204, and 205, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 206 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 207. In some embodiments, an antibody-drug conjugate provided herein binds to CD59. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1186, 1187, 202, 203, 204, and 205, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1 comprising the amino acid sequence of SEQ ID NO: 1186. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H2 comprising the amino acid sequence of SEQ ID NO: 1187. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 1188 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 207.

[0303] In some embodiments, an antibody-drug conjugate provided herein binds to CD25. In some embodiments, the antibody of the antibody drug conjugate is Clone123.

[0304] In some embodiments, an antibody-drug conjugate provided herein binds to CD229. In some embodiments, the antibody of the antibody drug conjugate is h8A10.

[0305] In some embodiments, an antibody-drug conjugate provided herein binds to CD19. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 208, 209, 210, 211, 212, and 213, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 214 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 215. In some embodiments, the anti-CD19 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1175 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1176. In some embodiments, the

antibody of the antibody drug conjugate is denintuzumab, which is also known as hBU12. See WO2009052431.

[0306] In some embodiments, an antibody-drug conjugate provided herein binds to CD70. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 216, 217, 218, 219, 220, and 221, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 222 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 223. In some embodiments, the antibody of the antibody drug conjugate is vorsetuzumab. In some cases, an antibody provided herein binds to CD70. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 1169, 1170, 1171, 1172, 1173 and 1174, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 1169, 1170, 1171, 1172, 1173 and 1174, respectively.

[0307] In some embodiments, an antibody-drug conjugate provided herein binds to B7H4. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 224, 225, 226, 227, 228, and 229, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 230 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 231. In some embodiments, the antibody of the antibody drug conjugate is mirzotamab.

[0308] In some cases, an antibody provided herein binds to B7H4. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) of which each sequence comprises at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, or 100% sequence identity to amino acid sequences from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 77-82, SEQ ID NOs: 91-96, SEQ ID NOs: 99-104, SEQ ID NOs: 985-990, SEQ ID NOs: 993-998, SEQ ID NOs: 1001-128, SEQ ID NOs: 1009-

1014, SEQ ID NOs: 1017-1022, SEQ ID NOs: 1025-1030, SEQ ID NOs: 1033-1038, SEQ ID NOs: 1041-1046, SEQ ID NOs: 1049-1054, SEQ ID NOs: 1057-1062, SEQ ID NOs: 1065-1070, SEQ ID NOs: 1073-1078, SEQ ID NOs: 1081-1086, SEQ ID NOs: 1089-1094, SEQ ID NOs: 1097-1102, SEQ ID NOs: 1105-1110, SEQ ID NOs: 1113-1118, and SEQ ID NOs: 1121-1126. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) each comprising at most one mutation relative to an amino acid sequence from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 77-82, SEQ ID NOs: 91-96, SEQ ID NOs: 99-104, SEQ ID NOs: 985-990, SEQ ID NOs: 993-998, SEQ ID NOs: 1001-1006, SEQ ID NOs: 1009-1014, SEQ ID NOs: 1017-1022, SEQ ID NOs: 1025-1030, SEQ ID NOs: 1033-1038, SEQ ID NOs: 1041-1046, SEQ ID NOs: 1049-1054, SEQ ID NOs: 1057-1062, SEQ ID NOs: 1065-1070, SEQ ID NOs: 1073-1078, SEQ ID NOs: 1081-1086, SEQ ID NOs: 1089-1094, SEQ ID NOs: 1097-1102, SEQ ID NOs: 1105-1110, SEQ ID NOs: 1113-1118, and SEQ ID NOs: 1121-1126. In some cases, the anti-B7H4 antibody comprises a heavy chain and a light chain comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 963 and 87, SEQ ID NO: 964 and 87, SEQ ID NO: 966 and 90, SEQ ID NO: 967 and 90, SEQ ID NO: 1129 and 1130, SEQ ID NO: 1131 11321131 and 1132, SEQ ID NO: 1133 and 1134, SEQ ID NO: 1135 and 1136, SEQ ID NO: 1137 and 1138, SEQ ID NO: 1139 and 1140, SEQ ID NO: 1141 and 1142, SEQ ID NO: 1143 and 1144, SEQ ID NO: 1145 and 1146, SEQ ID NO: 1147 and 1148, SEQ ID NO: 1149 and 1150, SEQ ID NO: 1151 and 1152, SEQ ID NO: 1153 and 1154, SEQ ID NO: 1155 and 1156, SEQ ID NO: 1157 and 1158, SEQ ID NO: 1159 and 1160, SEQ ID NO: 1161 and 1162, SEQ ID NO: 1163 and 1164, SEQ ID NO: 1165 and 1166, or SEQ ID NO: 1167 and 1168, respectively. In some embodiments, the anti-B7H4 antibody comprises a heavy chain variable region and a light chain variable region comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 961 and 962, SEQ ID NO: 975 and 98, SEQ ID NO: 983 and 984, SEQ ID NO: 991 and 992, SEQ ID NO: 999 and 1000, SEQ ID NO: 1007 and 1008, SEQ ID NO: 1015 and 1016, SEQ ID NO: 1031 and 1032, SEQ ID NO: 1039 and 1040, SEQ ID NO: 1047 and 1048, SEQ ID NO: 1055 and 1056, SEQ ID NO: 1063 and 1064, SEQ ID NO: 1071 and 1072, SEQ ID NO: 1079 and 1080, SEQ ID NO: 1087 and 1088, SEQ ID NO: 1095 and 1096, SEQ ID NO: 1103 and 1104, SEQ ID NO: 1111 and 1112, SEQ ID NO: 1119 and 1120, or SEQ ID NO: 1127 and 1128, respectively.

[0309] In some embodiments, an antibody-drug conjugate provided herein binds to CD138. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 232, 233, 234, 235, 236, and 237, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 238 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 239. In some embodiments, the antibody of the antibody drug conjugate is indatuxumab.

[0310] In some embodiments, an antibody-drug conjugate provided herein binds to CD166. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 240, 241, 242, 243, 244, and 245, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 246 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 247. In some embodiments, the antibody of the antibody drug conjugate is praluzatamab.

[0311] In some embodiments, an antibody-drug conjugate provided herein binds to CD51. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 248, 249, 250, 251, 252, and 253, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 254 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 255. In some embodiments, the antibody of the antibody drug conjugate is intetumumab.

[0312] In some embodiments, an antibody-drug conjugate provided herein binds to CD56. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 256, 257, 258, 259, 260, and 261, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 262 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 263. In some embodiments, the antibody of the antibody drug conjugate is lorvotuzumab.

[0313] In some embodiments, an antibody-drug conjugate provided herein binds to CD74. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 264, 265, 266, 267, 268, and 269, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 270 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 271. In some embodiments, the antibody of the antibody drug conjugate is milatuzumab.

[0314] In some embodiments, an antibody-drug conjugate provided herein binds to CEACAM5. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 272, 273, 274, 275, 276, and 277, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 278 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 279. In some embodiments, the antibody of the antibody drug conjugate is labetuzumab.

[0315] In some embodiments, an antibody-drug conjugate provided herein binds to CanAg. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 280, 281, 282, 283, 284, and 285, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 286 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 287. In some embodiments, the antibody of the antibody drug conjugate is cantuzumab.

[0316] In some embodiments, an antibody-drug conjugate provided herein binds to DLL-3. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 288, 289, 290, 291, 292, and 293, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 294 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 295. In some embodiments, the antibody of the antibody drug conjugate is rovalpituzumab.

[0317] In some embodiments, an antibody-drug conjugate provided herein binds to DPEP-3. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 296, 297, 298, 299, 300, and 301, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 302 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 303. In some embodiments, the antibody of the antibody drug conjugate is tamrintamab.

[0318] In some embodiments, an antibody-drug conjugate provided herein binds to EGFR. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 304, 305, 306, 307, 308, and 309, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 310 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 311. In some embodiments, the antibody of the antibody drug conjugate is laprituximab. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 312, 313, 314, 315, 316, and 317, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 318 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 319. In some embodiments, the antibody of the antibody drug conjugate is losatuxizumab. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 320, 321, 322, 323, 324, and 325, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 326 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 327. In some embodiments, the antibody of the antibody drug conjugate is serclutamab. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 328, 329, 330, 331, 332, and 333, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 334 and a light chain

variable region comprising the amino acid sequence of SEQ ID NO: 335. In some embodiments, the antibody of the antibody drug conjugate is cetuximab.

[0319] In some embodiments, an antibody-drug conjugate provided herein binds to FRa. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 336, 337, 338, 339, 340, and 341, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 342 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 343. In some embodiments, the antibody of the antibody drug conjugate is mirvetuximab. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 344, 345, 346, 347, 348, and 349, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 350 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 351. In some embodiments, the antibody of the antibody drug conjugate is farletuzumab.

[0320] In some embodiments, an antibody-drug conjugate provided herein binds to MUC-1. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 352, 353, 354, 355, 356, and 357, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 358 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 359. In some embodiments, the antibody of the antibody drug conjugate is gatipotuzumab.

[0321] In some embodiments, an antibody-drug conjugate provided herein binds to mesothelin. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 360, 361, 362, 363, 364, and 365, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 366 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 367. In some embodiments, the antibody of the antibody drug conjugate is anetumab.

[0322] In some embodiments, an antibody-drug conjugate provided herein binds to ROR-1. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 368, 369, 370, 371, 372, and 373, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 374 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 375. In some embodiments, the antibody of the antibody drug conjugate is zilovetamab.

[0323] In some embodiments, an antibody-drug conjugate provided herein binds to ASCT2. In some embodiments, an antibody-drug conjugate provided herein binds to B7H4. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 376, 377, 378, 379, 380, and 381, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 382 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 383. In some embodiments, the antibody of the antibody drug conjugate is 20502. See WO2019040780.

[0324] In some embodiments, an antibody-drug conjugate provided herein binds to B7-H3. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 384, 385, 386, 387, 388, and 389, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 390 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 391. In some embodiments, the antibody of the antibody drug conjugate is chAb-A (BRCA84D). In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 392, 393, 394, 395, 396, and 397, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 398 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 399. In some embodiments, the antibody of the antibody drug conjugate is hAb-B. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID

NOs: 400, 401, 402, 403, 404, and 405, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 406 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 407. In some embodiments, the antibody of the antibody drug conjugate is hAb-C. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 408, 409, 410, 411, 412, and 413, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 414 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 415. In some embodiments, the antibody of the antibody drug conjugate is hAb-D. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 416, 417, 418, 419, 420, and 421, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 422 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 423. In some embodiments, the antibody of the antibody drug conjugate is chM30. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 424, 425, 426, 427, 428, and 429, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 430 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 431. In some embodiments, the antibody of the antibody drug conjugate is hM30-H1-L4. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 432, 433, 434, 435, 436, and 437, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 438 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 439. In some embodiments, the antibody of the antibody drug conjugate is AbV_huAb18-v4. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 440, 441, 442, 443, 444, and 445, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising

the amino acid sequence of SEQ ID NO: 446 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 447. In some embodiments, the antibody of the antibody drug conjugate is AbV_huAb3-v6. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 448, 449, 450, 451, 452, and 453, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 454 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 455. In some embodiments, the antibody of the antibody drug conjugate is AbV_huAb3-v2.6. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 456, 457, 458, 459, 460, and 461, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 462 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 463. In some embodiments, the antibody of the antibody drug conjugate is AbV_huAb13-v1-CR. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 464, 465, 466, 467, 468, and 469, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 470 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 471. In some embodiments, the antibody of the antibody drug conjugate is 8H9-6m. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 472 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 473. In some embodiments, the antibody of the antibody drug conjugate is m8517. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 474, 475, 476, 477, 478, and 479, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 480 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 481. In some embodiments, the antibody of the antibody drug conjugate is TPP-5706. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 482 and a light chain

variable region comprising the amino acid sequence of SEQ ID NO: 483. In some embodiments, the antibody of the antibody drug conjugate is TPP-6642. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 484 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 485. In some embodiments, the antibody of the antibody drug conjugate is TPP-6850. In some embodiments, an antibody-drug conjugate provided herein binds to B7-H3. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 384, 1189, 1190, 1191, 1192, and 1193, respectively. In some embodiments, an antibody-drug conjugate provided herein binds to B7-H3. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H2, comprising the amino acid sequence of SEQ ID NO: 1189. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H3, comprising the amino acid sequence of SEQ ID NO: 1190. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-L1, comprising the amino acid sequence of SEQ ID NO: 1191. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-L2, comprising the amino acid sequence of SEQ ID NO: 1192. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-L3, comprising the amino acid sequence of SEQ ID NO: 1193. In some embodiments, the antibody of the antibody drug conjugate is chAb-A (BRCA84D). In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1194, 1195, 1196, 1197, 396, and 397, respectively. In some embodiments, the antibody of the antibody drug conjugate is chAb-A (BRCA84D). In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, comprising the amino acid sequence of SEQ ID NO: 1194. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H2, comprising the amino acid sequence of SEQ ID NO: 1195. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H3, comprising the amino acid sequence of SEQ ID NO: 1196. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-L1, comprising the amino acid sequence of SEQ ID NO: 1197. In some embodiments, the antibody of the antibody drug conjugate is hAb-B. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 400, 401, 402, 403, 404, and 1198, respectively. In some embodiments, the antibody of the antibody drug conjugate is

hAb-B. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-L3, comprising the amino acid sequence of SEQ ID NO: 1198. In some embodiments, the antibody of the antibody drug conjugate is hAb-C. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1199, 1200, 1201, 1202, 1203, and 1204, respectively. In some embodiments, the antibody of the antibody drug conjugate is hAb-C. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, comprising the amino acid sequence of SEQ ID NO: 1199. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H2, comprising the amino acid sequence of SEQ ID NO: 1200. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H3, comprising the amino acid sequence of SEQ ID NO: 1201. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-L1, comprising the amino acid sequence of SEQ ID NO: 1202. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-L2, comprising the amino acid sequence of SEQ ID NO: 1203. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-L3, comprising the amino acid sequence of SEQ ID NO: 1204. In some embodiments, the antibody of the antibody drug conjugate is hM30-H1-L4. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1205, 433, 434, 435, 436, and 437, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, comprising the amino acid sequence of SEQ ID NO: 1205. In some embodiments, the antibody of the antibody drug conjugate is hM30-H1-L4. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 438 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 1206. In some embodiments, the antibody of the antibody drug conjugate is AbV_huAb18-v4. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1207, 441, 1208, 443, 444, and 445, respectively. In some embodiments, the antibody of the antibody drug conjugate is AbV_huAb18-v4. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, comprising the amino acid sequence of SEQ ID NO: 1207. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H3, comprising the amino acid sequence of SEQ ID NO: 1208. In some embodiments, the antibody of the antibody drug conjugate is AbV_huAb3-v6. In some

embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1209, 449, 450, 451, 452, and 453, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, comprising the amino acid sequence of SEQ ID NO: 1209. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 454 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 1210. In some embodiments, the antibody of the antibody drug conjugate is AbV_huAb3-v2.6. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 1211, 457, 458, 459, 460, and 461, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, comprising the amino acid sequence of SEQ ID NO: 1211. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 462 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 1212. In some embodiments, the antibody of the antibody drug conjugate is AbV_huAb13-v1-CR. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 464, 1213, 466, 467, 468, and 1214, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H2, comprising the amino acid sequence of SEQ ID NO: 1213. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-L3, comprising the amino acid sequence of SEQ ID NO: 1214.

[0325] In some embodiments, an antibody-drug conjugate provided herein binds to CDCP1. In some embodiments, the antibody of the antibody drug conjugate is 10D7.

[0326] In some embodiments, an antibody-drug conjugate provided herein binds to HER3. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 486 and a light chain comprising the amino acid sequence of SEQ ID NO: 487. In some embodiments, the antibody of the antibody drug conjugate is patritumab. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 488 and a light chain comprising the amino acid sequence of SEQ ID NO: 489. In some embodiments, the antibody of the antibody drug conjugate is seribantumab. In some

embodiments, the antibody of the antibody drug conjugate comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 490 and a light chain comprising the amino acid sequence of SEQ ID NO: 491. In some embodiments, the antibody of the antibody drug conjugate is elgemtumab. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain the amino acid sequence of SEQ ID NO: 492 and a light chain comprising the amino acid sequence of SEQ ID NO: 493. In some embodiments, the antibody of the antibody drug conjugate is lumretuzumab.

[0327] In some embodiments, an antibody-drug conjugate provided herein binds to RON. In some embodiments, the antibody of the antibody drug conjugate is Zt/g4.

[0328] In some embodiments, an antibody-drug conjugate provided herein binds to claudin-2.

[0329] In some embodiments, an antibody-drug conjugate provided herein binds to HLA-G.

[0330] In some embodiments, an antibody-drug conjugate provided herein binds to PTK7. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 494, 495, 496, 497, 498, and 499, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 500 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 501. In some embodiments, the antibody of the antibody drug conjugate is PTK7 mab 1. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 502, 503, 504, 505, 506, and 507, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 508 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 509. In some embodiments, the antibody of the antibody drug conjugate is PTK7 mab 2. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 510, 511, 512, 513, 514, and 515, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 516 and a light chain variable region comprising the amino

acid sequence of SEQ ID NO: 517. In some embodiments, the antibody of the antibody drug conjugate is PTK7 mab 3.

[0331] In some embodiments, an antibody-drug conjugate provided herein binds to LIV1. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 518, 519, 520, 521, 522, and 523, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 524 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 525. In some embodiments, the antibody of the antibody drug conjugate is ladiratuzumab, which is also known as hLIV22 and hglg. See WO2012078668.

[0332] In some embodiments, an antibody-drug conjugate provided herein binds to avb6. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 526, 527, 528, 529, 530, and 531, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 532 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 533. In some embodiments, the antibody of the antibody drug conjugate is h2A2. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 534, 535, 536, 537, 538, and 539, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 540 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 541. In some embodiments, the antibody of the antibody drug conjugate is h15H3.

[0333] In some cases, an antibody provided herein binds to avB6. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 941, 942, 943, 944, 945, and 946, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 941, 942, 943, 944, 945, and 946, respectively. In some embodiments, the anti-H2A2 antibody

comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 947 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 948. In some embodiments, the anti-H2A2 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 949 or 950 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 951. In some embodiments, the anti-H2A2 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 952 or 953 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 954.

[0334] In some embodiments, an antibody-drug conjugate provided herein binds to CD48. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 542, 543, 544, 545, 546, and 547, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 548 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 549. In some embodiments, the antibody of the antibody drug conjugate is hMEM102. See WO2016149535.

[0335] In some embodiments, an antibody-drug conjugate provided herein binds to PD-L1. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 550, 551, 552, 553, 554, and 555, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 556 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 557. In some embodiments, the antibody of the antibody drug conjugate is SG-559-01 LALA mAb.

[0336] In some cases, an anti-PDL1 antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising at least 80% sequence identity, at least 85%

sequence identity, at least 90% sequence identity, at least 95%, at least 98%, or at least 99% sequence identity to the amino acid sequences of SEQ ID NOs: 902, 903, 903, 904, 905, 906, and 18 respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 902, 903, 903, 904, 905, 906, and 907, respectively.

[0337] In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 890-893 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 894. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 890 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 891 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 892 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 893 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5.

[0338] In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 895-898 and a light chain variable region comprising an amino acid sequence that is at least

95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 899. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 895 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 899. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 896 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 899. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 897 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 899. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 898 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 899.

[0339] In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 908 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 909.

[0340] In some embodiments, an antibody provided herein binds to EphA2. In some embodiments, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences that are at least 80%, at least 85%, at least

90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequences of SEQ ID NOs: 910, 911, 912, 913, 914, and 915, respectively.

[0341] In some embodiments, the anti-EphA2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 916 and a light chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 917. In some embodiments, the anti-EphA2 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 918 or SEQ ID NO: 919 and a light chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of the amino acid sequence of SEQ ID NO: 920. In some embodiments, the anti-EphA2 antibody comprises a heavy chain comprising the amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 921 or SEQ ID NO: 922 and a light chain comprising the amino acid sequence of SEQ ID NO: 923. In some embodiments, the anti-EphA2 antibody comprises a heavy chain that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 924 or SEQ ID NO: 925 and a light chain comprising the amino acid sequence of SEQ ID NO: 926. In some embodiments, the antibody is h1C1 or 1C1.

[0342] In some embodiments, the anti-EphA2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 916 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 917.

[0343] In some embodiments, an antibody-drug conjugate provided herein binds to IGF-1R. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 558, 559, 560, 561, 562, and 563, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 564 and a light chain variable region comprising the

amino acid sequence of SEQ ID NO: 565. In some embodiments, the antibody of the antibody drug conjugate is cixutumumab.

[0344] In some embodiments, an antibody-drug conjugate provided herein binds to claudin-18.2. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 566, 567, 568, 569, 570, and 571, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 572 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 573. In some embodiments, the antibody of the antibody drug conjugate is zolbetuximab (175D10). In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 574, 575, 576, 577, 578, and 579, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 580 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 581. In some embodiments, the antibody of the antibody drug conjugate is 163E12.

[0345] In some embodiments, an antibody-drug conjugate provided herein binds to Nectin-4. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 582, 583, 584, 585, 586, and 587, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 588 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 589. In some embodiments, the antibody of the antibody drug conjugate is enfortumab. See WO 2012047724.

[0346] In some embodiments, an antibody-drug conjugate provided herein binds to SLTRK6. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 590, 591, 592, 593, 594, and 595, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 596 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 597. In some embodiments, the antibody of the antibody drug conjugate is sirtratumab.

[0347] In some embodiments, an antibody-drug conjugate provided herein binds to CD228. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 598, 599, 600, 601, 602, and 603, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 604 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 605. In some embodiments, the antibody of the antibody drug conjugate is hL49. See WO 2020/163225.

[0348] In some cases, an antibody provided herein binds to CD228. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 927, 928, 929, 930, 931, and 932, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 927, 928, 929, 930, 931, and 932, respectively. In some embodiments, the anti-CD228 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 933 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 934. In some embodiments, the anti-CD228 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either of SEQ ID NO: 935 or 936 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 937. In some embodiments, the anti-CD228 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either of SEQ ID NO: 938 or 939 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 940.

[0349] In some embodiments, an antibody-drug conjugate provided herein binds to CD142 (tissue factor; TF). In some embodiments, the antibody of the antibody drug

conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 606, 607, 608, 609, 610, and 611, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 612 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 613. In some embodiments, the antibody of the antibody drug conjugate is tisotumab. See WO 2010/066803.

[0350] In some embodiments, an antibody-drug conjugate provided herein binds to STn. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 614, 615, 616, 617, 618, and 619, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 620 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 621. In some embodiments, the antibody of the antibody drug conjugate is h2G12.

[0351] In some embodiments, an antibody-drug conjugate provided herein binds to CD20. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 622, 623, 624, 625, 626, and 627, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 628 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 629. In some embodiments, the antibody of the antibody drug conjugate is rituximab.

[0352] In some embodiments, an antibody-drug conjugate provided herein binds to HER2. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 630, 631, 632, 633, 634, and 635, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 636 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 637. In some embodiments, the antibody of the antibody drug conjugate is trastuzumab.

[0353] In some embodiments, an antibody-drug conjugate provided herein binds to FLT3.

- [0354] In some embodiments, an antibody-drug conjugate provided herein binds to CD46.
- [0355] In some embodiments, an antibody-drug conjugate provided herein binds to GloboH.
- [0356] In some embodiments, an antibody-drug conjugate provided herein binds to AG7.
- [0357] In some embodiments, an antibody-drug conjugate provided herein binds to mesothelin.
- [0358] In some embodiments, an antibody-drug conjugate provided herein binds to FCRH5.
- [0359] In some embodiments, an antibody-drug conjugate provided herein binds to ETBR.
- [0360] In some embodiments, an antibody-drug conjugate provided herein binds to Tim-1.
- [0361] In some embodiments, an antibody-drug conjugate provided herein binds to SLC44A4.
- [0362] In some embodiments, an antibody-drug conjugate provided herein binds to ENPP3.
- [0363] In some embodiments, an antibody-drug conjugate provided herein binds to CD37.
- [0364] In some embodiments, an antibody-drug conjugate provided herein binds to CA9.
- [0365] In some embodiments, an antibody-drug conjugate provided herein binds to Notch3.
- [0366] In some embodiments, an antibody-drug conjugate provided herein binds to EphA2.
- [0367] In some embodiments, an antibody-drug conjugate provided herein binds to TRFC.
- [0368] In some embodiments, an antibody-drug conjugate provided herein binds to PSMA.

[0369] In some embodiments, an antibody-drug conjugate provided herein binds to LRRC15.

[0370] In some embodiments, an antibody-drug conjugate provided herein binds to 5T4.

[0371] In some embodiments, an antibody-drug conjugate provided herein binds to CD79b. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 638, 639, 640, 641, 642, and 643, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 644 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 645. In some embodiments, the antibody of the antibody drug conjugate is polatuzumab.

[0372] In some embodiments, an antibody-drug conjugate provided herein binds to NaPi2B. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 646, 647, 648, 649, 650, and 651, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 652 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 653. In some embodiments, the antibody of the antibody drug conjugate is lifastuzumab.

[0373] In some embodiments, an antibody-drug conjugate provided herein binds to Muc16. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 654, 655, 656, 657, 658, and 659, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 660 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 661. In some embodiments, the antibody of the antibody drug conjugate is sofituzumab.

[0374] In some embodiments, an antibody-drug conjugate provided herein binds to STEAP1. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 662, 663, 664, 665, 666, and 667, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable

region comprising the amino acid sequence of SEQ ID NO: 668 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 669. In some embodiments, the antibody of the antibody drug conjugate is vandortuzumab.

[0375] In some embodiments, an antibody-drug conjugate provided herein binds to BCMA. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 670, 671, 672, 673, 674, and 675, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 676 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 677. In some embodiments, the antibody of the antibody drug conjugate is belantamab.

[0376] In some embodiments, an antibody-drug conjugate provided herein binds to c-Met. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 678, 679, 680, 681, 682, and 683, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 684 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 685. In some embodiments, the antibody of the antibody drug conjugate is telisotuzumab.

[0377] In some embodiments, an antibody-drug conjugate provided herein binds to EGFR. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 686, 687, 688, 689, 690, and 691, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 692 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 693. In some embodiments, the antibody of the antibody drug conjugate is depatuxizumab.

[0378] In some embodiments, an antibody-drug conjugate provided herein binds to SLAMF7. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 694, 695, 696, 697, 698, and 699, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable

region comprising the amino acid sequence of SEQ ID NO: 700 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 701. In some embodiments, the antibody of the antibody drug conjugate is azintuxizumab.

[0379] In some embodiments, an antibody-drug conjugate provided herein binds to SLITRK6. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 702, 703, 704, 705, 706, and 707, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 708 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 709. In some embodiments, the antibody of the antibody drug conjugate is sirtratumab.

[0380] In some embodiments, an antibody-drug conjugate provided herein binds to C4.4a. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 710, 711, 712, 713, 714, and 715, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 716 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 717. In some embodiments, the antibody of the antibody drug conjugate is lupatumab.

[0381] In some embodiments, an antibody-drug conjugate provided herein binds to GCC. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 718, 719, 720, 721, 722, and 723, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 724 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 725. In some embodiments, the antibody of the antibody drug conjugate is indusatumab.

[0382] In some embodiments, an antibody-drug conjugate provided herein binds to Axl. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 726, 727, 728, 729, 730, and 731, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising

the amino acid sequence of SEQ ID NO: 732 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 733. In some embodiments, the antibody of the antibody drug conjugate is enapotamab.

[0383] In some embodiments, an antibody-drug conjugate provided herein binds to gpNMB. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 734, 735, 736, 737, 738, and 739, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 740 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 741. In some embodiments, the anti-gpNMB antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1179 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1180. In some embodiments, the antibody of the antibody drug conjugate is glembatumumab.

[0384] In some embodiments, an antibody-drug conjugate provided herein binds to Prolactin receptor. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 742, 743, 744, 745, 746, and 747, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 748 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 749. In some embodiments, the antibody of the antibody drug conjugate is rolinsatamab.

[0385] In some embodiments, an antibody-drug conjugate provided herein binds to FGFR2. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 750, 751, 752, 753, 754, and 755, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 756 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 757. In some embodiments, the antibody of the antibody drug conjugate is aprutumab.

[0386] In some embodiments, an antibody-drug conjugate provided herein binds to CDCP1. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 758, 759, 760, 761, 762, and 763, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 764 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 765. In some embodiments, the antibody of the antibody drug conjugate is Humanized CUB4 #135 HC4-H. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 766, 767, 768, 769, 770, and 771, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 772 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 773. In some embodiments, the antibody of the antibody drug conjugate is CUB4. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 774, 775, 776, 777, 778, 779, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 780 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 781. In some embodiments, the antibody of the antibody drug conjugate is CP13E10-WT. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 782, 783, 784, 785, 786, and 787, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 788 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 789. In some embodiments, the antibody of the antibody drug conjugate is CP13E10-54HCv13-89LCv1. In some embodiments, an antibody-drug conjugate provided herein binds to CDCP1. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 764 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 1215. In some embodiments, the antibody of the antibody drug conjugate is Humanized CUB4 #135 HC4-H. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:

772 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 1216. In some embodiments, the antibody of the antibody drug conjugate is CUB4. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 774, 775, 1217, 777, 778, 779, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H3, comprising the amino acid sequence of SEQ ID NO: 1209.

[0387] In some embodiments, an antibody-drug conjugate provided herein binds to ASCT2. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 790 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 791. In some embodiments, the antibody of the antibody drug conjugate is KM8094a. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 792 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 793. In some embodiments, the antibody of the antibody drug conjugate is KM8094b. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 794, 795, 796, 797, 798, and 799, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 800 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 801. In some embodiments, the antibody of the antibody drug conjugate is KM4018.

[0388] In some embodiments, an antibody-drug conjugate provided herein binds to CD123. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 802, 803, 804, 805, 806, and 807, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 808 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 809. In some embodiments, the antibody of the antibody drug conjugate is h7G3. See WO 2016201065.

[0389] In some embodiments, an antibody-drug conjugate provided herein binds to GPC3. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid

sequences of SEQ ID NOs: 810, 811, 812, 813, 814, and 815, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 816 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 817. In some embodiments, the antibody of the antibody drug conjugate is hGPC3-1. See WO 2019161174. In some embodiments, an antibody-drug conjugate provided herein binds to GPC3. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 810, 1218, 812, 1219, 814, and 815, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H2, comprising the amino acid sequence of SEQ ID NO: 1218. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-L1, comprising the amino acid sequence of SEQ ID NO: 1219.

[0390] In some embodiments, an antibody-drug conjugate provided herein binds to B6A. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 818, 819, 820, 821, 822, and 823, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 824 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 825. In some embodiments, the antibody of the antibody drug conjugate is h2A2. See PCT/US20/63390. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 826, 827, 828, 829, 830, and 831, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 832 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 833. In some embodiments, the antibody of the antibody drug conjugate is h15H3. See WO 2013/123152.

[0391] In some embodiments, an antibody-drug conjugate provided herein binds to PD-L1. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 834, 835, 836, 837, 838, and 839, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 840 and a light chain variable region comprising the

amino acid sequence of SEQ ID NO: 841. In some embodiments, the antibody of the antibody drug conjugate is SG-559-01. See PCT/US2020/054037.

[0392] In some embodiments, an antibody-drug conjugate provided herein binds to TIGIT. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 842, 843, 844, 845, 846, and 847, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 848 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 849. In some embodiments, the antibody of the antibody drug conjugate is Clone 13 (also known as ADI-23674 or mAb13). See WO 2020041541. In some embodiments, an antibody-drug conjugate provided herein binds to TIGIT. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 842, 843, 1220, 845, 846, and 847, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H3, comprising the amino acid sequence of SEQ ID NO: 1220.

[0393] In some embodiments, an antibody-drug conjugate provided herein binds to STN. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 850, 851, 852, 853, 854, and 855, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 856 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 857. In some embodiments, the antibody of the antibody drug conjugate is 2G12-2B2. See WO 2017083582.

[0394] In some embodiments, an antibody-drug conjugate provided herein binds to CD33. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 858, 859, 860, 861, 862, and 863, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 864 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 865. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 864 and a light chain variable region comprising the

amino acid sequence of SEQ ID NO: 1221. In some embodiments, the antibody of the antibody drug conjugate is h2H12. See WO2013173496.

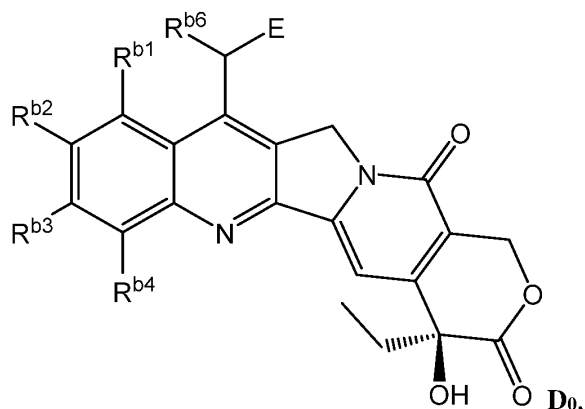
[0395] In some embodiments, an antibody-drug conjugate provided herein binds to NTBA (also known as CD352). In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 866, 867, 868, 869, 870, and 871, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 872 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 873. In some embodiments, the antibody of the antibody drug conjugate is h20F3 HDLD. See WO 2017004330.

[0396] In some embodiments, an antibody-drug conjugate provided herein binds to BCMA. In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 874, 875, 876, 877, 878, and 879, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 880 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 881. In some embodiments, the antibody of the antibody drug conjugate is SEA-BCMA (also known as hSG16.17). See WO 2017/143069.

[0397] In some embodiments, an antibody-drug conjugate provided herein binds to Tissue Factor (also known as TF). In some embodiments, the antibody of the antibody drug conjugate comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of SEQ ID NOs: 882, 883, 884, 885, 886, and 887, respectively. In some embodiments, the antibody of the antibody drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 888 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 889. In some embodiments, the antibody of the antibody drug conjugate is tisotumab. See WO 2010/066803 and US 9,150,658.

Camptothecin Compounds:

[0398] The Camptothecin compounds utilized in the various embodiments described herein are represented by the formula:



or a salt thereof; wherein;

E is $-\text{OR}^{\text{b5}}$ or $-\text{NR}^{\text{b5}}\text{R}^{\text{b5'}}$;

R^{b1} is selected from the group consisting of H, halogen, $-\text{CN}$, $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_1\text{-C}_8$ haloalkyl, $\text{C}_2\text{-C}_8$ alkenyl, $\text{C}_2\text{-C}_8$ alkynyl, $\text{C}_6\text{-C}_{12}$ aryl, 5- to 12-membered heteroaryl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, 3- to 10-membered heterocycloalkyl, $(\text{C}_6\text{-C}_{12} \text{ aryl})\text{-C}_2\text{-C}_8$ alkenyl-, $\text{C}_1\text{-C}_8$ hydroxyalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ aminoalkyl-, $\text{C}_1\text{-C}_8$ aminoalkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ alkyl-, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{C}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{O-C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-O-}$, $-\text{COOR}^{\text{a}}$, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; each optionally substituted with $\text{C}_1\text{-C}_3$ alkyl, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, $-\text{C}(\text{O})\text{R}^{\text{a}}$, and $-\text{SR}^{\text{a}}$; or

R^{b1} is combined with R^{b2} , R^{b5} , or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocycle or heterocycle;

R^{b2} is selected from the group consisting of H, halogen, $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_2\text{-C}_8$ alkynyl, $\text{C}_6\text{-C}_{12}$ aryl, 5- to 12-membered heteroaryl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, 3- to 10-membered heterocycloalkyl, $\text{C}_1\text{-C}_8$ haloalkyl, $\text{C}_1\text{-C}_8$ hydroxyalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{S}(\text{O})_2\text{-}$, $\text{C}_1\text{-C}_8$ aminoalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ aminoalkyl-, $\text{C}_1\text{-C}_8$ aminoalkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ alkyl-, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{O-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{C}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{O-C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-O-}$, $-\text{COOR}^{\text{a}}$, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; each optionally substituted with $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a;

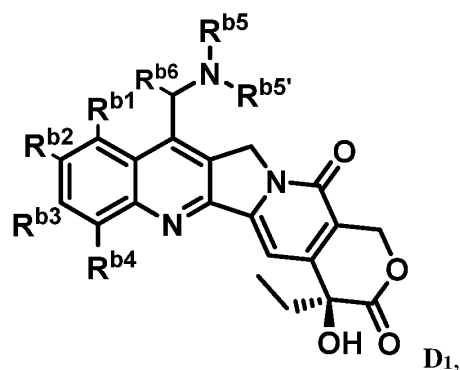
R^{b4} is selected from the group consisting of H or halogen;

each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₆ alkyl-O-C₁-C₆ alkyl-, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, heteroaryl-C₁-C₆ hydroxyalkyl, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and $R^{a'}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-; or



or a salt thereof; wherein;

R^{b1} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b1} is combined with R^{b2} , R^{b5} , or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;
each R^{b5} and $R^{b5'}$ are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, and heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or
 $R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;
 R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and
 R^a and $R^{a'}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-.

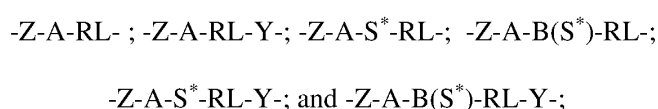
[0399] Still other Camptothecin compounds useful in the context of the Camptothecin Conjugates and Camptothecin Linker compounds described herein are Camptothecin compounds of formula **D1**, **D1a**, **D1b**, or any subformula thereof, or any of the compounds of Table I, which in some embodiments have an additional group including, but not limited to a hydroxyl, thiol, amine or amide functional group whose oxygen, sulfur or optionally substituted nitrogen atom is capable of incorporation into a linker, and is capable of being

released from a Camptothecin Conjugate as a free drug. In some embodiments, that functional group provides the only site on the camptothecin compound available for attachment to the Linker Unit (Q). The resulting drug-linker moiety of a Camptothecin Conjugate is one that is capable of releasing active free drug at the site targeted by its Ligand Unit in order to exert a cytotoxic, cytostatic or immunosuppressive effect.

[0400] “Free drug” refers to drug, as it exists once released from the drug-linker moiety. In some embodiments, the free drug includes a fragment of the Releasable Linker or Spacer Unit (Y) group. Free drug, which includes a fragment of the Releasable Linker or Spacer Unit (Y), are released from the remainder of the drug-linker moiety via cleavage of the releasable linker or released via the cleavage of a bond in the Spacer Unit (Y) group and is biologically active after release. In some embodiments, the free drug differs from the conjugated drug in that the functional group of the free drug for attachment to the self-immolative assembly unit is no longer associated with components of the Camptothecin Conjugate (other than a previously shared heteroatom). For example, the free hydroxyl functional group of an alcohol-containing drug can be represented as $D-O^*H$, whereas in the conjugated form the oxygen heteroatom designated by O^* is incorporated into the methylene carbamate unit of a self-immolative unit. Upon activation of the self-immolative moiety and release of free drug, the covalent bond to O^* is replaced by a hydrogen atom so that the oxygen heteroatom designated by O^* is present on the free drug as $-O-H$.

Linker Unit (Q)

[0401] As noted above, in some embodiments, the Linker Unit Q has a formula selected from the group consisting of:



wherein Z is a Stretcher Unit; A is a bond or a Connector Unit; B is a Parallel Connector Unit; S^* is a Partitioning Agent; RL is Releasable Linker; and Y is a Spacer Unit; and wherein the point of attachment of D to Q is through any one of the heteroatoms of the hydroxyl and primary and secondary amines present on formula **D1**, **D1a**, **D1b**, or any subformula thereof, or any of the compounds of Table I.

[0402] In other embodiments, the Linker Unit Q has a formula selected from the group consisting of:

-Z-A-; -Z-A-RL-; -Z-A-S^{*}-W-; -Z-A-B(S^{*})-W-; -Z-A-S^{*}-RL-; -Z-A-B(S^{*})-RL-;
 -Z-A-S^{*}-W-RL-; and -Z-A-B(S^{*})-W-RL-;

wherein Z is a Stretcher Unit, A is a bond or a Connector Unit; B is a Parallel Connector Unit; S^{*} is a Partitioning Agent; RL is a Releasable Linker other than a Glycoside (e.g., Glucuronide) Unit; and W is an Amino Acid Unit; and

wherein the point of attachment to Q is through the hydroxyl group substituent of the lactone ring of formula **D1**, **D1a**, **D1b**, or any subformula thereof, or any of the compounds of Table I.

[0403] In one group of embodiments, Q has a formula selected from the group consisting of: -Z-A-S^{*}-RL- and -Z-A-S^{*}-RL-Y-.

[0404] In another group of embodiments, Q has a formula selected from the group consisting of -Z-A-B(S^{*})-RL- and -Z-A-B(S^{*})-RL-Y-.

[0405] In still another group of embodiments, Q has a formula selected from the group consisting of -Z-A-RL- and -Z-A-RL-Y-.

Stretcher Unit (Z) or (Z'):

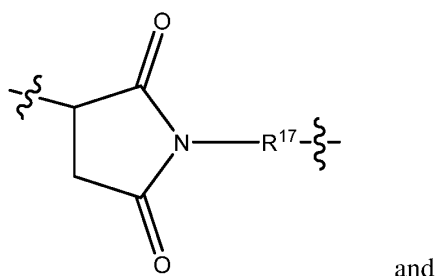
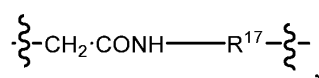
[0406] A Stretcher Unit (Z) is a component of a Camptothecin Conjugate or a Camptothecin-Linker Compound or other intermediate that acts to connect the Ligand Unit to the remainder of the conjugate. In that regard a Stretcher Unit, prior to attachment to a Ligand Unit (i.e. a Stretcher Unit precursor, Z'), has a functional group that can form a bond with a functional group of a targeting ligand.

[0407] In some embodiments, a Stretcher Unit precursor (Z') has an electrophilic group that is capable of interacting with a reactive nucleophilic group present on a Ligand Unit (e.g., an antibody) to provide a covalent bond between a Ligand Unit and the Stretcher Unit of a Linker Unit. Nucleophilic groups on an antibody having that capability include but are not limited to, sulfhydryl, hydroxyl and amino functional groups. The heteroatom of the nucleophilic group of an antibody can be reactive to an electrophilic group on a Stretcher Unit precursor and can provide a covalent bond between the Ligand Unit and Stretcher Unit of a Linker Unit or Drug-Linker moiety. Useful electrophilic groups for that purpose include, but are not limited to, maleimide, haloacetamide groups, and NHS esters. The electrophilic group provides a convenient site for antibody attachment to form a Camptothecin Conjugate or Ligand Unit-Linker intermediate.

[0408] In other embodiments, a Stretcher Unit precursor has a reactive site which has a nucleophilic group that is reactive to an electrophilic group present on a Ligand Unit (e.g., an antibody). Useful electrophilic groups on an antibody for that purpose include, but are not limited to, aldehyde and ketone carbonyl groups. The heteroatom of a nucleophilic group of a Stretcher Unit precursor can react with an electrophilic group on an antibody and form a covalent bond to the antibody. Useful nucleophilic groups on a Stretcher Unit precursor for that purpose include, but are not limited to, hydrazide, hydroxylamine, amino, hydrazine, thiosemicarbazone, hydrazine carboxylate, and arylhydrazide. The electrophilic group on an antibody provides a convenient site for antibody attachment to form a Camptothecin Conjugate or Ligand Unit-Linker intermediate.

[0409] In some embodiments, a sulfur atom of a Ligand Unit is bound to a succinimide ring system of a Stretcher Unit formed by reaction of a thiol functional group of a targeting ligand with a maleimide moiety of the corresponding Stretcher Unit precursor. In other embodiments, a thiol functional group of a Ligand Unit reacts with an alpha haloacetamide moiety to provide a sulfur-bonded Stretcher Unit by nucleophilic displacement of its halogen substituent.

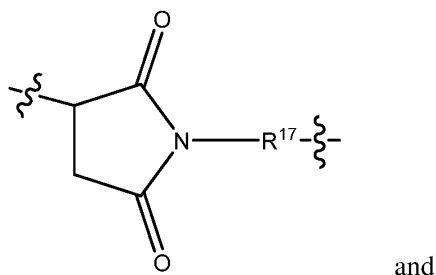
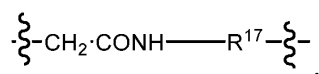
[0410] Representative Stretcher Units of such embodiments include those having the structures of:



wherein the wavy line adjacent to R¹⁷ indicates attachment to the Parallel Connector Unit (B) or Connector Unit (A) if B is absent, or a Partitioning Agent (S*), if B is absent, the other wavy line indicates covalent attachment to a sulfur atom of a Ligand Unit, and R¹⁷ is -C₁-C₁₀ alkylene-, C₁-C₁₀ heteroalkylene-, -C₃-C₈ carbocyclo-, -O-(C₁-C₈ alkylene)-, -arylene-, -C₁-C₁₀ alkylene-arylene-, -arylene-C₁-C₁₀ alkylene-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-, -(C₃-

C₈ carbocyclo)-C₁-C₁₀ alkylene-, -C₃-C₈ heterocyclo-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-, -C₁-C₁₀ alkylene-C(=O)-, C₁-C₁₀ heteroalkylene-C(=O)-, -C₃-C₈ carbocyclo-C(=O)-, -O-(C₁-C₈ alkylene)-C(=O)-, -arylene-C(=O)-, -C₁-C₁₀ alkylene-arylene-C(=O)-, -arylene-C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-C(=O)-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-C(=O)-, -C₃-C₈ heterocyclo-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-C(=O)-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ heteroalkylene-NH-, -C₃-C₈ carbocyclo-NH-, -O-(C₁-C₈ alkylene)-NH-, -arylene-NH-, -C₁-C₁₀ alkylene-arylene-NH-, -arylene-C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-NH-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-NH-, -C₃-C₈ heterocyclo-NH-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-NH-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ alkylene-S-, C₁-C₁₀ heteroalkylene-S-, -C₃-C₈ carbocyclo-S-, -O-(C₁-C₈ alkylene)-S-, -arylene-S-, -C₁-C₁₀ alkylene-arylene-S-, -arylene-C₁-C₁₀ alkylene-S-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-S-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-S-, -C₃-C₈ heterocyclo-S-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-S-, or -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-S-.

[0411] Representative Stretcher Units of such embodiments include those having the structures of:



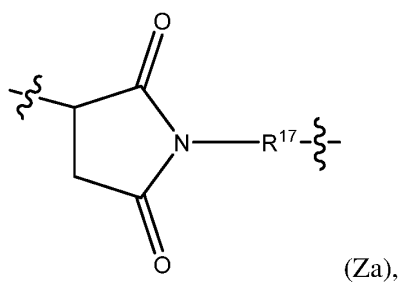
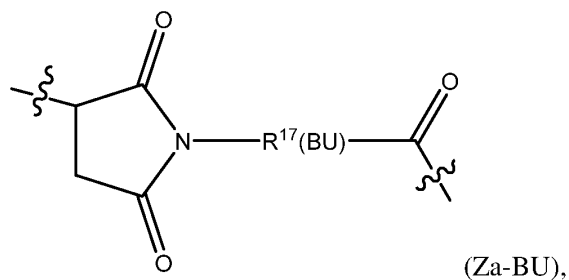
wherein the wavy line adjacent to R¹⁷ indicates attachment to the Parallel Connector Unit (B) or Connector Unit (A) if B is absent, or a Partitioning Agent (S*), if B is absent, the other wavy line indicates covalent attachment to a sulfur atom of a Ligand Unit, and R¹⁷ is -C₁-C₁₀ alkylene-, -CH₂-CH₂-(OCH₂CH₂)_k-, C₁-C₁₀ heteroalkylene-, -C₃-C₈ carbocyclo-, -O-(C₁-C₈ alkylene)-, -arylene-, -C₁-C₁₀ alkylene-arylene-, -arylene-C₁-C₁₀ alkylene-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-, -C₃-C₈ heterocyclo-, -C₁-C₁₀

alkylene-(C₃-C₈ heterocyclo)-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-, -C₁-C₁₀ alkylene-C(=O)-, C₁-C₁₀ heteroalkylene-C(=O)-, -C₃-C₈ carbocyclo-C(=O)-, -O-(C₁-C₈ alkylene)-C(=O)-, -arylene-C(=O)-, -C₁-C₁₀ alkylene-arylene-C(=O)-, -arylene-C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-C(=O)-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-C(=O)-, -C₃-C₈ heterocyclo-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-C(=O)-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ heteroalkylene-NH-, -C₃-C₈ carbocyclo-NH-, -O-(C₁-C₈ alkylene)-NH-, -arylene-NH-, -C₁-C₁₀ alkylene-arylene-NH-, -arylene-C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-NH-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-NH-, -C₃-C₈ heterocyclo-NH-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-NH-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ alkylene-S-, C₁-C₁₀ heteroalkylene-S-, -C₃-C₈ carbocyclo-S-, -O-(C₁-C₈ alkylene)-S-, -arylene-S-, -C₁-C₁₀ alkylene-arylene-S-, -arylene-C₁-C₁₀ alkylene-S-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-S-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-S-, -C₃-C₈ heterocyclo-S-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-S-, or -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-S-, wherein k is an integer ranging from 1 to 36. In some embodiments, R¹⁷ is -C₁-C₁₀ alkylene-. In some embodiments, R¹⁷ is -CH₂-CH₂-(OCH₂CH₂)_k-, wherein k is an integer ranging from 1 to 36.

[0412] In some embodiments, the R¹⁷ group is optionally substituted by a Basic Unit (BU) such as an aminoalkyl moiety, e.g. -(CH₂)_xNH₂, -(CH₂)_xNHR^a, and -(CH₂)_xNR^a₂, wherein subscript x is an integer of from 1-4 and each R^a is independently selected from the group consisting of C₁₋₆ alkyl and C₁₋₆ haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form an azetidiny, pyrrolidinyl or piperidinyl group.

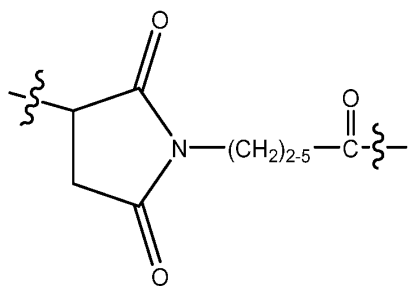
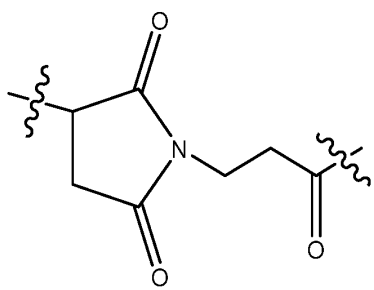
[0413] An illustrative Stretcher Unit is that of Formula Za or Za-BU in which R¹⁷ is -C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ heteroalkylene-C(=O)-, -C₃-C₈ carbocyclo-C(=O)-, -O-(C₁-C₈ alkylene)-C(=O)-, -arylene-C(=O)-, -C₁-C₁₀ alkylene-arylene-C(=O)-, -arylene-C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-C(=O)-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-C(=O)-, -C₃-C₈ heterocyclo-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-C(=O)-, or -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-C(=O)-.

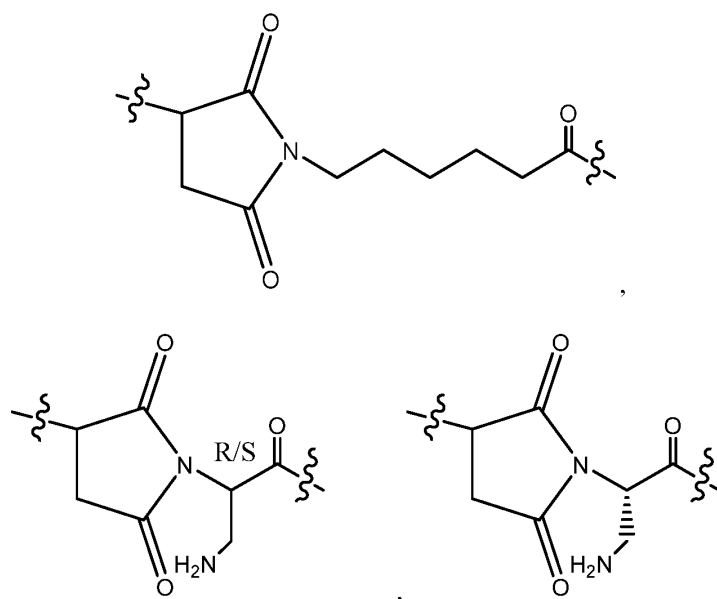
[0414] Accordingly, some preferred embodiments are represented by formula Za and Za-BU:



wherein the wavy line adjacent the carbonyl carbon atom indicates attachment to L^P , B, A, or S^* , in the formulae above, depending on the presence or absence of A and/or B, and the other wavy line indicates covalent bonding of the succinimide ring carbon atom to a sulfur atom of a Ligand Unit. During synthesis, the basic amino functional group of the Basic Unit (BU) can be protected by a protecting group.

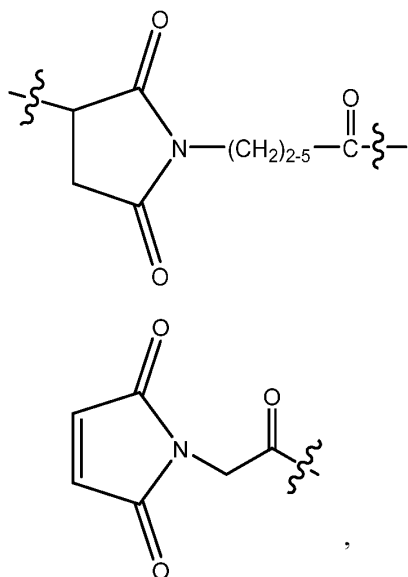
[0415] More preferred embodiments of Stretcher Units of formula Za and Za-BU are as follows:

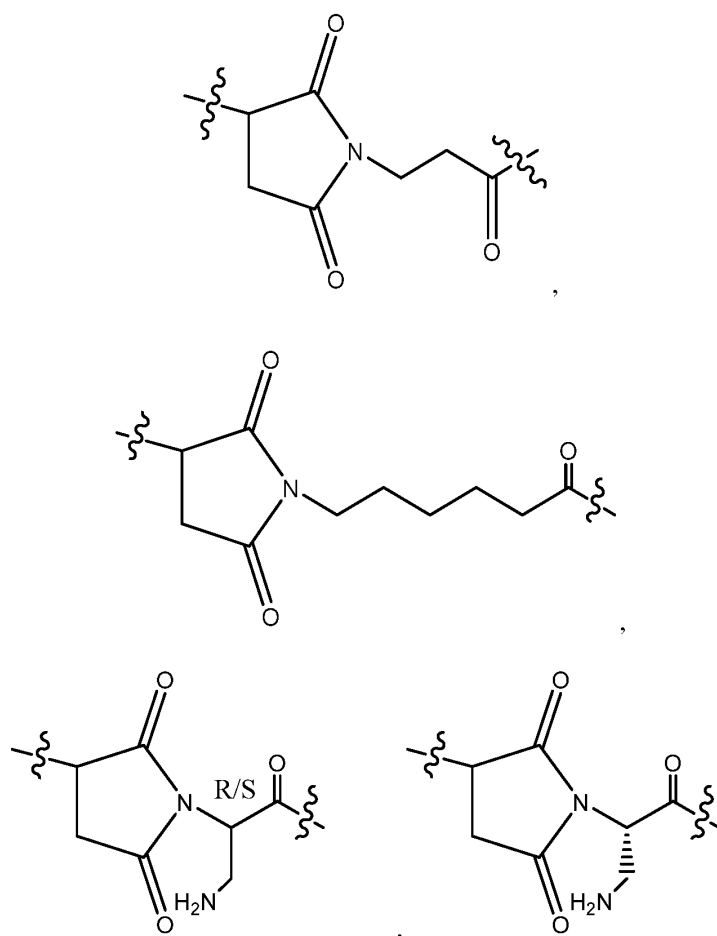




wherein the wavy line adjacent the carbonyl carbon atom indicates attachment to B, A, or S*, in the formulae above, depending on the presence or absence of A and/or B, and the other wavy line indicates covalent bonding of the succinimide ring carbon atom to a sulfur atom of a Ligand Unit.

[0416] Other preferred embodiments of Stretcher Units of formula Za and Za-BU are as follows:

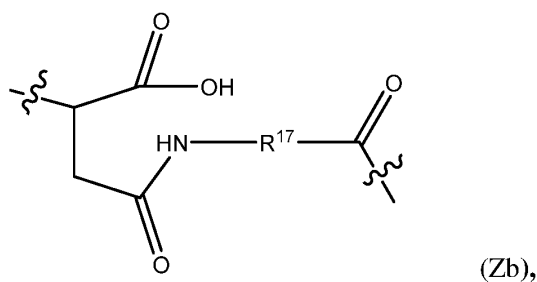
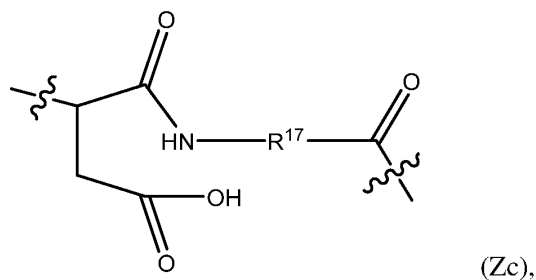
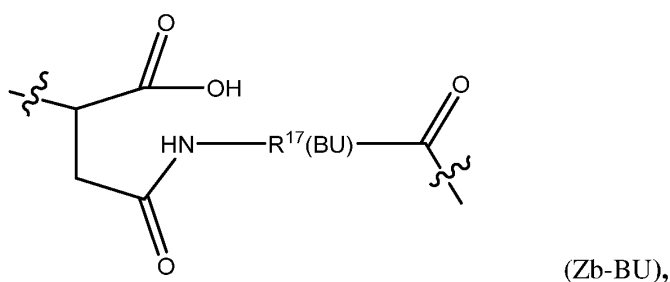
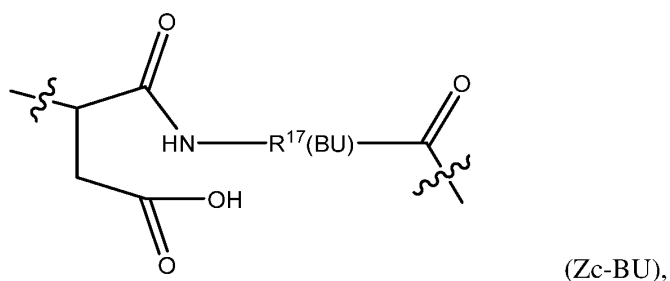




wherein the wavy line adjacent the carbonyl carbon atom indicates attachment to B, A, or S*, in the formulae above, depending on the presence or absence of A and/or B, and the other wavy line indicates covalent bonding of the succinimide ring carbon atom to a sulfur atom of a Ligand Unit.

[0417] It will be understood that a Ligand Unit-substituted succinimide may exist in hydrolyzed form(s). Those forms are exemplified below for hydrolysis of Za or Za-BU, wherein the structures representing the regioisomers from that hydrolysis have formula Zb and Zc or Zb-BU and Zc-BU.

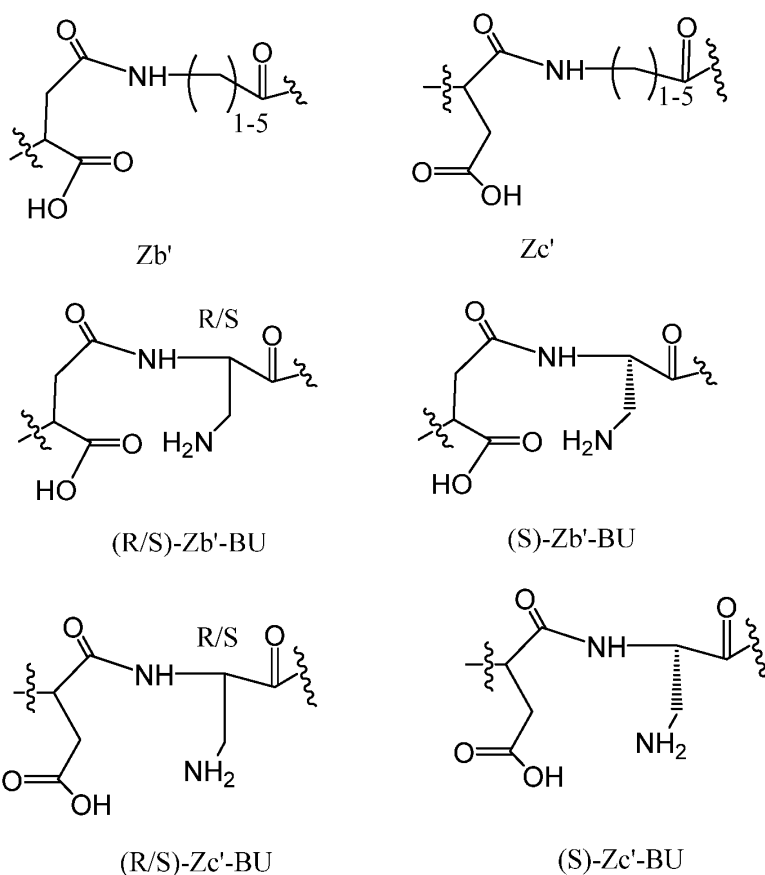
[0418] Accordingly, in other preferred embodiments a Stretcher unit (Z) is comprised of a succinic acid-amide moiety represented by the following:



wherein the wavy line adjacent to the carbonyl carbon atom bonded to R^{17} and the wavy line adjacent to the carbon atom of the acid-amide moiety is as defined for Za or Za-BU, depending on the presence or absence of A and/or B; and R^{17} is $-C_1-C_5$ alkylene-, wherein in Zb-BU and Zc-BU the alkylene is substituted by a Basic Unit (BU), wherein BU is $-(CH_2)_xNH_2$, $-(CH_2)_xNHR^a$, or $-(CH_2)_xN(R^a)_2$, wherein subscript x is an integer of from 1-4 and each R^a is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl, or both R^a together with the nitrogen to which they are attached define an azetidiny, pyrrolidiny or piperidiny group.

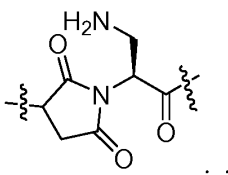
[0419] In more preferred embodiment, -Z-A- comprises a moiety derived from a maleimido-alkanoic acid moiety or an mDPR moiety. See, for example, see WO 2013/173337. In one group of embodiments, Z-A- is derived from a maleimido-propionyl moiety.

[0420] Accordingly, in some of those more preferred embodiments, a Stretcher unit (Z) is comprised of a succinic acid-amide moiety represented by the structure of formula Zb', Zc', (R/S)-Zb'-BU, (S)-Zb'-BU, (R/S)-Zc'-BU or (S)-Zc'-BU as follows:

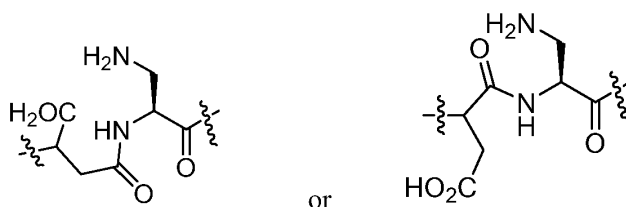


wherein the wavy lines are as defined for Za or Za-BU.

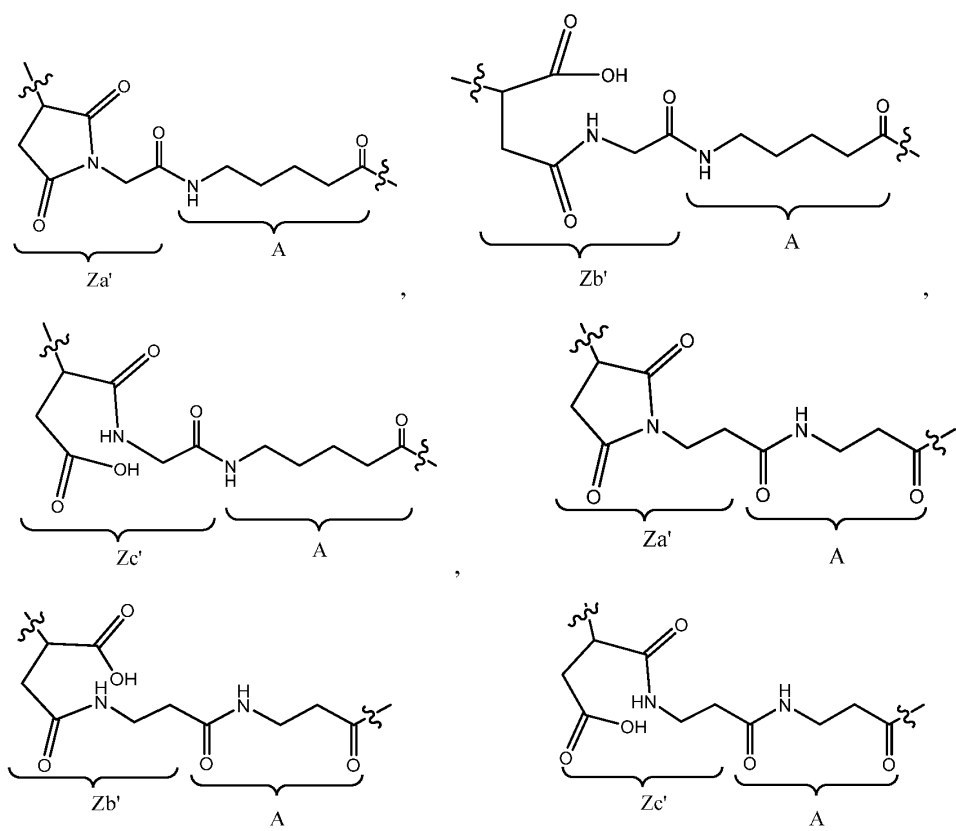
[0421] In particularly preferred embodiments, a Stretcher unit (Z) is comprised of a succinimide moiety represented by the structure of

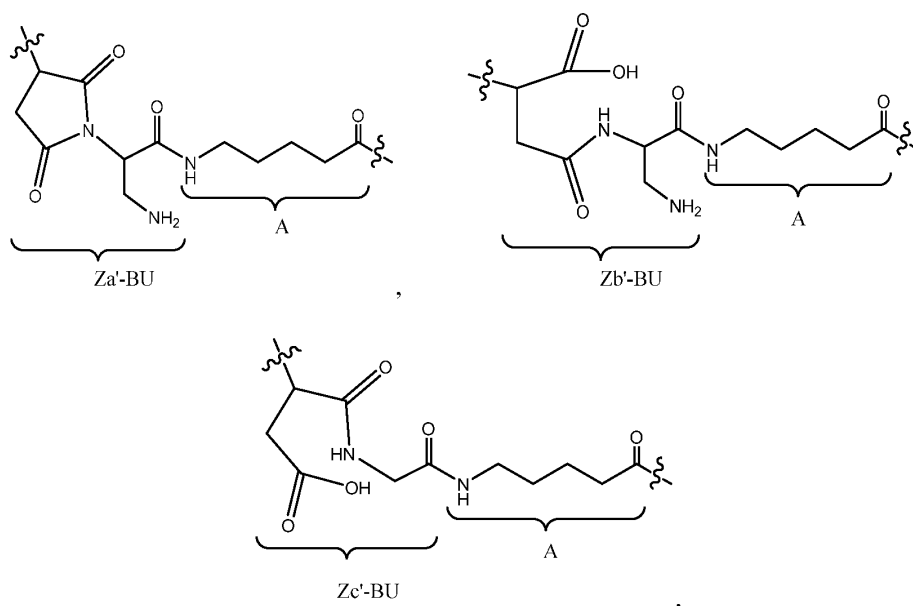


which may be generated from a maleimido-amino-propionyl (mDPR) analog (a 3-amino-2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoic acid derivative), or is comprised of a succinic acid-amide moiety represented by the structure of:



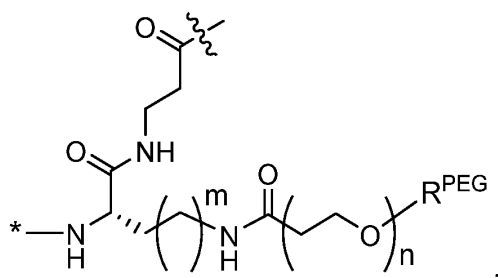
[0422] Illustrative Stretcher Units bonded to a Connector Unit (A) which are comprised of Za', Zb' or Zc', in which $-R^{17}-$ of Za, Zb or Zc is $-\text{CH}_2-$ or $-\text{CH}_2\text{CH}_2-$, or are comprised of Za'-BU, Zb'-BU or Zc'-BU in which $-R^{17}(\text{BU})-$ of Za-BU, Zb-BU or Zc-BU is $-\text{CH}(\text{CH}_2\text{NH}_2)-$, have the following structures:





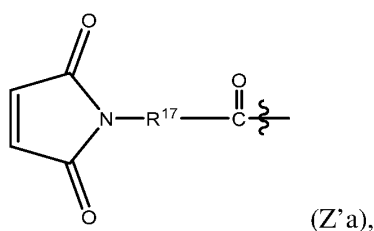
wherein the wavy lines are as defined for Za or Za-BU.

[0423] Other Stretcher Units bonded to a Ligand Unit (L) and a Connector Unit (A) have the structures above wherein A in any one of the above -Za-A-, -Za(BU)-A-, -Za'-A-, -Za'(BU)-A-, -Zb-A-, -Zb(BU)-A-, -Zb'-A-, -Zb'(BU)-A-, -Zc'-A- and Zc'(BU)-A- structures is replaced by a Parallel Connector Unit having the structure of:



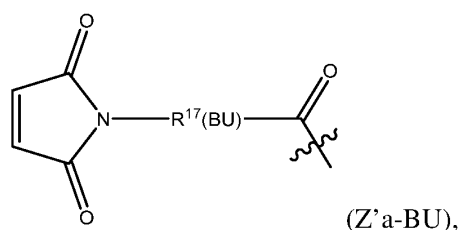
wherein subscript m ranges from 1 to 6; n ranges from 8 to 24; R^{PEG} is a PEG Capping Unit, preferably H, -CH₃, or -CH₂CH₂CO₂H, the asterisk (*) indicates covalent attachment to a Stretcher Unit corresponding in structure to formula Za, Za', Zb' or Zc' and the wavy line indicates covalent attachment to the Releasable Linker (RL).

[0424] Illustrative Stretcher Units prior to conjugation to the Ligand Unit (i.e., Stretcher Unit precursors) are comprised of a maleimide moiety and are represented by structures including that of formula Z'a



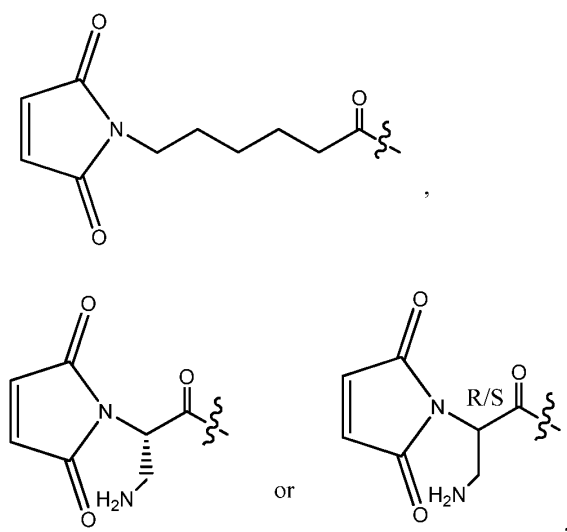
wherein the wavy line adjacent the carbonyl carbon atom indicates attachment to B, A, or S*, in the formulae above, depending on the presence or absence of A and/or B, R¹⁷ is -(CH₂)₁₋₅-, optionally substituted with a Basic Unit, such as an optionally substituted aminoalkyl, e.g., -(CH₂)_xNH₂, -(CH₂)_xNHR^a, and -(CH₂)_xN(R^a)₂, wherein subscript x is an integer of from 1-4 and each R^a is independently selected from the group consisting of C₁₋₆ alkyl and C₁₋₆ haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form an azetidiny, pyrrolidinyl or piperidinyl group.

[0425] Other illustrative Stretcher Units prior to conjugation to the Ligand Unit (i.e., Stretcher Unit precursors) are comprised of a maleimide moiety and are represented by structures including that of formula Z'a-BU.



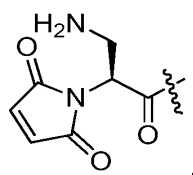
wherein the wavy line adjacent the carbonyl carbon atom indicates attachment to B, A, or S*, in the formulae above, depending on the presence or absence of A and/or B, R¹⁷ is -(CH₂)₁₋₅-, substituted with a Basic Unit, such as an optionally substituted aminoalkyl, e.g., -(CH₂)_xNH₂, -(CH₂)_xNHR^a, and -(CH₂)_xN(R^a)₂, wherein subscript x is an integer of from 1-4, preferably R¹⁷ is -CH₂- or -CH₂CH₂- and subscript x is 1 or 2, and each R^a is independently selected from the group consisting of C₁₋₆ alkyl and C₁₋₆ haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form an azetidiny, pyrrolidinyl or piperidinyl group.

[0426] In some preferred embodiments of formula Z'a, a Stretcher Unit precursor (Z') is represented by one of the following structures:



wherein the wavy line adjacent to the carbonyl is as defined for Z'a or Z'a-BU.

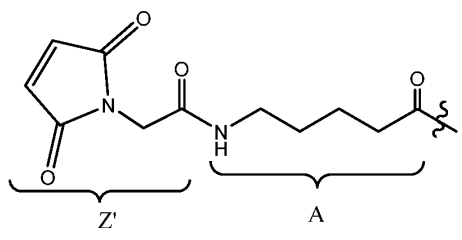
[0427] In more preferred embodiments the Stretcher unit precursor (Z') is comprised of a maleimide moiety and is represented by the structure of:

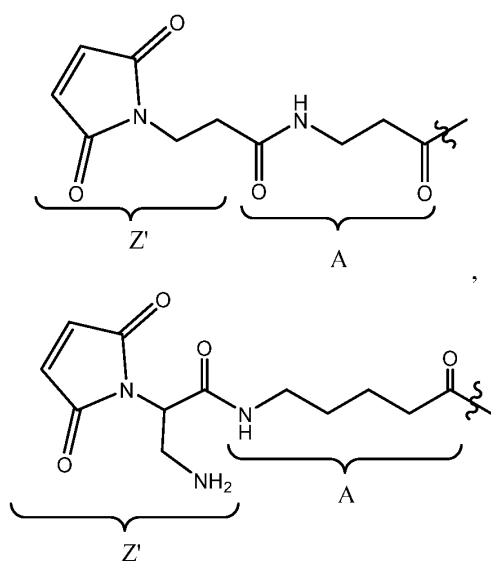


wherein the wavy line adjacent to the carbonyl is as defined for Za' and the amino group is optional protonated or protected by an amino protecting group.

[0428] In Stretcher Units having a BU moiety, it will be understood that the amino functional group of that moiety is typically protected by an amino protecting group during synthesis, e.g., an acid labile protecting group (e.g., BOC).

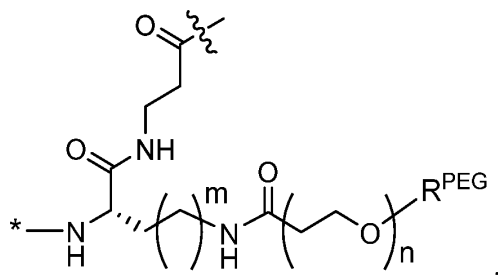
[0429] Illustrative Stretcher Unit precursors covalently attached to a Connector Unit that are comprised of the structure of Z'a or Z'a-BU in which $-R^{17}-$ or $-R^{17}(BU)-$ is $-\text{CH}_2-$, $-\text{CH}_2\text{CH}_2-$ or $-\text{CH}(\text{CH}_2\text{NH}_2)-$ have the following structures:





wherein the wavy line adjacent to the carbonyl is as defined for Z'a or Z'a-BU.

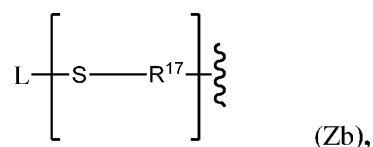
[0430] Other Stretcher Unit precursors bonded a Connector Unit (A) have the structures above wherein A in any one of the above Z'-A- and Z'(BU)-A- structures is replaced by a Parallel Connector Unit and Partitioning Agent (-B(S*)-) having the structure of



wherein subscript m ranges from 1 to 6; n ranges from 8 to 24; R^{PEG} is a PEG Capping Unit, preferably H, -CH₃, or -CH₂CH₂CO₂H, the asterisk (*) indicates covalent attachment to the Stretcher Unit precursor corresponding in structure to formula Za or Za' and the wavy line indicates covalent attachment to RL. In instances such as those shown here, the shown PEG group is meant to be exemplary of a variety of Partitioning Agents including PEG groups of different lengths and other Partitioning Agents that can be directly attached or modified for attachment to the Parallel Connector Unit.

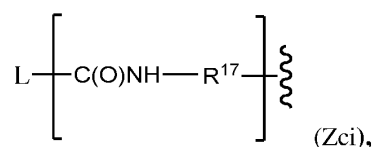
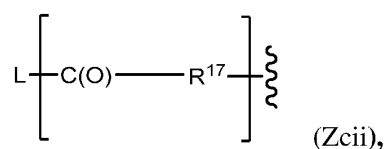
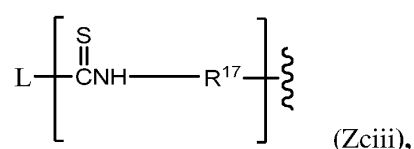
[0431] In another embodiment, the Stretcher Unit is attached to the Ligand Unit via a disulfide bond between a sulfur atom of the Ligand Unit and a sulfur atom of the Stretcher

unit. A representative Stretcher Unit of this embodiment is depicted within the square brackets of Formula Zb:



wherein the wavy line indicates attachment to the Parallel Connector Unit (B) or Connector Unit (A) if B is absent or a Partitioning Agent (S^*), if A and B are absent and R^{17} is -C₁-C₁₀ alkylene-, C₁-C₁₀ heteroalkylene-, -C₃-C₈ carbocyclo-, -O-(C₁-C₈ alkylene)-, -arylene-, -C₁-C₁₀ alkylene-arylene-, -arylene-C₁-C₁₀ alkylene-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-, -C₃-C₈ heterocyclo-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-, -C₁-C₁₀ alkylene-C(=O)-, C₁-C₁₀ heteroalkylene-C(=O)-, -C₃-C₈ carbocyclo-C(=O)-, -O-(C₁-C₈ alkylene)-C(=O)-, -arylene-C(=O)-, -C₁-C₁₀ alkylene-arylene-C(=O)-, -arylene-C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-C(=O)-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-C(=O)-, -C₃-C₈ heterocyclo-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-C(=O)-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ alkylene-NH-, C₁-C₁₀ heteroalkylene-NH-, -C₃-C₈ carbocyclo-NH-, -O-(C₁-C₈ alkylene)-NH-, -arylene-NH-, -C₁-C₁₀ alkylene-arylene-NH-, -arylene-C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-NH-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-NH-, -C₃-C₈ heterocyclo-NH-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-NH-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ alkylene-S-, C₁-C₁₀ heteroalkylene-S-, -C₃-C₈ carbocyclo-S-, -O-(C₁-C₈ alkylene)-S-, -arylene-S-, -C₁-C₁₀ alkylene-arylene-S-, -arylene-C₁-C₁₀ alkylene-S-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-S-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-S-, -C₃-C₈ heterocyclo-S-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-S-, or -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-S-.

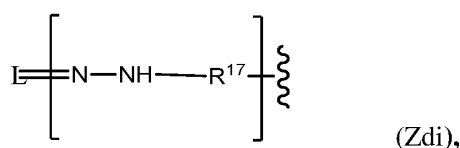
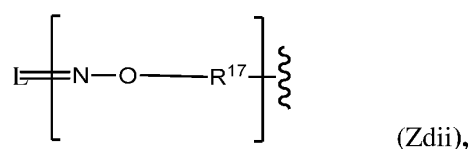
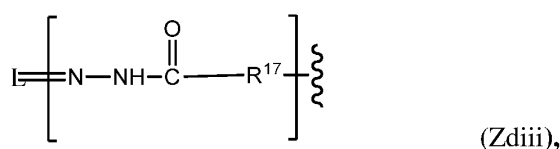
[0432] In yet another embodiment, the reactive group of a Stretcher Unit precursor contains a reactive site that can form a bond with a primary or secondary amino group of a Ligand Unit. Examples of these reactive sites include, but are not limited to, activated esters such as succinimide esters, 4-nitrophenyl esters, pentafluorophenyl esters, tetrafluorophenyl esters, anhydrides, acid chlorides, sulfonyl chlorides, isocyanates and isothiocyanates. Representative Stretcher Units of this embodiment are depicted within the square brackets of Formulas Zci, Zcii and Zciii:



wherein the wavy line indicates attachment to the Parallel Connector Unit (B) or Connector Unit (A) if B is absent or a Partitioning Agent (S^*), if A and B are absent and R^{17} is -C₁-C₁₀ alkylene-, C₁-C₁₀ heteroalkylene-, -C₃-C₈ carbocyclo-, -O-(C₁-C₈ alkylene)-, -arylene-, -C₁-C₁₀ alkylene-arylene-, -arylene-C₁-C₁₀ alkylene-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-, -C₃-C₈ heterocyclo-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-, -C₁-C₁₀ alkylene-C(=O)-, C₁-C₁₀ heteroalkylene-C(=O)-, -C₃-C₈ carbocyclo-C(=O)-, -O-(C₁-C₈ alkylene)-C(=O)-, -arylene-C(=O)-, -C₁-C₁₀ alkylene-arylene-C(=O)-, -arylene-C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-C(=O)-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-C(=O)-, -C₃-C₈ heterocyclo-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-C(=O)-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ alkylene-NH-, C₁-C₁₀ heteroalkylene-NH-, -C₃-C₈ carbocyclo-NH-, -O-(C₁-C₈ alkylene)-NH-, -arylene-NH-, -C₁-C₁₀ alkylene-arylene-NH-, -arylene-C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-NH-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-NH-, -C₃-C₈ heterocyclo-NH-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-NH-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ alkylene-S-, C₁-C₁₀ heteroalkylene-S-, -C₃-C₈ carbocyclo-S-, -O-(C₁-C₈ alkylene)-S-, -arylene-S-, -C₁-C₁₀ alkylene-arylene-S-, -arylene-C₁-C₁₀ alkylene-S-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-S-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-S-, -C₃-C₈ heterocyclo-S-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-S-, or -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-S-.

[0433] In still other embodiments, the reactive group of the Stretcher Unit precursor contains a reactive nucleophile that is capable of reacting with an electrophile present on, or introduced to, a Ligand Unit. For example, a carbohydrate moiety on a targeting ligand can

be mildly oxidized using a reagent such as sodium periodate and the resulting electrophilic functional group (-CHO) of the oxidized carbohydrate can be condensed with a Stretcher Unit precursor that contains a reactive nucleophile such as a hydrazide, an oxime, a primary or secondary amine, a hydrazine, a thiosemicarbazone, a hydrazine carboxylate, or an arylhydrazide such as those described by Kaneko, T. *et al.* (1991) Bioconjugate Chem. 2:133-41. Representative Stretcher Units of this embodiment are depicted within the square brackets of Formulas Zdi, Zdii, and Zdiii:



wherein the wavy line indicates attachment to the Parallel Connector Unit (B) or Connector Unit (A), or a Partitioning Agent (S*), if A and B are absent and R¹⁷ is -C₁-C₁₀ alkylene-, C₁-C₁₀ heteroalkylene-, -C₃-C₈ carbocyclo-, -O-(C₁-C₈ alkylene)-, -arylene-, -C₁-C₁₀ alkylene-arylene-, -arylene-C₁-C₁₀ alkylene-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-, -C₃-C₈ heterocyclo-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-, -C₁-C₁₀ alkylene-C(=O)-, C₁-C₁₀ heteroalkylene-C(=O)-, -C₃-C₈ carbocyclo-C(=O)-, -O-(C₁-C₈ alkylene)-C(=O)-, -arylene-C(=O)-, -C₁-C₁₀ alkylene-arylene-C(=O)-, -arylene-C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-C(=O)-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-C(=O)-, -C₃-C₈ heterocyclo-C(=O)-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-C(=O)-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-C(=O)-, -C₁-C₁₀ alkylene-NH-, C₁-C₁₀ heteroalkylene-NH-, -C₃-C₈ carbocyclo-NH-, -O-(C₁-C₈ alkylene)-NH-, -arylene-NH-, -C₁-C₁₀ alkylene-arylene-NH-, -arylene-C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-NH-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-NH-, -C₃-C₈ heterocyclo-NH-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-NH-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-NH-, -C₁-C₁₀ alkylene-S-, C₁-C₁₀ heteroalkylene-S-, -C₃-C₈ carbocyclo-S-, -O-

(C₁-C₈ alkylene)-S-, -arylene-S-, -C₁-C₁₀ alkylene-arylene-S-, -arylene-C₁-C₁₀ alkylene-S-, -C₁-C₁₀ alkylene-(C₃-C₈ carbocyclo)-S-, -(C₃-C₈ carbocyclo)-C₁-C₁₀ alkylene-S-, -C₃-C₈ heterocyclo-S-, -C₁-C₁₀ alkylene-(C₃-C₈ heterocyclo)-S-, or -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-S-.

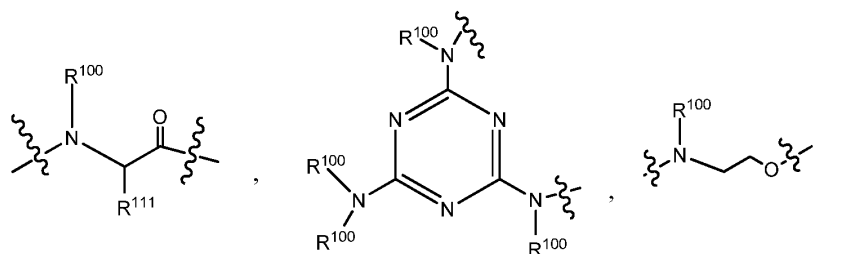
[0434] In some aspects of the present invention the Stretcher Unit has a mass of no more than about 1000 daltons, no more than about 500 daltons, no more than about 200 daltons, from about 30, 50, or 100 daltons to about 1000 daltons, from about 30, 50, or 100 daltons to about 500 daltons, or from about 30, 50, or 100 daltons to about 200 daltons.

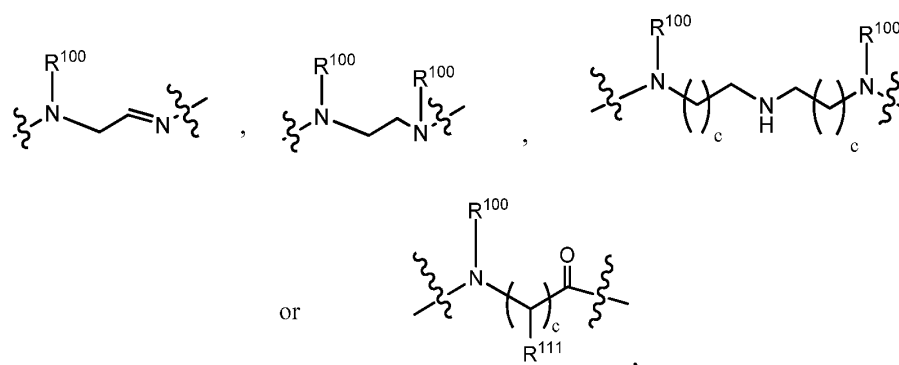
Connector Unit (A)

[0435] In some embodiments, a Connector Unit (A), is included in a Camptothecin Conjugate or Camptothecin-Linker Compound in instances where it is desirable to add additional distance between the Stretcher Unit (Z) or precursor thereof (Z') and the Releasable Linker. In some embodiments, the extra distance will aid with activation within RL. Accordingly, the Connector Unit (A), when present, extends the framework of the Linker Unit. In that regard, a Connector Unit (A) is covalently bonded with the Stretcher Unit (or its precursor) at one terminus and is covalently bonded to the optional Parallel Connector Unit or the Partitioning Agent (S*) at its other terminus.

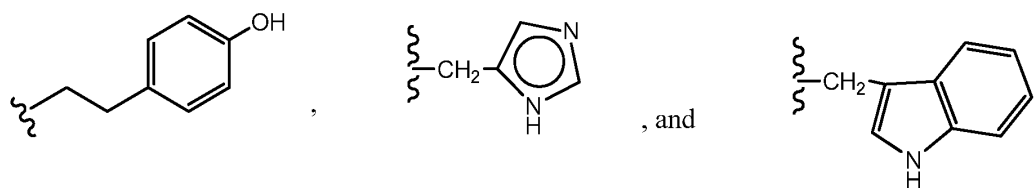
[0436] The skilled artisan will appreciate that the Connector Unit can be any group that serves to provide for attachment of the Releasable Linker to the remainder of the Linker Unit (Q). The Connector Unit can be, for example, comprised of one or more (e.g., 1-10, preferably, 1, 2, 3, or 4) proteinogenic or non-proteinogenic amino acid, amino alcohol, amino aldehyde, diamino residues. In some embodiments, the Connector Unit is a single proteinogenic or non-proteinogenic amino acid, amino alcohol, amino aldehyde, or diamino residue. An exemplary amino acid capable of acting as Connector units is β -alanine.

[0437] In some of those embodiments, the Connector Unit has the formula denoted below:



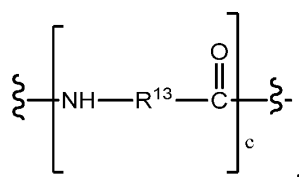


wherein the wavy lines indicate attachment of the Connector Unit within the Camptothecin Conjugate or Camptothecin Linker Compound; and wherein R^{111} is independently selected from the group consisting of hydrogen, *p*-hydroxybenzyl, methyl, isopropyl, isobutyl, *sec*-butyl, $-\text{CH}_2\text{OH}$, $-\text{CH}(\text{OH})\text{CH}_3$, $-\text{CH}_2\text{CH}_2\text{SCH}_3$, $-\text{CH}_2\text{CONH}_2$, $-\text{CH}_2\text{COOH}$, $-\text{CH}_2\text{CH}_2\text{CONH}_2$, $-\text{CH}_2\text{CH}_2\text{COOH}$, $-(\text{CH}_2)_3\text{NHC}(=\text{NH})\text{NH}_2$, $-(\text{CH}_2)_3\text{NH}_2$, $-(\text{CH}_2)_3\text{NHCOCH}_3$, $-(\text{CH}_2)_3\text{NHCHO}$, $-(\text{CH}_2)_4\text{NHC}(=\text{NH})\text{NH}_2$, $-(\text{CH}_2)_4\text{NH}_2$, $-(\text{CH}_2)_4\text{NHCOCH}_3$, $-(\text{CH}_2)_4\text{NHCHO}$, $-(\text{CH}_2)_3\text{NHCONH}_2$, $-(\text{CH}_2)_4\text{NHCONH}_2$, $-\text{CH}_2\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{NH}_2$, 2-pyridylmethyl-, 3-pyridylmethyl-, 4-pyridylmethyl-,



and each R^{100} is independently selected from hydrogen or $-\text{C}_1\text{-C}_3$ alkyl, preferably hydrogen or CH_3 ; and subscript *c* is an independently selected integer from 1 to 10, preferably 1 to 3.

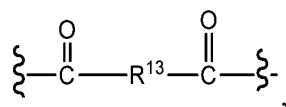
[0438] A representative Connector Unit having a carbonyl group for attachment to the Partitioning Agent (S^*) or to $-\text{B}(S^*)-$ is as follows:



wherein in each instance R^{13} is independently selected from the group consisting of $-\text{C}_1\text{-C}_6$ alkylene-, $-\text{C}_3\text{-C}_8$ carbocyclo-, -arylene-, $-\text{C}_1\text{-C}_{10}$ heteroalkylene-, $-\text{C}_3\text{-C}_8$ heterocyclo-, $-\text{C}_1\text{-C}_{10}$ alkylene-arylene-, -arylene- $-\text{C}_1\text{-C}_{10}$ alkylene-, $-\text{C}_1\text{-C}_{10}$ alkylene- $-(\text{C}_3\text{-C}_8\text{carbocyclo})-$, $-(\text{C}_3\text{-C}_8\text{carbocyclo})-\text{C}_1\text{-C}_{10}$ alkylene-, $-\text{C}_1\text{-C}_{10}$ alkylene- $-(\text{C}_3\text{-C}_8\text{ heterocyclo})-$, and $-(\text{C}_3\text{-C}_8$

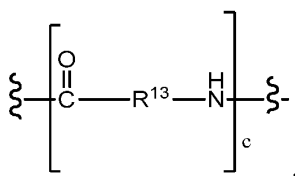
heterocyclo)-C₁-C₁₀ alkylene-, and the subscript c is an integer ranging from 1 to 4. In some embodiments R¹³ is -C₁-C₆ alkylene and c is 1.

[0439] Another representative Connector Unit having a carbonyl group for attachment to Partitioning Agent (S*) or to -B(S*)- is as follows:



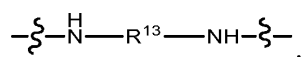
wherein R¹³ is -C₁-C₆ alkylene-, -C₃-C₈carbocyclo-, -arylene-, -C₁-C₁₀ heteroalkylene-, -C₃-C₈heterocyclo-, -C₁-C₁₀alkylene-arylene-, -arylene-C₁-C₁₀alkylene-, -C₁-C₁₀alkylene-(C₃-C₈carbocyclo)-, -(C₃-C₈carbocyclo)-C₁-C₁₀alkylene-, -C₁-C₁₀alkylene-(C₃-C₈ heterocyclo)-, or -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-. In some embodiments R¹³ is -C₁-C₆ alkylene.

[0440] A representative Connector Unit having a NH moiety that attaches to Partitioning Agent (S*) or to -B(S*)- is as follows:



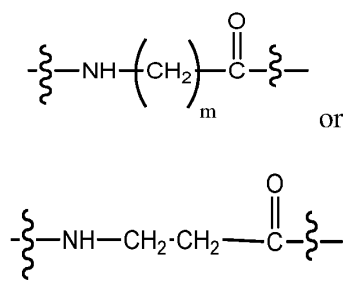
wherein in each instance, R¹³ is independently selected from the group consisting of -C₁-C₆ alkylene-, -C₃-C₈carbocyclo-, -arylene-, -C₁-C₁₀ heteroalkylene-, -C₃-C₈heterocyclo-, -C₁-C₁₀alkylene-arylene-, -arylene-C₁-C₁₀alkylene-, -C₁-C₁₀alkylene-(C₃-C₈carbocyclo)-, -(C₃-C₈carbocyclo)-C₁-C₁₀alkylene-, -C₁-C₁₀alkylene-(C₃-C₈ heterocyclo)-, and -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-, and subscript c is from 1 to 14. In some embodiments R¹³ is -C₁-C₆ alkylene and subscript c is 1.

[0441] Another representative Connector Unit having a NH moiety that attaches to Partitioning Agent (S*) or to -B(S*)- is as follows:



wherein R¹³ is -C₁-C₆ alkylene-, -C₃-C₈carbocyclo-, -arylene-, -C₁-C₁₀ heteroalkylene-, -C₃-C₈heterocyclo-, -C₁-C₁₀alkylene-arylene-, -arylene-C₁-C₁₀alkylene-, -C₁-C₁₀alkylene-(C₃-C₈carbocyclo)-, -(C₃-C₈carbocyclo)-C₁-C₁₀alkylene-, -C₁-C₁₀alkylene-(C₃-C₈ heterocyclo)-, -(C₃-C₈ heterocyclo)-C₁-C₁₀ alkylene-, -C(=O)-C₁-C₆ alkylene- or -C₁-C₆ alkylene-C(=O)-C₁-C₆ alkylene.

[0442] Selected embodiments of Connector Units include those having the following structure of:



wherein the wavy line adjacent to the nitrogen indicates covalent attachment a Stretcher Unit (Z) (or its precursor Z'), and the wavy line adjacent to the carbonyl indicates covalent attachment to Partitioning Agent (S*) or to -B(S*)-; and m is an integer ranging from 1 to 6, preferably 2 to 6, more preferably 2 to 4.

Releasable Linker (RL)

[0443] The Releasable Linker (RL) is capable of linking to the Spacer Unit (Y) or the Drug Unit (D). RL comprises a cleavable bond (i.e., a reactive site) that upon action by an enzyme present within a hyper-proliferating cell or hyper-activated immune cells or characteristic of the immediate environment of these abnormal or unwanted cells, or upon non-enzymatic action due to conditions more likely experienced by hyper-proliferating cells in comparison to normal cells, releases free drug. Alternatively, RL comprises a cleavable bond that is more likely acted upon intracellularly in a hyper-proliferating cell or hyper-activated immune cell due to preferential entry into such cells in comparison to normal cells.

Peptide Releasable Linkers

[0444] In some embodiments, the Releasable Linker is a Peptide Releasable Linker. In some embodiments, the Peptide Releasable Linker (RL) will comprise one or more contiguous or non-contiguous sequences of amino acids (e.g., so that RL has 1 to no more than 12 amino acids). The Peptide Releasable Linker can comprise or consist of, for example, an amino acid, a dipeptide, tripeptide, tetrapeptide, pentapeptide, hexapeptide, heptapeptide, octapeptide, nonapeptide, decapeptide, undecapeptide or dodecapeptide unit. In some aspects, in the presence of an enzyme (e.g., a tumor-associated protease), an amide linkage between the amino acids is cleaved, which ultimately leads to release of free drug.

[0445] Each amino acid can be proteinogenic or non-proteinogenic and/or a D- or L-isomer provided that RL comprises a cleavable bond that, when cleaved, initiates release of

the Camptothecin. In some embodiments, the Peptide Releasable Linker will comprise only proteinogenic amino acids. In some aspects, the Peptide Releasable Linker will have from 1 to no more than 12 amino acids in contiguous sequence.

[0446] In some embodiments, each amino acid is independently selected from the group consisting of alanine, arginine, aspartic acid, asparagine, histidine, glycine, glutamic acid, glutamine, phenylalanine, lysine, leucine, serine, tyrosine, threonine, isoleucine, proline, tryptophan, valine, cysteine, methionine, selenocysteine, ornithine, penicillamine, β -alanine, aminoalkanoic acid, aminoalkynoic acid, aminoalkanedioic acid, aminobenzoic acid, amino-heterocyclo-alkanoic acid, heterocyclo-carboxylic acid, citrulline, statine, diaminoalkanoic acid, and derivatives thereof. In some embodiments, each amino acid is independently selected from the group consisting of alanine, arginine, aspartic acid, asparagine, histidine, glycine, glutamic acid, glutamine, phenylalanine, lysine, leucine, serine, tyrosine, threonine, isoleucine, proline, tryptophan, valine, cysteine, methionine, and selenocysteine. In some embodiments, each amino acid is independently selected from the group consisting of alanine, arginine, aspartic acid, asparagine, histidine, glycine, glutamic acid, glutamine, phenylalanine, lysine, leucine, serine, tyrosine, threonine, isoleucine, proline, tryptophan, and valine. In some embodiments, each amino acid is selected from the proteinogenic or the non-proteinogenic amino acids.

[0447] In another embodiment, each amino acid is independently selected from the group consisting of the following L-(proteinogenic) amino acids: alanine, arginine, aspartic acid, asparagine, histidine, glycine, glutamic acid, glutamine, phenylalanine, lysine, leucine, serine, tyrosine, threonine, isoleucine, tryptophan, and valine.

[0448] In another embodiment, each amino acid is independently selected from the group consisting of the following D-isomers of these proteinogenic amino acids: alanine, arginine, aspartic acid, asparagine, histidine, glycine, glutamic acid, glutamine, phenylalanine, lysine, leucine, serine, tyrosine, threonine, isoleucine, tryptophan, and valine.

[0449] In certain embodiments, the Peptide Releasable Linker is comprised only of proteinogenic amino acids. In other embodiments, the Peptide Releasable Linker is comprised only of non-proteinogenic amino acids. In some embodiments, the Peptide Releasable Linker is comprised of a proteinogenic amino acid attached to a non-proteinogenic amino acid. In some embodiments, Peptide Releasable Linker is comprised of a proteinogenic amino acid attached to a D-isomer of a proteinogenic amino acid.

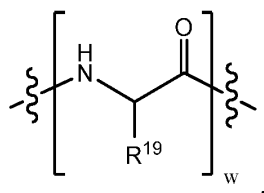
[0450] In another embodiment, each amino acid is independently selected from the group consisting of β -alanine, N-methylglycine, glycine, lysine, valine, and phenylalanine.

[0451] Exemplary Peptide Releasable Linkers include dipeptides or tripeptides such as -Val-Lys-Gly-, -Val-Cit-, -Phe-Lys-, or -Val-Ala-.

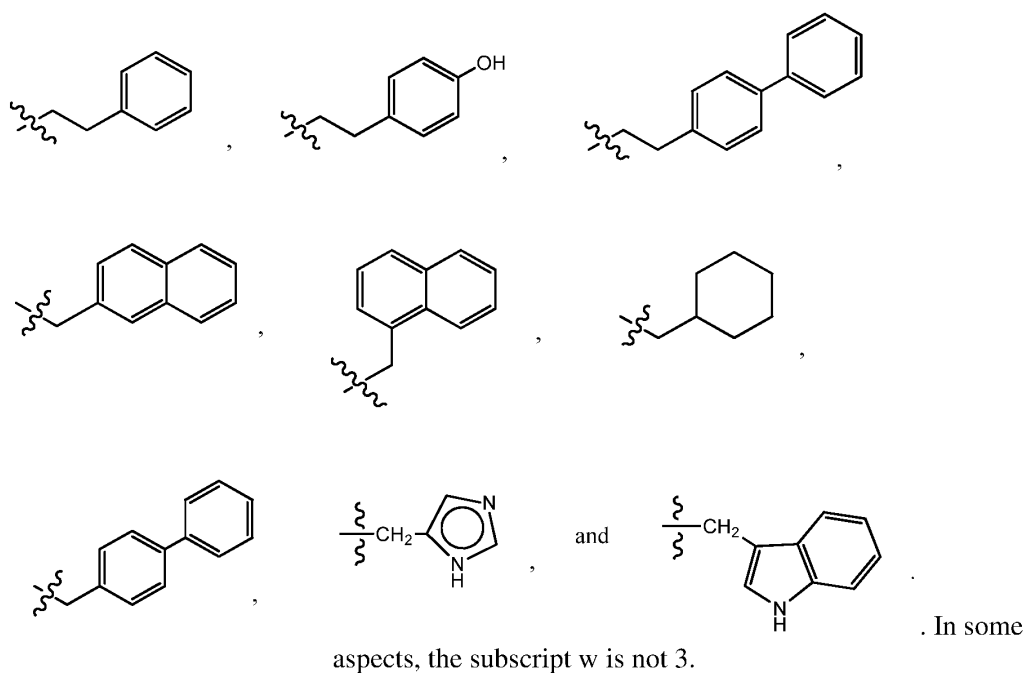
[0452] Useful Peptide Releasable Linkers can be designed and optimized in their selectivity for enzymatic cleavage by a particular enzyme, for example, a tumor-associated protease. In some embodiments, cleavage of a linkage is catalyzed by cathepsin B, C, or D, or a plasmin protease.

[0453] In some embodiments, the Peptide Releasable Linker (RL) will be represented by $-(AA)_1-12-$, or $(AA-AA)_1-6$ wherein AA is at each occurrence independently selected from proteinogenic or non-proteinogenic amino acids. In one aspect, AA is at each occurrence independently selected from proteinogenic amino acids. In another aspect, RL is a tripeptide having the formula: $AA_1-AA_2-AA_3$, wherein AA_1 , AA_2 and AA_3 are each independently an amino acid and wherein AA_1 attaches to $-NH-$ and AA_3 attaches to S^* . In yet another aspect, AA_3 is gly or β -ala.

[0454] In some embodiments, the Peptide Releasable Linker has the formula denoted below in the square brackets, the subscript w is an integer ranging from 1 to 12; or w is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12; or w is 2, 3, or 4; or w is 3; or w is 4:

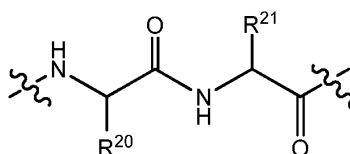


wherein R^{19} is, in each instance, independently selected from the group consisting of hydrogen, methyl, isopropyl, isobutyl, *sec*-butyl, benzyl, *p*-hydroxybenzyl, $-\text{CH}_2\text{OH}$, $-\text{CH}(\text{OH})\text{CH}_3$, $-\text{CH}_2\text{CH}_2\text{SCH}_3$, $-\text{CH}_2\text{CONH}_2$, $-\text{CH}_2\text{COOH}$, $-\text{CH}_2\text{CH}_2\text{CONH}_2$, $-\text{CH}_2\text{CH}_2\text{COOH}$, $-(\text{CH}_2)_3\text{NHC}(=\text{NH})\text{NH}_2$, $-(\text{CH}_2)_3\text{NH}_2$, $-(\text{CH}_2)_3\text{NHCOCH}_3$, $-(\text{CH}_2)_3\text{NHCHO}$, $-(\text{CH}_2)_4\text{NHC}(=\text{NH})\text{NH}_2$, $-(\text{CH}_2)_4\text{NH}_2$, $-(\text{CH}_2)_4\text{NHCOCH}_3$, $-(\text{CH}_2)_4\text{NHCHO}$, $-(\text{CH}_2)_3\text{NHCONH}_2$, $-(\text{CH}_2)_4\text{NHCONH}_2$, $-\text{CH}_2\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{NH}_2$, 2-pyridylmethyl-, 3-pyridylmethyl-, 4-pyridylmethyl-, phenyl, cyclohexyl,



[0455] In some aspects, each R^{19} is independently hydrogen, methyl, isopropyl, isobutyl, *sec*-butyl, $-(CH_2)_3NH_2$, or $-(CH_2)_4NH_2$. In some aspects, each R^{19} is independently hydrogen, isopropyl, or $-(CH_2)_4NH_2$.

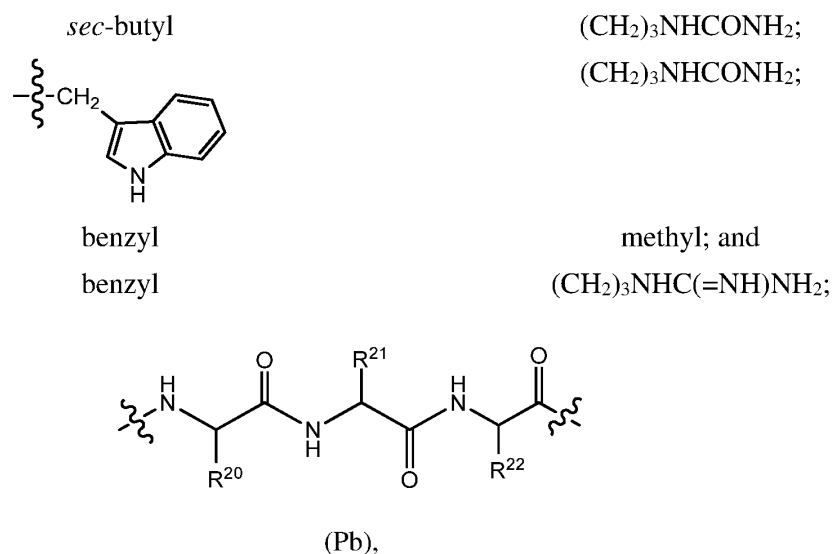
[0456] Illustrative Peptide Releasable Linkers are represented by formulae (Pa), (Pb) and (Pc):



(Pa),

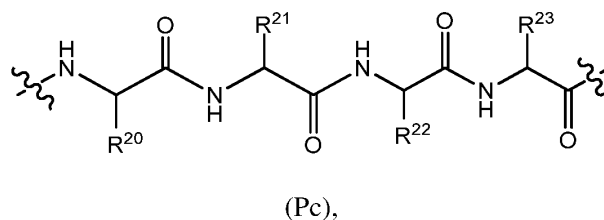
wherein R^{20} and R^{21} are as follows:

R^{20}	R^{21}
benzyl	$(CH_2)_4NH_2$;
methyl	$(CH_2)_4NH_2$;
isopropyl	$(CH_2)_4NH_2$;
isopropyl	$(CH_2)_3NHCONH_2$;
benzyl	$(CH_2)_3NHCONH_2$;
isobutyl	$(CH_2)_3NHCONH_2$;



wherein R^{20} , R^{21} and R^{22} are as follows:

R^{20}	R^{21}	R^{22}
benzyl	benzyl	$-(\text{CH}_2)_4\text{NH}_2$
isopropyl	benzyl	$-(\text{CH}_2)_4\text{NH}_2$
H	Benzyl	$-(\text{CH}_2)_4\text{NH}_2$
isopropyl	$-(\text{CH}_2)_4\text{NH}_2$	-H



wherein R^{20} , R^{21} , R^{22} and R^{23} are as follows:

R^{20}	R^{21}	R^{22}	R^{23}
H	benzyl	isobutyl	H; and
methyl	isobutyl	methyl	isobutyl.

[0457] In some embodiments, RL comprises a peptide selected from the group consisting of gly-gly, gly-gly-gly, gly-gly-gly-gly (SEQ ID NO: 1222), val-gly-gly, val-cit-gly, val-gln-gly, val-glu-gly, phe-lys-gly, leu-lys-gly, gly-val-lys-gly (SEQ ID NO: 1223), val-lys-gly-gly (SEQ ID NO: 1224), val-lys-gly, val-lys-ala, val-lys-leu, leu-leu-gly, gly-gly-phe-gly (SEQ ID NO: 1225), gly-gly-phe-gly-gly (SEQ ID NO: 1226), val-gly, and val-lys- β -ala.

[0458] In other embodiments, RL comprises a peptide selected from the group consisting of gly-gly-gly, gly-gly-gly-gly (SEQ ID NO: 1222), val-gly-gly, val-cit-gly, val-gln-gly, val-glu-gly, phe-lys-gly, leu-lys-gly, gly-val-lys-gly (SEQ ID NO: 1223), val-lys-gly-gly (SEQ ID NO: 1224), val-lys-gly, val-lys-ala, val-lys-leu, leu-leu-gly, gly-gly-phe-gly (SEQ ID NO: 1225), and val-lys- β -ala.

[0459] In still other embodiments, RL comprises a peptide selected from the group consisting of gly-gly-gly, val-gly-gly, val-cit-gly, val-gln-gly, val-glu-gly, phe-lys-gly, leu-lys-gly, val-lys-gly, val-lys-ala, val-lys-leu, leu-leu-gly and val-lys- β -ala.

[0460] In yet other embodiments, RL comprises a peptide selected from the group consisting of gly-gly-gly-gly (SEQ ID NO: 1222), gly-val-lys-gly (SEQ ID NO: 1223), val-lys-gly-gly (SEQ ID NO: 1224), and gly-gly-phe-gly (SEQ ID NO: 1225).

[0461] In other embodiments, RL is a peptide selected from the group consisting of val-gln-gly, val-glu-gly, phe-lys-gly, leu-lys-gly, val-lys-gly, val-lys-ala, val-lys-leu, leu-leu-gly and val-lys- β -ala.

[0462] In still other embodiments, RL is val-lys-gly.

[0463] In still other embodiments, RL is val-lys- β -ala.

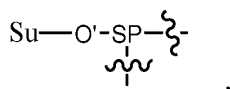
Glycoside Unit Releasable Linkers

[0464] In some embodiments, the Releasable Linker is a Glycoside (e.g., Glucuronide) Unit. In such embodiments, a self-immolation cascade is activated by operation of a glycosidase on a carbohydrate moiety of the Glycoside (e.g., Glucuronide) Unit. A number of sugars are useful in the embodiments described herein. Particular carbohydrate moieties include those of Galactose, Glucose, Mannose, Xylose, Arabinose, Mannose-6-phosphate, Fucose, Rhamnose, Gulose, Allose, 6-deoxy-glucose, Lactose, Maltose, Cellobiose, Gentiobiose, Maltotriose, GlcNAc, GalNAc, and maltohexaose.

[0465] A Glycoside (e.g., Glucuronide) Unit typically comprises a sugar moiety (Su) linked via an oxygen glycosidic bond to a self-immolative spacer. Cleavage of the oxygen glycosidic bond initiates the self-immolation reaction sequence that result in release of free drug. In some embodiments, the self-immolation sequence is activated from cleavage by β -glucuronidase of a Glycoside (e.g., Glucuronide) Unit, which is an exemplary glycoside unit. The Glycoside (e.g., Glucuronide) Unit comprises an activation unit and a self-immolative

Spacer Unit. The Glycoside (e.g., Glucuronide) Unit comprises a sugar moiety (Su) linked via an oxygen glycosidic bond to a self-immolative Spacer Unit.

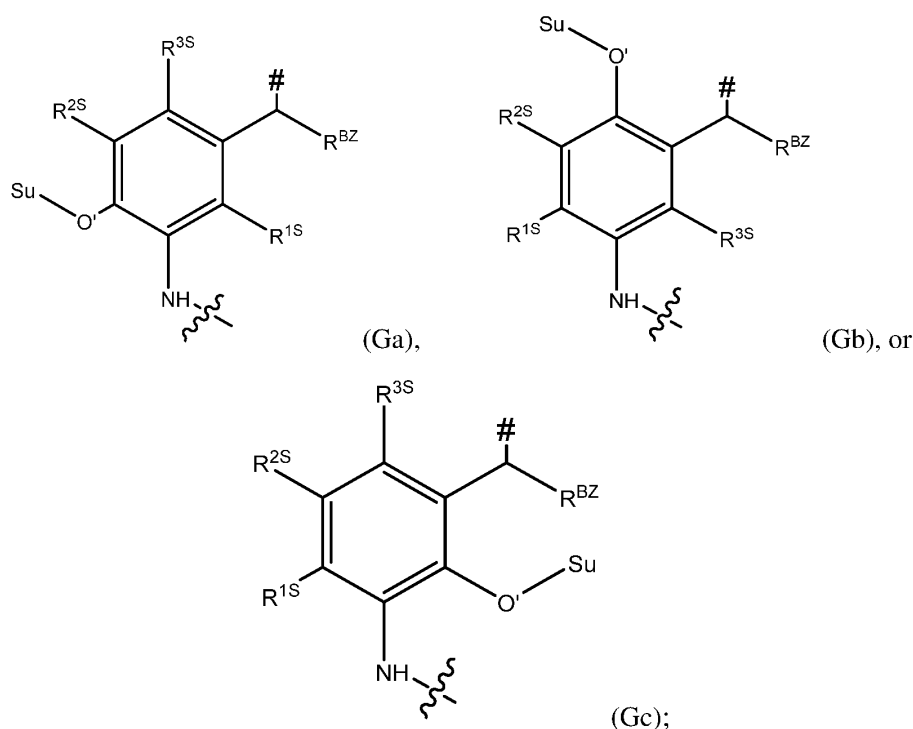
[0466] In some embodiments, a Glycoside (e.g., Glucuronide) Unit comprises a sugar moiety (Su) linked via an oxygen glycoside bond (-O'-) to a Self-immolative Unit (SP) of the formula:



wherein the wavy lines indicate covalent attachment to the Drug Unit of any one of formula **D1**, **D1a**, **D1b**, or any subformula thereof, or to a Spacer Unit that is attached to the Drug Unit (a Camptothecin Compound), and to the Stretcher Unit (Z) or its precursor (Z'), either directly or indirectly through the Connector Unit (A) or Parallel Connector Unit (B), Partitioning Agent (S*) or combinations of the Connector Unit and Parallel Connector Unit, as the case may be.

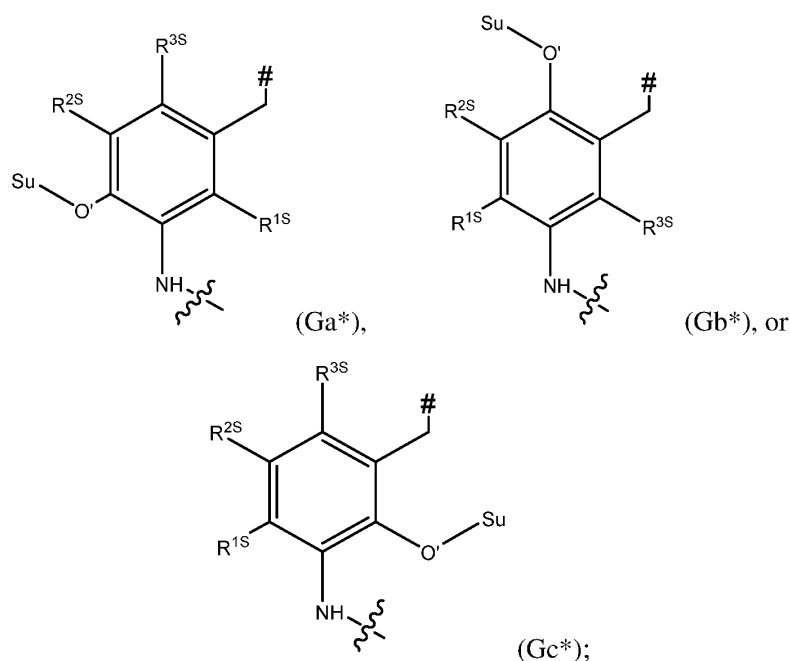
[0467] The oxygen glycosidic bond (-O'-) is typically a β-glucuronidase-cleavage site (i.e., Su is from glucuronide), such as a glycoside bond cleavable by human lysosomal β-glucuronidase.

[0468] In some embodiments, the Glycoside (e.g., Glucuronide) Unit can be represented by formula Ga, Gb, or Gc:



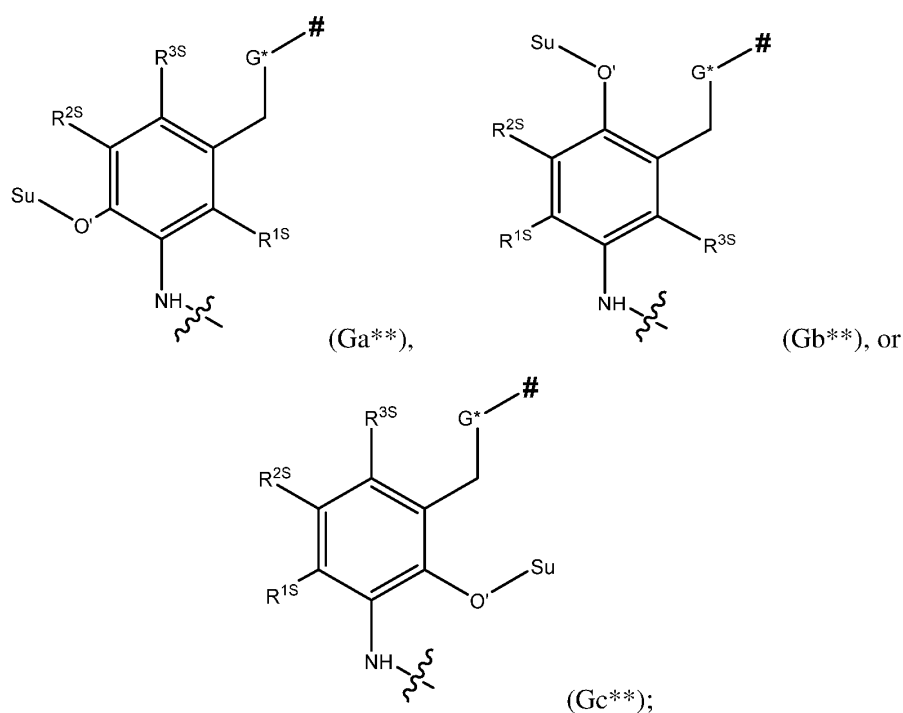
wherein Su is a Sugar moiety, -O' represents an oxygen glycosidic bond; R^{1S}, R^{2S} and R^{3S} independently are hydrogen, a halogen, -CN, -NO₂, or other electron withdrawing group, or an electron donating group; R^{BZ} is selected from the group consisting of C₁-C₆ alkyl, C₁-C₆ haloalkyl, a PEG unit, a cyclodextrin unit, a polyamide, a hydrophilic peptide, a polysaccharide, and a dendrimer; and wherein the wavy line indicates attachment to a Stretcher Unit (Z) (or its precursor (Z')), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit); and # indicates attachment to the Camptothecin or to a Spacer (either directly or indirectly via an intervening functional group or other moiety).

[0469] In some embodiments, the Glycoside (e.g., Glucuronide) Unit can be represented by formula Ga*, Gb*, or Gc*:



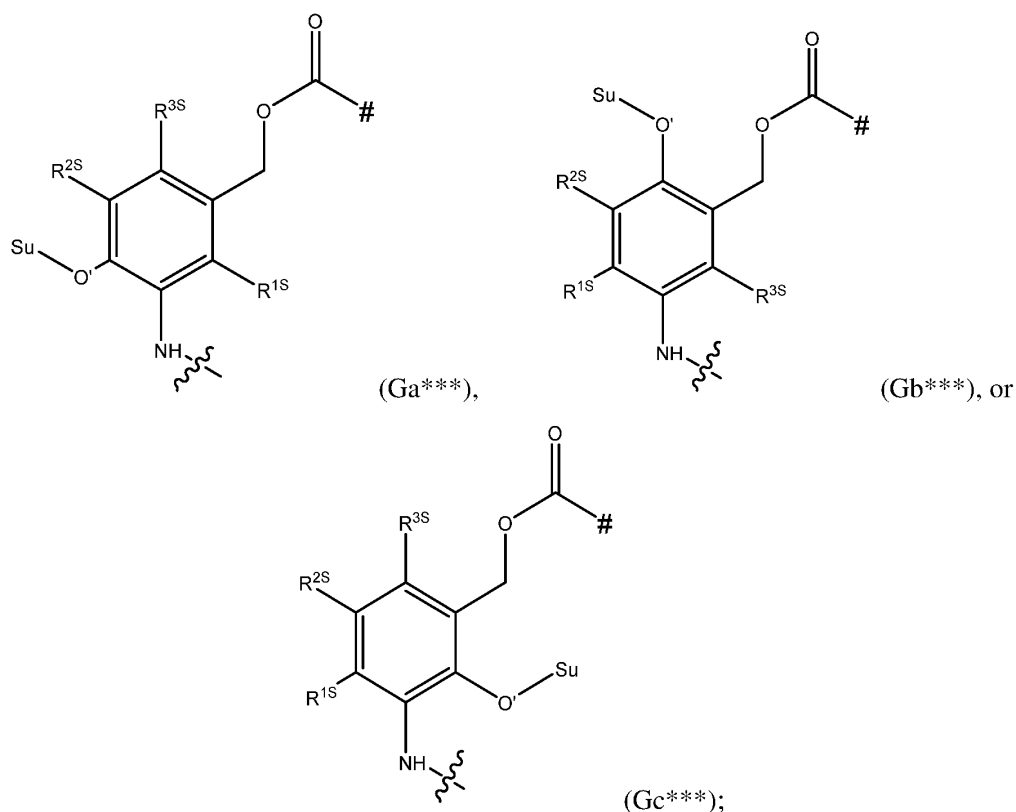
[0470] wherein Su is a Sugar moiety, $-O'$ represents an oxygen glycosidic bond; R^{1S} , R^{2S} and R^{3S} independently are hydrogen, a halogen, $-CN$, $-NO_2$, or other electron withdrawing group, or an electron donating group; and wherein the wavy line indicates attachment to a Stretcher Unit (Z) (or its precursor (Z')), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit); and $\#$ indicates attachment to the Camptothecin or to a Spacer (either directly or indirectly via an intervening functional group or other moiety).

[0471] In some embodiments, the Glycoside (e.g., Glucuronide) Unit can be represented by formula Ga^{**} , Gb^{**} , or Gc^{**} :



wherein Su is a Sugar moiety, -O' represents an oxygen glycosidic bond; R^{1S}, R^{2S} and R^{3S} independently are hydrogen, a halogen, -CN, -NO₂, or other electron withdrawing group, or an electron donating group; and wherein the wavy line indicates attachment to a Stretcher Unit (Z) (or its precursor (Z')), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit); # indicates attachment to the Camptothecin, optionally through a Spacer Unit; and G* is an intervening moiety comprising a functional group that is capable of attachment to the Spacer Unit or the Camptothecin. In some embodiments, the intervening moiety is -O-C(O)-.

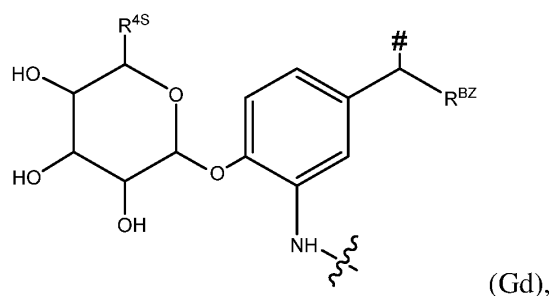
[0472] In some embodiments, the Glycoside (e.g., Glucuronide) Unit can be represented by formula Ga***, Gb***, or Gc***:



wherein Su is a Sugar moiety, -O' represents an oxygen glycosidic bond; R^{1S} , R^{2S} and R^{3S} independently are hydrogen, a halogen, -CN, -NO₂, or other electron withdrawing group, or an electron donating group; and wherein the wavy line indicates attachment to a Stretcher Unit (Z) (or its precursor (Z')), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit); and # indicates attachment to the Camptothecin, optionally through a Spacer Unit.

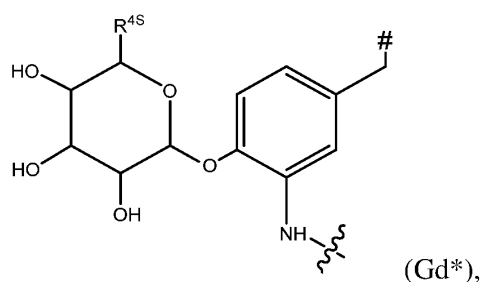
[0473] In preferred embodiments R^{1S} , R^{2S} , and R^{3S} are independently selected from hydrogen, halogen, -CN, or -NO₂. In other preferred embodiments, R^{1S} , R^{2S} , and R^{3S} are each hydrogen. In other preferred embodiments R^{2S} is an electron withdrawing group, preferably NO₂, and R^{1S} and R^{3S} are each hydrogen.

[0474] In some embodiments, the activatable self-immolative group capable of glycosidase cleavage to initiate the self-immolative reaction sequence is represented by the formula Gd:



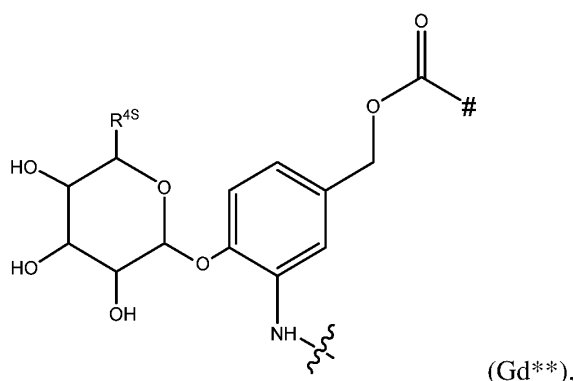
wherein R^{4S} is CH_2OH or $-CO_2H$, the wavy line indicates covalent attachment to a Stretcher Unit (Z) (or its precursor Z'), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit, and the hash mark (#) indicates covalent attachment to the methylene carbamate unit.

[0475] In some embodiments, the activatable self-immolative group capable of glycosidase cleavage to initiate the self-immolative reaction sequence is represented by the formula Gd*:



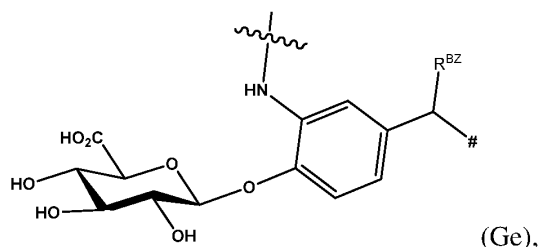
wherein R^{4S} is CH_2OH or $-CO_2H$, the wavy line indicates covalent attachment to a Stretcher Unit (Z) (or its precursor Z'), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit, and the hash mark (#) indicates covalent attachment to a $-OC(O)-$ unit that connects to a Spacer Unit or Camptothecin. In some embodiments, the $-OC(O)-$ unit connects to a nitrogen atom of a Spacer Unit or Camptothecin to form a methylene carbamate moiety. In some embodiments, the $-OC(O)-$ unit connects to an oxygen atom of a Spacer Unit or Camptothecin to form a methylene carbonate moiety.

[0476] In some embodiments, the activatable self-immolative group capable of glycosidase cleavage to initiate the self-immolative reaction sequence is represented by the formula Gd**:



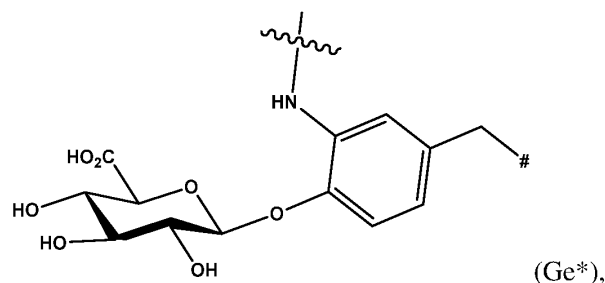
wherein R^{4S} is CH_2OH or $-CO_2H$, the wavy line indicates covalent attachment to a Stretcher Unit (Z) (or its precursor Z'), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit, and the hash mark (#) indicates covalent attachment to Spacer Unit or the Camptothecin. In some embodiments, the $-OC(O)-$ unit connects to a nitrogen atom of a Spacer Unit or Camptothecin to form a methylene carbamate moiety. In some embodiments, the $-OC(O)-$ unit connects to an oxygen atom of a Spacer Unit or Camptothecin to form a methylene carbonate moiety.

[0477] In some embodiments wherein the activatable self-immolative moiety is comprised of a Glycoside (e.g., Glucuronide) Unit, the moiety is represented by the following formula Ge:



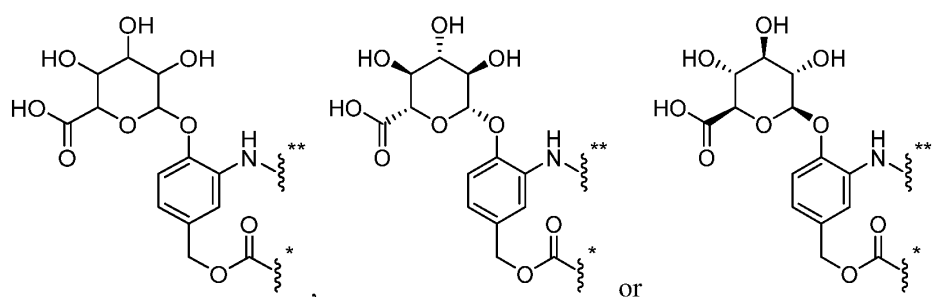
wherein the wavy line indicates covalent attachment to a Stretcher Unit (Z) (or its precursor Z'), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit and the hash mark (#) indicates covalent attachment of the benzylic carbon of a Spacer or functional group attached to the Camptothecin. In some embodiments, the functional group is $-O-C(O)-$. In some embodiments, the structure of formula Ge is attached to the Drug Unit via a quaternized tertiary amine (N^+), wherein the nitrogen atom is from a tertiary amine functional group on the unconjugated Drug Unit.

[0478] In some embodiments wherein the activatable self-immolative moiety is comprised of a Glycoside (e.g., Glucuronide) Unit, the moiety is represented by the following formula Ge:

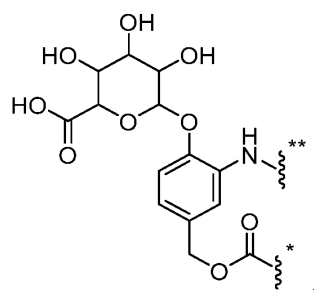


[0479] wherein the wavy line indicates covalent attachment to a Stretcher Unit (Z) (or its precursor Z'), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit and the hash mark and # indicates attachment to the Camptothecin or to a Spacer Unit (either directly or indirectly via an intervening functional group or other moiety). In some embodiments, the intervening functional group is -O-C(O)-. In some embodiments, the structure of formula Ge is attached to the Drug Unit via a quaternized tertiary amine (N⁺), wherein the nitrogen atom is from a tertiary amine functional group on the unconjugated Drug Unit.

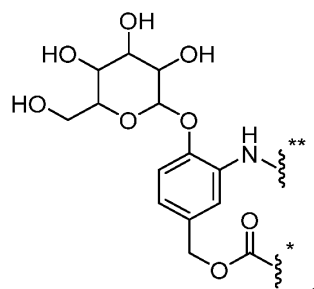
[0480] In some embodiments, the Releasable Linker has the structure:



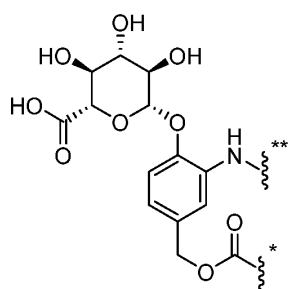
[0481] In some embodiments, the Releasable Linker has the structure:



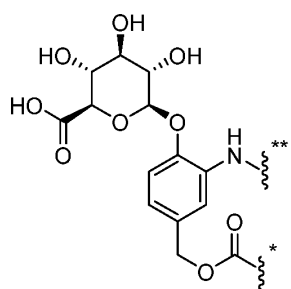
[0482] In some embodiments, the Releasable Linker has the structure:



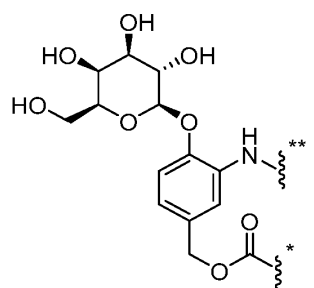
[0483] In some embodiments, the Releasable Linker has the structure:



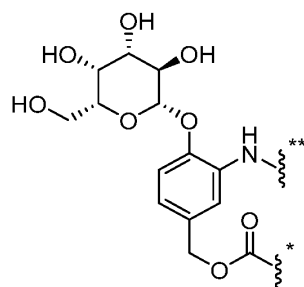
[0484] In some embodiments, the Releasable Linker has the structure:



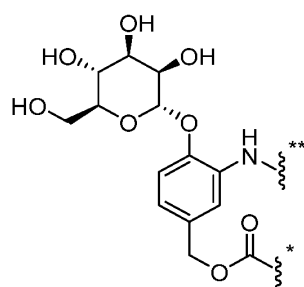
[0485] In some embodiments, the Releasable Linker has the structure:



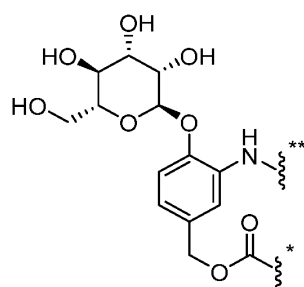
[0486] In some embodiments, the Releaseable Linker has the structure:



[0487] In some embodiments, the Releaseable Linker has the structure:



[0488] In some embodiments, the Releaseable Linker has the structure:

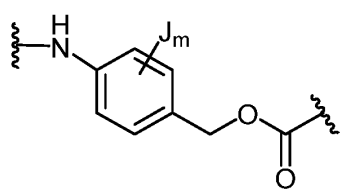


[0489] Another type of Releasable Linker that provides a mechanism for separation of the Camptothecin from the Ligand Unit and other components of the Linker Unit through activation of a self-immolation cascade within the Linker Unit is comprised of a p-aminobenzyloxycarbonyl (PAB) moiety whose phenylene component is substituted with J_m wherein the subscript m indicating the number of substituents is an integer ranging from 0-4, and each J is independently -C₁-C₈ alkyl, -O-(C₁-C₈ alkyl), -halogen, -nitro, or -cyano.

[0490] In some embodiments, RL is a self-immolative group capable of releasing -D without the need for a separate hydrolysis step or subsequent self-immolative event. In some embodiments, -RL- is a PAB moiety that is linked to the carbonyl of -W- via the amino

nitrogen atom of the PAB group, and connected directly to -D via a carbonate group. In related embodiments, -RL- is comprised of a PAB moiety that is linked to the carbonyl of -A-, -S* or -B- via the amino nitrogen atom of the PAB group, and connected directly to -D via a carbonate group. Without being bound by any particular theory or mechanism, a possible mechanism of Drug release from RL comprised of a PAB moiety in which RL is attached directly to -D via a carbonate group is shown in Toki *et al.* (2002) J Org. Chem. 67:1866-1872.

[0491] In some embodiments, RL units containing a PAB moiety are represented by the formula:

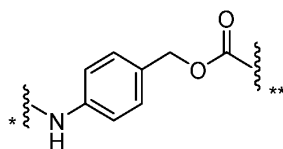


wherein subscript m is an integer ranging from 0-4, and each J is independently -C₁-C₈ alkyl, -O-(C₁-C₈ alkyl), -halogen, -nitro, or -cyano.

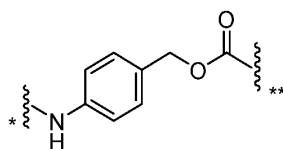
[0492] Other examples of self-immolative groups include, but are not limited to, aromatic compounds that are electronically similar to the PAB moiety such as 2-aminoimidazol-5-methanol derivatives (Hay *et al.* (1999) Bioorg. Med. Chem. Lett. 9:2237) and ortho or para-aminobenzylacetals. Other RLs undergo cyclization upon amide bond hydrolysis, such as substituted and unsubstituted 4-aminobutyric acid amides (Rodrigues *et al.*, Chemistry Biology, 1995, 2, 223), appropriately substituted bicyclo[2.2.1] and bicyclo[2.2.2] ring systems (Storm, *et al.*, J. Amer. Chem. Soc., 1972, 94, 5815) and 2-aminophenylpropionic acid amides (Amsberry, *et al.*, J. Org. Chem., 1990, 55, 5867).

[0493] In one embodiment, RL is a branched bis(hydroxymethyl)styrene (BHMS) unit.

[0494] In some embodiments, RL has the formula:



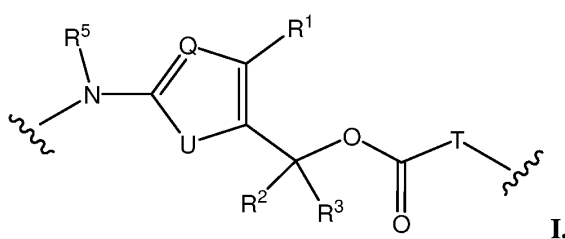
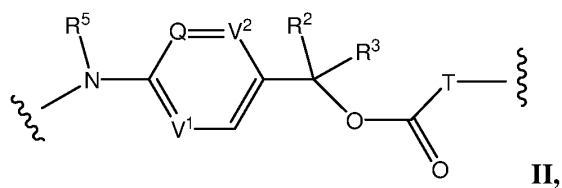
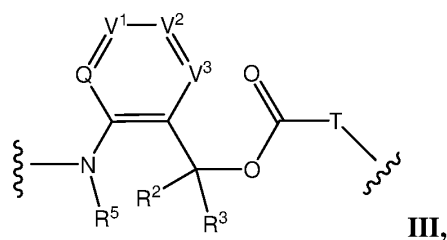
[0495] wherein the wavy line marked with ** indicates the site of attachment to D; and the wavy line marked with * indicates the point of attachment to additional linker components of Q. In some embodiments, RL comprises the formula:



wherein the wavy line marked with ** indicates the site of attachment to D; and the wavy line marked with * indicates the point of attachment to other portions of RL, such as Peptide Releasable Linkers or Glycosidide Unit Relasable Linkers described herein.

[0496] In some embodiments, RL comprises a heterocyclic “self-immolating moiety” of Formulas **I**, **II**, or **III** bound to the drug and incorporates an amide group that upon hydrolysis by an intracellular protease initiates a reaction that ultimately cleaves the self-immolative moiety from the drug such that the drug is released from the conjugate in an active form. The linker moiety further comprises a peptide sequence adjacent to the self-immolative moiety that is a substrate for an intracellular enzyme, for example an intracellular protease such as a cathepsin (e.g., cathepsin B), that cleaves the peptide at the amide bond shared with the self-immolative moiety. For embodiments disclosed herein, a PAB-containing RL is directly attached to the tertiary hydroxyl of the lactone ring present in each of formula **D1**, **D1a**, **D1b**, or any subformula thereof, or any of the compounds of Table I.

[0497] In some embodiments, a heterocyclic self-immolating group (RL) is selected from Formulas **I**, **II**, and **III**:



wherein the wavy lines indicate the covalent attachment sites to the cell-specific ligand and the D' drug moiety, and wherein U is O, S or NR⁶; Q is CR⁴ or N; V¹, V², and V³ are independently CR⁴ or N provided that for formula **II** and **III** at least one of Q, V¹ and V² is N; T is the heteroatom of a hydroxyl or thiol or primary or secondary or N-heterocycle or N-amide or N-carbamate of a Drug Unit of formula D₁, D_{1a}, or D₂, wherein T and D' together form a Drug Unit of formula **D₁**, **D_{1a}**, **D_{1b}**, or any subformula thereof, or any of the compounds of Table I; R¹, R², R³ and R⁴ are independently selected from the group consisting of H, F, Cl, Br, I, OH, -N(R⁵)₂, -N(R⁵)₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, -SO₂R⁵, -S(=O)R⁵, -SR⁵, -SO₂N(R⁵)₂, -C(=O)R⁵, -CO₂R⁵, -C(=O)N(R⁵)₂, -CN, -N₃, -NO₂, C₁-C₈ alkoxy, C₁-C₈ halosubstituted alkyl, polyethyleneoxy, phosphonate, phosphate, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₂-C₈ alkenyl, C₂-C₈ substituted alkenyl, C₂-C₈ alkynyl, C₂-C₈ substituted alkynyl, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₁-C₂₀ heterocycle, and C₁-C₂₀ substituted heterocycle; or when taken together, R² and R³ form a carbonyl (=O), or spiro carbocyclic ring of 3 to 7 carbon atoms; and R⁵ and R⁶ are independently selected from H, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₂-C₈ alkenyl, C₂-C₈ substituted alkenyl, C₂-C₈ alkynyl, C₂-C₈ substituted alkynyl, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₁-C₂₀ heterocycle, and C₁-C₂₀ substituted heterocycle; wherein C₁-C₈ substituted alkyl, C₂-C₈ substituted alkenyl, C₂-C₈ substituted alkynyl, C₆-C₂₀ substituted aryl, and C₂-C₂₀ substituted heterocycle are independently substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, OH, -N(R⁵)₂, -N(R⁵)₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, C₁-C₈ alkylsulfonate, C₁-C₈ alkylamino, 4-dialkylaminopyridinium, C₁-C₈ alkylhydroxyl, C₁-C₈ alkylthiol, -SO₂R⁵, -S(=O)R⁵, -SR⁵, -SO₂N(R⁵)₂, -C(=O)R⁵, -CO₂R⁵, -C(=O)N(R⁵)₂, -CN, -N₃, -NO₂, C₁-C₈ alkoxy, C₁-C₈ trifluoroalkyl, C₁-C₈ alkyl, C₃-C₁₂ carbocycle, C₆-C₂₀ aryl, C₂-C₂₀ heterocycle, polyethyleneoxy, phosphonate, and phosphate.

[0498] The conjugate can be stable extracellularly, or in the absence of an enzyme capable of cleaving the amide bond of the self-immolative moiety. However, upon entry into a cell, or exposure to a suitable enzyme, an amide bond can be cleaved initiating a spontaneous self-immolative reaction resulting in the cleavage of the bond covalently linking the self-immolative moiety to the drug, to thereby effect release of the drug in its underivatized or pharmacologically active form.

[0499] The self-immolative moiety in conjugates of the invention can either incorporate one or more heteroatoms and thereby provide improved solubility, improve the rate of cleavage, and/or decrease propensity for aggregation of the conjugate. These improvements of the heterocyclic self-immolative linker constructs of the present invention over non-heterocyclic, PAB-type linkers can in some instances result in surprising and unexpected biological properties such as increased efficacy, decreased toxicity, and/or improvements in one or more desirable pharmacokinetic and/or pharmacodynamic properties.

[0500] Not to be limited by theory or any particular mechanism, the presence of electron-withdrawing groups on the heterocyclic ring of formula **I**, **II**, or **III** linkers can moderate the rate of cleavage.

[0501] In one embodiment, the self-immolative moiety is the group of formula **I** in which Q is N, and U is O or S. Such a group has a non-linearity structural feature which can improve the solubility of the conjugates. In this context R can be H, methyl, nitro, or CF₃. In one embodiment, Q is N and U is O thereby forming an oxazole ring and R is H. In another embodiment, Q is N and U is S thereby forming a thiazole ring optionally substituted at R with an Me or CF₃ group.

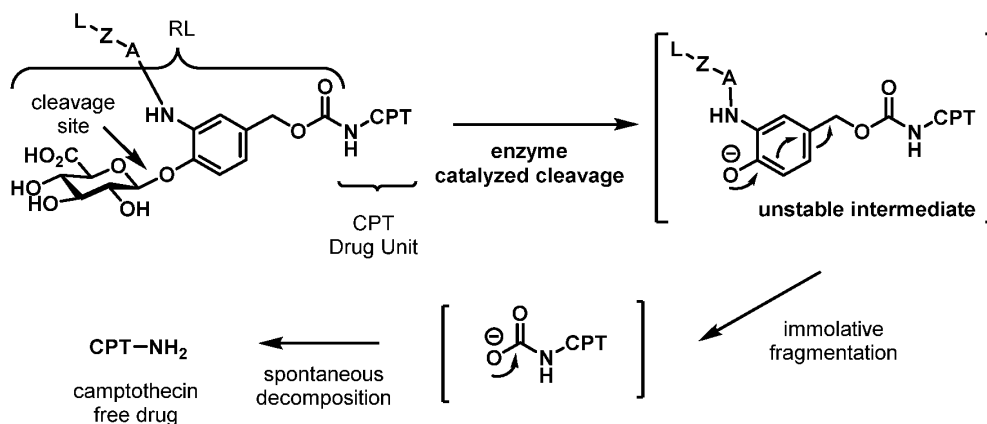
[0502] In another exemplary embodiment, the self-immolative moiety is the group of formula **II** in which Q is N and V¹ and V² are independently N or CH. In another embodiment, Q, V¹, and V² are each N. In another embodiment, Q and V¹ are N while V² is CH. In another embodiment, Q and V² are N while V¹ is CH. In another embodiment, Q and V¹ are both CH and V² is N. In another embodiment, Q is N while V¹ and V² are both CH.

[0503] In another embodiment, the self-immolative moiety is the group of formula **III** in which Q, V¹, V², and V³ are each independently N or CH. In another embodiment Q is N while V¹, V², and V³ are each N. In another embodiment, Q, V¹, and V² are each CH while V³ is N. In another embodiment Q, V², and V³ are each CH while V¹ is N. In another embodiment, Q, V¹, and V³ are each CH while V² is N. In another embodiment, Q and V² are both N while V¹ and V³ are both CH. In another embodiment Q and V² are both CH while V¹ and V³ are both N. In another embodiment, Q and V³ are both N while V¹ and V² are both CH.

[0504] Without being bound by theory, Scheme 1a depicts a mechanism of free drug release from a Camptothecin Drug Unit attached through a nitrogen atom of an amine

substituent from the free drug to a Releasable Linker that is a Glycoside (e.g., Glucuronide) Unit.

Scheme 1a:



Partitioning Agent (S*):

[0505] The Camptothecin Conjugates described herein can also include a Partitioning Agent (S*). The Partitioning Agent portions are useful, for example, to mask the hydrophobicity of particular Camptothecin Drug Units or Linking Unit components. In some embodiments, masking the hydrophobicity of the Camptothecin Drug Unit or Linking Unit improves the pharmacokinetic properties (e.g., plasma concentration over time, plasma AUC, plasma clearance rate) of the Camptothecin Conjugate. Without being bound by theory, it is believed that certain hydrophilic or amphiphilic moieties, when matched in size and/or hydrophilicity to the masked moiety's hydrophobicity and incorporated in a suitable location, can counteract negative pharmacokinetic effects caused by the hydrophobic moiety. Masking the hydrophobicity of particular Camptothecin Drug Units or Linking Unit components may allow for a corresponding Ligand Drug Conjugate to achieve higher loading (e.g., drug-antibody ratio (DAR)) compared to a similar conjugate that lacks the masking component.

[0506] Representative Partitioning Agents include polyethylene glycol (PEG) units, cyclodextrin units, polyamides, hydrophilic peptides, polysaccharides and dendrimers.

[0507] When the polyethylene glycol (PEG) units, cyclodextrin units, polyamides, hydrophilic peptides, polysaccharides or dendrimers are included in Q, the groups may be present as an 'in line' component or as a side chain or branched component. For those embodiments in which a branched version is present, the Linker Units can include a lysine residue (or Parallel Connector Unit, B) that provides simple functional conjugation of, for example, the PEG unit, to the remainder of the Linking Unit.

Polyethylene Glycol Unit (PEG)

[0508] Polydisperse PEGs, monodisperse PEGs and discrete PEGs can be used as part of the Partitioning Agents in Compounds of the present invention. Polydisperse PEGs are a heterogeneous mixture of sizes and molecular weights whereas monodisperse PEGs are typically purified from heterogeneous mixtures and are therefore provide a single chain length and molecular weight. Preferred PEG Units are discrete PEGs, compounds that are synthesized in stepwise fashion and not via a polymerization process. Discrete PEGs provide a single molecule with defined and specified chain length.

[0509] The PEG Unit provided herein can comprise one or multiple polyethylene glycol chains. A polyethylene glycol chain is composed of at least two ethylene oxide ($\text{CH}_2\text{CH}_2\text{O}$) subunits. In some embodiments the polyethylene glycol chains are linked together, for example, in a linear, branched or star shaped configuration. Typically, at least one of the PEG chains is derivitized at one end for covalent attachment to an appropriate site on a component of the Linker Unit (e.g. B) or can be used as an in-line (e.g., bifunctional) linking group within to covalently join two of the Linker Unit components (e.g., Z-A-S^{*}-RL- , Z-A-S^{*}-RL-Y-). Exemplary attachments within the Linker Unit are by means of non-conditionally cleavable linkages or via conditionally cleavable linkages. Exemplary attachments are via amide linkage, ether linkages, ester linkages, hydrazone linkages, oxime linkages, disulfide linkages, peptide linkages or triazole linkages. In some embodiments, attachment within the Linker Unit is by means of a non-conditionally cleavable linkage. In some embodiments, attachment within the Linker Unit is not via an ester linkage, hydrazone linkage, oxime linkage, or disulfide linkage. In some embodiments, attachment within the Linker Unit is not via a hydrazone linkage.

[0510] A conditionally cleavable linkage refers to a linkage that is not substantially sensitive to cleavage while circulating in the plasma but is sensitive to cleavage in an intracellular or intratumoral environment. A non-conditionally cleavable linkage is one that is not substantially sensitive to cleavage in any biological environment. Chemical hydrolysis of a hydrazone, reduction of a disulfide, and enzymatic cleavage of a peptide bond or glycosidic linkage are examples of conditionally cleavable linkages.

[0511] In some embodiments, the PEG Unit can be directly attached to a Parallel Connector Unit B. The other terminus (or termini) of the PEG Unit can be free and untethered and may take the form of a methoxy, carboxylic acid, alcohol, or other suitable functional group. The methoxy, carboxylic acid, alcohol, or other suitable functional group

acts as a cap for the terminal PEG subunit of the PEG Unit. By untethered, it is meant that the PEG Unit will not be attached at that untethered site to a Camptothecin, to an antibody, or to another linking component. The skilled artisan will understand that the PEG Unit in addition to comprising repeating ethylene glycol subunits may also contain non-PEG material (e.g., to facilitate coupling of multiple PEG chains to each other). Non-PEG material refers to the atoms in the PEG Unit that are not part of the repeating $-\text{CH}_2\text{CH}_2\text{O}-$ subunits. In some embodiments provided herein, the PEG Unit comprises two monomeric PEG chains attached to each other via non-PEG elements. In other embodiments provided herein, the PEG Unit comprises two linear PEG chains attached to a central core or Parallel Connector Unit (i.e., the PEG Unit itself is branched).

[0512] There are a number of PEG attachment methods available to those skilled in the art, [see, e.g., Goodson, et al. (1990) *Bio/Technology* **8**:343 (PEGylation of interleukin-2 at its glycosylation site after site-directed mutagenesis); EP 0 401 384 (coupling PEG to G-CSF); Malik, et al., (1992) *Exp. Hematol.* **20**:1028-1035 (PEGylation of GM-CSF using tresyl chloride); PCT Pub. No. WO 90/12874 (PEGylation of erythropoietin containing a recombinantly introduced cysteine residue using a cysteine-specific mPEG derivative); U.S. Pat. No. 5,757,078 (PEGylation of EPO peptides); U.S. Pat. No. 5,672,662 (Poly(ethylene glycol) and related polymers monosubstituted with propionic or butanoic acids and functional derivatives thereof for biotechnical applications); U.S. Pat. No. 6,077,939 (PEGylation of an N-terminal α -carbon of a peptide); Veronese et al., (1985) *Appl. Biochem. Biotechnol* **11**:141-142 (PEGylation of an N-terminal α -carbon of a peptide with PEG-nitrophenylcarbonate ("PEG-NPC") or PEG-trichlorophenylcarbonate); and Veronese (2001) *Biomaterials* **22**:405-417 (Review article on peptide and protein PEGylation)].

[0513] For example, PEG may be covalently bound to amino acid residues via a reactive group. Reactive groups are those to which an activated PEG molecule may be bound (e.g., a free amino or carboxyl group). For example, N-terminal amino acid residues and lysine (K) residues have a free amino group; and C-terminal amino acid residues have a free carboxyl group. Thiol groups (e.g., as found on cysteine residues) can also be useful as a reactive group for attaching PEG. In addition, enzyme-assisted methods for introducing activated groups (e.g., hydrazide, aldehyde, and aromatic-amino groups) specifically at the C-terminus of a polypeptide have been described (see Schwarz, et al. (1990) *Methods Enzymol.* **184**:160; Rose, et al. (1991) *Bioconjugate Chem.* **2**:154; and Gaertner, et al. (1994) *J. Biol. Chem.* **269**:7224].

[0514] In some embodiments, PEG molecules may be attached to amino groups using methoxylated PEG ("mPEG") having different reactive moieties. Non-limiting examples of such reactive moieties include succinimidyl succinate (SS), succinimidyl carbonate (SC), mPEG-imidate, para-nitrophenylcarbonate (NPC), succinimidyl propionate (SPA), and cyanuric chloride. Non-limiting examples of such mPEGs include mPEG-succinimidyl succinate (mPEG-SS), mPEG₂-succinimidyl succinate (mPEG₂-SS); mPEG-succinimidyl carbonate (mPEG-SC), mPEG₂-succinimidyl carbonate (mPEG₂-SC); mPEG-imidate, mPEG-para-nitrophenylcarbonate (mPEG-NPC), mPEG-imidate; mPEG₂-para-nitrophenylcarbonate (mPEG₂-NPC); mPEG-succinimidyl propionate (mPEG-SPA); mPEG₂-succinimidyl propionate (mPEG₂-SPA); mPEG-N-hydroxy-succinimide (mPEG-NHS); mPEG₂-N-hydroxy-succinimide (mPEG₂-NHS); mPEG-cyanuric chloride; mPEG₂-cyanuric chloride; mPEG₂-Lysinol-NPC, and mPEG₂-Lys-NHS.

[0515] Generally, at least one of the PEG chains that make up the PEG Unit is functionalized so that it is capable of covalent attachment to other Linker Unit components.

[0516] Functionalization includes, for example, via an amine, thiol, NHS ester, maleimide, alkyne, azide, carbonyl, or other functional group. In some embodiments, the PEG Unit further comprises non-PEG material (i.e., material not comprised of -CH₂CH₂O-) that provides coupling to other Linker Unit components or to facilitate coupling of two or more PEG chains.

[0517] The presence of the PEG Unit (or other Partitioning Agent) in the Linker Unit can have two potential impacts upon the pharmacokinetics of the resulting Camptothecin Conjugate. The desired impact is a decrease in clearance (and consequent increase in exposure) that arises from the reduction in non-specific interactions induced by the exposed hydrophobic elements of the Camptothecin Conjugate or to the Camptothecin itself. The second impact is undesired and is a decrease in volume and rate of distribution that sometimes arises from the increase in the molecular weight of the Camptothecin Conjugate.

[0518] Increasing the number of PEG subunits increases the hydrodynamic radius of a conjugate, typically resulting in decreased diffusivity. In turn, decreased diffusivity typically diminishes the ability of the Camptothecin Conjugate to penetrate into a tumor (Schmidt and Wittrup, *Mol Cancer Ther* 2009;8:2861-2871). Because of these two competing pharmacokinetic effects, it is desirable to use a PEG that is sufficiently large to decrease the Camptothecin Conjugate clearance thus increasing plasma exposure, but not so large as to

greatly diminish its diffusivity, to an extent that it interferes with the ability of the Camptothecin Conjugate to reach the intended target cell population. See the examples (e.g., examples 1, 18, and 21) of US2016/0310612, which are incorporated by reference herein, for methodology for selecting an optimal PEG size for a particular drug-linker.

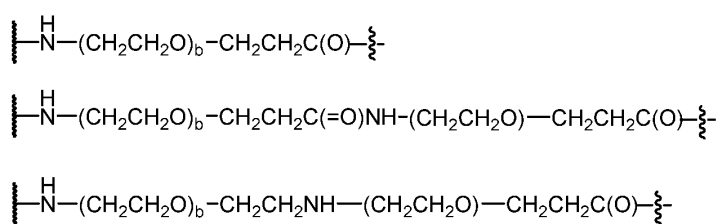
[0519] In one group of embodiments, the PEG Unit comprises one or more linear PEG chains each having at least 2 subunits, at least 3 subunits, at least 4 subunits, at least 5 subunits, at least 6 subunits, at least 7 subunits, at least 8 subunits, at least 9 subunits, at least 10 subunits, at least 11 subunits, at least 12 subunits, at least 13 subunits, at least 14 subunits, at least 15 subunits, at least 16 subunits, at least 17 subunits, at least 18 subunits, at least 19 subunits, at least 20 subunits, at least 21 subunits, at least 22 subunits, at least 23 subunits, or at least 24 subunits. In preferred embodiments, the PEG Unit comprises a combined total of at least 4 subunits, at least 6 subunits, at least 8 subunits, at least 10 subunits, or at least 12 subunits. In some such embodiments, the PEG Unit comprises no more than a combined total of about 72 subunits, preferably no more than a combined total of about 36 subunits.

[0520] In another group of embodiments, the PEG Unit comprises a combined total of from 4 to 72, 4 to 60, 4 to 48, 4 to 36 or 4 to 24 subunits, from 5 to 72, 5 to 60, 5 to 48, 5 to 36 or 5 to 24 subunits, from 6 to 72, 6 to 60, 6 to 48, 6 to 36 or from 6 to 24 subunits, from 7 to 72, 7 to 60, 7 to 48, 7 to 36 or 7 to 24 subunits, from 8 to 72, 8 to 60, 8 to 48, 8 to 36 or 8 to 24 subunits, from 9 to 72, 9 to 60, 9 to 48, 9 to 36 or 9 to 24 subunits, from 10 to 72, 10 to 60, 10 to 48, 10 to 36 or 10 to 24 subunits, from 11 to 72, 11 to 60, 11 to 48, 11 to 36 or 11 to 24 subunits, from 12 to 72, 12 to 60, 12 to 48, 12 to 36 or 12 to 24 subunits, from 13 to 72, 13 to 60, 13 to 48, 13 to 36 or 13 to 24 subunits, from 14 to 72, 14 to 60, 14 to 48, 14 to 36 or 14 to 24 subunits, from 15 to 72, 15 to 60, 15 to 48, 15 to 36 or 15 to 24 subunits, from 16 to 72, 16 to 60, 16 to 48, 16 to 36 or 16 to 24 subunits, from 17 to 72, 17 to 60, 17 to 48, 17 to 36 or 17 to 24 subunits, from 18 to 72, 18 to 60, 18 to 48, 18 to 36 or 18 to 24 subunits, from 19 to 72, 19 to 60, 19 to 48, 19 to 36 or 19 to 24 subunits, from 20 to 72, 20 to 60, 20 to 48, 20 to 36 or 20 to 24 subunits, from 21 to 72, 21 to 60, 21 to 48, 21 to 36 or 21 to 24 subunits, from 22 to 72, 22 to 60, 22 to 48, 22 to 36 or 22 to 24 subunits, from 23 to 72, 23 to 60, 23 to 48, 23 to 36 or 23 to 24 subunits, or from 24 to 72, 24 to 60, 24 to 48, 24 to 36 or 24 subunits.

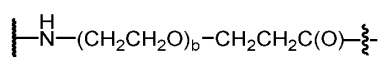
[0521] In some embodiments, the Partitioning Agent S* is a linear PEG Unit comprising from 2 to 20, or from 2 to 12, or from 4 to 12, or 4, 8, or 12 -CH₂CH₂O- subunits. In some embodiments, the linear PEG Unit is connected at one end of the PEG Unit to the RL Unit

and at the other end of the PEG Unit to the Stretcher/Connector Units (Z-A-). In some embodiments, the PEG Unit is connected to the RL Unit via a $-\text{CH}_2\text{CH}_2\text{C}(\text{O})-$ group that forms an amide bond with the RL Unit (e.g., $-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2\text{C}(\text{O})-\text{RL}$) and to the Stretcher Unit/Connector Unit (Z-A-) via an $-\text{NH}-$ group (e.g., $\text{Z-A-NH}-(\text{CH}_2\text{CH}_2\text{O})_n-$) that forms an amide bond with the Z-A- portion.

[0522] Illustrative embodiments for PEG Units that are connected to the RL and Stretcher/Connector Units (Z-A-) are shown below:



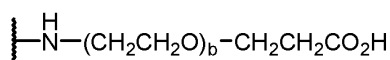
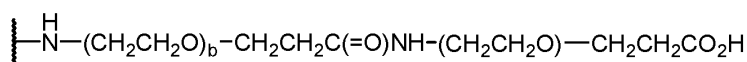
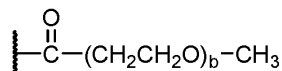
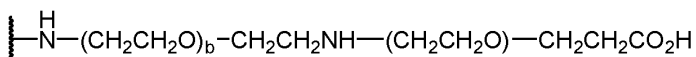
and in a particular embodiment, the PEG Unit is:



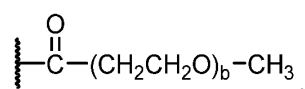
wherein the wavy line on the left indicates the site of attachment to Z-A-, the wavy line on the right indicates the site of attachment to RL, and each b is independently selected from 2 to 72, 4 to 72, 6 to 72, 8 to 72, 10 to 72, 12 to 72, 2 to 24, 4 to 24, 6 to 24, or 8 to 24, 2 to 12, 4 to 12, 6 to 12, and 8 to 12. In some embodiments, subscript b is 2, 4, 8, 12, or 24. In some embodiments, subscript b is 2. In some embodiments, subscript b is 4. In some embodiments, subscript b is 8. In some embodiments, subscript b is 12.

[0523] In some embodiments, the linear PEG Unit that is connected to the Parallel Connector Unit at one end and comprises a terminal cap at the other end. In some embodiments, the PEG Unit is connected to the Parallel Connector Unit via a carbonyl group that forms an amide bond with the Parallel Connector Unit lysine residue amino group (e.g., $-(\text{OCH}_2\text{CH}_2)_n-\text{C}(\text{O})-\text{B}-$) and includes a PEG Unit terminal cap group selected from the group consisting of $\text{C}_{1-4}\text{alkyl}$ and $\text{C}_{1-4}\text{alkyl}-\text{CO}_2\text{H}$. In some embodiments, the Partitioning Agent S^* is a linear PEG Unit comprising 4, 8, or 12 $-\text{CH}_2\text{CH}_2\text{O}-$ subunits and a terminal methyl cap.

[0524] Illustrative linear PEG Units that can be used in any of the embodiments provided herein are as follows:



and in a particular embodiment, the PEG Unit is:



wherein the wavy line indicates site of attachment to the Parallel Connector Unit (B), and each n is independently selected from 4 to 72, 6 to 72, 8 to 72, 10 to 72, 12 to 72, 6 to 24, or 8 to 24. In some embodiments, subscript b is about 4, about 8, about 12, or about 24.

[0525] As used to herein, terms “PEG2”, “PEG4”, “PEG8”, and “PEG12” refers to specific embodiments of PEG Unit which comprises the number of PEG subunits (i.e., the number of subscription “b”). For example, “PEG2” refers to embodiments of PEG Unit that comprises 2 PEG subunits, “PEG4” refers to embodiments of PEG Unit that comprises 4 PEG subunits, “PEG8” refers to embodiments of PEG Unit that comprises 8 PEG subunits, and “PEG12” refers to embodiments of PEG Unit that comprises 12 PEG subunits.

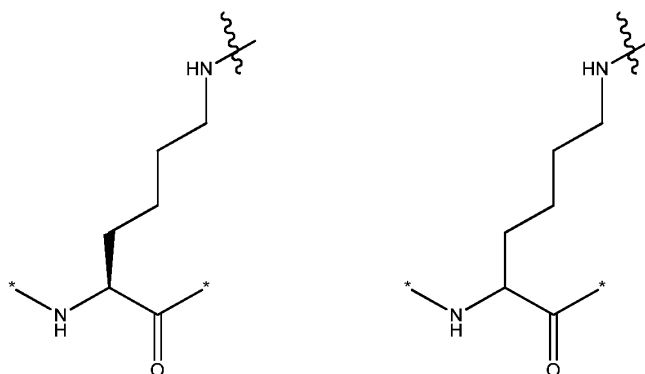
[0526] As described herein, the PEG unit is selected such that it improves clearance of the resultant Camptothecin Conjugate but does not significantly impact the ability of the Conjugate to penetrate into the tumor. In embodiments, the PEG unit to be selected for use will preferably have from 2 subunits to about 24 subunits, from 4 subunits to about 24 subunits, more preferably about 4 subunits to about 12 subunits.

[0527] In preferred embodiments of the present disclosure the PEG Unit is from about 300 daltons to about 5 kilodaltons; from about 300 daltons, to about 4 kilodaltons; from about 300 daltons, to about 3 kilodaltons; from about 300 daltons, to about 2 kilodaltons; or from about 300 daltons, to about 1 kilodalton. In some such aspects, the PEG Unit has at least 6 subunits or at least 8, 10, or 12 subunits. In some such aspects, the PEG Unit has at least 6 subunits or at least 8, 10, or 12 subunits but no more than 72 subunits, preferably no more than 36 subunits.

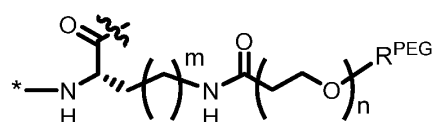
[0528] It will be appreciated that when referring to PEG subunits, and depending on context, the number of subunits can represent an average number, e.g., when referring to a population of Camptothecin Conjugates or Camptothecin-Linker Compounds, and/or using polydisperse PEGs.

Parallel Connector Unit (B):

[0529] In some embodiments, the Camptothecin Conjugates and Camptothecin Linker Compounds will comprise a Parallel Connector Unit to provide a point of attachment to a Partitioning Agent (shown in the Linker Units as $-B(S^*)-$). As a general embodiment, the PEG Unit can be attached to a Parallel Connector Unit such as lysine as shown below wherein the wavy line and asterisks indicate covalent linkage within the Linker Unit of a Camptothecin Conjugate or Camptothecin Linker Compound:



[0530] In some embodiments, the Parallel Connector Unit (L^P) and Partitioning Agent (S^*) (together, $-B(S^*)-$) have the structure of



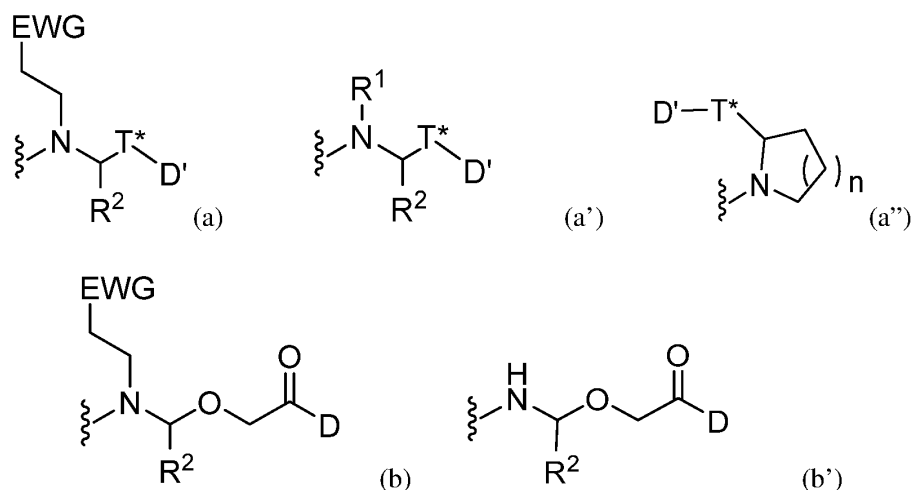
wherein m ranges from 0 to 6; n ranges from 2 to 24; R^{PEG} is a PEG Capping Unit, preferably H, $-CH_3$, or $-CH_2CH_2CO_2H$, the asterisk (*) indicates covalent attachment to a Connector Unit A corresponding in formula Za, Za', Zb' or Zc' and the wavy line indicates covalent attachment to the Releasable Linker (RL). In some embodiments, the structure is attached to a Connector Unit A in formula Za or Za'. In some embodiments, n is 2, 4, 8, or 12. In instances such as those shown here, the shown PEG group is meant to be exemplary of a variety of Partitioning Agents including PEG groups of different lengths and other

Partitioning Agents that can be directly attached or modified for attachment to the Parallel Connector Unit.

Spacer Unit (Y):

[0531] In some embodiments, the Camptothecin Conjugates provided herein will have a Spacer (Y) between the Releasable Linker (RL) and the Drug Unit. The Spacer Unit can be a functional group to facilitate attachment of RL to the Drug Unit, or it can provide additional structural components to further facilitate release of the Drug Unit from the remainder of the Conjugate (e.g., a methylene carbamate unit or a self-immolative para-aminobenzyl (PAB) component).

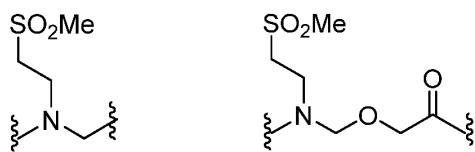
[0532] In those embodiments to further facilitate release of the Drug Unit as free drug, the Spacer Unit-Drug Unit group ($-Y-T^*-D$ or $-Y-D$) is represented by one of the following formulae:



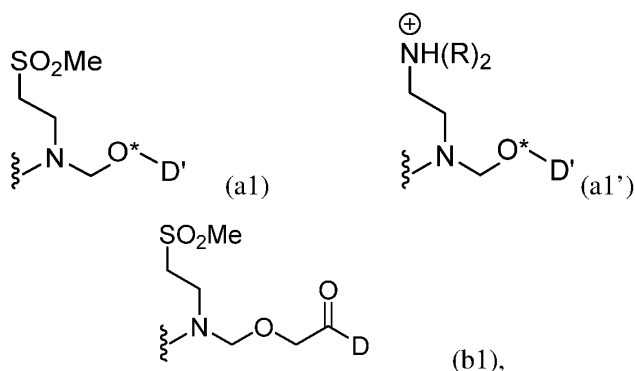
wherein R¹ and R² are independently selected from H, C₁-C₈ alkyl, C₁-C₈ substituted alkyl, C₂-C₈ alkenyl, C₂-C₈ substituted alkenyl, C₂-C₈ alkynyl, C₂-C₈ substituted alkynyl, C₆-C₂₀ aryl, C₆-C₂₀ substituted aryl, C₁-C₂₀ heterocycle, and C₁-C₂₀ substituted heterocycle; wherein the C₁-C₈ substituted alkyl, C₂-C₈ substituted alkenyl, C₂-C₈ substituted alkynyl, C₆-C₂₀ substituted aryl, and C₂-C₂₀ substituted heterocycle are independently optionally substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, OH, -N(R⁵)₂, -N(R⁵)₃⁺, C₁-C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, C₁-C₈ alkylsulfonate, C₁-C₈ alkylamino, 4-dialkylaminopyridinium, C₁-C₈ alkylhydroxyl, C₁-C₈ alkylthiol, -SO₂R⁵, -S(=O)R⁵, -SR⁵, -SO₂N(R⁵)₂, -C(=O)R⁵, -CO₂R⁵, -C(=O)N(R⁵)₂, -CN, -N₃, -NO₂, C₁-C₈ alkoxy, C₁-C₈ trifluoroalkyl, C₁-C₈ alkyl, C₃-C₁₂ carbocycle, C₆-C₂₀ aryl,

C₂–C₂₀ heterocycle, polyethyleneoxy, phosphonate, and phosphate; subscript n is 1 or 2; wherein EWG represents an electron-withdrawing group; T* is the heteroatom of a hydroxyl or thiol or primary or secondary amine or N-heterocycle or N-amide or N-carbamate of a Drug Unit of formula **D₀**, **D₁**, **D_{1a}**, **D_{1b}**, or any subformula thereof; D' is the remainder of a Drug Unit, wherein T* and D' together form a Drug Unit of formula **D₀**, **D₁**, **D_{1a}**, **D_{1b}**, or any subformula thereof (*i.e.* T* + D' = D); D is a Drug Unit of formula **D₀**, **D₁**, **D_{1a}**, **D_{1b}**, or any subformula thereof; and the wavy line adjacent to the nitrogen atom is the point of covalent attachment to RL. In some embodiments, EWG is selected from the group consisting of -CN, -NO₂, -CX₃, -X, -C(=O)OR', -C(=O)N(R')₂, -C(=O)R', -C(=O)X, -S(=O)₂R', -S(=O)₂OR', -S(=O)₂NHR', -S(=O)₂N(R')₂, -P(=O)(OR')₂, -P(=O)(CH₃)NHR', -NO, -N(R')₃⁺, wherein X is -F, -Br, -Cl, or -I, and R' is independently selected from the group consisting of hydrogen and C₁–C₆ alkyl.

[0533] In some embodiments, the Spacer Unit is represented by one of the following formulae:



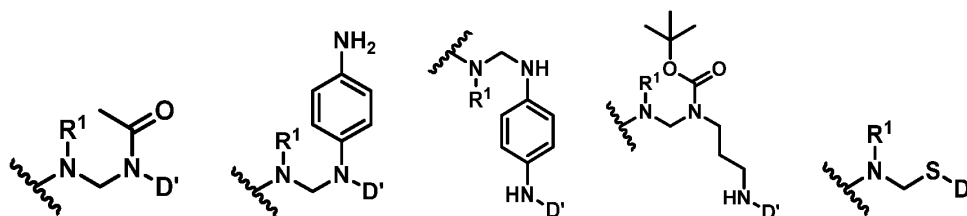
[0534] In still other embodiments, the Spacer Unit-Drug Unit group (–Y–T*–D or –Y–D) comprises a methylene carbamate unit and is represented by one of the following the formulae:



wherein formula (a1) and formula (a1') in which each R is independently –H or C₁–C₄ alkyl represents Spacer Units in which O* is the oxygen atom from the hydroxyl substituent to the lactone ring of a Drug Unit of formula **D₀**, **D₁**, **D_{1a}**, **D_{1b}**, or any subformula thereof, or of any one of compounds of Table I, and the wavy lines of formula (a1), formula (a1') and formula

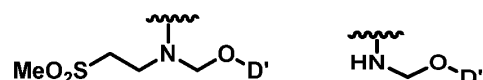
(b1) retain their previous meanings from formulae (a), (a') and (b), respectively. In formula (a1') the $-\text{CH}_2\text{CH}_2\text{N}^+(\text{R})_2$ moiety represents exemplary Basic Units in protonated form.

[0535] In some embodiments, the Spacer Unit-Drug Unit group $-\text{Y}-\text{T}^*-\text{D}'$ is represented by one of the following formulae:



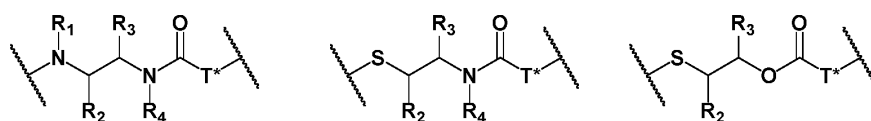
wherein R^1 is as defined for formula (a'), the wavy line adjacent to the nitrogen atom is the point of covalent attachment to RL, T^* is as defined above, and D' represents the remainder of the Drug Unit, wherein T^* and D' together form a Drug Unit of formula **D₀**, **D₁**, **D_{1a}**, **D_{1b}**, or any subformula thereof.

[0536] In some embodiments, the Spacer Unit-Drug Unit group $(-\text{Y}-\text{T}^*-\text{D})$ is represented by one of the following formulae:



wherein the wavy line adjacent is the point of covalent attachment to RL, T^* is as defined above, and D' represents the remainder of the Drug Unit, wherein T^* and D' together form a Drug Unit of formula **D₀**, **D₁**, **D_{1a}**, **D_{1b}**, or any subformula thereof.

[0537] In some embodiments, the Spacer Unit-Drug Unit group $(-\text{Y}-\text{T}^*-\text{D})$ is represented by one of the following formulae:

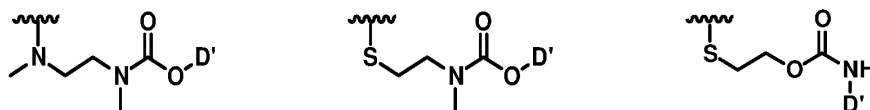


wherein R^1 and R^4 are independently selected from H, $\text{C}_1\text{--C}_8$ alkyl, $\text{C}_1\text{--C}_8$ substituted alkyl, $\text{C}_2\text{--C}_8$ alkenyl, $\text{C}_2\text{--C}_8$ substituted alkenyl, $\text{C}_2\text{--C}_8$ alkynyl, $\text{C}_2\text{--C}_8$ substituted alkynyl, $\text{C}_6\text{--C}_{20}$ aryl, $\text{C}_6\text{--C}_{20}$ substituted aryl, $\text{C}_1\text{--C}_{20}$ heterocycle, and $\text{C}_1\text{--C}_{20}$ substituted heterocycle; wherein the $\text{C}_1\text{--C}_8$ substituted alkyl, $\text{C}_2\text{--C}_8$ substituted alkenyl, $\text{C}_2\text{--C}_8$ substituted alkynyl, $\text{C}_6\text{--C}_{20}$ substituted aryl, and $\text{C}_2\text{--C}_{20}$ substituted heterocycle are independently substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, OH, $-\text{N}(\text{R}^5)_2$,

$-N(R^5)_3^+$, C₁–C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, C₁–C₈ alkylsulfonate, C₁–C₈ alkylamino, 4-dialkylaminopyridinium, C₁–C₈ alkylhydroxyl, C₁–C₈ alkylthiol, $-SO_2R^5$, $-S(=O)R^5$, $-SR^5$, $-SO_2N(R^5)_2$, $-C(=O)R^5$, $-CO_2R^5$, $-C(=O)N(R^5)_2$, $-CN$, $-N_3$, $-NO_2$, C₁–C₈ alkoxy, C₁–C₈ trifluoroalkyl, C₁–C₈ alkyl, C₃–C₁₂ carbocycle, C₆–C₂₀ aryl, C₂–C₂₀ heterocycle, polyethyleneoxy, phosphonate, and phosphate; R² is selected from the group consisting of H, C₁–C₈ alkyl, C₁–C₈ substituted alkyl, C₂–C₈ alkenyl, C₂–C₈ substituted alkenyl, C₂–C₈ alkynyl, C₂–C₈ substituted alkynyl, C₆–C₂₀ aryl, C₆–C₂₀ substituted aryl, C₁–C₂₀ heterocycle, and C₁–C₂₀ substituted heterocycle; wherein the C₁–C₈ substituted alkyl, C₂–C₈ substituted alkenyl, C₂–C₈ substituted alkynyl, C₆–C₂₀ substituted aryl, and C₂–C₂₀ substituted heterocycle are independently substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, OH, $-N(R^5)_2$, $-N(R^5)_3^+$, C₁–C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, C₁–C₈ alkylsulfonate, C₁–C₈ alkylamino, 4-dialkylaminopyridinium, C₁–C₈ alkylhydroxyl, C₁–C₈ alkylthiol, $-SO_2R^5$, $-S(=O)R^5$, $-SR^5$, $-SO_2N(R^5)_2$, $-C(=O)R^5$, $-CO_2R^5$, $-C(=O)N(R^5)_2$, $-CN$, $-N_3$, $-NO_2$, C₁–C₈ alkoxy, C₁–C₈ trifluoroalkyl, C₁–C₈ alkyl, C₃–C₁₂ carbocycle, C₆–C₂₀ aryl, C₂–C₂₀ heterocycle, polyethyleneoxy, phosphonate, and phosphate, or is combined with R³ and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; R³ is selected from the group consisting of H, C₁–C₈ alkyl, C₁–C₈ substituted alkyl, C₂–C₈ alkenyl, C₂–C₈ substituted alkenyl, C₂–C₈ alkynyl, C₂–C₈ substituted alkynyl, C₆–C₂₀ aryl, C₆–C₂₀ substituted aryl, C₁–C₂₀ heterocycle, and C₁–C₂₀ substituted heterocycle; wherein the C₁–C₈ substituted alkyl, C₂–C₈ substituted alkenyl, C₂–C₈ substituted alkynyl, C₆–C₂₀ substituted aryl, and C₂–C₂₀ substituted heterocycle are independently substituted with one or more substituents selected from the group consisting of F, Cl, Br, I, OH, $-N(R^5)_2$, $-N(R^5)_3^+$, C₁–C₈ alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, C₁–C₈ alkylsulfonate, C₁–C₈ alkylamino, 4-dialkylaminopyridinium, C₁–C₈ alkylhydroxyl, C₁–C₈ alkylthiol, $-SO_2R^5$, $-S(=O)R^5$, $-SR^5$, $-SO_2N(R^5)_2$, $-C(=O)R^5$, $-CO_2R^5$, $-C(=O)N(R^5)_2$, $-CN$, $-N_3$, $-NO_2$, C₁–C₈ alkoxy, C₁–C₈ trifluoroalkyl, C₁–C₈ alkyl, C₃–C₁₂ carbocycle, C₆–C₂₀ aryl, C₂–C₂₀ heterocycle, polyethyleneoxy, phosphonate, and phosphate, or is combined with R² and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; T* is the heteroatom of a hydroxyl or thiol or primary or secondary amine or N-heterocycle or N-amide or N-carbamate of a Drug Unit of formula **D0**, **D1**, **D1a**, **D1b**, or any subformula thereof; D' is the remainder of a Drug Unit, wherein T* and D' together form a Drug Unit of formula **D0**, **D1**,

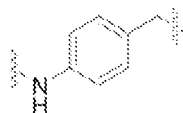
D_{1a}, D_{1b}, or any subformula thereof (*i.e.* $T^* + D' = D$); D is a Drug Unit of formula **D₀, D₁, D_{1a}, D_{1b}**, or any subformula thereof; and the wavy line adjacent to the nitrogen atom is the point of covalent attachment to RL.

[0538] In some embodiments, the Spacer Unit-Drug Unit ($-Y-T^*-D'$) is represented by one of the following formulae:



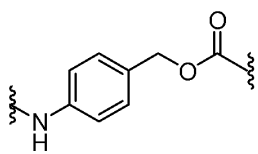
wherein the wavy line adjacent to the nitrogen atom is the point of covalent attachment to RL, T^* is as defined above, and D' represents the remainder of the Drug Unit, wherein T^* and D' together form a Drug Unit of formula **D₀, D₁, D_{1a}, D_{1b}**, or any subformula thereof.

[0539] In some embodiments, the Spacer Unit is represented by the formula:



wherein the wavy line adjacent to the nitrogen atom is the point of covalent attachment to RL, as defined above, and the wavy line next to the benzylic carbon atom connects to a Drug Unit. In some embodiments, the Drug Unit is attached to the benzylic carbon atom via a quaternized tertiary amine (N^+) of D.

[0540] In still other embodiments, the Spacer Unit is represented by the formula:



wherein the wavy line adjacent to the nitrogen atom is the point of covalent attachment to RL, as defined above, and the wavy line next to the $-OC(O)-$ group connects to a Drug Unit. In some embodiments, the Drug Unit is attached via T^* , wherein T^* is the heteroatom of a hydroxyl or thiol or primary amine, secondary amine, or N-heterocycle or N-amide or N-carbamate of a Drug Unit of formula **D₀, D₁, D_{1a}, D_{1b}**, or any subformula thereof.

Subscript “p”

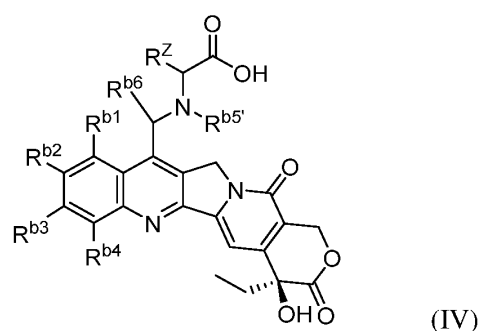
[0541] In one group of embodiments of the invention, subscript p represents the number of Drug Linker moieties on a Ligand Unit of an individual Camptothecin Conjugate and is an

integer preferably ranging from 1 to 16, 1 to 12, 1 to 10, or 1 to 8. Individual Camptothecin Conjugates can be also be referred to as a Camptothecin Conjugate compound. In any of the embodiments herein, there can be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 Drug Linker moieties conjugated to a Ligand Unit of an individual Camptothecin Conjugate. In another group of embodiments of the invention, a Camptothecin Conjugate describes a population of individual Camptothecin Conjugate compounds substantially identical except for the number of Camptothecin Drug-Linker moieties bound to each Ligand Unit (i.e., a Camptothecin Conjugate composition) so that subscript p represents the average number of Camptothecin drug linker moieties bound to the Ligand Units of the Camptothecin Conjugate composition. In that group of embodiments, subscript p is a number ranging from 1 to about 16, 1 to about 12, 1 to about 10, or 1 to about 8, from 2 to about 16, 2 to about 12, 2 to about 10, or 2 to about 8. In some embodiments, p is about 2. In some embodiments, p is about 4. In some embodiments, p is about 8. In some embodiments, p is about 16. In some embodiments, p is 2. In some embodiments, p is 4. In some embodiments, p is 8. In some embodiments, p is 16. In some embodiments, the value of subscript p refers to the average drug loading as well as the drug loading of the predominate ADC in the composition.

[0542] In some embodiments, conjugation will be via the interchain disulfides and there will from 1 to about 8 Camptothecin Linker Compound molecules conjugated to a targeting agent that becomes a Ligand Unit. In some embodiments, conjugation will be via an introduced cysteine residue as well as interchain disulfides and there will be from 1 to 10 or 1 to 12 or 1 to 14 or 1 to 16 Camptothecin Linker Compound moieties conjugated to a Ligand Unit. In some embodiments, conjugation will be via an introduced cysteine residue and there will be 2 or 4 Camptothecin Linker Compound molecules conjugated to a Ligand Unit.

Partially Released Free Drug

[0543] In some embodiments, are compounds where the RL unit in the conjugate has been cleaved, leaving the drug moiety with one amino acid residue bound thereto. In some embodiments, the partially released Free Drug (Drug-Amino Acid Conjugate) is a compound of Formula (IV):



or a stereoisomer or mixture of stereoisomers thereof, or a pharmaceutically acceptable salt thereof, wherein R^Z is an amino acid sidechain as described herein. In some embodiments, R^x is H, methyl, isopropyl, benzyl, or $-(CH_2)_4-NH_2$. In some embodiments, R^Z is H or methyl. In some embodiments, R^Z is H. In some embodiments, R^Z is methyl.

[0544] In some embodiments, the compound of Formula (IV) is a biologically active compound. In some embodiments, such compounds are useful in a method of inhibiting topoisomerase, killing tumor cells, inhibiting growth of tumor cells, cancer cells, or of a tumor, inhibiting replication of tumor cells or cancer cells, lessening of overall tumor burden or decreasing the number of cancerous cells, or ameliorating one or more symptoms associated with a cancer or autoimmune disease. Such methods comprise, for example, contacting a cancer cell with a compound of Formula (IV).

Camptothecin Conjugate Mixtures and Compositions

[0545] The present invention provides Camptothecin Conjugate mixtures and pharmaceutical compositions comprising any of the Camptothecin Conjugates described herein. The mixtures and pharmaceutical compositions comprise a plurality of conjugates. In some embodiments, each of the conjugates in the mixture or composition is identical or substantially identical, however, the distribution of drug-linkers on the ligands in the mixture or compositions may vary as well as the drug loading. For example, the conjugation technology used to conjugate drug-linkers to antibodies as the targeting agent in some embodiments results in a composition or mixture that is heterogeneous with respect to the distribution of Camptothecin Linker Compounds on the antibody (Ligand Unit) within the mixture and/or composition. In some of those embodiments, the loading of Camptothecin Linker Compounds on each of the antibody molecules in a mixture or composition of such molecules is an integer that ranges from 1 to 16.

[0546] In those embodiments, when referring to the composition as a whole, the loading of drug-linkers is a number ranging from 1 to about 16. Within the composition or mixture,

there sometimes is a small percentage of unconjugated antibodies. The average number of drug-linkers per Ligand Unit in the mixture or composition (i.e., average drug-load) is an important attribute as it determines the maximum amount of drug that can be delivered to the target cell. Typically, the average drug load is 1, 2 or about 2, 3 or about 3, 4 or about 4, 5 or about 5, 6 or about 6, 7 or about 7, 8 or about 8, 9 or about 9, 10 or about 10, 11 or about 11, 12 or about 12, 13 or about 13, 14 or about 14, 15 or about 15, 16 or about 16.

[0547] In some embodiments, the mixtures and pharmaceutical compositions comprise a plurality (i.e., population) of conjugates, however, the conjugates are identical or substantially identical and are substantially homogenous with respect to the distribution of drug-linkers on the ligand molecules within the mixture and/or composition and with respect to loading of drug-linkers on the ligand molecules within the mixture and/or composition. In some such embodiments, the loading of drug-linkers on an antibody Ligand Unit is 2 or 4. Within the composition or mixture, there may also be a small percentage of unconjugated antibodies. The average drug load in such embodiments is about 2 or about 4. Typically, such compositions and mixtures result from the use of site-specific conjugation techniques and conjugation is due to an introduced cysteine residue.

[0548] The average number of Camptothecins or Camptothecin-Linker Compounds per Ligand Unit in a preparation from a conjugation reaction may be characterized by conventional means such as mass spectrometry, ELISA assay, HPLC (e.g., HIC). In those instances, the quantitative distribution of Camptothecin Conjugates in terms of subscript *p* may also be determined. In other instances, separation, purification, and characterization of homogeneous Camptothecin Conjugates may be achieved by conventional means such as reverse phase HPLC or electrophoresis.

[0549] In some embodiments, the compositions are pharmaceutical compositions comprising the Camptothecin Conjugates described herein and a pharmaceutically acceptable carrier. In some of those embodiments, the pharmaceutical composition is in liquid form. In some embodiments, the pharmaceutical composition is a solid. In other of those embodiments, the pharmaceutical composition is a lyophilized powder.

[0550] The compositions, including pharmaceutical compositions, can be provided in purified form. As used herein, “purified” means that when isolated, the isolate contains at least 95%, and in other embodiments at least 98% of Conjugate by weight of the isolate.

Methods of Use

Treatment of Cancer

[0551] The Camptothecin Conjugates are useful for inhibiting the multiplication of a tumor cell or cancer cell, causing apoptosis in a tumor or cancer cell, or for treating a cancer in a patient. The Camptothecin Conjugates are used accordingly in a variety of settings for the treatment of cancers. The Camptothecin Conjugates are intended to deliver a drug to a tumor cell or cancer cell. Without being bound by theory, in one embodiment, the Ligand Unit of a Camptothecin Conjugate binds to or associates with a cancer-cell or a tumor-cell-associated antigen, and the Camptothecin Conjugate is taken up (internalized) inside the tumor cell or cancer cell through receptor-mediated endocytosis or other internalization mechanism. In some embodiments, the antigen is attached to a tumor cell or cancer cell or is an extracellular matrix protein associated with the tumor cell or cancer cell. Once inside the cell, via activation of the Activation Unit, the drug is released within the cell. In an alternative embodiment, the free drug is released from the Camptothecin Conjugate outside the tumor cell or cancer cell, and the free drug subsequently penetrates the cell.

[0552] In one embodiment, the Ligand Unit binds to the tumor cell or cancer cell.

[0553] In another embodiment, the Ligand Unit binds to a tumor cell or cancer cell antigen which is on the surface of the tumor cell or cancer cell.

[0554] In another embodiment, the Ligand Unit binds to a tumor cell or cancer cell antigen that is an extracellular matrix protein associated with the tumor cell or cancer cell.

[0555] The specificity of the Ligand Unit for a particular tumor cell or cancer cell is an important consideration for determining the tumors or cancers that are most effectively treated. For example, Camptothecin Conjugates that target a cancer cell antigen present on hematopoietic cancers are useful treating hematologic malignancies (e.g., anti-CD30, anti-CD70, anti-CD19, anti-CD33 binding Ligand Unit (e.g., antibody) are useful for treating hematologic malignancies). Camptothecin Conjugates that target a cancer cell antigen present on solid tumors in some embodiments are useful treating such solid tumors.

[0556] Cancers that are intended to be treated with a Camptothecin Conjugate include, but are not limited to, hematopoietic cancers such as, for example, lymphomas (Hodgkin Lymphoma and Non-Hodgkin Lymphomas) and leukemias and solid tumors. Examples of hematopoietic cancers include, follicular lymphoma, anaplastic large cell lymphoma, mantle cell lymphoma, acute myeloblastic leukemia, chronic myelocytic leukemia, chronic

lymphocytic leukemia, diffuse large B cell lymphoma, and multiple myeloma. Examples of solid tumors include fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon cancer, colorectal cancer, kidney cancer, pancreatic cancer, bone cancer, breast cancer, ovarian cancer, prostate cancer, esophageal cancer, stomach cancer, oral cancer, nasal cancer, throat cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, uterine cancer, testicular cancer, small cell lung carcinoma, bladder carcinoma, lung cancer, epithelial carcinoma, glioma, glioblastoma multiforme, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, neuroblastoma, and retinoblastoma.

[0557] In preferred embodiments, the treated cancer is any one of the above-listed lymphomas and leukemias.

Multi-Modality Therapy for Cancer

[0558] Cancers, including, but not limited to, a tumor, metastasis, or other disease or disorder characterized by uncontrolled cell growth are intended to be treated or inhibited by administration of an effective amount of a Camptothecin Conjugate.

[0559] In one group of embodiments, methods for treating cancer are provided, including administering to a patient in need thereof an effective amount of a Camptothecin Conjugate and a chemotherapeutic agent. In one embodiment the chemotherapeutic agent is one in which treatment of the cancer has not been found to be refractory to that agent. In another embodiment, the chemotherapeutic agent one in which the treatment of cancer has been found to be refractory to that agent.

[0560] In another group of embodiments, the Camptothecin Conjugate is administered to a patient that has also undergone surgery as treatment for the cancer. In such embodiments a chemotherapeutic agent is typically administered over a series of sessions, or one or a combination of the chemotherapeutic agents, such a standard of care chemotherapeutic agent(s), is administered.

[0561] In either group of embodiments, the patient also receives an additional treatment, such as radiation therapy. In a specific embodiment, the Camptothecin Conjugate is administered concurrently with the chemotherapeutic agent or with radiation therapy. In another specific embodiment, the chemotherapeutic agent or radiation therapy is administered prior or subsequent to administration of a Camptothecin Conjugate.

[0562] Additionally, methods of treatment of cancer with a Camptothecin Conjugate are provided as an alternative to chemotherapy or radiation therapy where the chemotherapy or the radiation therapy has proven or can prove too toxic, *e.g.*, results in unacceptable or unbearable side effects, for the subject being treated. The patient being treated is optionally treated with another cancer treatment such as surgery, radiation therapy or chemotherapy, depending on which treatment is found to be acceptable or bearable.

Treatment of Autoimmune Diseases

[0563] The Camptothecin Conjugates are intended to be useful for killing or inhibiting the unwanted replication of cells that produce an autoimmune disease or for treating an autoimmune disease.

[0564] The Camptothecin Conjugates are used accordingly in a variety of settings for the treatment of an autoimmune disease in a patient. The Camptothecin Conjugates are typically used to deliver a camptothecin drug to a target cell. Without being bound by theory, in one embodiment, the Camptothecin Conjugate associates with an antigen on the surface of a pro-inflammatory or inappropriately stimulated immune cell, and the Camptothecin Conjugate is then taken up inside the targeted cell through receptor-mediated endocytosis. Once inside the cell, the Linker Unit is cleaved, resulting in release of the Camptothecin Drug Unit as free drug. The Camptothecin free drug is then able to migrate within the cytosol and induce a cytotoxic or cytostatic activity. In an alternative embodiment, the Camptothecin Drug Unit is cleaved from the Camptothecin Conjugate outside the target cell, and the Camptothecin free drug resulting from that release subsequently penetrates the cell.

[0565] In one embodiment, the Ligand Unit binds to an autoimmune antigen. In one such embodiment, the antigen is on the surface of a cell involved in an autoimmune condition.

[0566] In one embodiment, the Ligand Unit binds to activated lymphocytes that are associated with the autoimmune disease state.

[0567] In a further embodiment, the Camptothecin Conjugate kills or inhibits the multiplication of cells that produce an autoimmune antibody associated with a particular autoimmune disease.

[0568] Particular types of autoimmune diseases intended to be treated with the Camptothecin Conjugates include, but are not limited to, Th2 lymphocyte related disorders (*e.g.*, atopic dermatitis, atopic asthma, rhinoconjunctivitis, allergic rhinitis, Omenn's syndrome, systemic sclerosis, and graft versus host disease); Th1 lymphocyte-related disorders (*e.g.*, rheumatoid arthritis, multiple sclerosis, psoriasis, Sjorgren's syndrome, Hashimoto's thyroiditis, Grave's disease, primary biliary cirrhosis, Wegener's granulomatosis, and tuberculosis); and activated B lymphocyte-related disorders (*e.g.*, systemic lupus erythematosus, Goodpasture's syndrome, rheumatoid arthritis, and type I diabetes).

Multi-Drug Therapy of Autoimmune Diseases

[0569] Methods for treating an autoimmune disease are also disclosed including administering to a patient in need thereof an effective amount of a Camptothecin Conjugate and another therapeutic agent known for the treatment of an autoimmune disease.

Compositions and Methods of Administration

[0570] The present invention provides pharmaceutical compositions comprising the Camptothecin Conjugates described herein and at least one pharmaceutically acceptable carrier. The pharmaceutical composition is in any form that allows the compound to be administered to a patient for treatment of a disorder associated with expression of the antigen to which the Ligand unit binds. For example, the conjugates are in the form of a liquid or solid. The preferred route of administration is parenteral. Parenteral administration includes subcutaneous injections, intravenous, intramuscular, intrasternal injection or infusion techniques. In one embodiment, the pharmaceutical compositions is administered parenterally. In one embodiment, the conjugates are administered intravenously. Administration is by any convenient route, for example by infusion or bolus injection.

[0571] Pharmaceutical compositions are formulated to allow a Camptothecin Conjugate to be bioavailable upon administration of the composition to a patient. Compositions sometimes take the form of one or more dosage units.

[0572] Materials used in preparing the pharmaceutical compositions are preferably non-toxic in the amounts used. It will be evident to those of ordinary skill in the art that the

optimal dosage of the active ingredient(s) in the pharmaceutical composition will depend on a variety of factors. Relevant factors include, without limitation, the type of animal (*e.g.*, human), the particular form of the compound, the manner of administration, and the composition employed.

[0573] The composition in some embodiments is in the form of a liquid. The liquid in some of those embodiments is useful for delivery by injection. In some embodiments a composition for administration by injection, in addition to the Camptothecin Conjugate, contains one or more excipients selected from the group consisting of a surfactant, preservative, wetting agent, dispersing agent, suspending agent, buffer, stabilizer and isotonic agent.

[0574] The liquid compositions, whether they are solutions, suspensions or other like form, in some embodiments include one or more of the following: sterile diluents such as water for injection, saline solution, preferably physiological saline, Ringer's solution, isotonic sodium chloride, fixed oils such as synthetic mono or diglycerides which can serve as the solvent or suspending medium, polyethylene glycols, glycerin, cyclodextrin, propylene glycol or other solvents; antibacterial agents such as benzyl alcohol or methyl paraben; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as amino acids, acetates, citrates or phosphates; detergents, such as nonionic surfactants, polyols; and agents for the adjustment of tonicity such as sodium chloride or dextrose. A parenteral composition is sometimes enclosed in ampoule, a disposable syringe or a multiple-dose vial made of glass, plastic or other material. Physiological saline is an exemplary adjuvant. An injectable composition is preferably sterile.

[0575] The amount of the conjugate that is effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, which in some embodiments is determined by standard clinical techniques. In addition, *in vitro* or *in vivo* assays are optionally employed to help identify optimal dosage ranges. The precise dose to be employed in the compositions will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances.

[0576] The compositions comprise an effective amount of a Camptothecin Conjugate such that a suitable dosage amount will be obtained. Typically, that amount is at least about 0.01% of a compound by weight of the composition.

[0577] For intravenous administration, the pharmaceutical composition typically comprises from about 0.01 to about 100 mg of a Camptothecin Conjugate per kg of the animal's body weight. In one embodiment, the composition can include from about 1 to about 100 mg of a Camptothecin Conjugate per kg of the animal's body weight. In another aspect, the amount administered will be in the range from about 0.1 to about 25 mg/kg of body weight of a compound. Depending on the drug used, the dosage can be even lower, for example, 1.0 µg/kg to 5.0 mg/kg, 4.0 mg/kg, 3.0 mg/kg, 2.0 mg/kg or 1.0 mg/kg, or 1.0 µg/kg to 500.0 µg/kg of the subject's body weight.

[0578] Generally, the dosage of a conjugate administered to a patient is typically about 0.01 mg/kg to about 100 mg/kg of the subject's body weight or from 1.0 µg/kg to 5.0 mg/kg of the subject's body weight. In some embodiments, the dosage administered to a patient is between about 0.01 mg/kg to about 15 mg/kg of the subject's body weight. In some embodiments, the dosage administered to a patient is between about 0.1 mg/kg and about 15 mg/kg of the subject's body weight. In some embodiments, the dosage administered to a patient is between about 0.1 mg/kg and about 20 mg/kg of the subject's body weight. In some embodiments, the dosage administered is between about 0.1 mg/kg to about 5 mg/kg or about 0.1 mg/kg to about 10 mg/kg of the subject's body weight. In some embodiments, the dosage administered is between about 1 mg/kg to about 15 mg/kg of the subject's body weight. In some embodiments, the dosage administered is between about 1 mg/kg to about 10 mg/kg of the subject's body weight. In some embodiments, the dosage administered is between about 0.1 to 4 mg/kg, even more preferably 0.1 to 3.2 mg/kg, or even more preferably 0.1 to 2.7 mg/kg of the subject's body weight over a treatment cycle.

[0579] The term "carrier" refers to a diluent, adjuvant or excipient, with which a compound is administered. Such pharmaceutical carriers in some embodiments is a liquid, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil. Other carriers include saline, gum acacia, gelatin, starch paste, talc, keratin, colloidal silica, urea. In addition, auxiliary, stabilizing, thickening, lubricating and coloring agents are sometimes used. In one embodiment, when administered to a patient, the Camptothecin Conjugate or compositions thereof and pharmaceutically acceptable carriers are sterile.

[0580] Water is an exemplary carrier when the compounds are administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are often employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical carriers also include excipients such as starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol. The present compositions, if desired, also contain minor amounts of wetting or emulsifying agents, or pH buffering agents.

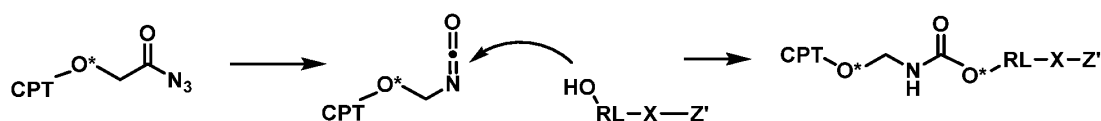
[0581] In an embodiment, the conjugates are formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to animals, particularly human beings. Typically, the carriers or vehicles for intravenous administration are sterile isotonic aqueous buffer solutions. Where necessary, the compositions include a solubilizing agent. Compositions for intravenous administration optionally comprise a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachets indicating the quantity of active agent. Where a conjugate is to be administered by infusion, it is typically dispensed, for example, with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the conjugate is administered by injection, an ampoule of sterile water for injection or saline is sometimes provided so that the ingredients can be mixed prior to administration.

[0582] The pharmaceutical compositions are generally formulated as sterile, substantially isotonic and in full compliance with all Good Manufacturing Practice (GMP) regulations of the U.S. Food and Drug Administration.

Methods of Preparing Camptothecin Conjugates

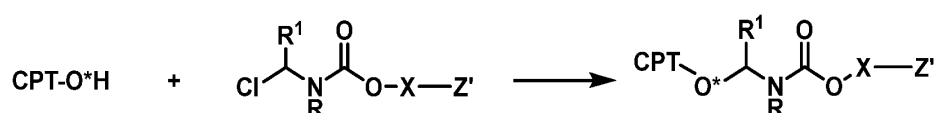
[0583] The Camptothecin Conjugates described herein are prepared in either a serial construction of antibodies, linkers, and drug units, or in a convergent fashion by assembling portions followed by a completed assembly step. The Curtius Rearrangement or a Chloramine synthesis can be used to provide a methylene carbamate linker (Spacer) which is useful in a number of embodiments of the Conjugates described herein.

[0584] *Scheme 2: Preparation of Exemplary Camptothecin Drug-Linker compounds of formula Z'-A-RL-Y-D, Z'-A-S*-RL-Y-D or Z'-A-B(S*)-RL-Y-D wherein Y has formula (a')* using the Curtius Rearrangement Reaction:



[0585] *Scheme 2* illustrates a synthetic strategy involving a Curtius rearrangement of an acyl azide derivative of the free drug, wherein CPT is a Camptothecin Drug Unit corresponding in structure to a Camptothecin compound having a hydroxyl functional group, such as one of formula **D1**, **D1a**, **D1b**, or any subformula thereof, or any of the compounds of Table I, whose oxygen atom, which is represented by O*, is incorporated into the methylene carbamate unit formed as a consequence of the rearrangement, Z' is a Stretcher Unit precursor, RL is a Releasable Linker and X is -A-, -A-S*- or -A-B(S*)- wherein A is a Connector Unit, S* is a Partitioning agent and B is a Parallel Connector Unit. That strategy may be applied to Camptothecin drugs containing multiple alcohols, or other heteroatoms, as a means for acquiring regioselectivity, as there are many complementary methods of alkylation to form an acyl azide such as: halo ester alkylation, halo acid alkylation or metal carbene insertion with ethyl or methyl diazoacetate, *see* Doyle, M. *et al.* *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley: New York, 1998. The acyl azide is then heated with at least a stoichiometric amount of alcohol-containing Linker Unit intermediate of formula Z'-X-RL-OH.

[0586] *Scheme 3*: Alternative preparation of exemplary Camptothecin Drug-Linker compounds of formula Z'-A-RL-Y-D, Z'-A-S*-RL-Y-D or Z'-A-B(S*)-RL-Y-D wherein Spacer Unit Y is a methylene carbamate unit of formula (a) or formula (a') via N-chloromethylamine synthesis:



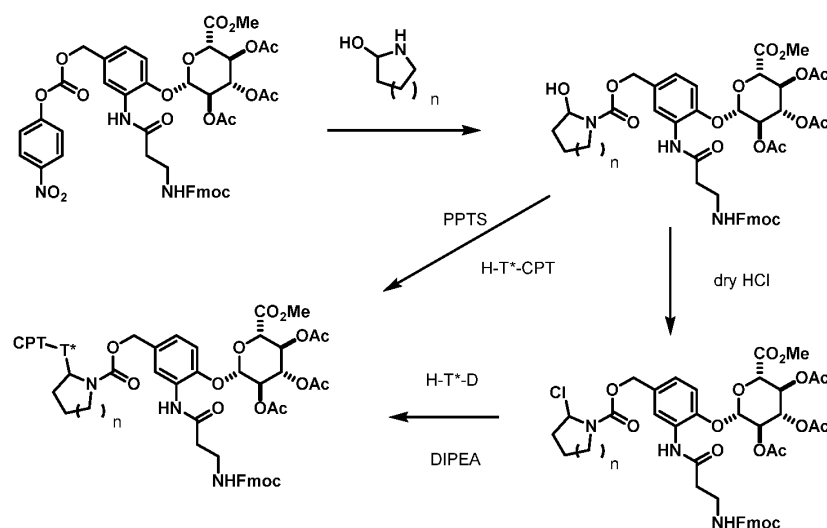
wherein R¹ is hydrogen or C₁-C₄ alkyl, R is -H or -CH₂CH₂SO₂Me and the other the variable groups have their meanings from Scheme 2.

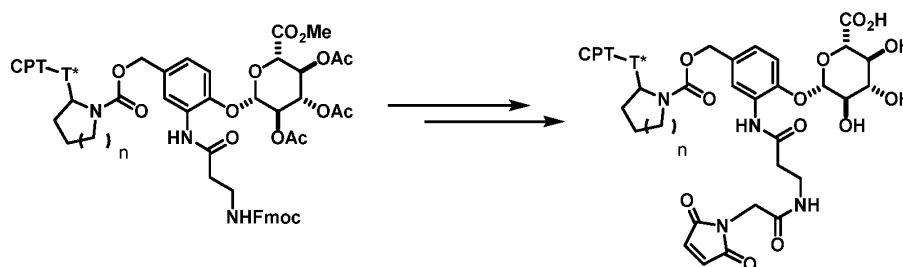
[0587] The N-chloromethylamine synthesis is an alternative to the Curtius rearrangement in that it allows for the introduction of an unmodified alcohol or other heteroatom containing Camptothecin compound, whose use may not be compatible with the conditions required to form the acyl azide of *Scheme 2*, and proceeds by condensation with a reactive N-

chloromethylamine. That methodology is also more appropriate for introducing certain types of methylene carbamate units as shown for example by *Scheme 4*.

[0588] *Scheme 4* demonstrates synthesis of exemplary Camptothecin-Linker Compounds of formula $Z'-A-RL-Y-D$, $Z'-A-S^*-RL-Y-D$ or $Z'-A-B(S^*)-RL-Y-D$ wherein the Spacer Unit (Y) is a methylene carbamate unit of formula (a''). Reaction of the p-nitro-phenyl carbonate with the cyclic aminol provides a carbamate, which is then converted to the chlorocycloalkylamine for alkylation with a nucleophile from the thiol, hydroxyl, amine or amide functional group of free camptothecin drug. Alternatively, the carbamate can be treated with acid in the presence of the drug moiety to assemble the drug-linker intermediate shown. The alkylation product is deprotected followed by condensation of the resulting free amine with 3-maleimidopropionic acid N-hydroxysuccinimide ester, which introduces a Stretcher Unit precursor covalently attached to a Connector Unit thus providing Camptothecin-Linker Compounds. The resulting Camptothecin-Linker Compounds are then condensed with a thiol-containing targeting agent to provide Camptothecin Conjugates having a Spacer Unit comprising a self-immolative moiety and the methylene carbamate unit of formula a''.

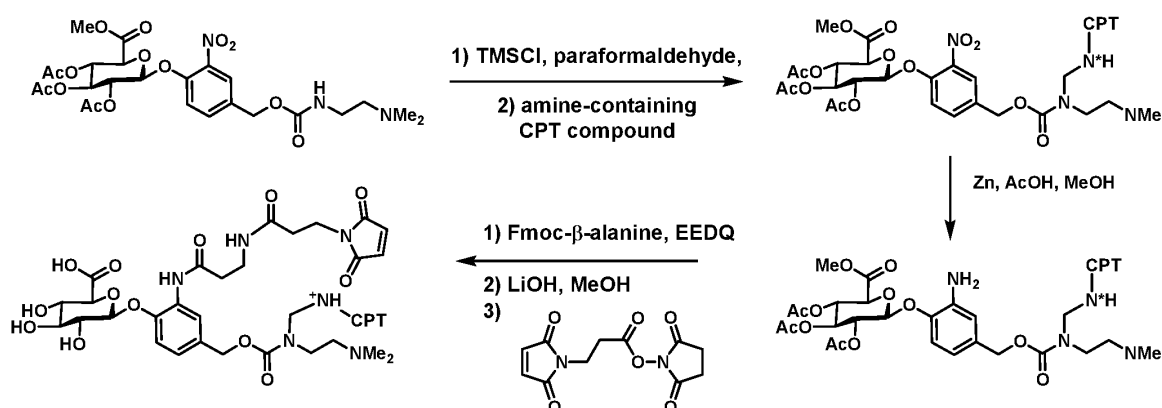
[0589] *Scheme 4*: Preparation of exemplary Camptothecin Drug-Linker compounds of formula $Z'-A-RL-Y-D$ wherein Spacer Unit Y is a formula (a'') methylene carbamate unit.





[0590] For Camptothecin-Linker Compounds and Camptothecin Conjugates having a methylene carbamate unit wherein T* is the nitrogen atom from a primary or secondary amine substituent of a Camptothecin compound direct alkylation with a chlormethylamine following the generalized procedures provided by *Scheme 3* or *Scheme 4* may not be suitable due to excessive or undesired over-alkylation of the nitrogen heteroatom from the amine functional group of free drug. In those instances, the method embodied by *Scheme 5* may be used.

[0591] *Scheme 5:*



[0592] In Scheme 5 an intermediate carbamate is prepared already having a Basic Unit (i.e., the dimethylaminoethyl moiety) as the R substituent for a formula (a1') methylene carbamate unit. The nitrogen of that carbamate is condensed with formaldehyde and the resulting intermediate quenched with the amine functional group of an aliphatic amine-containing camptothecin drug. N* represents the nitrogen atom from that functional group. That condensation forms the methylene carbamate of formula (a1') covalently attached to a Camptothecin Drug Unit, wherein R¹ is hydrogen and R is dimethylaminoethyl. The phenyl nitro group is then reduced to an amine in order to provide a handle for sequential introduction of a Connector Unit (A) and a Stretcher Unit precursor (Z').

EXAMPLES

Materials and Methods

[0593] The following materials and methods are applicable to the synthetic procedures described in this section unless indicated otherwise. All commercially available anhydrous solvents were used without further purification. Starting materials, reagents and solvents were purchased from commercial suppliers (SigmaAldrich and Fischer). Products were purified by flash column chromatography utilizing a Biotage Isolera One flash purification system (Charlotte, NC). UPLC-MS was performed on a Waters single quad detector mass spectrometer interfaced to a Waters Acquity UPLC system. UPLC methods are described below. Preparative HPLC was carried out on a Waters 2454 Binary Gradient Module solvent delivery system configured with a Waters 2998 PDA detector or Teledyne ISCO ACCQPrep HP150. Products were purified with the appropriate diameter of column of a Phenomenex Max-RP 4 μ m Synergi 80 Å 250 mm reverse phase column eluting with 0.05% trifluoroacetic acid in water and 0.05% trifluoroacetic acid in acetonitrile unless otherwise specified.

General Method:

[0594] Column - Waters CORTECS C18 1.6 μ m, 2.1 x 50 mm, reversed-phase column

[0595] Solvent A - 0.1% aqueous formic acid

[0596] Solvent B - acetonitrile with 0.1% formic acid

Time (min)	Flow (mL/min)	A%	B%	Gradient
Initial	0.6	97	3	
1.70	0.6	40	60	Linear
2.00	0.6	5	95	Linear
2.50	0.6	5	95	Linear
2.80	0.6	97	3	Linear
3.00	0.6	97	3	Linear
2.80	0.6	97	3	Linear

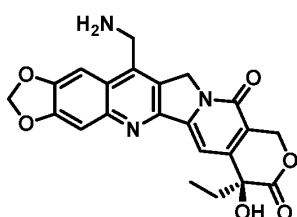
List Of Abbreviations

AcOH	acetic acid
Boc	tert-butyloxycarbonyl protecting group
DCM	dichloromethane
DIPEA	N, N-diisopropylethylamine
DMA	N,N-dimethylacetamide
DMF	N,N-dimethylformamide
EtOAc	ethyl acetate
EtOH	ethanol

Fmoc	9-fluorenylmethyl carbamate
HATU	1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate
Hex	hexanes
HPLC	high performance liquid chromatography
MeCN	acetonitrile
MeOH	methanol
MP	3-maleimidopropyl
MS	Mass spectrometry
OSu	N-hydroxysuccinimide
PEG	polyethylene glycol
PPTS	pyridinium para-toluene sulfonic acid
pTSA	para-toluene sulfonic acid
Prep	preparative
TFA	trifluoroacetic acid
TSTU	N,N,N',N'-tetramethyl-O-(N-succinimidyl)uronium tetrafluoroborate
UPLC	Ultra Performance Liquid Chromatography

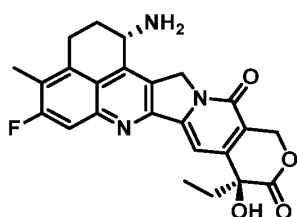
Experimental Methods

Example 1



[0597] Preparation of compound **1** was described in patent WO 2019195665

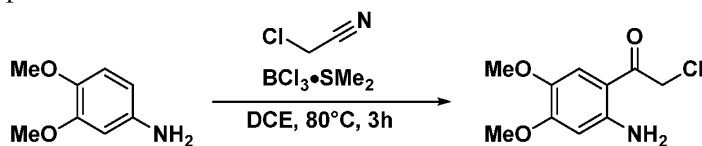
Example 1a



[0598] Compound **1a** (Exatecan) was purchased from Advanced ChemBlock (Catalog # 10484).

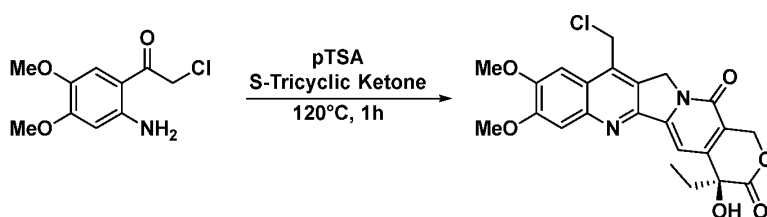
Example 2: Preparation of Compound 2ao.

Step 1:



[0599] Boron trichloride methyl sulfide complex (2M in DCM, 1.10 eq, 18 mL, 35.9 mmol) was diluted in DCE (110 mL) and the mixture was cooled to 0°C under nitrogen atmosphere. 3,4-dimethoxyaniline (1.00 eq, 5000 mg, 32.6 mmol) diluted in DCE (20 mL) was added dropwise. The resulting solution was stirred for 15 minutes, and 2-chloroacetonitrile (1.10 eq, 2.3 mL, 35.9 mmol) was added. The reaction was warmed to room temperature, stirred for 15 minutes, and then heated at reflux for 3 hours. Nearly complete conversion to the imine/ketone intermediate was observed by UPLC-MS. The reaction was cooled to room temperature and 2M HCl (130 mL) was added. The reaction was heated to reflux for 30 minutes, then cooled to room temperature, and poured into ice water (150 mL). The aqueous was extracted with DCM (3 x 250 mL) and the combine organic extracts were washed with water (3x500 mL). Organic phase was dried with MgSO_4 , filtered and concentrated in vacuo. The crude material was purified by FCC 0-50% MeCN in DCM. Fractions containing the desired product were concentrated in vacuo to afford a tan solid 1-(2-amino-4,5-dimethoxy-phenyl)-2-chloro-ethanone (1573 mg, 6.85 mmol, 20.98 % yield). $\text{Rt} = 1.25$ min General Method UPLC. MS (m/z) $[\text{M}+\text{H}]^+$ calc. for $\text{C}_{10}\text{H}_{13}\text{ClNO}_3$ 230.06, found 230.28.

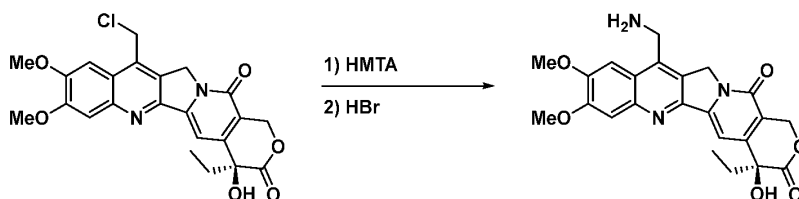
Step 2:



[0600] (2-amino-4,5-dimethoxyphenyl)-2-chloro-ethanone (1.00 eq, 200 mg, 0.871 mmol), Para-toluenesulfonic acid (1.00 eq, 150.0 mg, 0.871 mmol) and (4S)-4-ethyl-4-hydroxy-7,8-dihydro-1H-pyrano[3,4-f]indolizine-3,6,10-trione (1.10 eq, 252 mg, 0.958 mmol) were charged in a flask. DCM (2 mL) was added to homogenize the solids, and then evaporated under nitrogen. The neat solids were heated to 120°C under high vacuum (1

mbar) for 60 minutes. The reaction was cooled to room temperature, the crude product was precipitated with water, filtered, washed with water and dried under high vacuum to afford a brown solid (257 mg, 0.563 mmol, 64.67 % yield), which was used in the next step without further purification. Rt = 1.35 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₂₃H₂₂ClN₂O₆ 457.12, found 457.56.

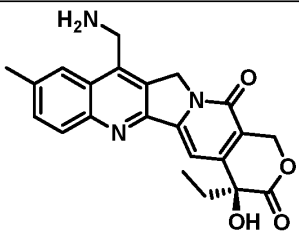
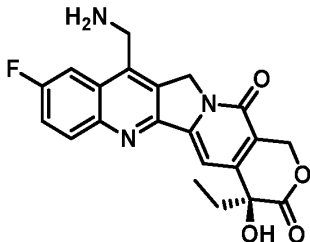
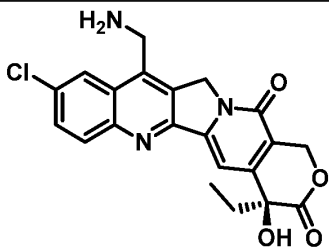
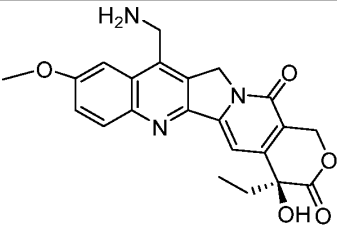
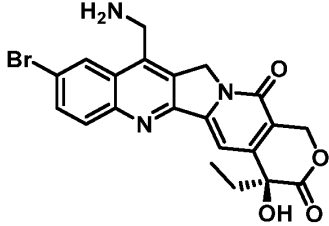
Step 3:

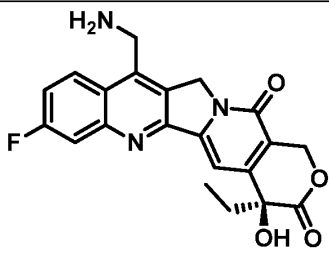
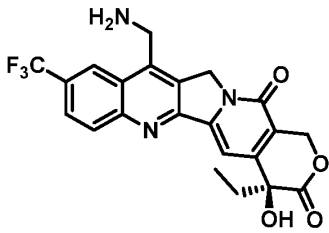
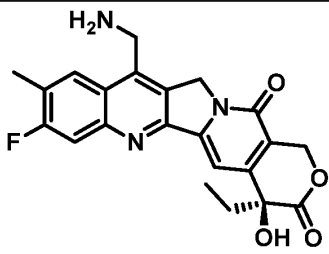
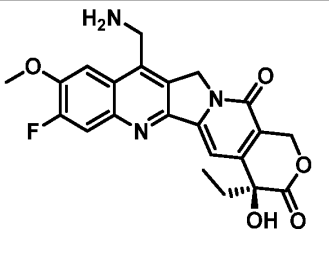
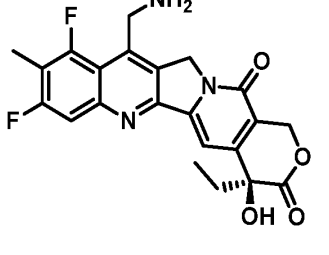


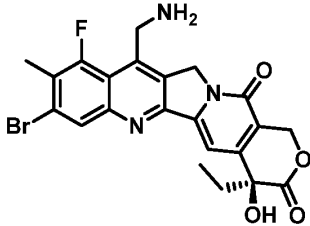
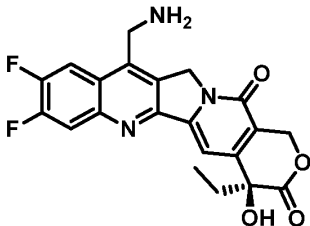
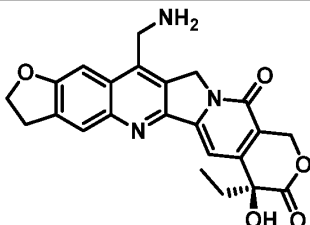
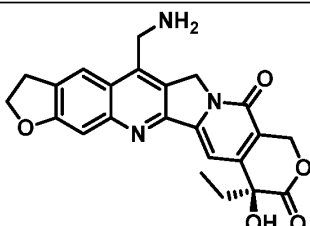
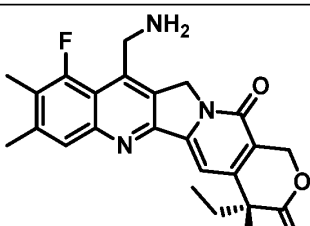
[0601] (19S)-10-(chloromethyl)-19-ethyl-19-hydroxy-6,7-dimethoxy-17-oxa-3,13-diazapentacyclo[11.8.0.02,11.04,9.015,20]henicosa-1(21),2,4(9),5,7,10,15(20)-heptaene-14,18-dione (1.00 eq, 257 mg, 0.563 mmol) was dissolved in Ethanol (4 mL). 1,3,5,7-tetrazatricyclo[3.3.1.13,7]decane (3.00 eq, 237 mg, 1.69 mmol) was added and the reaction was stirred at 65 °C for 24 hours. The reaction was quenched with a mixture of EtOH (4 mL) and 48% w/w aqueous HBr (0.8 mL). The reaction was stirred at 65 °C for 1 hour. The reaction was cooled to room temperature and concentrated in vacuo. The crude product was purified by prep-HPLC using a Synergi Max-RP 30 x 250 mm column eluting with MeCN in water 0.05% TFA. Fractions containing the desired product were concentrated in vacuo to afford a yellow solid (19S)-10-(aminomethyl)-19-ethyl-19-hydroxy-6,7-dimethoxy-17-oxa-3,13-diazapentacyclo[11.8.0.02,11.04,9.015,20]henicosa-1(21),2,4(9),5,7,10,15(20)-heptaene-14,18-dione (Compound **2ao**) (32 mg, 0.0722 mmol, 12.84 % yield). Rt = 0.84 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₂₃H₂₄N₃O₆ 438.17, found 438.35.

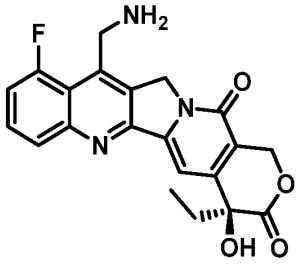
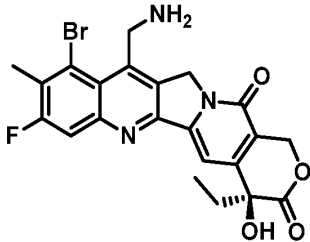
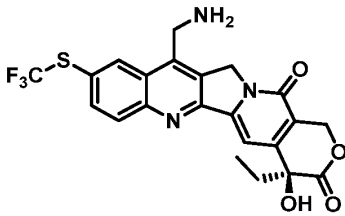
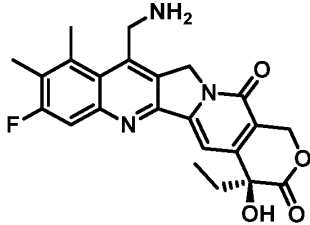
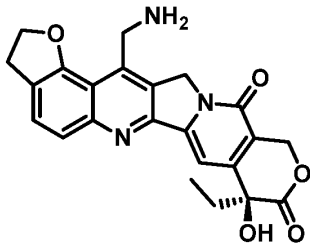
[0602] **Table 2.** Compounds listed below were made following the general procedures outlined for compound 2ao.

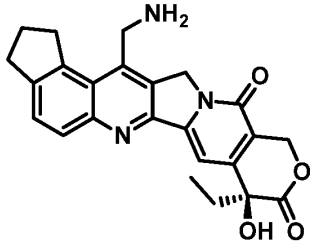
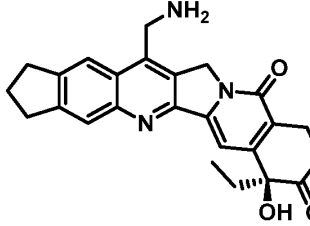
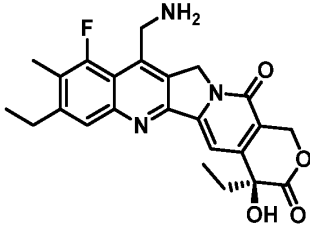
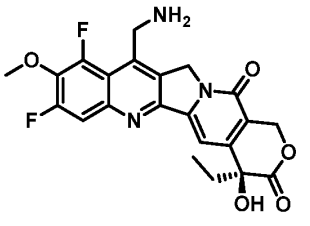
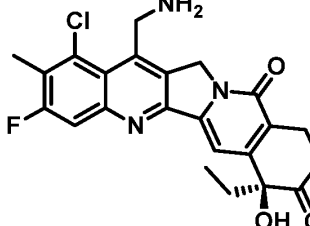
No.	Structure	Exact Mass	Calc. [M+H] ⁺	m/z	Rt (min)

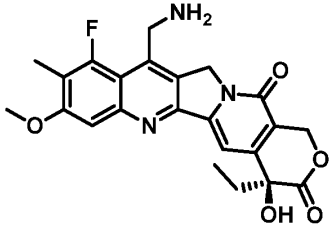
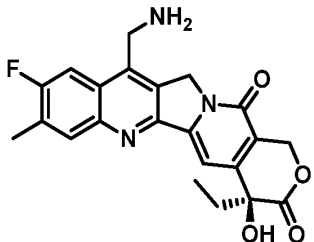
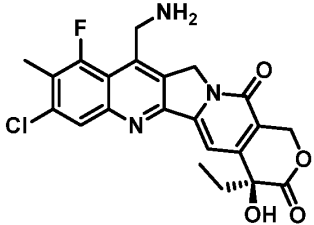
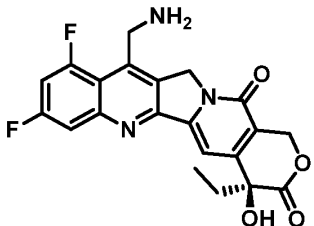
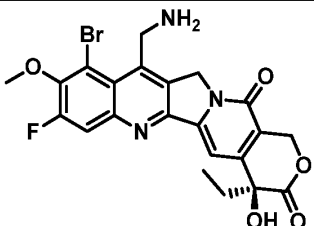
2a		391.15	392.16	392.37	0.87
2b		395.13	396.14	396.93	0.82
2c		411.1	412.11	412.26	0.91
2d		407.15	408.16	408.67	0.89
2e		455.05	456.06	456.4	0.98

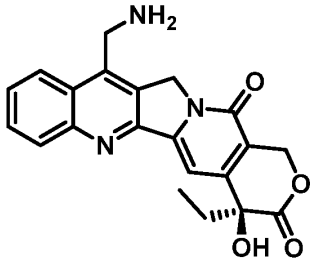
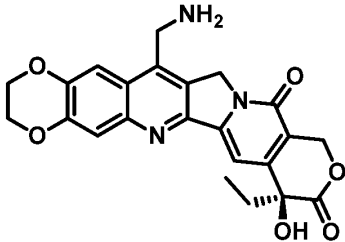
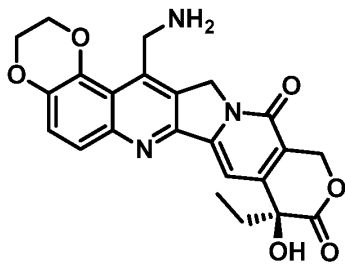
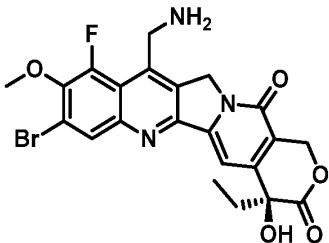
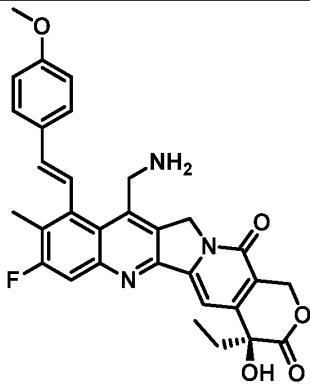
2f		395.13	396.14	396.64	0.9
2g		445.12	446.13	446.99	1
2h		409.14	410.15	410.32	1.03
2i		425.14	426.15	426.38	0.98
2j		427.13	428.14	428.46	0.98

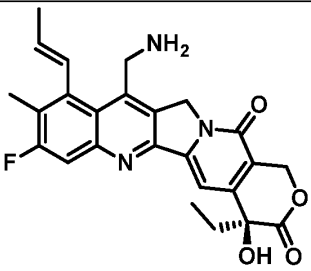
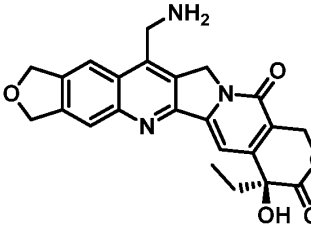
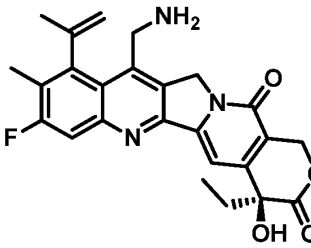
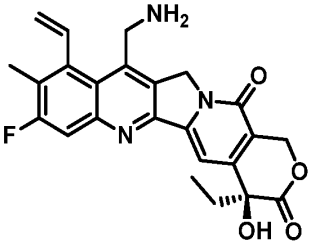
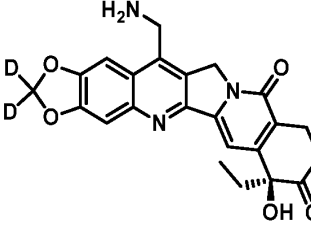
2k		487.05	488.06	488.6	1.15
2l		413.12	414.13	414.53	0.95
2m		419.15	420.16	420.6	0.83
2n		419.15	420.16	420.6	0.88
2o		423.16	424.17	424.58	0.95

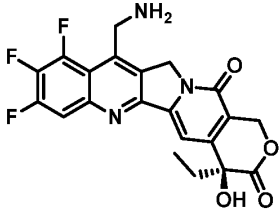
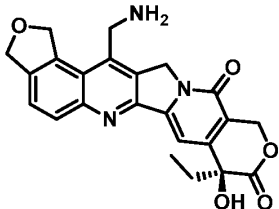
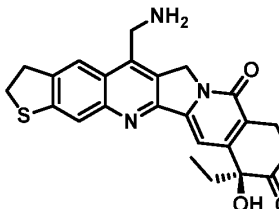
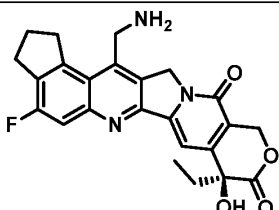
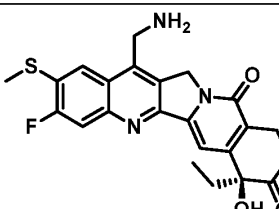
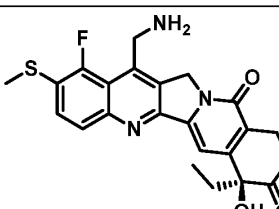
2p		395.13	396.14	396.25	0.82
2q		487.05	488.06	488.57	1.11
2r		477.1	478.11	478.32	1.13
2s		423.16	424.17	424.68	1.04
2t		419.15	420.16	420.6	0.9

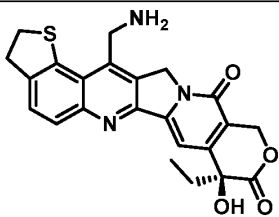
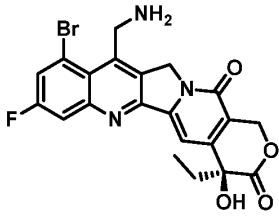
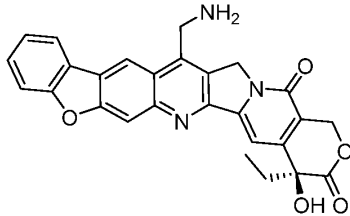
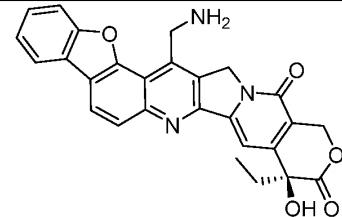
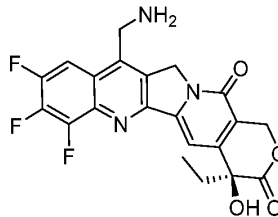
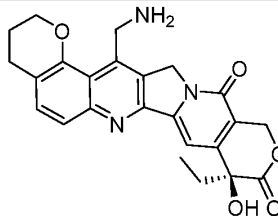
2u		417.17	418.18	418.66	0.97
2v		417.17	418.18	418.56	0.99
2w		437.18	438.19	438.64	1.06
2x		443.13	444.14	444.46	0.92
2y		443.1	444.11	444.46	1.01

2z		439.15	440.16	440.54	1
2aa		409.14	410.15	410.22	0.97
2ab		443.1	444.11	444.66	1.05
2ac		413.12	414.13	414.59	0.84
2ad		503.05	504.06	504.32	1.05

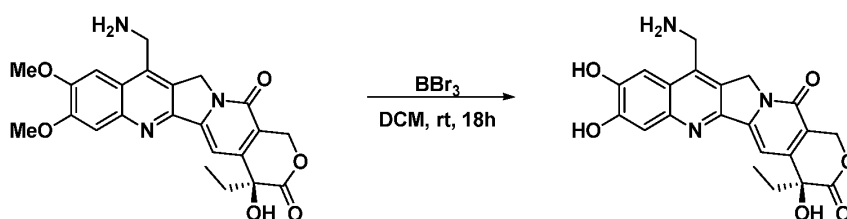
2ae		377.14	378.15	378.6	0.78
2af		435.14	436.15	436.61	0.88
2ag		435.14	436.15	436.51	0.9
2ah		503.05	504.06	504.41	0.96
2ai		541.2	542.21	542.05	1.32

2aj		449.18	450.19	450.19	1.11
2ak		419.15	420.16	420.60	0.79
2al		449.18	450.19	450.38	1.06
2am		435.16	436.17	436.22	1.03
2an		423.14	424.15	424.48	0.86

2ap		431.11	432.12	432.05	0.99
2aq		419.15	420.16	420.47	1.00
2ar		435.13	436.14	436.32	1.06
2as		435.16	436.17	435.84	1.09
2at		441.12	442.13	442.20	1.04
2au		441.12	442.13	442.11	1.16

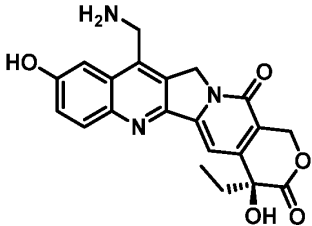
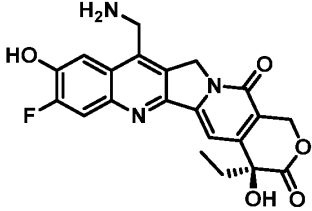
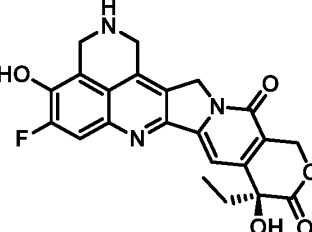
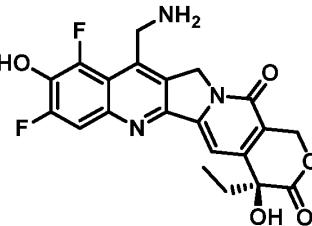
2av		435.13	436.14	436.41	1.13
2aw		473.04	474.05	475.11	1.09
2ax		467.15	468.16	468.48	1.17
2ay		467.15	468.16	468.33	1.12
2az		431.11	432.12	432.33	0.72
2aaa		433.16	434.17	434.33	0.74

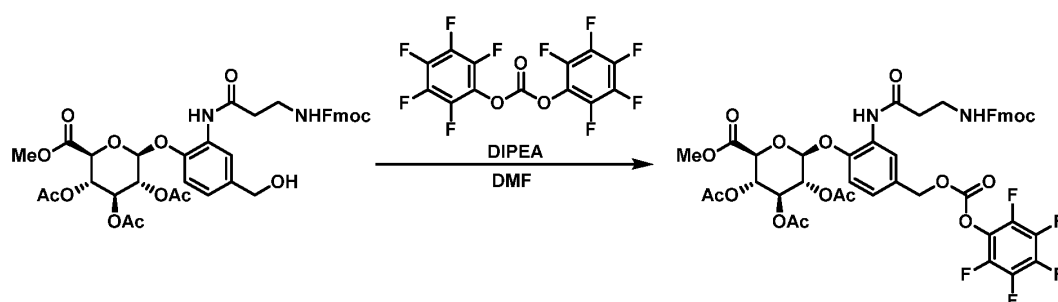
2aab		462.19	463.20	463.52	0.71
2aac		433.16	434.17	434.33	0.73

Example 3: Preparation of Compound 3e.

[0603] rac-(19S)-10-(aminomethyl)-19-ethyl-19-hydroxy-6,7-dimethoxy-17-oxa-3,13-diazapentacyclo[11.8.0.02,11.04,9.015,20]henicosa-1(21),2,4,6,8,10,15(20)-heptaene-14,18-dione (1.00 eq, 26 mg, 0.0594 mmol) was dissolved in DCM (0.5944mL). Boron tribromide (10.0 eq, 0.59 mL, 0.594 mmol) was added and the reaction was stirred for 15 hours. The reaction was diluted into a stirred mixture of methanol (20 mL) and concentrated in vacuo. The crude product was purified by prep-HPLC using a Synergi Max-RP 21.2 x 250 column eluting with MeCN in water 0.05% TFA. Fractions containing the desired product were concentrated in vacuo to afford a yellow solid (19S)-10-(aminomethyl)-19-ethyl-6,7,19-trihydroxy-17-oxa-3,13-diazapentacyclo[11.8.0.02,11.04,9.015,20]henicosa-1(21),2,4(9),5,7,10,15(20)-heptaene-14,18-dione **Compound 3e** (2.1 mg, 0.00520 mmol, 8.75 % yield). Rt = 0.69 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₂₁H₂₀N₃O₆ 410.14, found 410.61.

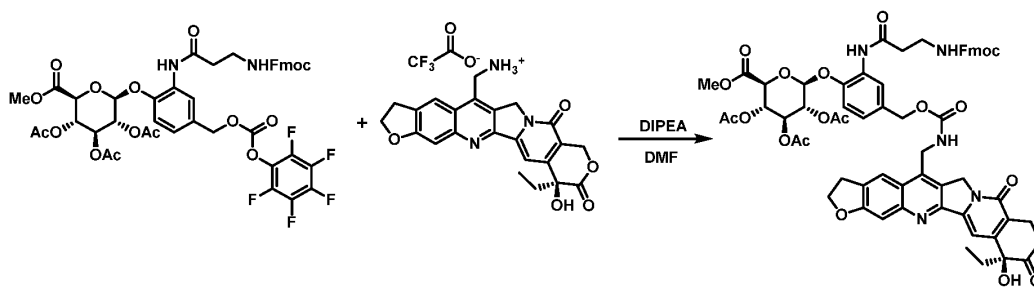
[0604] **Table 3.** Compounds 3a-3d were made following the general procedures outlined for Compound 3e.

No.	Structure	Exact Mass	Calc. [M+H] ⁺	m/z	Rt (min)
3a		393.13	394.14	394.22	0.78
3b		411.12	412.13	412.26	0.8
3c		423.12	424.13	424.58	0.76
3d		429.11	430.12	430.01	0.82

Example 4. Preparation of Compound 4.

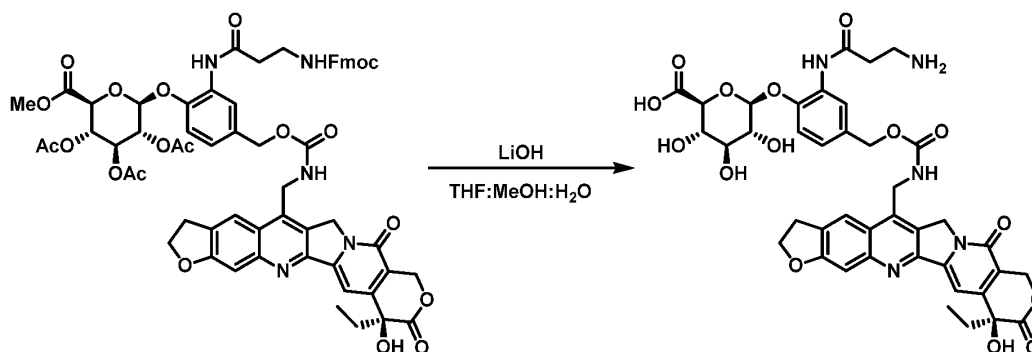
[0605] methyl rac-(2S,3S,4S,5R,6S)-3,4,5-triacetoxy-6-[2-[3-(9H-fluoren-9-ylmethoxycarbonylamino)propanoylamino]-4-(hydroxymethyl)phenoxy]tetrahydropyran-2-carboxylate (1.00 eq, 2000 mg, 2.67 mmol), prepared according to the procedure of

Bioconjugate Chem. (2006) 17: 831–840), was dissolved in DMF (8.904 mL). Bis(pentafluorophenyl) carbonate (1.50 eq, 1579 mg, 4.01 mmol) was added to the reaction followed by N,N-Diisopropylethylamine (2.00 eq, 0.93 mL, 5.34 mmol). The reaction was stirred for 30 minutes at which point complete conversion was observed by UPLC-MS. The reaction was diluted with EtOAc (100 mL), washed with 13% NaCl (2x100 mL), washed with brine, dried MgSO₄, filtered and concentrated in vacuo. The crude product was purified by FCC 10-100% EtOAc in Hex. Fractions containing the desired product were concentrated in vacuo to afford a colorless solid methyl (2S,3S,4S,5R,6S)-3,4,5-triacetoxy-6-[2-[3-(9H-fluoren-9-ylmethoxycarbonylamino)propanoylamino]-4-[(2,3,4,5,6-pentafluorophenoxy)carbonyloxymethyl]phenoxy]tetrahydropyran-2-carboxylate (2.27 g, 2.37 mmol, 88.57 % yield). Rt = 2.26 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₄₅H₄₀F₅N₂O₁₆ 959.23, found 959.32.

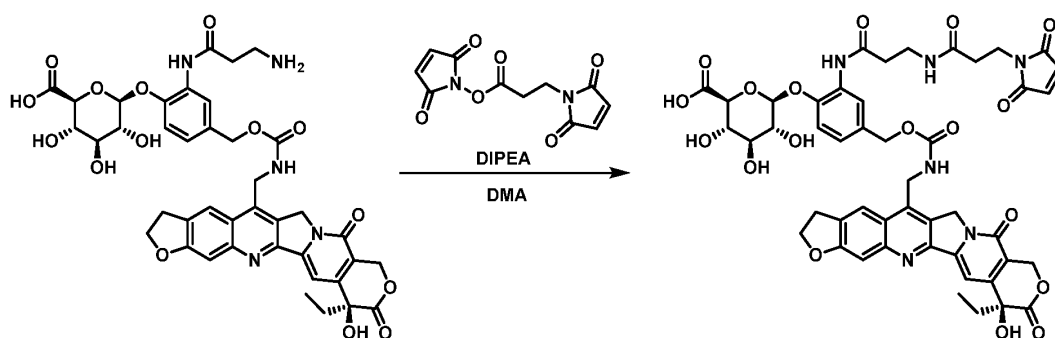


[0606] (5S)-14-(aminomethyl)-5-ethyl-5-hydroxy-7,20-dioxo-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(24),2,4(9),13,15(23),16,21-heptaene-6,10-dione; 2,2,2-trifluoroacetic acid **Compound 2n** (1.00 eq, 135 mg, 0.254 mmol) and methyl (2S,3S,4S,5R,6S)-3,4,5-triacetoxy-6-[2-[3-(9H-fluoren-9-ylmethoxycarbonylamino)propanoylamino]-4-[(2,3,4,5,6-pentafluorophenoxy)carbonyloxymethyl]phenoxy]tetrahydropyran-2-carboxylate (1.00 eq, 243 mg, 0.254 mmol) were dissolved in DMF (1 mL). N,N-Diisopropylethylamine (1.50 eq, 0.066 mL, 0.380 mmol) was added and the reaction was stirred for 20 minutes. Complete conversion was observed by UPLC-MS. The reaction was acidified with AcOH (100 μ L), and concentrated in vacuo. The residue was purified by FCC 25G Sfar Silica HC-D 0-12% MeOH in DCM. Fractions containing the desired product were concentrated in vacuo to afford a yellow amorphous solid methyl (2S,3S,4S,5R,6S)-3,4,5-triacetoxy-6-[4-[(5S)-5-ethyl-5-hydroxy-6,10-dioxo-7,20-dioxo-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(13),2,4(9),14,16,21,23-heptaen-14-yl]methylcarbamoyloxymethyl]-2-[3-(9H-fluoren-9-

ylmethoxycarbonylamino)propanoylamino]phenoxy]tetrahydropyran-2-carboxylate (203 mg, 0.170 mmol, 67.05 % yield). Rt = 2.04 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₆₂H₆₀N₅O₂₀ 1194.38, found 1194.55.



[0607] methyl (2S,3S,4S,5R,6S)-3,4,5-triacetoxy-6-[4-[[[(5S)-5-ethyl-5-hydroxy-6,10-dioxo-7,20-dioxa-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(13),2,4(9),14,16,21,23-heptaen-14-yl]methylcarbamoyloxymethyl]-2-[3-(9H-fluoren-9-ylmethoxycarbonylamino)propanoylamino]phenoxy]tetrahydropyran-2-carboxylate (1.00 eq, 203 mg, 0.170 mmol) was dissolved in Methanol (2mL) and THF (2mL). The reaction was cooled to 0°C with an ice/water bath then lithium hydroxide (30.0 eq, 122 mg, 5.10 mmol) was added. The reaction was stirred for 10 minutes at which point complete acetate deprotection was observed. Water (2mL) was added to the reaction and stirred for 10 minutes at which point complete deprotection was observed. Note: reversible lactone hydrolysis is observed (M+18). The reaction was acidified with AcOH (500 mL) and concentrated in vacuo. Purified by prep-HPLC 30x250 mm MaxRP 10-30-95% MeCN in H₂O 0.05% TFA. Fractions containing the desired product were concentrated in vacuo to afford a yellow solid (2S,3S,4S,5R,6S)-6-[2-(3-aminopropanoylamino)-4-[[[(5S)-5-ethyl-5-hydroxy-6,10-dioxo-7,20-dioxa-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(13),2,4(9),14,16,21,23-heptaen-14-yl]methylcarbamoyloxymethyl]phenoxy]-3,4,5-trihydroxy-tetrahydropyran-2-carboxylic acid (100 mg, 0.120 mmol, 70.51 % yield). Rt = 0.98 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₄₀H₄₂N₅O₁₅ 832.27, found 832.42.



[0608] (2S,3S,4S,5R,6S)-6-[2-(3-aminopropanoylamino)-4-[(5S)-5-ethyl-5-hydroxy-6,10-dioxo-7,20-dioxa-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(13),2,4(9),14,16,21,23-heptaen-14-yl]methylcarbamoyloxymethyl]phenoxy]-3,4,5-trihydroxy-tetrahydropyran-2-carboxylic acid (1.00 eq, 100 mg, 0.120 mmol) was dissolved in DMA (1mL). 2,5-dioxopyrrolidin-1-yl 3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoate (1.20 eq, 38 mg, 0.144 mmol) was added followed by N,N-Diisopropylethylamine (1.50 eq, 0.031 mL, 0.180 mmol). The reaction was stirred for 5 minutes at which point complete conversion was observed by UPLC-MS. The reaction was acidified with AcOH (50 uL) and purified by prep-HPLC 5-40-95% MeCN in H₂O 0.05% TFA. Fractions containing the desired product were concentrated in vacuo to afford a yellow solid (2S,3S,4S,5R,6S)-6-[2-[3-[3-(2,5-dioxopyrrol-1-yl)propanoylamino]propanoylamino]-4-[(5S)-5-ethyl-5-hydroxy-6,10-dioxo-7,20-dioxa-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(13),2,4(9),14,16,21,23-heptaen-14-yl]methylcarbamoyloxymethyl]phenoxy]-3,4,5-trihydroxy-tetrahydropyran-2-carboxylic acid **Compound 4** (91 mg, 0.0931 mmol, 77.59 % yield). Rt = 1.11 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₄₇H₄₇N₆O₁₈ 983.30, found 983.30.

[0609] **Table 4.** Compounds listed below were made following the general procedures outlined for Compound 4.

No.	Z'-A	RL	Camptothecin (N-link)
4	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2n
4a	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2u
4b	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2am
4c	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2al
4d	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2j
4e	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2k
4f	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 1
4g	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2i

4h	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2x
4i	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2ap
4j	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2ac
4k	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2as
4l	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2aq
4m	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 6d
4n	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2ag
4o	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2h
4p	Mal-CH ₂ CH ₂ C(O)-N(CH ₃)CH ₂ C(O)-	MAC	Compound 15d
4q	Mal-CH ₂ CH ₂ C(O)-N(CH ₃)CH ₂ C(O)-	MAC	Compound 15c
4r	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 6e
4s	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 6g
4t	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 6p
4u	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2q
4v	Mal-CH ₂ CH ₂ C(O)-N(CH ₃)CH ₂ C(O)-	MAC	Compound 15a
4w	Mal-CH ₂ CH ₂ C(O)-N(CH ₃)CH ₂ C(O)-	MAC	Compound 15b
4x	Mal-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ C(O)- NHCH ₂ CH ₂ C(O)-	Glucuronide	Compound 2n
4y	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Mannose	Compound 2n
4z	Mal-CH ₂ CH ₂ C(O)-Lys(PEG12)-Val-Cit-	PABC	Compound 2n
4aa	Mal-CH ₂ CH ₂ C(O)-NHCH ₂ CH ₂ C(O)-	Galactose	Compound 2n
4ab	Mal-CH ₂ CH ₂ C(O)-		Compound 2n

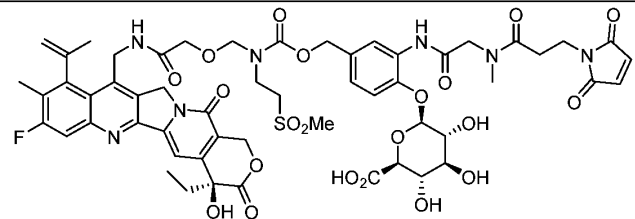
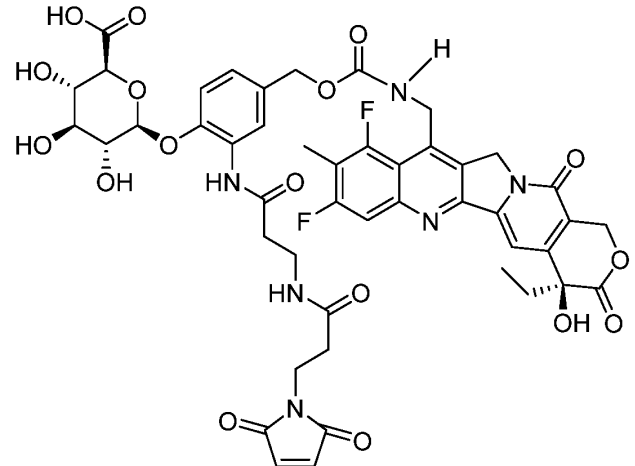
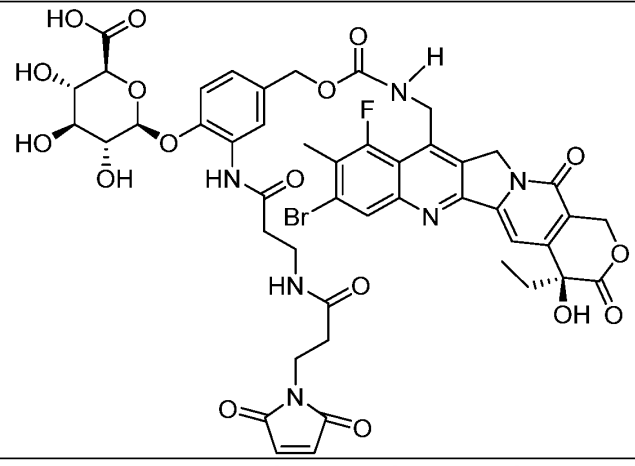
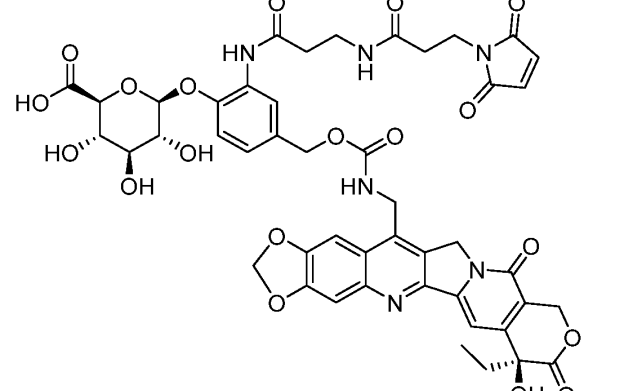
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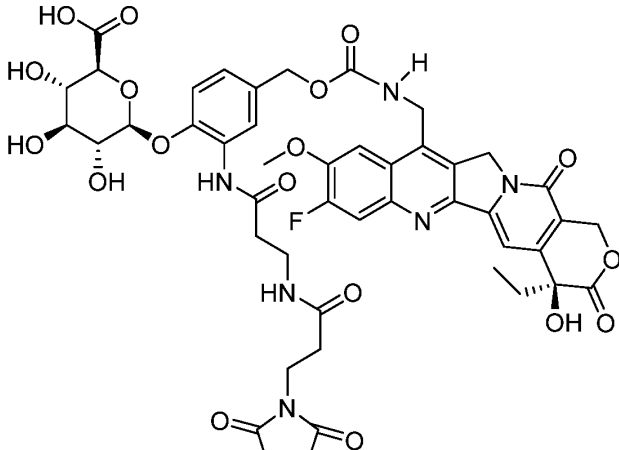
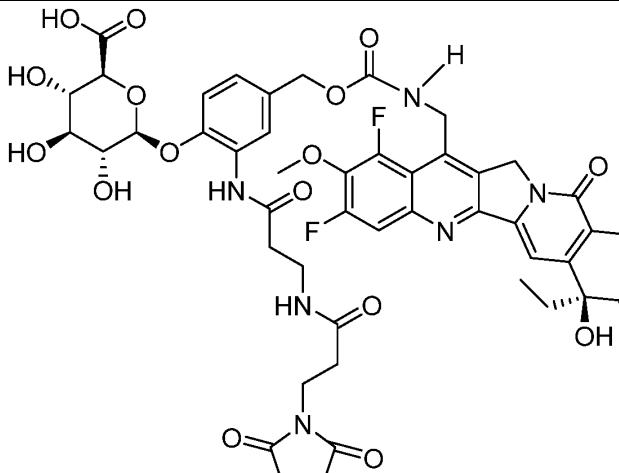
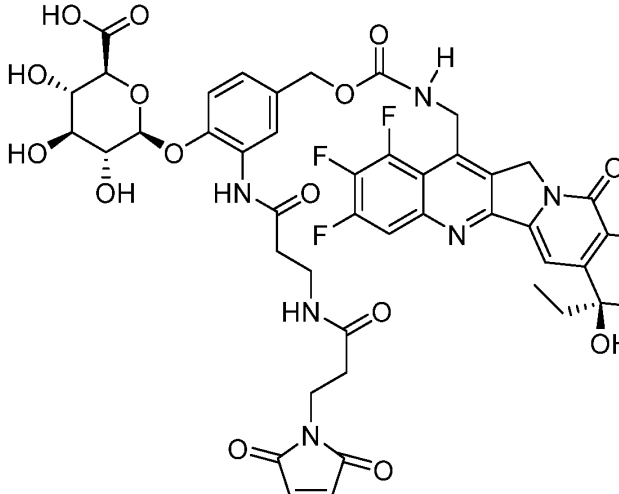
Compound No.	Parent Exact Mass	Calc'd MS (m/z) [M+H] ⁺	Observed MS (m/z)	RT
4	982.29	983.30	983.30	1.11
4a	980.31	981.32	981.96	1.48
4b	998.30	999.31	999.80	1.56
4c	1012.30	1013.31	1013.57	1.40
4d	990.27	991.28	991.64	1.45
4e	1050.20	1051.21	1051.63	1.59
4f	984.27	985.28	985.45	1.24
4g	988.28	989.29	989.28	1.28
4h	1006.27	1007.28	1007.72	1.35
4i	994.25	995.26	995.39	1.27
4j	976.26	977.27	977.62	1.31
4k	998.30	999.31	999.75	1.45
4l	982.29	983.29	983.27	1.21
4m	1040.31	1041.32	1041.35	1.40
4n	1042.30	1043.31	1043.80	1.35
4o	972.28	973.29	972.97	1.42
4p	1177.31	1178.32	1178.87	1.29
4q	1175.33	1176.34	1176.81	1.31
4r	1084.28	1085.29	1085.86	1.46
4s	1054.27	1055.28	1055.09	1.63

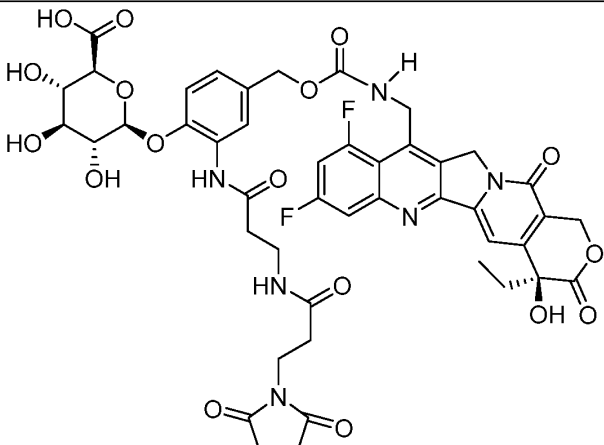
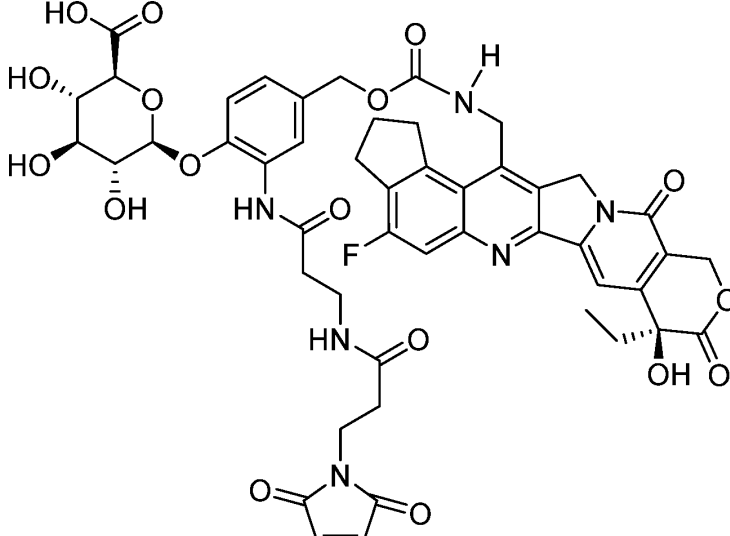
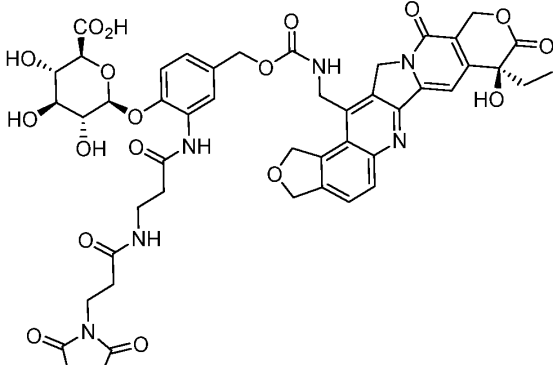
4t	1038.29	1039.30	1039.01	1.58
4u	1050.19	1051.20	1051.04	1.55
4v	1191.34	1192.35	1191.96	1.45
4w	1205.35	1206.36	1206.98	1.50
4x	1024.33	1025.34	1025.13	1.38
4y	968.31	969.32	969.19	1.28
4z	1675.80	1675.81	1675.73	1.51
4aa	968.31	969.32	969.12	1.26
4ab	570.18	571.19	570.95	1.33

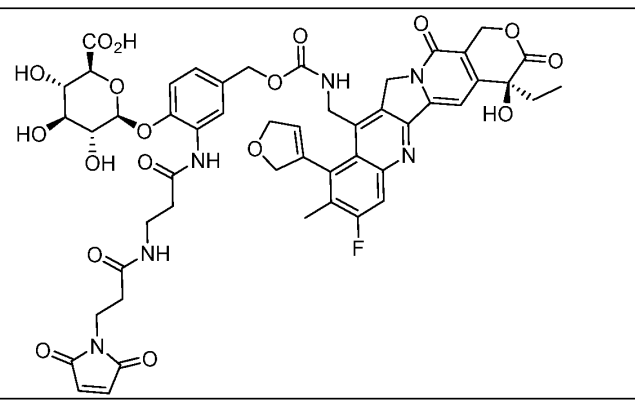
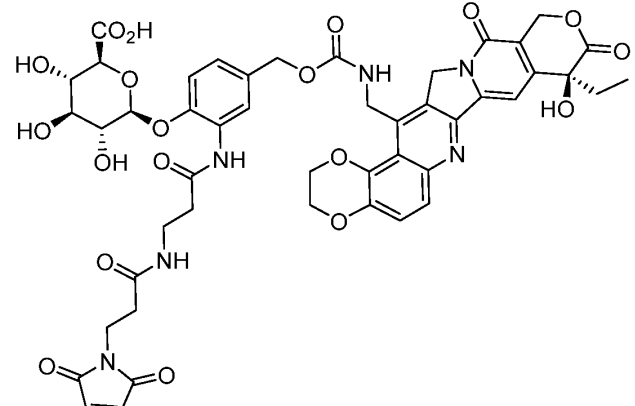
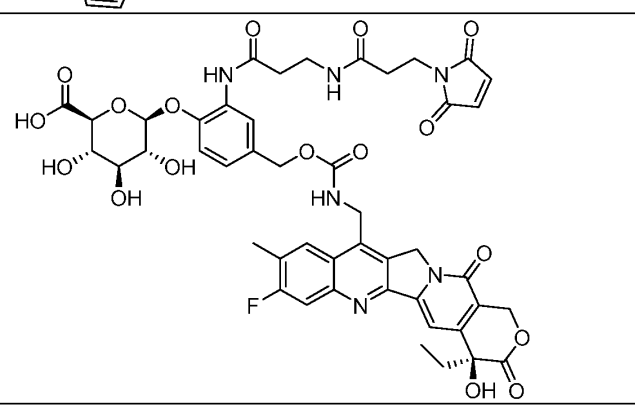
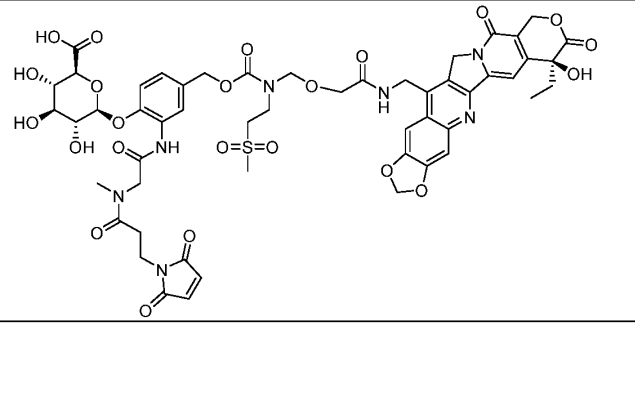
Structures

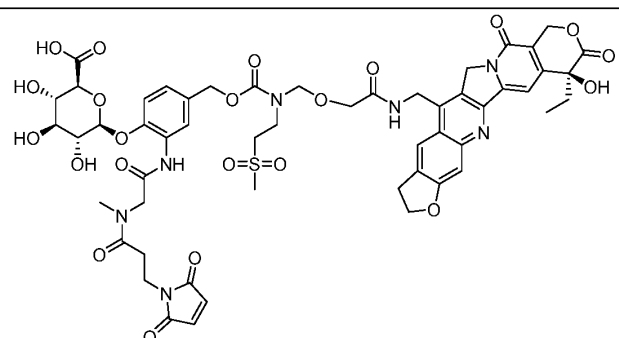
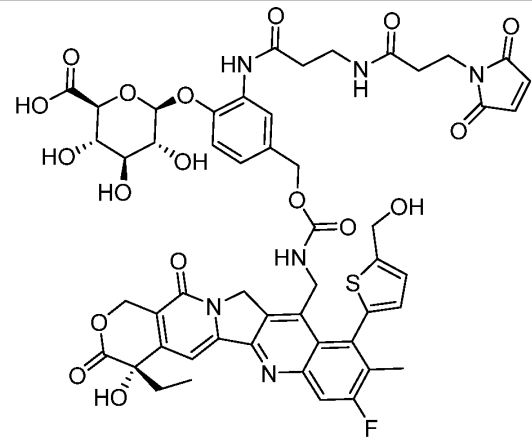
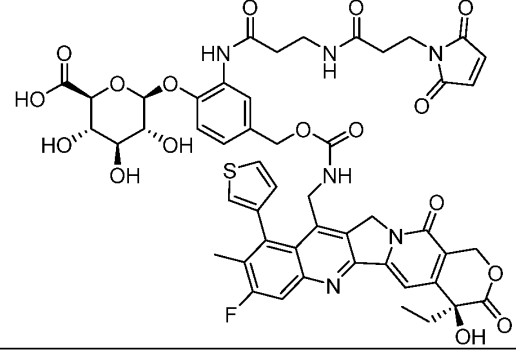
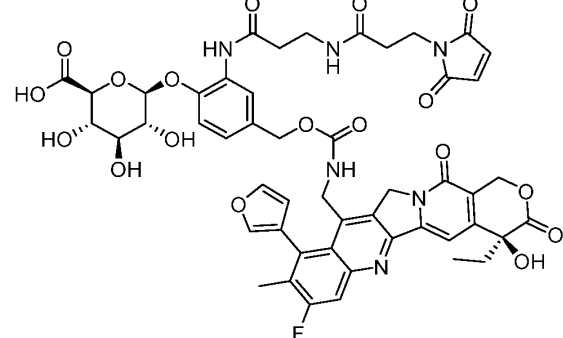
No.	Structure
4	
4a	
4b	

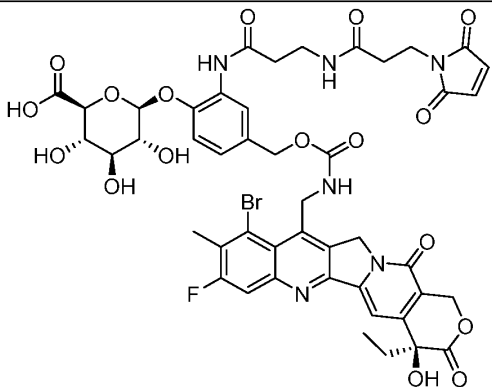
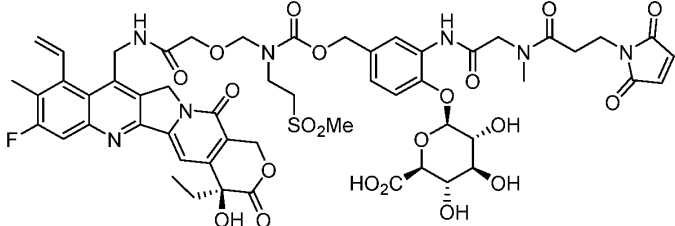
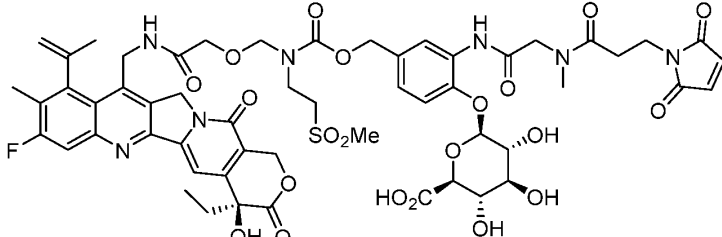
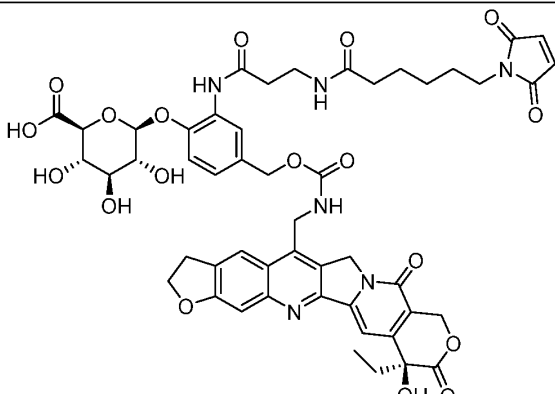
4c	
4d	
4e	
4f	

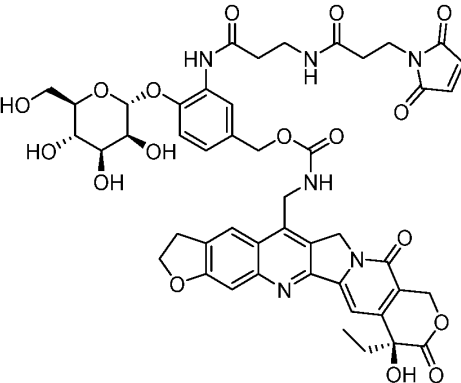
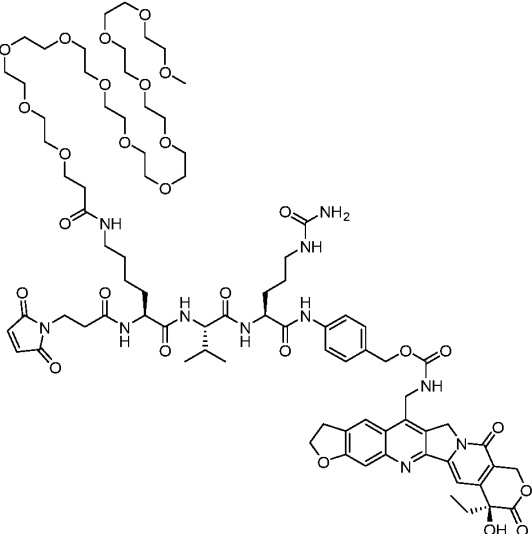
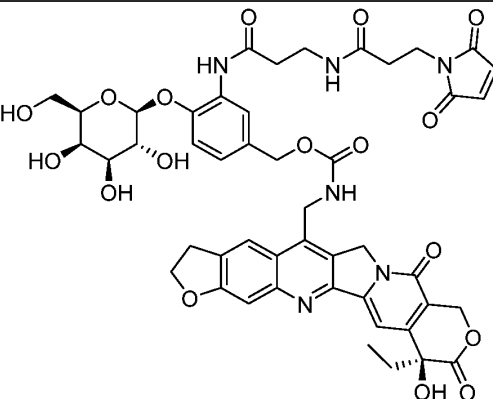
4g	
4h	
4i	

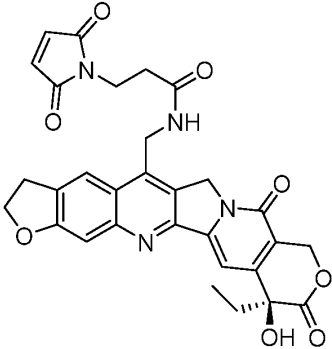
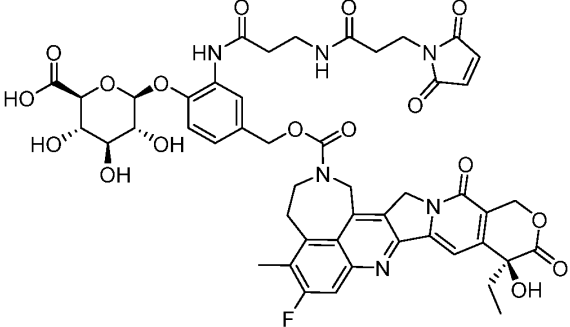
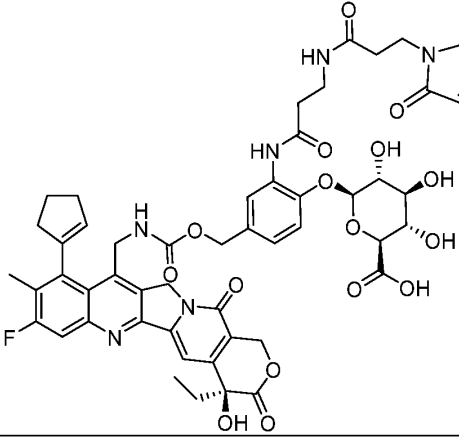
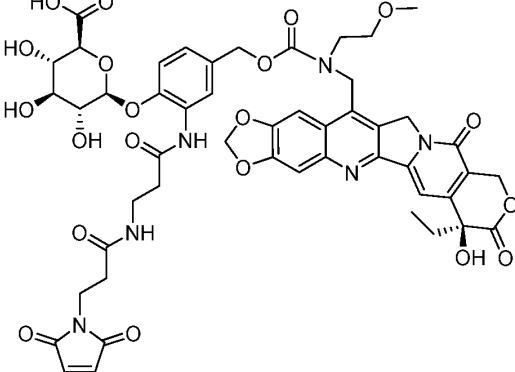
4j	
4k	
4l	

4m	
4n	
4o	
4p	

4q	
4r	
4s	
4t	

4u	
4v	
4w	
4x	

4y	
4z	
4aa	

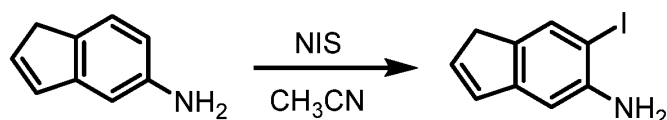
4ab	
4ac	
4ad	
4ae	

Aggregation Levels

[0610] Table 5. ADC aggregations levels for camptothecin drug-linkers (DAR = 8) linked to a Ag4 antibody or to an alternative target-specific antibody referred to as Ag1. ADC aggregation was determined by Size Exclusion Chromatography (SEC).

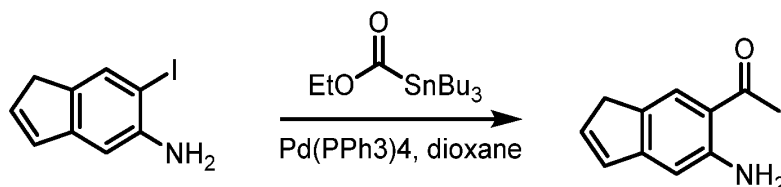
ADC	Description	DAR	Conc. (mg/mL)	HMW%
Ag1-Ex_4	Glucuronide-Ex_2n	7.7	0.65	1.98
Ag4 -Ex_4	Glucuronide-Ex_2n	8	0.86	1.65
Ag1-Ex_4a	Glucuronide-Ex_2u	7.7	0.27	2.18
Ag4 -Ex_4a	Glucuronide-Ex_2u	7.8	0.78	1.62
Ag1-Ex_4b	Glucuronide-Ex_2am	7.8	0.46	1.92
Ag4 -Ex_4b	Glucuronide-Ex_2am	8	0.71	1.36
Ag1-Ex_4c	Glucuronide-Ex_2al	7.6	0.55	1.98
Ag4 -Ex_4c	Glucuronide-Ex_2al	8	0.65	1.49
Ag1-Ex_4f	Glucuronide-Ex_1	7.5	0.87	1.82
Ag4 -Ex_4f	Glucuronide-Ex_1	8	0.89	1.15
Ag1-Ex_4i	Glucuronide-Ex_2ap	8	0.49	1.4
Ag4-Ex_4i	Glucuronide-Ex_2ap	8	0.78	0.9
Ag1-Ex_4g	Glucuronide-Ex_2i	7.9	0.65	1.4
Ag4-Ex_4g	Glucuronide-Ex_2i	8	0.59	0.9
Ag1-Ex_4k	Glucuronide-Ex_2as	7.8	0.76	1.5
Ag4-Ex_4k	Glucuronide-Ex_2as	8	0.96	1.2
Ag1-Ex_4h	Glucuronide-Ex_2x	7.5	0.62	1.5
Ag4-Ex_4h	Glucuronide-Ex_2x	8	0.96	1.3
Ag1-Ex_4j	Glucuronide-Ex_2ac	7.7	0.69	1.9
Ag4-Ex_4j	Glucuronide-Ex_2ac	8	0.94	1.2
Ag4-Ex_4ad	Glucuronide-Ex_6c	7.9	0.78	6.4
Ag1-Ex_4ad	Glucuronide-Ex_6c	8	0.84	5.4
Ag4-Ex_4ac	Glucuronide-Ex_9	7.9	0.68	2.4
Ag1-Ex_4ac	Glucuronide-Ex_9	8	0.87	1.5
Ag4-Ex_4l	Glucuronide-Ex_2aq	7.7	0.87	2.6
Ag1-Ex_4l	Glucuronide-Ex_2aq	8	1.06	2.7
Ag4-Ex_4m	Glucuronide-Ex_6d	8	0.69	2.5
Ag1-Ex_4m	Glucuronide-Ex_6d	8	0.64	1.6
Ag4-Ex_4q	Glucuronide-Ex_15c	8	0.52	9.7
Ag1-Ex_4q	Glucuronide-Ex_15c	8	0.65	15.62

Example 5: Preparation of Compounds 5a-5c and 2ak



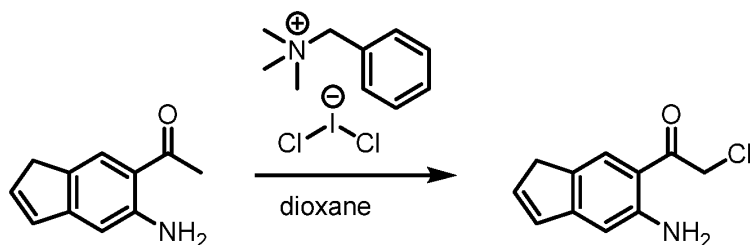
[0611] To a solution of 1*H*-indene-5-amine (3 g, 22.92 mmol) in acetonitrile (MeCN, 135 mL) was added a solution of NIS (5.21 g, 23.15 mmol) in acetonitrile (MeCN, 30 mL) dropwise at -15°C. The mixture was stirred at -15°C for 15 min. The reaction mixture was quenched by addition of a saturated Na₂S₂O₃ (150 mL) at -15°C, and then extracted with ethyl acetate (3×500 mL). The combined organic layer was dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give a residue. The residue was purified by flash silica gel chromatography Eluent of 0~10% Ethyl acetate/Petroleum ether to afford product 6-iodo-1*H*-inden-5-amine (10.1 g, yield: 28.6%)

¹H NMR (400MHz, CDCl₃): δ = 7.72 (s, 1H), 6.85 (s, 1H), 6.77 - 6.69 (m, 1H), 6.52 (td, *J* = 1.6, 5.6 Hz, 1H), 4.05 (br s, 2H), 3.30 (s, 2H).



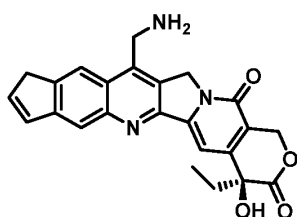
[0612] To a solution of 6-iodo-1*H*-inden-5-amine (4.8 g, 18.67 mmol) in dioxane (120 mL) was added tributyl(1-ethoxyvinyl)stannane (11.47 g, 31.74 mmol). Then Pd(PPh₃)₄ (2.16 g, 1.87 mmol) was added under nitrogen. The mixture was stirred at 100°C for 16 h. The mixture was cooled to room temperature, then HCl (2M, 300mL) was added and stirred for 10 min. The reaction mixture was extracted with ethyl acetate (2×300 mL). And a solution of Na₂CO₃ in H₂O was added to aqueous phase to pH>7. Then the mixture was extracted with ethyl acetate (3×500 mL). The combined organic phase was dried over Na₂SO₄ and concentrated. The residue was purified by flash silica gel chromatography, eluent of 0~6% ethyl acetate/Petroleum ether gradient gave a product 1-(5-amino-1*H*-inden-6-yl)-2-chloroethan-1-one (320 mg, 5%).

[0613] ¹H NMR (400MHz, CDCl₃): δ = 7.76 (s, 1H), 6.76 (s, 2H), 6.68 (s, 1H), 3.39 (d, *J* = 0.4 Hz, 2H), 2.60 (s, 3H).



[0614] To a solution of 1-(5-amino-1*H*-inden-6-yl)ethan-1-one (80 mg, 461.87 μmol) in dioxane (10 mL) was added benzyltrimethylammonium dichloroiodate (385.81 mg, 1.11 mmol). The mixture was stirred at 70°C for 6 h. The mixture was poured into a solution of $\text{Na}_2\text{S}_2\text{O}_3$ and NaHCO_3 , stirred at 25°C for 5 min. The phases were separated, and the aqueous phase was extracted twice with ethyl acetate (80 mL). The combined extracts were dried over Na_2SO_4 and concentrated to give a residue. The residue was purified by preparative HPLC to afford product 1-(5-amino-1*H*-inden-6-yl)-2-chloroethan-1-one (34 mg, 9%).

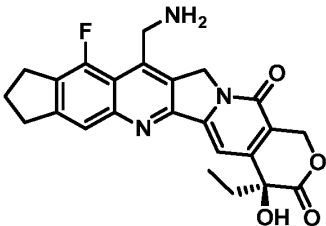
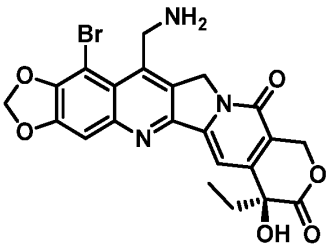
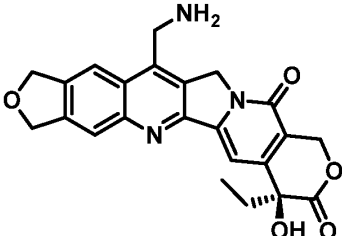
General Method UPLC-MS: $t_{\text{R}} = 1.80$ min, m/z (ES+) 208.05 ($\text{M}+\text{H}$)⁺, found 208.01



[0615] (5-amino-1*H*-inden-6-yl)-2-chloroethan-1-one was used to prepare **compound 5** using similar procedures as defined in Example 2.

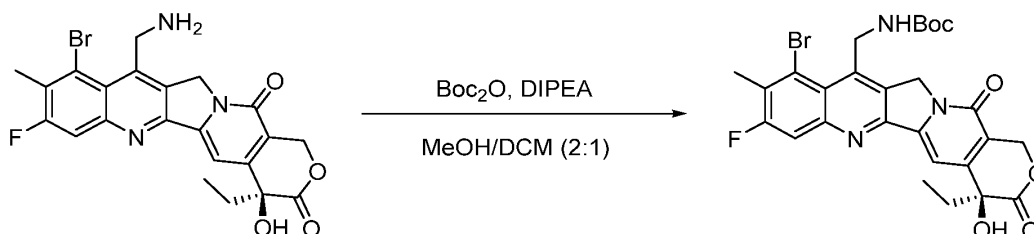
[0616] **Table 6.** Compounds 5a-5c and 2ak were made following the procedures outlined for Compound 5.

No.	Structure	Exact Mass	Calc. [M+H] ⁺	m/z	Rt (min)
5		415.15	416.16	416.7 5	2.98
5a		407.15	408.16	407.8 5	1.00

5b		435.16	436.17	436.0 3	1.10
5c		499.04	500.05	500.3 3	1.04
2ak		419.15	420.16	420.6	0.79

Example 6: Preparation of Compounds 6a-6i, 2ai, 2aj, 2al and 2am.

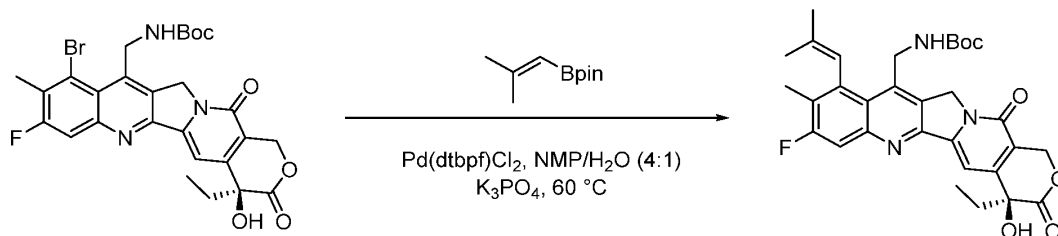
***tert*-butyl (*S*)-((10-bromo-4-ethyl-8-fluoro-4-hydroxy-9-methyl-3,14-dioxo-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-11-yl)methyl)carbamate**



[0617] In a 4 mL vial equipped with a stir bar, (*S*)-11-(aminomethyl)-10-bromo-4-ethyl-8-fluoro-4-hydroxy-9-methyl-1,12-dihydro-14*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-3,14(4*H*)-dione (**Compound 2q**, 230 mg, 0.47 mmol) was added into MeOH/DCM (2:1, 1.5 mL). Boc₂O (113 mg, 0.52 mmol) and DIPEA (164 μ L, 0.94 mmol) were added to the above solution at RT. The resulting solution was stirred at RT for 2 h. The reaction solution was concentrated in vacuo and residue was purified by silica gel column chromatography (0-20% MeOH:DCM) to afford product (193 mg, 70% yield).

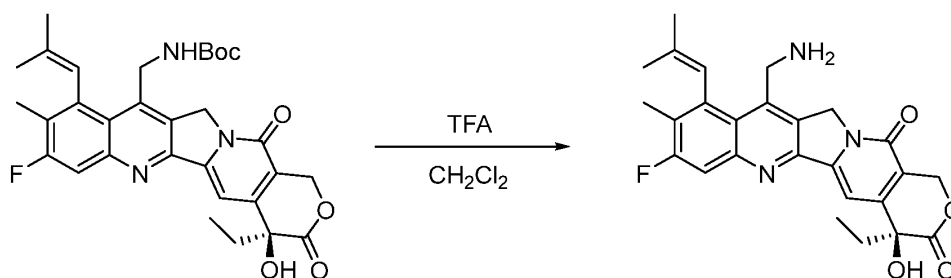
General Method UPLC-MS: t_R = 2.26 min, m/z (ES⁺) 589.43 (M+H)⁺, found 589.75.

***tert*-butyl (S)-((4-ethyl-8-fluoro-4-hydroxy-9-methyl-10-(2-methylprop-1-en-1-yl)-3,14-dioxo-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-11-yl)methyl)carbamate**



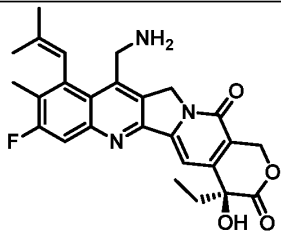
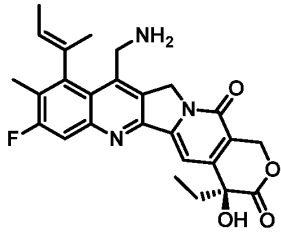
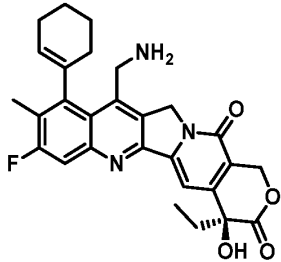
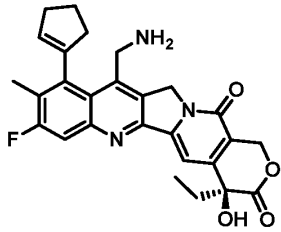
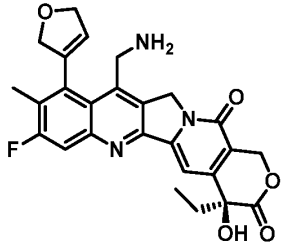
[0618] To a mixture of *tert*-butyl (S)-((10-bromo-4-ethyl-8-fluoro-4-hydroxy-9-methyl-3,14-dioxo-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-11-yl)methyl)carbamate (15 mg, 0.03 mmol) and 0.5 M K₃PO₄ (204 μ L, 0.10 mmol) in NMP (0.4 mL) was added Pd(dtbpf)Cl₂ (1.8 mg, 2.50 μ mol) under nitrogen. The mixture was degassed and purged with N₂ for 3 times, and 4,4,5,5-tetramethyl-2-(2-methylprop-1-en-1-yl)-1,3,2-dioxaborolane (18.6 mg, 0.10 mmol) was added via syringe, followed by addition of degassed H₂O (0.1 mL). Then the mixture was stirred at 60°C for 2 h under nitrogen. The reaction solution was added AcOH to pH=5, filtered and the filtrate was purified by preparative HPLC to afford product (7.6 mg, yield: 53 %). General Method UPLC-MS: *t*_R = 2.33 min, *m/z* (ES⁺) 563.63 (M+H)⁺, found 563.84.

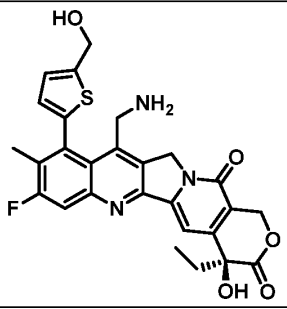
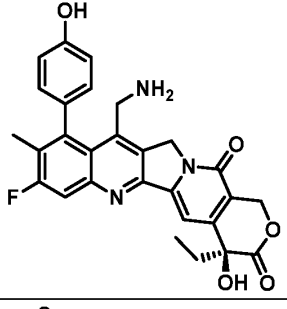
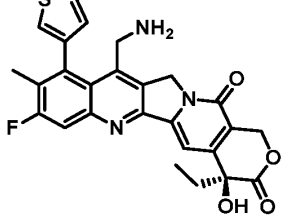
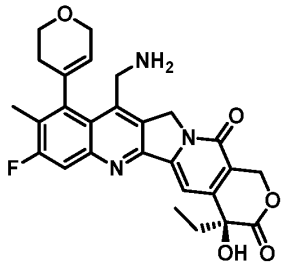
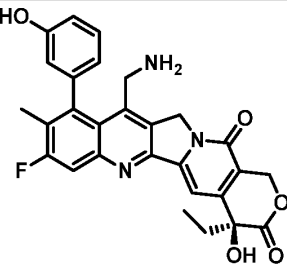
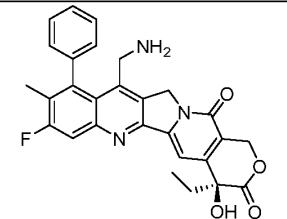
(S)-11-(aminomethyl)-4-ethyl-8-fluoro-4-hydroxy-9-methyl-10-(2-methylprop-1-en-1-yl)-1,12-dihydro-14*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-3,14(4*H*)-dione

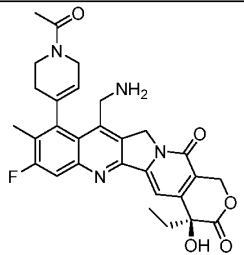
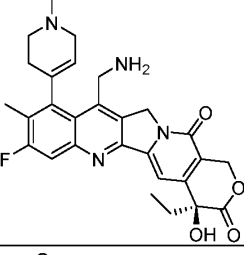
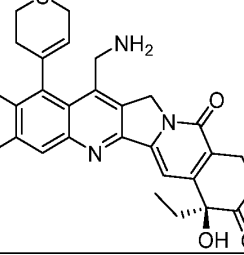
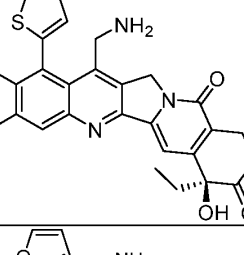
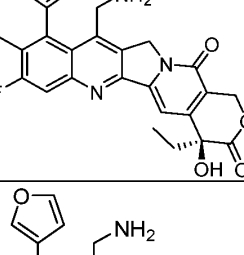
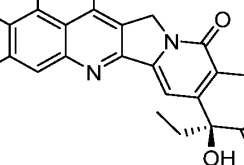


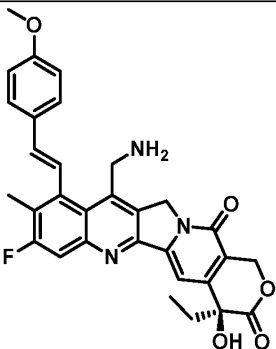
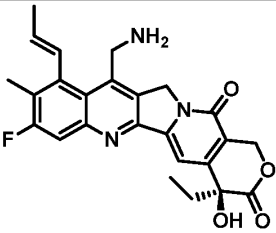
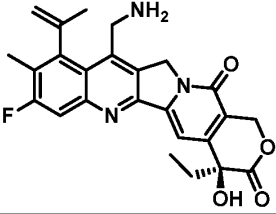
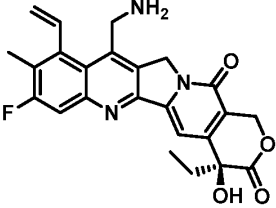
[0619] *tert*-butyl (S)-((4-ethyl-8-fluoro-4-hydroxy-9-methyl-10-(2-methylprop-1-en-1-yl)-3,14-dioxo-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-11-yl)methyl)carbamate (7.6 mg, 13.5 μ mol) was dissolved in 20% TFA/DCM (0.5 mL) at RT. The reaction solution was stirred at RT for 1 h. The solvent was removed in vacuo and the material purified by preparative HPLC to afford product **Compound 6** (3.4 mg, yield: 55%). General Method UPLC-MS: *t*_R = 1.44 min, *m/z* (ES⁺) 463.19 (M+H)⁺, found 463.85.

[0620] Table 7. Compounds 6a-6i, 2ai, 2aj, 2al and 2am were made following the procedures outlined for Compound 6.

No.	Structure	Exact Mass	Calc. [M+H] ⁺	m/z	Rt (min)
6		463.19	464.20	463.85	1.44
6a		463.19	464.20	464.92	1.35
6b		489.21	490.22	489.77	1.47
6c		475.19	476.20	475.68	1.35
6d		477.17	478.18	477.67	1.16

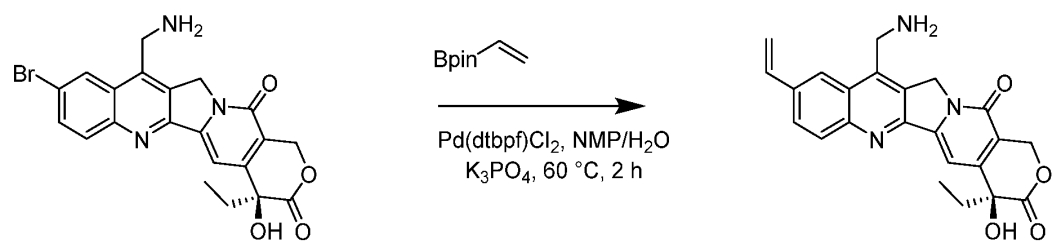
6e		521.14	522.15	521.72	1.24
6f		501.17	502.18	501.59	1.26
6g		491.13	492.14	491.63	1.31
6h		491.18	492.20	491.63	1.18
6i		501.17	502.18	501.66	1.28
6j		485.18	486.18	485.71	1.29

6k		532.21	533.22	532.75	1.09
6l		504.22	505.23	504.91	0.84
6m		507.16	508.17	508.08	1.28
6n		491.13	492.14	491.75	1.34
6o		475.15	476.15	475.43	1.23
6p		475.15	476.16	475.81	1.25

2ai		541.20	542.21	542.05	1.32
2aj		449.18	450.19	450.19	1.11
2al		449.18	450.19	450.38	1.06
2am		435.16	436.17	436.22	1.03

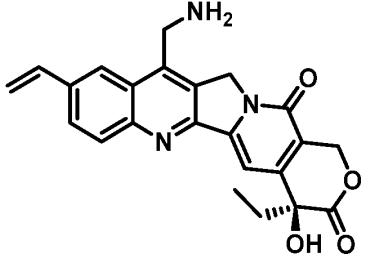
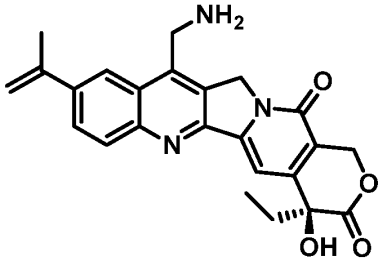
Example 7: Preparation of Compounds 33 and 33a.

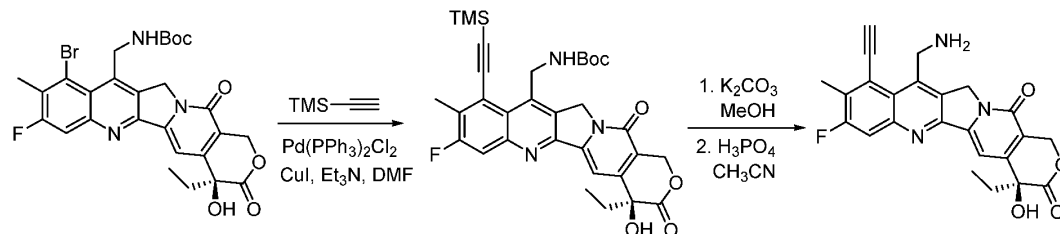
(19S)-10-(aminomethyl)-19-ethyl-19-hydroxy-7-vinyl-17-oxa-3,13-diazapentacyclo[11.8.0.02,11.04,9.015,20]henicosa-1(21),2,4,6,8,10,15(20)-heptaene-14,18-dione



[0621] To a mixture of (19S)-10-(aminomethyl)-7-bromo-19-ethyl-19-hydroxy-17-oxa-3,13-diazapentacyclo[11.8.0.02,11.04,9.015,20]henicosa-1(21),2,4,6,8,10,15(20)-heptaene-14,18-dione (15 mg, 0.03 mmol) and 0.5 M K₃PO₄ (263 uL, 0.13 mmol) in NMP (0.4 mL) was added Pd(dtbpf)Cl₂ (2.3 mg, 3.3 umol) under nitrogen. The mixture was degassed and purged with N₂ for 3 times, and 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (22.3 uL, 0.13 mmol) was added via syringe, followed by addition of degassed H₂O (0.1 mL). Then the mixture was stirred at 60°C for 2 h under nitrogen. The reaction solution was added AcOH to pH=5, filtered and the filtrate was purified by preparative HPLC to afford product **Compound 33** (3.6 mg, yield: 27%). General Method UPLC-MS: t_R = 1.08 min, m/z (ES+) 403.44 (M+H)⁺, found 403.73.

[0622] **Table 8.** Compound 33a was made following the procedure outlined for Compound 33.

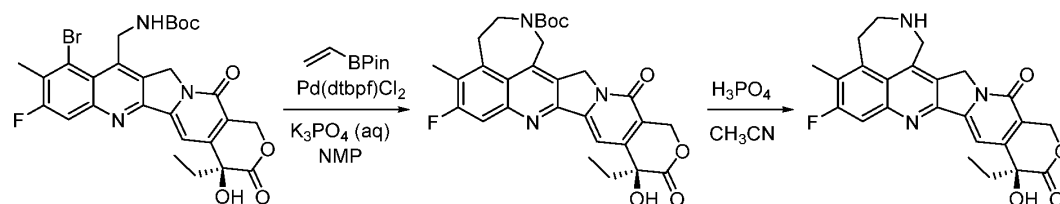
No.	Structure	Exact Mass	Calc. [M+H] ⁺	m/z	Rt (min)
33		403.15	404.16	403.73	1.08
33a		417.17	418.18	418.15	1.19

Example 8: Preparation of Compound 34.**(S)-11-(aminomethyl)-4-ethyl-10-ethynyl-8-fluoro-4-hydroxy-9-methyl-1,12-dihydro-14H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H)-dione**

[0623] *Tert*-butyl (*S*)-((10-bromo-4-ethyl-8-fluoro-4-hydroxy-9-methyl-3,14-dioxo-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-11-yl)methyl)carbamate (10 mg, 20 μ mol), trimethylsilylacetylene (4 mg, 41 μ mol) and DMF (0.2 mL) were added to a 4 mL vial equipped with stir bar. CuI (1.9 mg, 10 μ mol), Pd(PPh₃)₂Cl₂ (0.8 mg, 4 μ mol) and triethylamine (0.2 mL) were added to the mixture. The reaction system was degassed and recharged with nitrogen. The mixture was stirred at 25°C for 6 h under nitrogen. LCMS showed the reaction was completed. The reaction mixture was filtered and concentrated in vacuo. The crude product was purified by preparatory HPLC.

[0624] *Tert*-butyl (*S*)-((4-ethyl-8-fluoro-4-hydroxy-9-methyl-3,14-dioxo-10-((trimethylsilyl)ethynyl)-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-11-yl)methyl)carbamate (3.1 mg, 6 μ mol) and MeOH (0.2 mL) was added to a 4 mL vial equipped with stir bar. K₂CO₃ (2.4 mg, 18 μ mol) was added to the solution at 0°C and the reaction was warmed to RT and stirred for 3 h. Reaction was then concentrated to dryness in vacuo, and the crude product was dissolved in a mixture of H₃PO₄ (0.17 mL), acetonitrile (0.17 mL) and H₂O (0.17 mL). The reaction solution was filtered and prepped by HPLC to afford product **Compound 34** (0.3 mg, 4.5%).

General Method UPLC-MS: t_R = 1.23 min, m/z (ES⁺) 434.15 (M+H)⁺, found 434.49

Example 9: Preparation of Compound 9**(S)-10-ethyl-6-fluoro-10-hydroxy-5-methyl-2,3,4,10,13,16-hexahydro-14H-azepino[3,4,5-de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-11,14(1H)-dione**

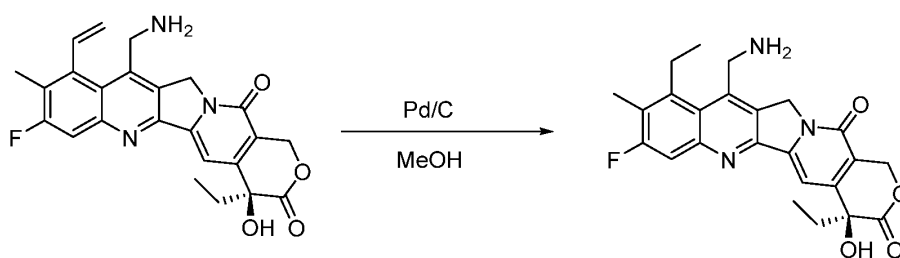
[0625] To a mixture of *tert*-butyl (*S*)-((10-bromo-4-ethyl-8-fluoro-4-hydroxy-9-methyl-3,14-dioxo-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-11-yl)methyl)carbamate (100 mg, 17 μ mol) and K_3PO_4 (180 mg, 0.85 mmol) in NMP (3 mL) was added $Pd(dtbpf)Cl_2$ (11 mg, 17 μ mol) under nitrogen. 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (104 mg, 0.7 mmol) was added via syringe, followed by addition of degassed H_2O (0.6 mL). Then the mixture was stirred at 80°C for 16 h under nitrogen. The reaction solution was acidified with AcOH to pH 5, and then poured into water and extracted with ethyl acetate for 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4 , filtered and concentrated to give a residue. The residue was purified by silica gel column chromatography (petroleum ether: ethyl acetate=10: 1 to 0:1).

[0626] H_3PO_4 (0.17 mL), acetonitrile (0.17 mL) and H_2O (0.17 mL) were premixed, and *tert*-butyl (*S*)-10-ethyl-6-fluoro-10-hydroxy-5-methyl-11,14-dioxo-3,4,10,11,14,16-hexahydro-13*H*-azepino[3,4,5-*de*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-2(1*H*)-carboxylate (55 mg, 0.10 mmol) was added at 25 °C. The resulting solution was stirred at 25 °C for 16 h. LCMS showed the reaction was completed. The reaction solution was filtered and purified by prep HPLC to afford product **Compound 9** (20 mg, 45%).

General Method UPLC-MS: t_R = 1.06 min, m/z (ES+) 436.17 ($M+H$)⁺, found 436.14.

Example 10: Preparation of Compound 10.

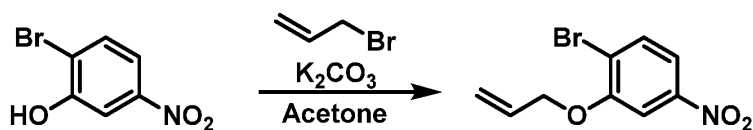
(*S*)-11-(aminomethyl)-4,10-diethyl-8-fluoro-4-hydroxy-9-methyl-1,12-dihydro-14*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-3,14(4*H*)-dione



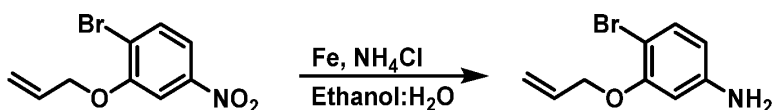
[0627] In a 4 mL vial equipped with a stir bar, the (*S*)-11-(aminomethyl)-4-ethyl-8-fluoro-4-hydroxy-9-methyl-10-vinyl-1,12-dihydro-14*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-3,14(4*H*)-dione was dissolved (**Compound 2am**, 5.4 mg, 0.012 mmol) in methanol (300 μ L) and palladium on carbon was added (0.26 mg, 0.003 mmol). Reaction was stirred for 2 h at RT. Reaction was filtered, and solvent removed in vacuo. Residue was purified by preparative HPLC to afford product **Compound 10** (1.9 mg, yield = 35.2 %).

General Method UPLC-MS: $t_R = 1.20$ min, m/z (ES+) 438.18 (M+H)⁺, found 438.41.

Example 11. Preparation of Compounds 11 and 11a.

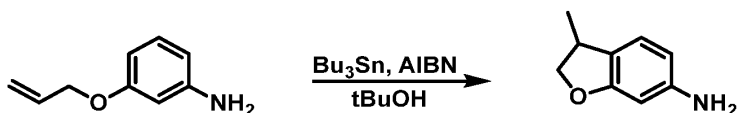


[0628] 2-bromo-5-nitro-phenol (1.00 eq, 500 mg, 2.29 mmol) was dissolved in Acetone (20mL). Allyl bromide (1.50 eq, 0.30 mL, 3.44 mmol) was added followed by dipotassium carbonate (2.00 eq, 634 mg, 4.59 mmol). The reaction was heated at 60 °C for 2h at which point complete conversion was observed. The reaction was cooled to room temperature and concentrated in vacuo. The residue was dissolved in EtOAc (50 mL), washed with water (3x50 mL), washed brine, dried MgSO₄, filtered and concentrated in vacuo to afford the desired product as a colorless solid 2-allyloxy-1-bromo-4-nitro-benzene (544 mg, 2.11 mmol, 91.94 % yield). Used in the next step without further purification.



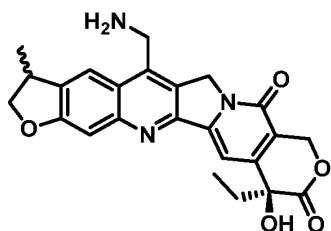
[0629] 2-allyloxy-1-bromo-4-nitro-benzene (1.00 eq, 468 mg, 1.81 mmol), ammonium chloride (10.0 eq, 969 mg, 18.1 mmol), and iron (10.0 eq, 1012 mg, 18.1 mmol) were dissolved in Ethanol (29.881mL) and Water (7.4702mL). The reaction was stirred at 80 °C for 2h at which point complete conversion was observed. The reaction was filtered, and the eluent was concentrated in vacuo. The residue was diluted with EtOAc, washed with water (2x50 mL), washed brine (30 mL), dried MgSO₄, filtered and concentrated in vacuo to afford the desired product as a yellow oil g 3-allyloxy-4-bromo-aniline (401 mg, 1.76 mmol, 96.95 % yield). $R_t = 1.51$ min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₉H₉BrNO 228.00, found 228.07.

¹H NMR (500 MHz, Chloroform-d) δ 7.28 (d, $J = 8.4$ Hz, 1H), 6.28 (d, $J = 2.5$ Hz, 1H), 6.22 (dd, $J = 8.4, 2.5$ Hz, 1H), 6.08 (ddt, $J = 17.2, 10.5, 4.9$ Hz, 1H), 5.50 (dq, $J = 17.3, 1.7$ Hz, 1H), 5.32 (dq, $J = 10.6, 1.5$ Hz, 1H), 4.57 (dt, $J = 4.9, 1.7$ Hz, 2H), 3.77 (s, 2H).



[0630] 3-allyloxy-4-bromo-aniline (1.00 eq, 401 mg, 1.76 mmol) was dissolved in tert-butanol (17.563mL). tributylstannane (10.0 eq, 4.7 mL, 17.6 mmol) was added to the reaction followed by 2,2'-Azobis(2-methylpropionitrile) (0.0600 eq, 17 mg, 0.105 mmol). The reaction was stirred at 80 °C for 90 minutes at which point conversion to the desired product was observed. The reaction was cooled to room temperature and 10% KF (15 mL) was added the reaction was stirred for 30 minutes. EtOAc (100 mL) was added, washed sat NaHCO₃ (2x100 mL), washed brine (50 mL), dried MgSO₄ filtered and concentrated in vacuo. The residue was purified by FCC 0-50% EtOAc in Hex. Fractions containing the desired product were concentrated in vacuo to afford a colorless oil 3-methyl-2,3-dihydrobenzofuran-6-amine (227 mg, 1.52 mmol, 86.52 % yield). Rt = 0.59 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₉H₁₂NO 150.09, found 149.82

¹H NMR (500 MHz, Chloroform-d) δ 6.91 (d, J = 7.8 Hz, 1H), 6.25 – 6.20 (m, 1H), 6.18 (d, J = 2.1 Hz, 1H), 4.65 (t, J = 8.7 Hz, 1H), 4.03 (t, J = 7.9 Hz, 1H), 3.76 (m, 2H), 3.44 (h, J = 7.1 Hz, 1H), 1.27 (d, J = 6.8 Hz, 3H).

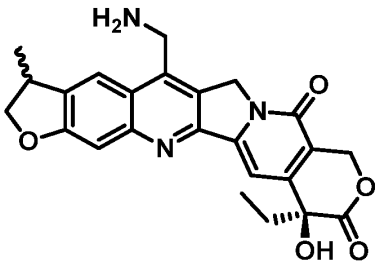
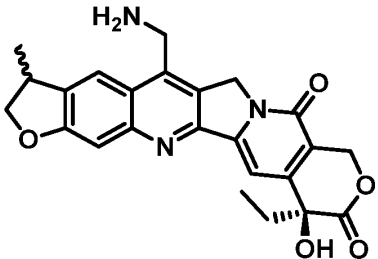


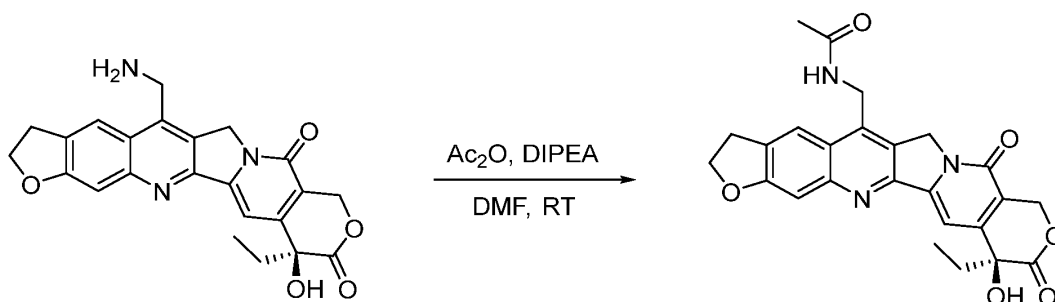
(5-amino-1H-inden-6-yl)-2-chloroethan-1-one was used to prepare **Compound 11** and **Compound 11a** using similar procedures as defined in Example 2. Two separable diastereomer products were isolated:

[0631] **Compound 11** (5S)-14-(aminomethyl)-5-ethyl-5-hydroxy-18-methyl-7,20-dioxo-11,24 diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(24),2,4(9),13,15(23),16,21-heptaene-6,10-dione (16 mg, 0.0369 mmol, 16.12 % yield). Rt = 1.04 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₂₄H₂₃N₃O₅ 434.17, found 434.25.

[0632] **Compound 11a** (5S)-14-(aminomethyl)-5-ethyl-5-hydroxy-18-methyl-7,20-dioxo-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(24),2,4(9),13,15(23),16,21-heptaene-6,10-dione (19 mg, 0.0430 mmol, 18.75 % yield). Rt = 1.03 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₂₄H₂₃N₃O₅ 434.17, found 434.33.

[0633] Table 9. Compounds 11 and 11a.

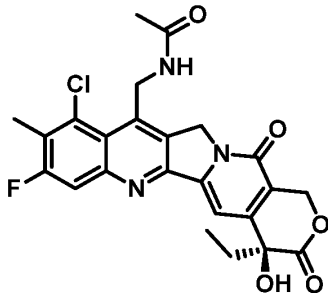
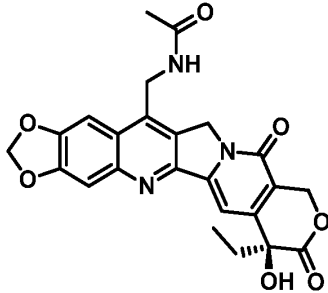
No.	Structure	Exact Mass	Calc. [M+H] ⁺	m/z	Rt (min)
11		433.16	434.17	434.25	1.04
11a		433.16	434.17	434.33	1.03

Example 12: Preparation of Compounds 12 and 12a-12b.

[0634] In a 4 mL vial equipped with a stir bar, (*S*)-5-(aminomethyl)-12-ethyl-12-hydroxy-2,3,9,12-tetrahydro-8*H*-furo[3,2-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(6*H*)-dione (10 mg, 0.02 mmol) in DMF (0.5 mL). Acetic anhydride (2.9 mg, 0.03 mmol) and DIPEA (6.2 μ L, 0.04 mmol) were added to the vial and reaction was stirred at RT for 2 h. Crude material was purified by preparative HPLC to yield product **Compound 12** (1.7 mg, 15% yield).

General Method UPLC-MS: t_R = 1.25 min, m/z (ES⁺) 462.17 (M+H)⁺, found 462.13.

[0635] **Table 10.** Compounds 12a-12b were made following the procedures outlined for Compound 12.

No.	Structure	Exact Mass	Calc. [M+H] ⁺	m/z	Rt (min)
12a		485.12	486.13	486.43	1.58
12b		463.14	464.15	464.54	1.08

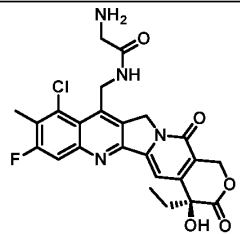
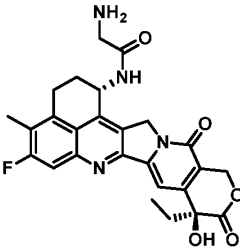
Example 13: Preparation of Compounds 13 and 13a-13b.

[0636] In a 4 mL vial equipped with a stir bar, dissolve Boc-Gly (4.2 mg, 0.02 mmol) in DMF (0.5 mL). Add HATU (7.9 mg, 0.02 mmol) and DIPEA (5.7 μ L, 0.04 mmol) to the vial and let stir for 20 minutes. Add (*S*)-5-(aminomethyl)-12-ethyl-12-hydroxy-2,3,9,12-tetrahydro-8*H*-furo[3,2-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(6*H*)-dione (9.2 mg, 0.02 mmol) to the vial and let reaction stir for 3 hours. Confirm coupling by UPLC-MS.

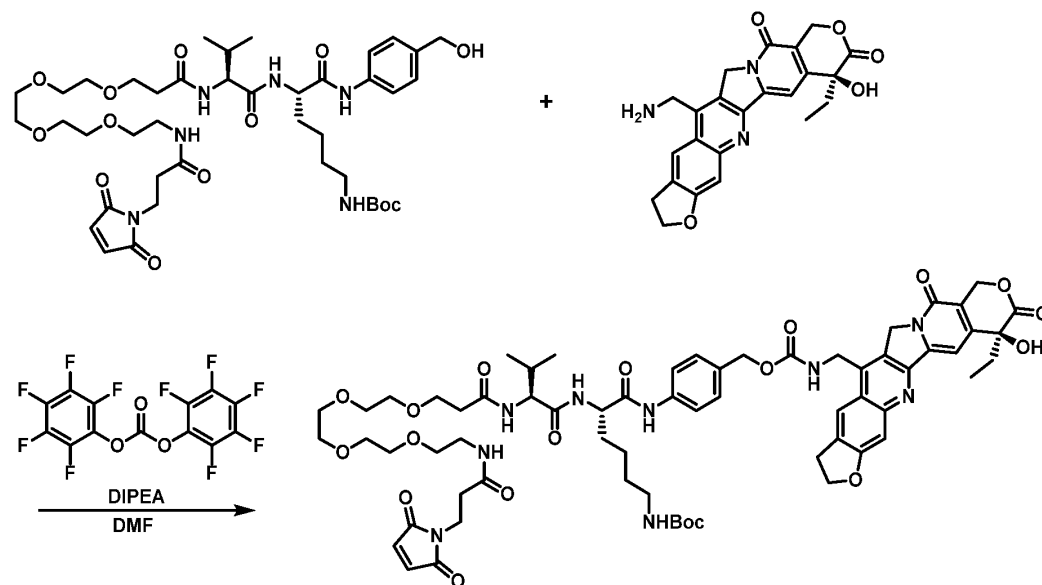
[0637] Remove DMF in vacuo and dissolve residue in 20% TFA in DCM and let stir for 1 hour. Crude was purified by preparatory HPLC to afford product **Compound 13** (2.4 mg, 23% yield – 2 steps).

[0638] General Method UPLC-MS: t_R = 1.03 min, m/z (ES⁺) 477.17 (M+H)⁺, found 477.51.

[0639] **Table 11.** Compounds 13a-13b were made following the procedures outlined for Compound 13.

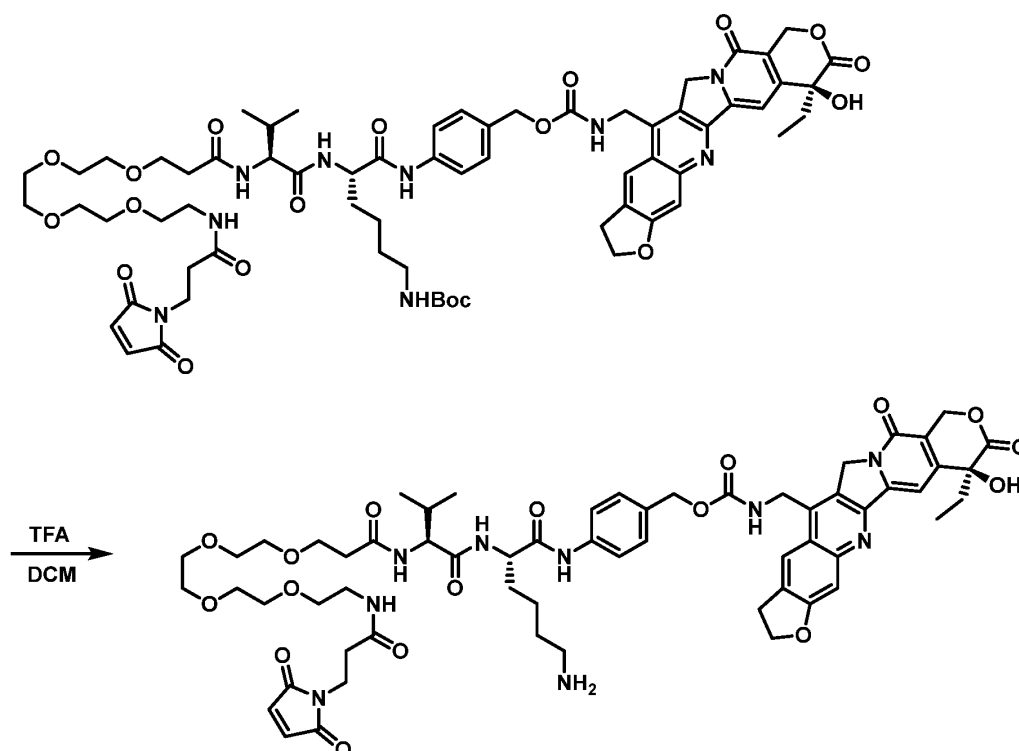
No.	Structure	Exact Mass	Calc. [M+H] ⁺	m/z	Rt (min)
13a		500.13	501.14	501.23	1.20
13b		492.18	493.19	493.17	1.15

Example 14: Preparation of Camptothecin Drug Linker Compounds.



[0640] tert-butyl N-[(5S)-5-[[[(2S)-2-[3-[2-[2-[2-[2-[3-(2,5-dioxopyrrol-1-yl)propanoylamino]ethoxy]ethoxy]ethoxy]ethoxy]propanoylamino]-3-methylbutanoyl]amino]-6-[4-(hydroxymethyl)anilino]-6-oxo-hexyl]carbamate (1.25 eq, 76 mg, 0.0900 mmol), prepared according to the procedure reported in WO2019195665, was

dissolved in DMF (1 mL). Bis(pentafluorophenyl) carbonate (1.50 eq, 43 mg, 0.108 mmol) was added to the reaction followed by N,N-Diisopropylethylamine (2.00 eq, 0.025 mL, 0.144 mmol). Complete conversion to the activated PFP intermediate was observed by UPLC-MS after 5 minutes. (5S)-14-(aminomethyl)-5-ethyl-5-hydroxy-7,20-dioxo-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(24),2,4(9),13,15,17(21),22-heptaene-6,10-dione (1.00 eq, 30 mg, 0.0720 mmol) was added to the reaction and stirred for 5 minutes at which point complete conversion was observed by UPLC-MS. The reaction was acidified with AcOH (30 μ L) and purified by Prep-HPLC 21x250 mm MaxRP 30-50-95% MeCN in H₂O 0.1% FA. Fractions containing the desired product were concentrated in vacuo to afford a yellow solid tert-butyl N-[(5S)-5-[(2S)-2-[3-[2-[2-[2-[2-[3-(2,5-dioxopyrrol-1-yl)propanoylamino]ethoxy]ethoxy]ethoxy]ethoxy]propanoylamino]-3-methylbutanoyl]amino]-6-[4-[(5S)-5-ethyl-5-hydroxy-6,10-dioxo-7,20-dioxo-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(13),2,4(9),14,16,21,23-heptaen-14-yl]methylcarbamoyloxymethyl]anilino]-6-oxo-hexyl]carbamate (35 mg, 0.0269 mmol, 37.34 % yield). Rt = 1.58 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₆₅H₈₄N₉O₁₉ 1294.59, found 1294.52.



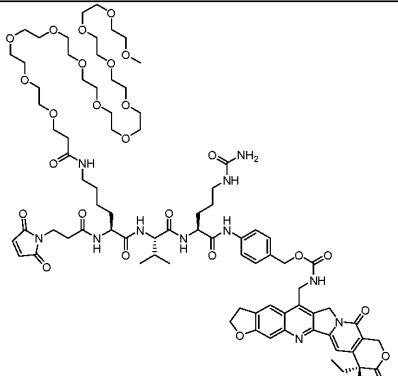
[0641] tert-butyl N-[(5S)-5-[[[(2S)-2-[3-[2-[2-[2-[2-[3-(2,5-dioxopyrrol-1-yl)propanoylamino]ethoxy]ethoxy]ethoxy]ethoxy]propanoylamino]-3-methylbutanoyl]amino]-6-[4-[[[(5S)-5-ethyl-5-hydroxy-6,10-dioxo-7,20-dioxo-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(13),2,4(9),14,16,21,23-heptaen-14-yl]methylcarbamoyloxymethyl]anilino]-6-oxo-hexyl]carbamate (1.00 eq, 35 mg, 0.0269 mmol) was dissolved in 10% DCM (2mL) in TFA. Stirred for 30 minutes and concentrated in vacuo. Complete conversion observed by UPLC-MS. The reaction was purified by prep-HPLC 21x250 mm MaxRP 20-35-95% MeCN in H₂O 0.05% TFA. Fractions containing the desired product were concentrated in vacuo to afford a yellow solid [4-[[[(2S)-6-amino-2-[[[(2S)-2-[3-[2-[2-[2-[2-[3-(2,5-dioxopyrrol-1-yl)propanoylamino]ethoxy]ethoxy]ethoxy]ethoxy]propanoylamino]-3-methylbutanoyl]amino]hexanoyl]amino]phenyl]methyl N-[(5S)-5-ethyl-5-hydroxy-6,10-dioxo-7,20-dioxo-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(13),2,4(9),14,16,21,23-heptaen-14-yl]methyl]carbamate;2,2,2-trifluoroacetic acid **Compound 14** (16 mg, 0.0120 mmol, 44.64 % yield). Rt = 1.22 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₆₀H₇₆N₉O₁₇ 1194.54, found 1194.60.

[0642] **Table 12.** Compound 14a was made following the general procedures outlined for Compound 14. Compound 14b was made following the general procedures outline for Compound 14.

No.	Z'-A	S* or L ^P (S*)	RL	Y	Camptothecin (N-link)
14	Mal-CH ₂ CH ₂ C(O)-	-NH(CH ₂ CH ₂ O) ₄ -CH ₂ CH ₂ C(O)-	Val-Lys	PABC	Compound 2n
14a	Mal-CH ₂ CH ₂ C(O)-	-NH(CH ₂ CH ₂ O) ₄ -CH ₂ CH ₂ C(O)-	Val-Lys	PABC	Compound 1
4z	Mal-CH ₂ CH ₂ -C(O)	-NH((CH ₂) ₅ -NH-C(O)(CH ₂ CH ₂ O) ₁₂ CH ₃)C(O)-	Val-Cit	PABC	Compound 2n

The following example was prepared using similar procedures as described for Compound 14.

Compound Number	STRUCTURE	Exact Mass	Calc. [M+H] ⁺	m/z	Rt (min)
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4z		1673.80	1674.81	1675.73	1.51
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Characterization Data

No.	Parent Exact Mass	Calc'd MS (m/z) [M+H] ⁺	Observed MS (m/z)	RT
14	1193.53	1194.54	1194.60	1.22
14a	1195.51	1196.52	1196.23	1.22

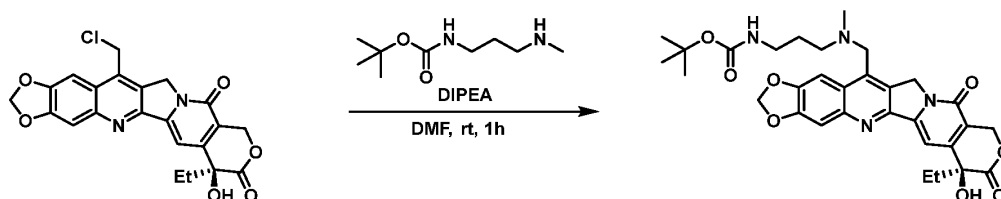
Aggregation Levels

[0643] **Table 13.** ADC aggregations levels for camptothecin drug-linkers (DAR = 8).

ADC aggregation was determined by Size Exclusion Chromatography (SEC).

ADC	Description	DAR	Conc. (mg/mL)	HMW %
Ag1-Ex_14	Glucuronide-Ex_2n	8.2	1.15	11.64
Ag4 -Ex_14	Glucuronide-Ex_2n	8.2	0.99	9.05
Ag1-Ex_14a	Glucuronide-Ex_2u	8.5	0.94	22.44
Ag4 -Ex_14a	Glucuronide-Ex_2u	8.4	1.00	16.49

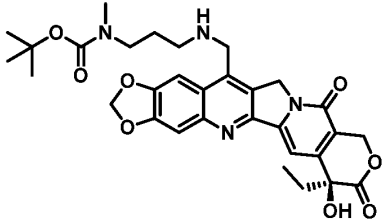
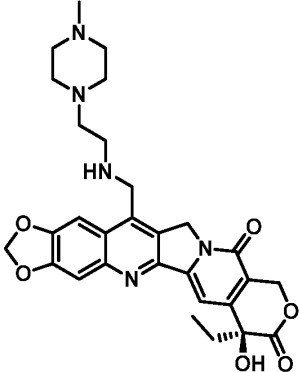
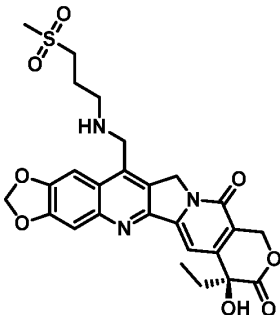
Example 15. Preparation of Compound 7

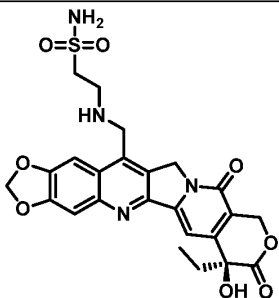
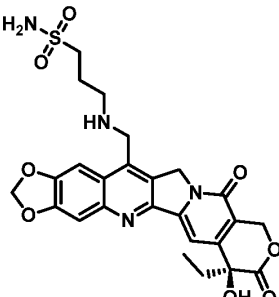
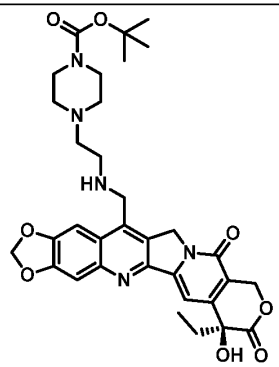
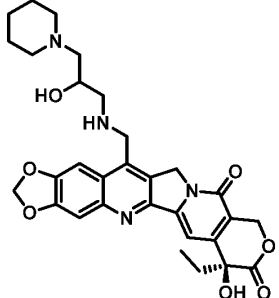
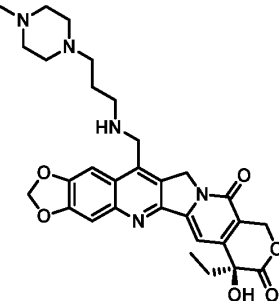


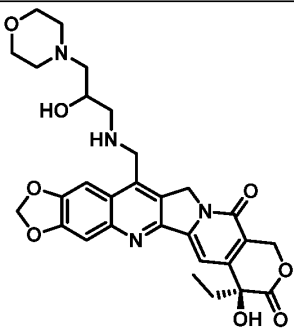
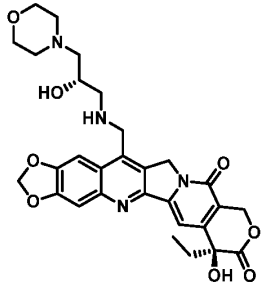
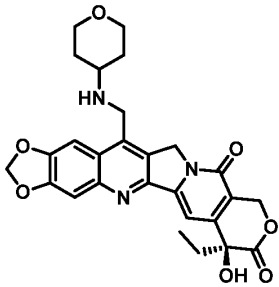
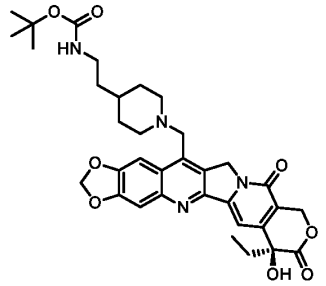
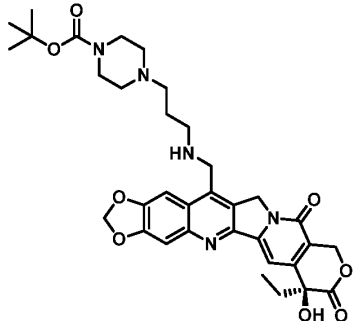
[0644] rac-(5S)-14-(chloromethyl)-5-ethyl-5-hydroxy-7,18,20-trioxa-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(13),2,4(9),14,16,21,23-heptaene-6,10-dione (1.00 eq, 50 mg, 0.113 mmol) was dissolved in DMF (1mL) and added to tert-butyl N-[3-(methylamino)propyl]carbamate (3.00 eq, 64 mg, 0.340 mmol). Lithium

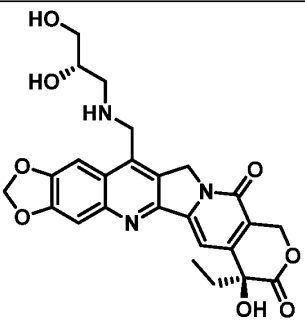
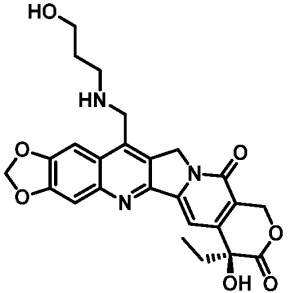
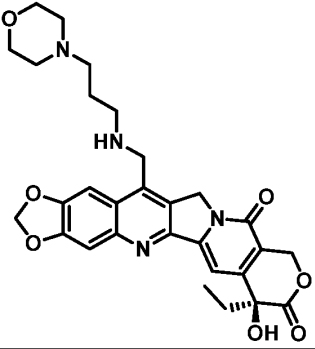
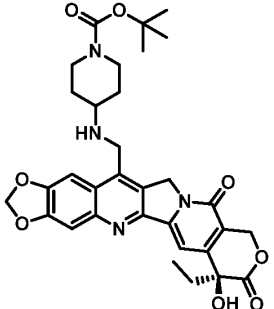
iodide (1.00 eq, 15 mg, 0.113 mmol) was added followed by N,N-Diisopropylethylamine (6.00 eq, 0.12 mL, 0.681 mmol). The reaction was stirred for 1h, and then acidified with AcOH (200 uL) and purified by prep-HPLC. Fractions containing the desired product were concentrated in vacuo to afford a yellow solid tert-butyl N-[3-[[[(5S)-5-ethyl-5-hydroxy-6,10-dioxo-7,18,20-trioxa-11,24-diazahehexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(13),2,4(9),14,16,21,23-heptaen-14-yl]methyl-methyl-amino]propyl]carbamate **Compound 7** (45.13 mg, 0.0762 mmol, 67.14 % yield). Rt = 1.18 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₃₁H₃₇N₄O₈ 593.26, found 593.56.

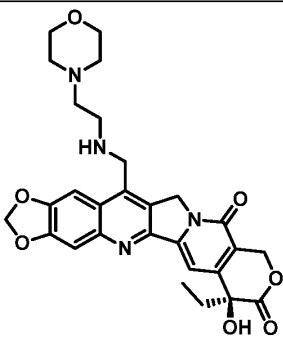
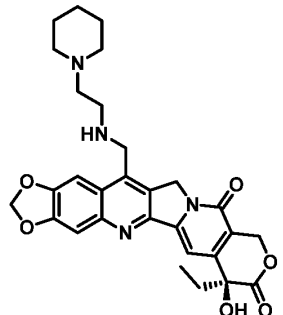
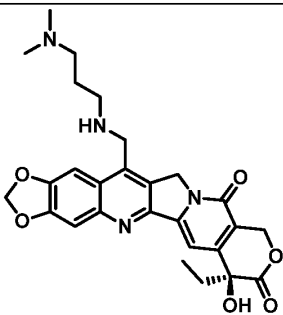
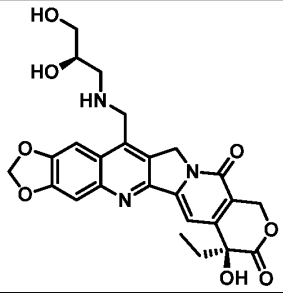
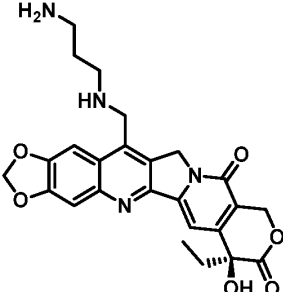
[0645] **Table 14.** The compounds of Table 14 were made following the general procedures outlined for Compound 7.

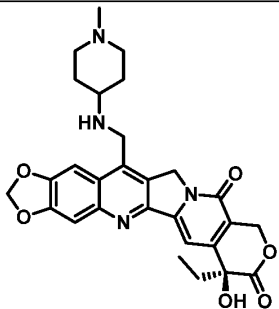
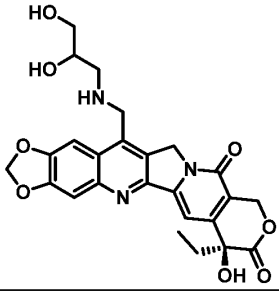
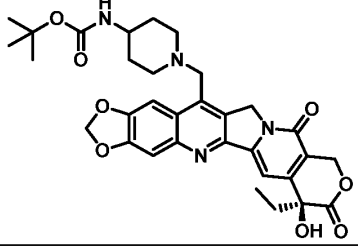
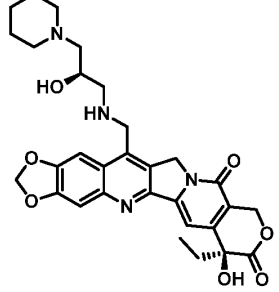
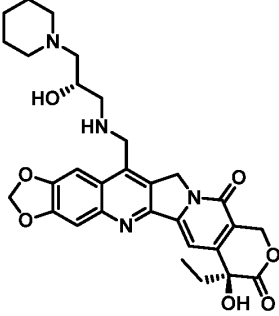
Compound #	Structure	Calc. [M+H] ⁺	m/z	RT (min)
7a		593.26	593.46	1.31
7b		548.25	548.55	1.07
7c		542.16	542.54	0.88

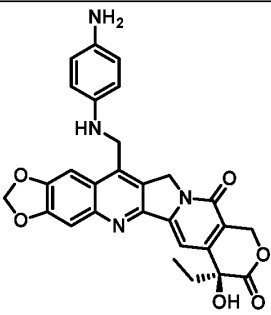
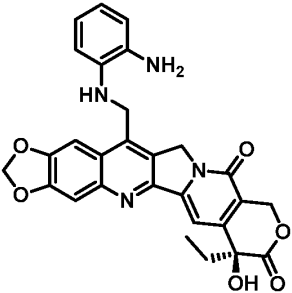
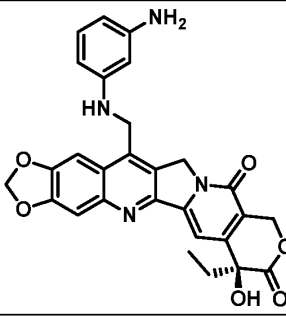
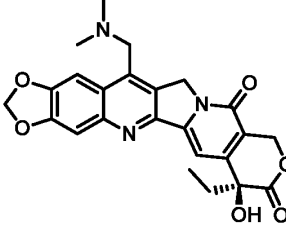
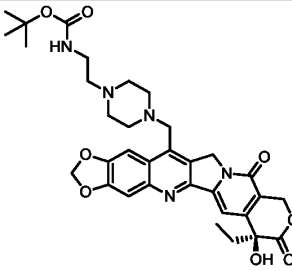
7d		529.14	529.44	0.86
7e		543.16	543.12	0.87
7f		634.29	634.5	1.69
7g		563.25	563.59	1.12
7h		562.27	562.62	1.07

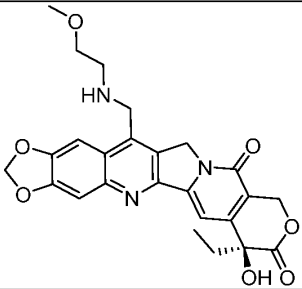
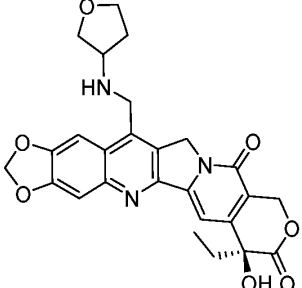
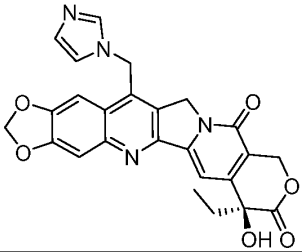
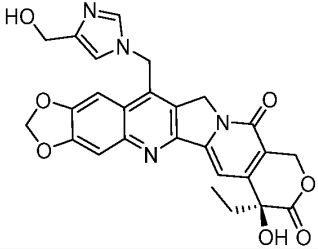
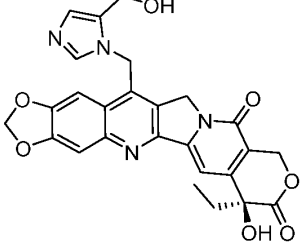
7i		565.23	565.43	1.06
7j		565.23	565.43	1.07
7k		506.19	506.55	0.89
7l				
7m		648.31	648.66	1.34

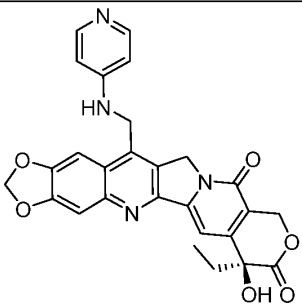
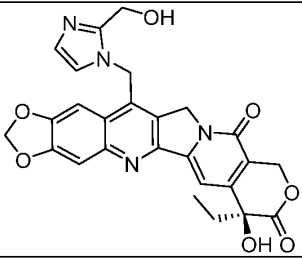
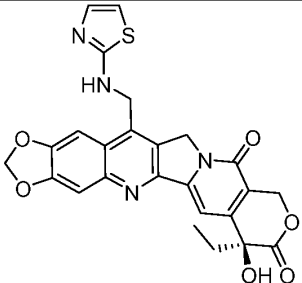
7n		496.17	496.56	1.06
7o		480.18	480.55	1.26
7p		549.24	549.52	1.09
7q		605.26	605.59	1.16

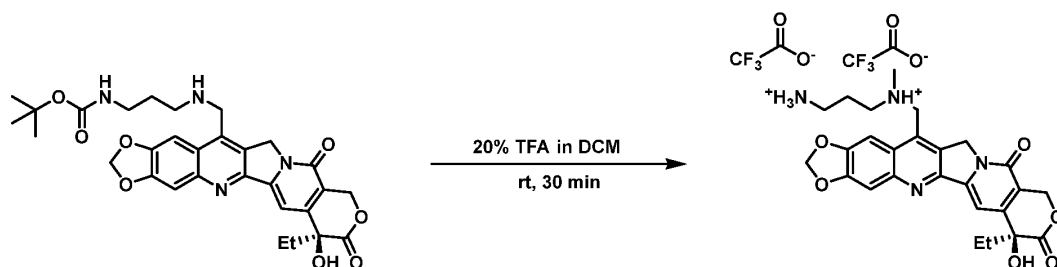
7r		535.22	535.55	1.04
7s		533.24	533.22	1.09
7t		507.23	507.61	1.07
7u		496.17	496.46	1.12
7v		479.2	479.48	1.04

7w		519.23	519.74	1.09
7x		496.17	496.46	1.13
7y		605.26	605.49	1.15
7z		563.25	563.49	1.15
7aa		563.25	563.68	1.14

7ab		513.18	513.08	1.08
7ac		513.18	513.17	1.44
7ad		513.218	513.45	1.24
7ae		450.17	450.48	0.81
7af		633.29	634.3	1.21

7ag		480.18	479.93	1.03
7ah		492.18	491.96	0.99
7ai		473.15	473.25	0.99
7aj		203.16	203.24	0.98
7ak		503.16	503.24	0.98

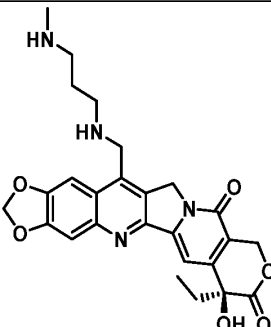
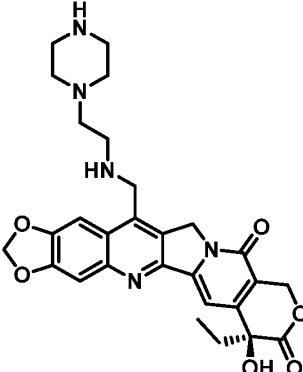
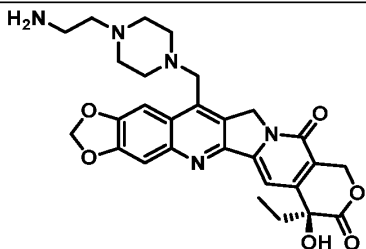
7al		499.16	498.97	1.03
7am		503.16	503.14	0.98
7an		504.12	505.32	0.99

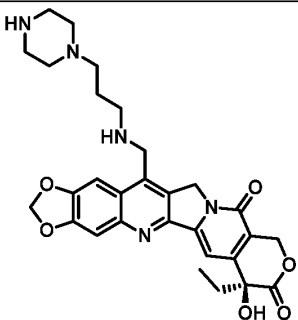
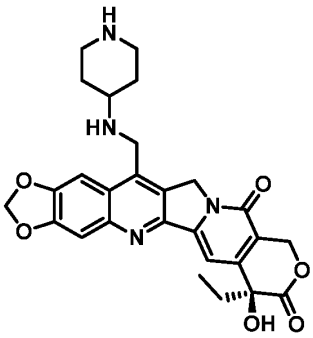
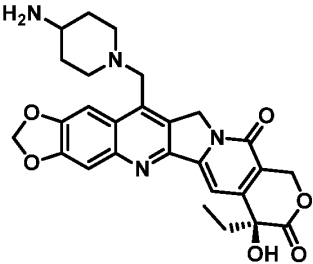
Example 16. Preparation of Compounds 8a-8f

[0646] tert-butyl N-[3-[[[(5S)-5-ethyl-5-hydroxy-6,10-dioxo-7,18,20-trioxa-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(13),2,4(9),14,16,21,23-heptaen-14-yl]methyl-methyl-amino]propyl]carbamate (1.00 eq, 45 mg, 0.0762 mmol) was dissolved in 20% TFA in DCM (1 mL). The reaction was stirred for 30 minutes at which point complete conversion was observed. The reaction was concentrated in vacuo and purified by prep-HPLC. Fractions containing the desired product were concentrated in vacuo to afford a yellow solid (5S)-14-[[[3-aminopropyl(methyl)amino]methyl]-5-ethyl-5-hydroxy-

7,18,20-trioxa-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracosal(13),2,4(9),14,16,21,23-heptaene-6,10-dione;2,2,2-trifluoroacetic acid **Compound 8** (42 mg, 0.0580 mmol, 76.18 % yield). Rt = 0.58 min General Method UPLC. MS (m/z) [M+H]⁺ calc. for C₂₆H₂₉N₄O₆ 493.21, found 493.55.

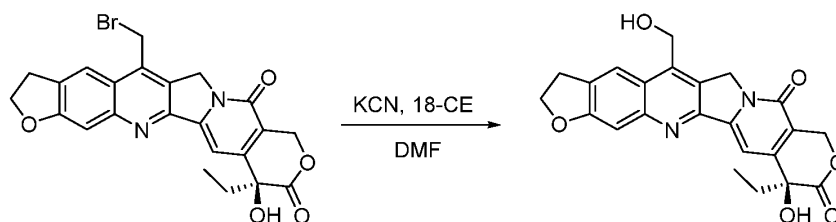
[0647] **Table 15.** Camptothecin derivatives prepared following the general procedures outlined for Compound 8.

Compound #	Structure	Calc. [M+H] ⁺	m/z	RT (min)
8a		493.21	493.65	0.83
8b		534.24	534.39	0.88
8c		534.24	534.58	0.92

8d		548.25	548.55	1.05
8e		505.21	505.58	0.78
8f		505.21	505.58	0.87

Camptothecin Conjugation Method

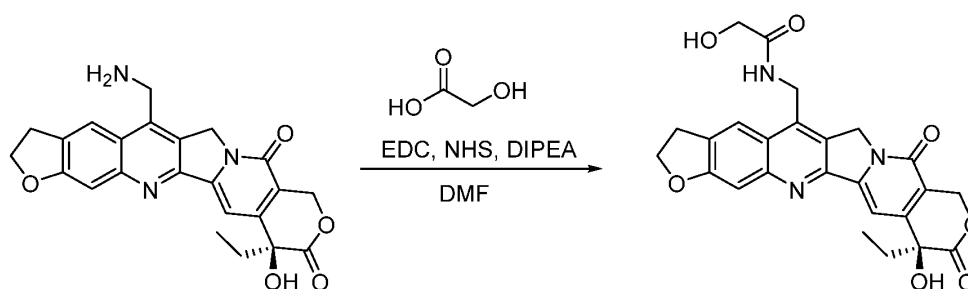
[0648] Fully or partially reduced ADCs were prepared in 50% propylene glycol (PG) IX PBS mixture. A half portion of the PG was added to reduced mAb, and half PG was added to the 1 mM DMSO camptothecin drug-linker stock. The PG/drug-linker mix was added to reduced mAb in 25% portions. After the addition of drug-linker was complete, excess drug-linker was removed by treating with activated charcoal (1 mg of charcoal to 1 mg of mAb). The charcoal was then removed via filtration, and the resulting ADC was buffer exchanged using a NAP5 or PD10 column, into 1X PBS pH 7.4.

Example 17. Preparation of Compound 35

[0649] In a 4 mL vial equipped with a stir bar, (*S*)-5-(bromomethyl)-12-ethyl-12-hydroxy-2,3,9,12-tetrahydro-8*H*-furo[3,2-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(6*H*)-dione (30 mg, 0.07 mmol) was dissolved in DMF (0.5 mL). KCN (8.9 mg, 0.14 mmol) and crown ether (18.1 mg, 0.07 mmol) were added to the reaction, and the reaction was stirred for 2 h at RT. Confirm reaction by UPLC-MS and remove solvent in vacuo. Product was purified by preparatory HPLC to afford product **compound 35** (3.7 mg, 13% yield). General Method UPLC-MS: R_t = 1.29 min, m/z (ES+) 421.14 ($M+H$)⁺, found 421.42.

[0650] **Table 16.** Camptothecin derivatives prepared following the general procedures outlined for Compound 35.

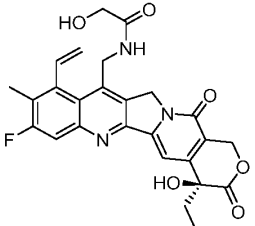
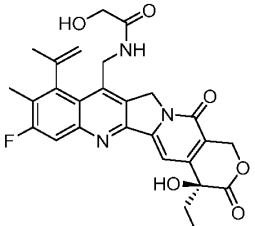
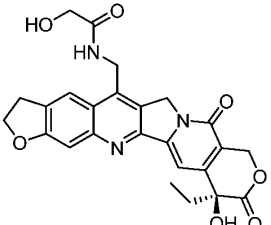
Compound #	Structure	Calc. $[M+H]^+$	m/z	RT (min)
35		421.14	421.42	1.29

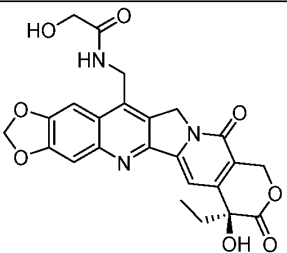
Example 18. Preparation of Compound 15c

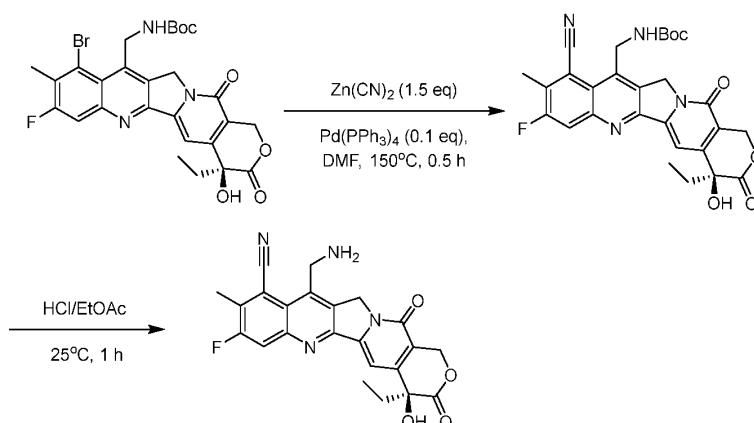
[0651] Glycolic acid (12.51 mg, 0.1645 mmol) was dissolved in DMF (1 mL). *N*-hydroxysuccinimide (18.18 mg, 0.1579 mmol) was added followed by 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (37.84 mg, 0.1974 mmol). The reaction

was stirred for 20 minutes and then the solution was added to a vial containing (5S)-14-(aminomethyl)-5-ethyl-5-hydroxy-7,20-dioxo-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(24),2,4(9),13,15,17(21),22-heptaene-6,10-dione (46 mg, 0.1097 mmol). DIPEA (38.2 μ L, 0.219 mmol) was added to the reaction mixture and stirred for 5 minutes at which point complete conversion to the desired product was observed by UPLC-MS. The reaction was acidified with AcOH (50 μ L) and purified by prep-HPLC 30x250 mm Max-RP, 10-35-95% MeCN in H₂O 0.05% TFA. Fractions containing the desired product were concentrated in vacuo to afford a yellow solid (S)-N-((12-ethyl-12-hydroxy-8,11-dioxo-2,3,6,9,11,12-hexahydro-8H-furo[3,2-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-5-yl)methyl)-2-hydroxyacetamide (**Compound 15c**, 24.1 mg, 0.0505 mmol, 46.0%). General Method UPLC-MS: R_t = 1.24 min, m/z (ES+) 478.16 (M+H)⁺, found 478.27.

[0652] Table 17. Camptothecin derivatives prepared following the general procedures outlined for Compound 15c.

Compound #	Structure	Calc. [M+H] ⁺	m/z	RT (min)
15a		494.17	493.95	1.40
15b		508.19	508.23	1.61
15c		478.16	478.27	1.24

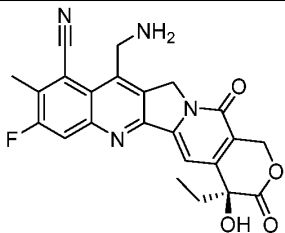
15d		480.14	480.07	1.25
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Example 18. Preparation of Compound 16

[0653] To a solution of CPT (100 mg, 170 μmol) in DMF (5 mL) was added $\text{Pd(PPh}_3)_4$, (40 mg, 35 μmol) and zinc cyanide (80 mg, 680 μmol) at 20°C in a microwave tube. The reaction was heated at 150°C for 0.5 h under microwave. The resulting mixture was partitioned between ethyl acetate (100 mL) and water (200 mL), and then the aqueous phase was further extracted with ethyl acetate (3×30 mL). The organic phase was washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC (TFA condition) to give Boc-protected intermediate (12 mg, yield 13%).

[0654] A mixture of CPT intermediate (12 mg, 22.5 μmol) in HCl/EtOAc (4 M, 1 mL) was stirred at 25°C for 2 h. LCMS analysis showed reactant was consumed completely and one main peak with desired mass was detected. The resulting mixture was concentrated to give a residue which was purified by prep-HPLC (TFA condition) to give final product **Compound 16** (5 mg, 41% yield). General Method UPLC-MS: $R_t = 1.07$ min, m/z (ES+) 435.15 ($\text{M}+\text{H}$)⁺, found 435.29

[0655] **Table 18.** Camptothecin derivatives prepared following the general procedures outlined for Compound 16.

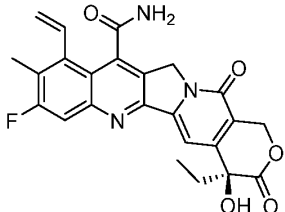
Compound #	Structure	Calc. [M+H] ⁺	m/z	RT (min)
16		435.15	435.29	1.07

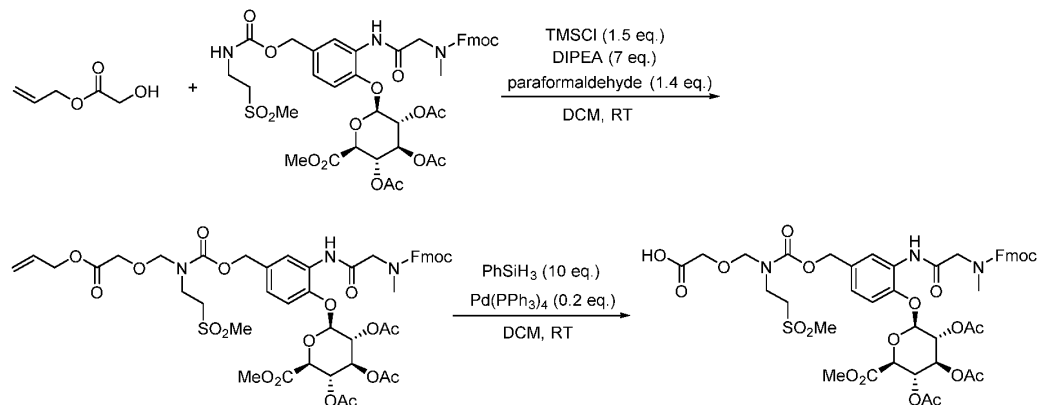
Example 19. Preparation of Compound 17

[0656] To a solution of CPT (20 mg, 37.34 mmol) in H₂O (0.3 mL) and tert-butanol (1 mL) was added AD-mix-beta (58.1 mg, 74.6 mmol) at 0°C. The reaction mixture was warmed to 20°C and stirred at 20°C for 48 h. LCMS analysis showed starting material was consumed completely and one main peak with desired mass was detected. The resulting mixture was purified by pre-HPLC (TFA condition) to afford intermediate (5 mg, 12% yield).

[0657] A mixture of CPT intermediate (12 mg, 22.5 mmol) in HCl/EtOAc (4 M, 1 mL) was stirred at 25°C for 2 h. LCMS analysis showed reactant was consumed completely and one main peak with desired mass was detected. The resulting mixture was concentrated to give a residue which was purified by reverse phase HPLC (9n) to afford product **Compound 17** (5 mg, 41% yield). General Method UPLC-MS: *t_R* = 1.71 min, *m/z* (ES⁺) 450.15 (M+H)⁺, found 450.00.

[0658] **Table 19.** Camptothecin derivatives prepared following the general procedures outlined for Compound 17.

Compound #	Structure	Calc. [M+H] ⁺	m/z	RT (min)
17		450.15	450.00	1.71

Example 20. Preparation of Compound 18

[0659] The allyl ester of glycolic acid was made according to literature *ACS Cent. Sci.* 2020, 6, 2, 226.

[0660] In a scintillation vial equipped with stir bar, MAC linker precursor (450 mg, 0.5 mmol) was dissolved in DCM and added TMSCl (96 μ L, 0.75 mmol) and paraformaldehyde (21 mg, 0.7 mmol) and stirred at room temp overnight. Solution was clear and DIPEA (323 mg, 2.5 mmol) was added to the reaction mixture. Glycolic acid allyl ester (290 μ L, 2.5 mmol) was added to the reaction and stirred overnight. Reverse phase biotage (5-95% ACN:H₂O + 0.5 % formic acid) afforded the intermediate (225 mg, 45% y).

[0661] In scintillation vial equipped with stir bar, intermediate (225 mg, 0.22 mmol) was dissolved in DCM (0.5 mL) and THF (0.5 mL). PhSiH₃ (237 mg, 2.2 mmol) was added followed by Pd(PPh₃)₄ (58 mg, 0.05 SGD-9493mmol). Reaction was stirred for 2 h at 25°C. Reverse phase biotage (5-95% ACN:H₂O + 0.5 % formic acid) afforded the desired product **Compound 18** (160 mg, 73% yield). General Method UPLC-MS: t_R = 2.11 min, m/z (ES+) 986.26 (M+H)⁺, found 986.37.

Example 20. Preparation of Compound 19

[0662] To a 4 mL scintillation vial equipped with stir bar was added carboxylate 2-((((3-(2-(((9H-fluoren-9-yl)methoxy)carbonyl)(methyl)amino)acetamido)-4-(((2S,3R,4S,5S,6S)-3,4,5-triacetoxy-6-(methoxycarbonyl)tetrahydro-2H-pyran-2-yl)oxy)benzyl)oxy)carbonyl)(2-(methylsulfonyl)ethyl)amino)methoxy)acetic acid (19.8 mg, 0.02 mmol), HATU (7.6 mg, 0.02 mmol), DIPEA (7.7 μ L, 0.06 mmol) and DMF (0.2 mL). The reaction was stirred for 10 min at 25°C. (S)-11-(aminomethyl)-4-ethyl-8-fluoro-4-hydroxy-9-methyl-10-vinyl-1,12-dihydro-14H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H)-dione (8.7 mg, 0.02 mmol) was added to the reaction and stirred for 3 h. Solvent was removed in vacuo purified

by reverse phase HPLC (5-95% ACN:H₂O + 0.5 % formic acid) to afford the intermediate (9.8 mg, 70% yield).

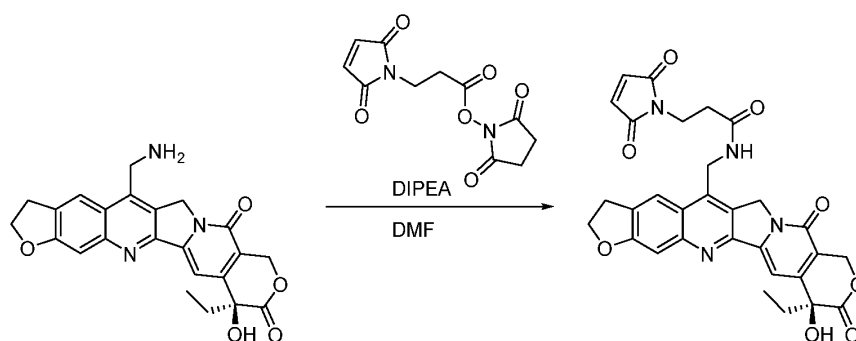
[0663] To a 4 mL scintillation vial equipped with stir bar was added (2*S*,3*R*,4*S*,5*S*,6*S*)-2-(2-(2-(((9*H*-fluoren-9-yl)methoxy)carbonyl)(methyl)amino)acetamido)-4-(10-((*S*)-4-ethyl-8-fluoro-4-hydroxy-9-methyl-3,14-dioxo-10-vinyl-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-11-yl)-4-(2-(methylsulfonyl)ethyl)-3,8-dioxo-2,6-dioxa-4,9-diazadecyl)phenoxy)-6-(methoxycarbonyl)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (9.8 mg, 0.014 mmol), THF (0.2 mL), and MeOH (0.2 mL). The reaction was cooled to -20°C and stirred for 10 minutes. LiOH in water (420 uL, 84 mmol, 20 mM) was added to the reaction and stirred for 1 h at -20°C and 6 h at 25°C. Solvent was removed in vacuo purified by reverse phase HPLC (5-95% ACN:H₂O + 0.5 % formic acid) to afford the intermediate (4.6 mg, 62% yield).

[0664] To a 4 mL scintillation vial equipped with stir bar was added (2*S*,3*S*,4*S*,5*R*,6*S*)-6-(4-(10-((*S*)-4-ethyl-8-fluoro-4-hydroxy-9-methyl-3,14-dioxo-10-vinyl-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-11-yl)-4-(2-(methylsulfonyl)ethyl)-3,8-dioxo-2,6-dioxa-4,9-diazadecyl)-2-(2-(methylamino)acetamido)phenoxy)-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-carboxylic acid (1.27 mg, 0.001 mmol), DIPEA (0.43 uL, 0.002 mmol), and MP-OSu (0.39 mg, 0.002 mmol), and DMF (500 µL). The reaction was and stirred for 3 hours at room temperature. Solvent was removed in vacuo purified by reverse phase HPLC (5-95% ACN:H₂O + 0.5 % formic acid) to afford the product **Compound 19** (0.70 mg, 48.13% yield). General Method UPLC-MS: *t_R* = 1.45 min, *m/z* (ES+) 1192.35 (M+H)⁺, found 1191.96.

[0665] **Table 20.** Camptothecin derivatives prepared following the general procedures outlined for Compound 19.

Compound #	Structure	Calc. [M+H] ⁺	m/z	RT (min)
19		1192.35	1191.96	1.45
19a		1206.36	1206.98	1.50
19b		1178.32	1178.87	1.29
19c		1176.34	1176.81	1.31

Example 21. Preparation of Compound 21



[0666] (5S)-14-(aminomethyl)-5-ethyl-5-hydroxy-7,20-dioxo-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(24),2,4(9),13,15,17(21),22-heptaene-6,10-dione (3.0 mg, 0.0072 mmol) was dissolved in DMF (0.25 mL). 2,5-dioxopyrrolidin-1-yl 3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoate (2.3 mg, 0.0086 mmol) was added followed by DIPEA (2.5 μ L, 0.014 mmol). Complete conversion was

observed by UPLC-MS after 30 minutes. The reaction was acidified with AcOH (10 μ L) and purified by prep-HPLC 10x250 mm Max-RP 5-60-95% MeCN in H₂O 0.05% TFA. Fractions containing the desired product were concentrated in vacuo to afford a yellow solid 3-(2,5-dioxopyrrol-1-yl)-N-[[[(5S)-5-ethyl-5-hydroxy-6,10-dioxo-7,20-dioxo-11,24-diazahexacyclo[11.11.0.02,11.04,9.015,23.017,21]tetracos-1(24),2,4(9),13,15,17(21),22-heptaen-14-yl]methyl]propenamide (**Compound 21**, 1.91 mg, 0.0033 mmol, 46 %). General Method UPLC-MS: t_R = 1.33 min, m/z (ES+) 571.19 (M+H)⁺, found 570.95.

Biological Examples

***In vitro* Small Molecule and ADC Evaluation**

[0667] *In vitro* potency was assessed on multiple cancer cell lines. All cell lines were authenticated by STR profiling at IDEXX BioResearch and cultured for no more than 2 months after resuscitation. Cells cultured in log-phase growth were seeded for 24 hours in 96-well plates containing 150 μ i RPMI 1640 supplemented with 20% FBS. Serial dilutions of antibody-drug conjugates in cell culture media were prepared at 4x working concentrations, and 50 μ L of each dilution was added to the 96-well plates. Following addition of test articles, cells were incubated with test articles for 4 days at 37 $^{\circ}$ C. After 96 hours, growth inhibition was assessed by CellTiterGlo[®] (Promega, Madison, WI) and luminescence was measured on a plate reader. The IC₅₀ value, determined in triplicate, is defined here as the concentration that results in 50% reduction in cell growth relative to untreated controls.

[0668] In the following Tables IC₅₀ values for ADCs and camptothecin free drugs are given in ng/mL and nmol/L concentrations, respectively, with values in the parenthesis representing percent cells remaining at highest concentration tested (1000 ng/mL for ADCs and 1 μ M for camptothecin free compound, unless otherwise indicated) relative to untreated cells. Cell viability was determined by CellTiter-Glo staining after 96h exposure to ADC. ND = Not Determined. In the following tables, "Ex_" refers to a drug linker number. For example, "Ag4-Ex_4a" refers to a conjugate of an Ag4 antibody with drug linker 4a.

[0669] **Table 21.** In vitro potency (IC₅₀ values) of CPT free drugs (nmol/L) targeting renal carcinoma cells (786-O), melanoma cells (A2058), pancreatic cancer cells (BxPC3), non-small-cell lung cancer cells (Calu1), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), breast cancer cells (MDA-MB-231), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Drug	786-O IC ₅₀	A2058 IC ₅₀	BxPC3 IC ₅₀	Calu1 IC ₅₀	DEL IC ₅₀	DELBVR IC ₅₀
2n	5	3	3	18	1	1
2ad	9	ND	22	ND	1	1
2ah	108	ND	199	ND	12	11
2ai	64	ND	57	ND	6	5
2aj	2	ND	3	ND	0.3	0.3
2ak	57	ND	88	ND	6	6
2al	4	ND	7	ND	1	1
2am	2	ND	4	ND	0.3	0.3
2ap	8	ND	14	ND	1	1
13a	6	ND	5	ND	0.3	1
12a	1	ND	2	ND	0.2	0.2
13	139	ND	94	ND	8	21
12	13	ND	12	ND	1	1
13b	27	ND	21	ND	1	4
2aq	11	18	27	1	2	3
10	54	33	64	95	7	15
14	4	2	6	9	0.6	1
5b	69	17	128	54	17	15
2ar	26	7	43	26	7	5
2as	3	3	5	4	1	1
2at	50	20	84	37	11	8
2au	4	3	6	7	1	1
2av	22	4	34	25	5	4
5c	1	5	8	4	0.3	
5a	56	16	154	389	7	10
5	16	7	40	129	4	4
2aw	58	18	149	269	15	15
11	8	3	12	69	1	2
11a	15	5	23	131	2	4
6	5	5	8	17	1	3
6a	6	5	8	21	2	3
33	10	6	11	36	2	2
33a	34	18	50	120	7	12
6b	23	15	18	32	5	5
6c	4	5	5	15	1	2
6d	23	13	15	43	3	12
6g	6	4	7	25	1	1
6f	97	17	46	294	9	8
12b	12	ND	11	ND	0	1
6e	29	11	65	155	4	4
6h	36	20	100	155	6	7

6i	5	2	10	26	1	1
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[0670] Table 22 (cont.) *In vitro* potency (IC₅₀ values) of CPT free drugs (nmol/L) targeting renal carcinoma cells (786-O), melanoma cells (A2058), pancreatic cancer cells (BxPC3), non-small-cell lung cancer cells (Calu1), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), breast cancer cells (MDA-MB-231), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Drug	Karpas299 IC ₅₀	L540cy IC ₅₀	Ls174T IC ₅₀	MDAMB 231 IC ₅₀	MOLM-13 IC ₅₀	SU-DHL-4 IC ₅₀
2n	5	2	4	8	29	1
2ad	7	4	17	15	5	4
2ah	65	54	152	149	125	29
2ai	47	47	64	79	34	13
2aj	2	1	5	5	1	1
2ak	40	22	50	147	129	11
2al	4	2	11	9	2	1
2am	2	1	5	5	2	1
2ap	5	2	4	13	5	2
13a	1	1	44	5	2	1
12a	1	0.4	7	2	1	0.4
13	126	45	195	177	88	18
12	24	5	19	27	5	1
13b	11	6	58	30	23	2
2aq	7	4	12	12	39	5
10	57	51	33	59	149	15
14	4	2	3	5	22	1
5b	46	10	45	36	>1000	27
2ar	29	4	14	14	258	13
2as	3	1	2	1	51	2
2at	38	4	30	21	264	23
2au	5	1	2	1	40	2
2av	26	5	11	9	236	8
5c	1	0.8	6	2	2	0.5
5a	28	20	>1K	350	73	12
5	10	9	>1K	218	258	7
2aw	36	25	>1K	456	199	22
11	14	4	>1K	41	108	4
11a	13	6	>1K	100	14	3
6	4	4	21	7	4	2

6a	5	4	12	7	4	2
33	8	4	14	18	85	4
33a	28	21	18	36	258	14
6b	14	13	85	35	9	9
6c	3	3	18	7	4	2
6d	12	11	31	21	6	4
6g	4	4	14	12	6	2
6f	59	23	>1K	139	51	19
12b	8	4	22	28	3	1
6e	31	18	17	57	17	7
6h	28	19	48	102	31	14
6i	4	3	10	11	2	2

[0671] Table 23. *In vitro* potency (IC₅₀ values) of CPT free drugs (nmol/L) targeting renal carcinoma cells (786-O), melanoma cells (A2058), pancreatic cancer cells (BxPC3), non-small-cell lung cancer cells (Calu1), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), breast cancer cells (MDA-MB-231), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Drug	786-O IC ₅₀	A2058 IC ₅₀	BxPC3 IC ₅₀	Calu1 IC ₅₀	DEL IC ₅₀	DELBVR IC ₅₀
7w	15	ND	13	ND	2	2
7n	66	ND	47	ND	5	6
7i	118	ND	57	ND	9	17
7h	44	ND	43	ND	5	6
7aa	131	ND	66	ND	17	19
7z	123	ND	127	ND	17	16
8f	267	ND	166	ND	14	30
8e	104	ND	62	ND	7	10
8d	15	ND	14	ND	2	2
8c	27	ND	14	ND	3	4
8b	102	ND	51	ND	8	13
8a	11	ND	15	ND	1	2
8	113	ND	52	ND	8	16

[0672] Table 23 (cont.) *In vitro* potency (IC₅₀ values) of CPT free drugs (nmol/L) targeting renal carcinoma cells (786-O), melanoma cells (A2058), pancreatic cancer cells (BxPC3), non-small-cell lung cancer cells (Calu1), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), breast cancer

cells (MDA-MB-231), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Drug	Karpas29 9 IC ₅₀	L540cy IC ₅₀	Ls174T IC ₅₀	MDAMB 231 IC ₅₀	MOLM- 13 IC ₅₀	SU-DHL- 4 IC ₅₀
7w	8	6	16	26	26	6
7n	57	23	39	96	137	21
7i	84	48	110	183	183	32
7h	57	23	40	67	93	21
7aa	63	51	188	228	69	19
7z	150	48	79	306	143	39
8f	110	84	236	207	32	32
8e	72	36	109	102	89	25
8d	9	6	19	25	37	6
8c	28	14	32	57	69	7
8b	62	56	111	260	91	17
8a	8	5	48	22	3	4
8	54	44	131	125	47	15

[0673] Table 24. *In vitro* potency (IC₅₀ values) of CPT ADCs (ng/mL) targeting renal carcinoma cells (786-O), melanoma cells (A2058), pancreatic cancer cells (BxPC3), non-small-cell lung cancer cells (Calu1), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), breast cancer cells (MDA-MB-231), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Drug	786-O IC ₅₀	A2058 IC ₅₀	BxPC3 IC ₅₀	Calu1 IC ₅₀	DEL IC ₅₀	DELBVR IC ₅₀
Ag4-Ex_4a	>1K	>1K	>1K	>1K	>1K	>1K
Ag4-Ex_4b	>1K	>1K	>1K	>1K	12	23
Ag4-Ex_4	>1K	>1K	>1K	>1K	1	4
Ag4-Ex_4c	>1K	>1K	>1K	>1K	176	>1K
Ag4-Ex_4f	>1K	>1K	>1K	>1K	2	6
Ag4-Ex_14	>1000	637	845	>1000	2	4
Ag4-Ex_14a	880	541	609	>1000	3	4
Ag1-Ex_4a	>1K	>1K	>1K	>1K	>1K	>1K
Ag1-Ex_4b	>1K	>1K	739	>1K	18	13

Ag1-Ex_4	>1K	241	106	>1K	3	3
Ag1-Ex_4c	>1K	>1K	>1K	>1K	139	55
Ag1-Ex_4f	>1K	>1K	268	>1K	6	6
Ag1-Ex_14	394	32	175	>1000	4	3
Ag1-Ex_14a	280	28	76	>1000	4	4

[0674] Table 24 (cont.) *In vitro* potency (IC₅₀ values) of CPT ADCs (ng/mL) targeting renal carcinoma cells (786-O), melanoma cells (A2058), pancreatic cancer cells (BxPC3), non-small-cell lung cancer cells (Calu1), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), breast cancer cells (MDA-MB-231), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Drug	Karpas299 IC ₅₀	L540cy IC ₅₀	Ls174T IC ₅₀	MDAMB 231 IC ₅₀	MOLM-13 IC ₅₀	SU-DHL-4 IC ₅₀
Ag4-Ex_4a	ND	>1K	>1K	>1K	>1K	>1K
Ag4-Ex_4b	477	13	>1K	>1K	>1K	>1K
Ag4-Ex_4	535	7	>1K	>1K	>1K	>1K
Ag4-Ex_4c	>1K	54	>1K	>1K	>1K	>1K
Ag4-Ex_4f	35	7	>1K	>1K	>1K	>1K
Ag4-Ex_14	123	15	ND	>1000	>1000	>1000
Ag4-Ex_14a	18	9	ND	>1000	>1000	>1000
Ag1-Ex_4a	ND	>1K	>1K	>1K	>1K	>1K
Ag1-Ex_4b	882	16	>1K	>1K	234	72
Ag1-Ex_4	6	79	35	>1K	60	9
Ag1-Ex_4c	>1K	61	>1K	>1K	432	521
Ag1-Ex_4f	54	16	109	>1K	94	26
Ag1-Ex_14	50	20	ND	>1000	131	14
Ag1-Ex_14a	16	16	ND	>1000	180	23

[0675] Table 25. In vitro potency (IC₅₀ values) of CPT free drugs (nmol/L) targeting renal carcinoma cells (786-O), melanoma cells (A2058), pancreatic cancer cells (BxPC3), non-small-cell lung cancer cells (Calu1), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), breast cancer cells (MDA-MB-231), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Compound No.	786-O IC ₅₀	A2058 IC ₅₀	BxPC3 IC ₅₀	Calu1 IC ₅₀	DEL IC ₅₀	DELBVR IC ₅₀
35	4	2	6	9	0.6	1
6j	12	10	30	36	4	5
6l	38	16	51	73	6	15
6k	80	17	95	170	7	11
6p	ND	2	ND	8	0.9	2
6o	ND	4	ND	26	2	3
6n	ND	16	ND	56	6	7
6m	ND	7	ND	35	2	6
7ag	0.9	0.6	ND	6	0.3	0.3
7ah	0.8	0.5	ND	10	0.2	0.2
16	8	3	ND	67	1	1
15c	22	6	ND	184	1	3
7aj	99	57	103	>1K	14	16
7ai	12	3	17	81	1	3

[0676] Table 25 (cont.) In vitro potency (IC₅₀ values) of CPT free drugs (nmol/L) targeting renal carcinoma cells (786-O), melanoma cells (A2058), pancreatic cancer cells (BxPC3), non-small-cell lung cancer cells (Calu1), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), breast cancer cells (MDA-MB-231), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Drug	Karpas299 IC ₅₀	L540cy IC ₅₀	Ls174T IC ₅₀	MDAMB 231 IC ₅₀	MOLM-13 IC ₅₀	SU-DHL-4 IC ₅₀
35	4	2	3	5	22	1
6j	9	9	12	103	15	14
6l	25	20	29	177	16	18
6k	40	16	46	368	13	21
6p	3	2	5	10	3	1
6o	8	5	9	35	14	4
6n	24	17	47	70	30	13

6m	12	8	22	38	7	5
7ag	1	0.9	3	9	2	0.8
7ah	1	0.8	2	6	0.9	0.5
16	7	5	6	38	30	3
15c	22	10	>1K	69	18	3
7aj	55	56	64	706	81	34
7ai	6	4	8	52	9	3

[0677] Table 26. *In vitro* potency (IC₅₀ values) of CPT ADCs (ng/mL) targeting renal carcinoma cells (786-O), melanoma cells (A2058), pancreatic cancer cells (BxPC3), non-small-cell lung cancer cells (Calu1), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), breast cancer cells (MDA-MB-231), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Drug	786-O IC ₅₀	A2058 IC ₅₀	BxPC3 IC ₅₀	Calu1 IC ₅₀	DEL IC ₅₀	DELBVR IC ₅₀
Ag1-Ex_4i	>1K	>1K	>1K	>1K	4	15
Ag4-Ex_4i	>1K	>1K	>1K	>1K	63	>1K
Ag1-Ex_4g	>1K	>1K	>1K	>1K	6	6
Ag4-Ex_4g	153	121	130	551	4	14
Ag1-Ex_4k	>1K	>1K	>1K	>1K	65	52
Ag4-Ex_4k	>1K	>1K	>1K	>1K	73	>1K
Ag1-Ex_4h	>1K	>1K	>1K	>1K	>1K	>1K
Ag4-Ex_4h	>1K	>1K	>1K	>1K	>1K	>1K
Ag1-Ex_4j	>1K	>1K	>1K	>1K	474	233
Ag4-Ex_4j	>1K	>1K	>1K	>1K	>1K	>1K
Ag4-Ex_4ad	ND	>1K	ND	>1K	>1K	>1K
Ag1-Ex_4ad	ND	>1K	ND	>1K	55	53
Ag4-Ex_4ac	ND	>1K	ND	>1K	5	16
Ag1-Ex_4ac	ND	>1K	ND	>1K	10	14
Ag4-Ex_4l	ND	>1K	ND	>1K	68	>1K
Ag1-Ex_4l	ND	>1K	ND	>1K	119	65
Ag4-Ex_4m	ND	>1K	ND	>1K	9	>1K

Ag1-Ex_4m	ND	>1K	ND	>1K	9	22
Ag4-Ex_4q	>1K	>1K	>1K	>1K	0.3	0.8
Ag1-Ex_4q	61	32	>1K	>1K	0.9	1

[0678] Table 26 (cont.) *In vitro* potency (IC₅₀ values) of CPT ADCs (ng/mL) targeting renal carcinoma cells (786-O), melanoma cells (A2058), pancreatic cancer cells (BxPC3), non-small-cell lung cancer cells (Calu1), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), breast cancer cells (MDA-MB-231), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Drug	786-O IC ₅₀	A2058 IC ₅₀	BxPC3 IC ₅₀	Calu1 IC ₅₀	DEL IC ₅₀	DELBVR IC ₅₀
Ag1-Ex_4i	>1K	>1K	>1K	>1K	4	15
Ag4-Ex_4i	>1K	>1K	>1K	>1K	63	>1K
Ag1-Ex_4g	>1K	>1K	>1K	>1K	6	6
Ag4-Ex_4g	153	121	130	551	4	14
Ag1-Ex_4k	>1K	>1K	>1K	>1K	65	52
Ag4-Ex_4k	>1K	>1K	>1K	>1K	73	>1K
Ag1-Ex_4h	>1K	>1K	>1K	>1K	>1K	>1K
Ag4-Ex_4h	>1K	>1K	>1K	>1K	>1K	>1K
Ag1-Ex_4j	>1K	>1K	>1K	>1K	474	233
Ag4-Ex_4j	>1K	>1K	>1K	>1K	>1K	>1K
Ag4-Ex_4ad	ND	>1K	ND	>1K	>1K	>1K
Ag1-Ex_4ad	ND	>1K	ND	>1K	55	53
Ag4-Ex_4ac	ND	>1K	ND	>1K	5	16
Ag1-Ex_4ac	ND	>1K	ND	>1K	10	14
Ag4-Ex_4l	ND	>1K	ND	>1K	68	>1K
Ag1-Ex_4l	ND	>1K	ND	>1K	119	65
Ag4-Ex_4m	ND	>1K	ND	>1K	9	>1K
Ag1-Ex_4m	ND	>1K	ND	>1K	9	22
Ag4-Ex_4q	>1K	>1K	>1K	>1K	0.3	0.8
Ag1-Ex_4q	61	32	>1K	>1K	0.9	1

[0679] Table 27. *In vitro* potency (IC₅₀ values) of CPT ADCs (ng/mL) targeting melanoma cells (A2058), pancreatic cancer cells (BxPC3), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Drug	A2058 IC ₅₀	BxPC3 IC ₅₀	DEL IC ₅₀	DELBVR IC ₅₀
Ag1-Ex_4f(8)	344	>1K	7	4
Ag4-Ex_4f(8)	>1K	>1K	4	6
Ag1-Ex_4(8)	211	535	5	2
Ag4-Ex_4(8)	>1K	>1K	2	4
Ag1-Ex_4x(8)	223	>1K	3	4
Ag4-Ex_4x(8)	>1K	>1K	0.9	4
Ag1-Ex_4y(8)	539	>1K	2	3
Ag4-Ex_4y(8)	>1K	>1K	0.6	5
Ag1-Ex_4ab(8)	126	>1K	1	1
Ag4-Ex_4ab(8)	>1K	>1K	0.1	1
Ag1-Ex_4aa(8)	168	88	2	1
Ag4-Ex_4aa(8)	>1K	>1K	0.6	2
Ag1-Ex_4z(8)	342	233	2	3
Ag4-Ex_4z(8)	>1K	>1K	1	7

[0680] Table 27 (cont.) *In vitro* potency (IC₅₀ values) of CPT ADCs (ng/mL) targeting melanoma cells (A2058), pancreatic cancer cells (BxPC3), anaplastic large cell lymphoma cells (DEL, DELBVR, Karpas299), Hodgkin's lymphoma cells (L540cy, Ls174T), acute myeloid leukemia cells (MOLM-13), and B-lymphocyte cancer cells (SU-DHL4).

Drug	Karpas299 IC ₅₀	Ls174T IC ₅₀	MOLM-13 IC ₅₀	SU-DHL-4 IC ₅₀	L540cy IC ₅₀
Ag1-Ex_4f(8)	25	ND	160	22	14
Ag4-Ex_4f(8)	19	ND	>1K	>1K	8
Ag1-Ex_4(8)	123	ND	131	16	9
Ag4-Ex_4(8)	59	ND	>1K	>1K	6
Ag1-Ex_4x(8)	51	56	106	14	ND
Ag4-Ex_4x(8)	7	>1K	>1K	>1K	ND
Ag1-Ex_4y(8)	27	18	39	11	ND
Ag4-Ex_4y(8)	16	>1K	>1K	>1K	ND
Ag1-Ex_4ab(8)	46	>1K	23	9	ND
Ag4-Ex_4ab(8)	44	>1K	>1K	>1K	ND
Ag1-Ex_4aa(8)	21	17	34	7	ND
Ag4-Ex_4aa(8)	16	>1K	>1K	>1K	ND

Ag1-Ex_4z(8)	63	72	28	7	ND
Ag4-Ex_4z(8)	33	>1K	>1K	>1K	ND

In vivo Model Methods

[0681] All experiments were conducted in concordance with the Animal Care and Use Committee in a facility fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care. Efficacy experiments were conducted in the L540cy, OV90, EBC-1, and 768-O xenografts models. Tumor cells, as a cell suspension, were implanted subcutaneous in immune-compromised SCID or nude mice. Upon tumor engraftment, mice were randomized to study groups (5 mice per group) when the average tumor volume reached about 100 mm³. The ADC or controls were dosed once via intraperitoneal injection. The average number of drug-linker attached to an antibody is indicated in the parenthesis next to the ADC (also referred to herein as Drug-Antibody Ratio (DAR) number, e.g., DAR4, DAR8, etc.). Ag1 refers to an antibody that targets a ubiquitously expressed cell surface antigen. Ag2 refers to an antibody that targets a surface antigen expressed on tumor cells and is involved in self-tolerance. Ag3 refers to an antibody that targets O-glycans overexpressed on the surface of cancer cells. Ag4 refers to an antibody that targets a surface antigen characteristically overexpressed in hematopoietic malignancies. Ag5 refers to an antibody that targets a surface antigen highly expressed in hemtologic malignancies and renal cell carcinoma. h00 is a non-binding control antibody. Tumor volume as a function of time was determined using the formula (L x W²)/2. Animals were euthanized when tumor volumes reached 750 mm³. Mice showing durable regressions were terminated after 10-12 weeks post implant.

[0682] Animals were implanted with L540cy cells. After 12 days, the animals were sorted into groups with an average tumor size of 100 mm³, and then treated with a single dose of camptothecin ADC Ag4-Ex_4f(8), Ag4-Ex_14a(8) or Ag4-Ex_14(8) at 0.3 or Ag4-Ex_4f(8), Ag4-Ex_14a(8), Ag4-Ex-14(8), h00-Ex_4f(8), h00-Ex_14a(8) or h00-Ex_14a(8) at 1 mg/kg. Animals were evaluated for tumor size and in-life signs during the course of the study. The results are shown in Figures 1A and 1B.

[0683] Animals were implanted with EBC-1 cells. On day 7, the animals were sorted into groups with an average tumor size of 100mm³, and then treated with a single dose of camptothecin ADC Ag2-Ex_4f(8), Ag2-Ex_4c(8), Ag2-Ex_4b(8) or Ag2-Ex_4(8), at 5

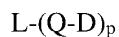
mg/kg. Animals were evaluated for tumor size and in-life signs during the course of the study. The results are shown in Figure 2.

[0684] Animals were implanted with OV-90 cells. After 17 days, the animals were sorted into groups with an average tumor size of 100mm³, and then treated with a single dose of camptothecin ADC Ag3-Ex_4f(8), Ag3-Ex_4c(8), Ag3-Ex_4b(8) or Ag3-Ex_4(8), at 5 mg/kg. Animals were evaluated for tumor size and in-life signs during the course of the study. The results are shown in Figure 3.

[0685] Animals were implanted with 786-O cells. After 15 days, the animals were sorted into groups with an average tumor size of 100mm³, and then treated with a single dose of camptothecin ADC Ag5-Ex_4(8) or Ag5-Ex_4f(8), at 3 mg/kg. Animals were evaluated for tumor size and in-life signs during the course of the study. The results are shown in Figure 4.

ENUMERATED EMBODIMENTS

Embodiment 1. A Camptothecin Conjugate having the formula of

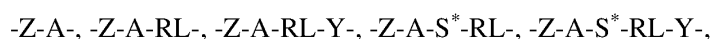
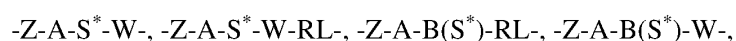
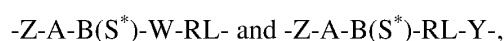


or a salt thereof, wherein

L is a Ligand Unit from a targeting agent, in particular from an antibody that selectively binds to a cancer cell antigen;

subscript p is an integer ranging from 1 to 16;

Q is a Linker Unit having a formula selected from the group consisting of:



wherein Z is a Stretcher Unit;

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

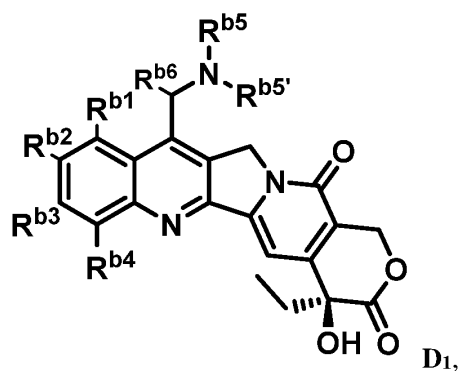
S^{*} is a Partitioning Agent;

RL is a Releasable Linker;

W is a Amino Acid Unit;

Y is a Spacer Unit; and

D is a Drug Unit D having a formula of



or a salt thereof; wherein

R^{b1} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl,

C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)-O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;
each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, and heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -

OH, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

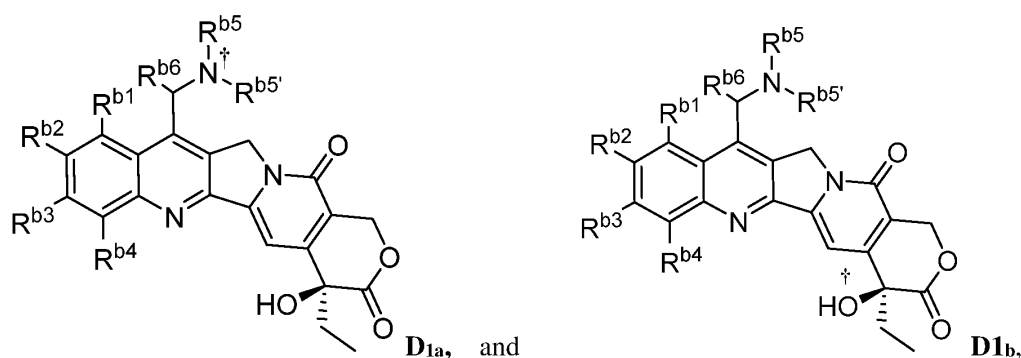
R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and R^{a'} are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

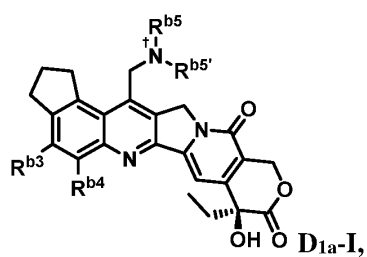
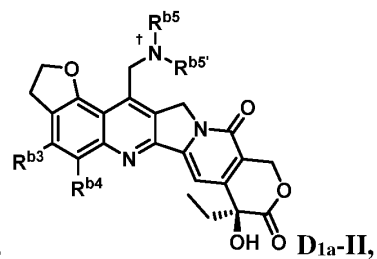
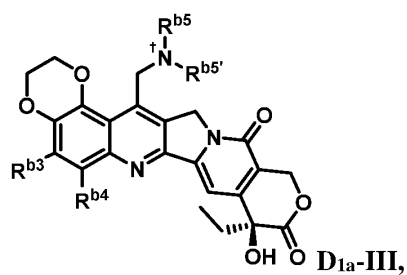
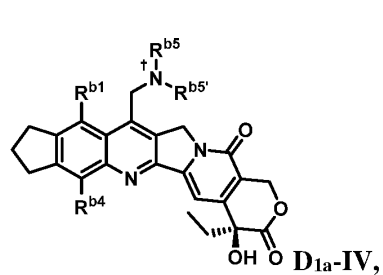
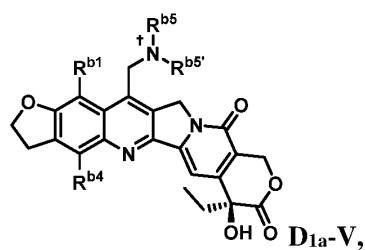
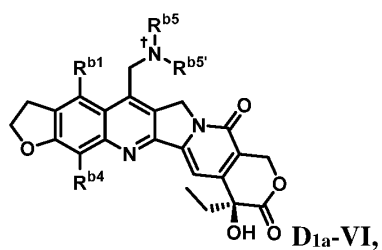
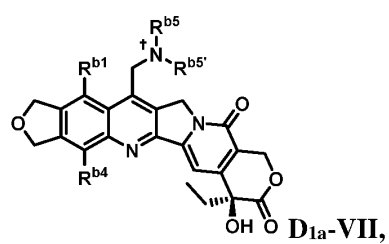
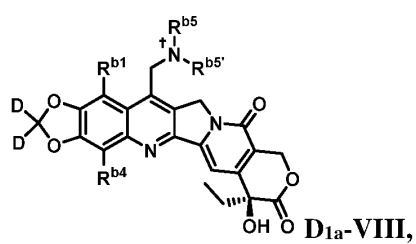
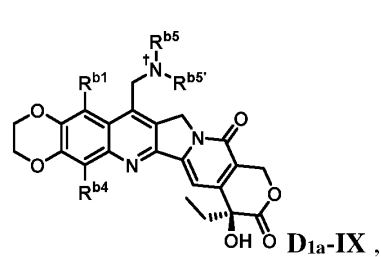
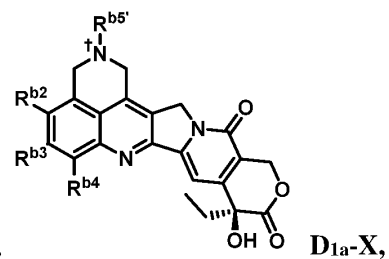
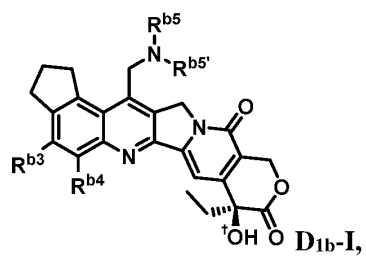
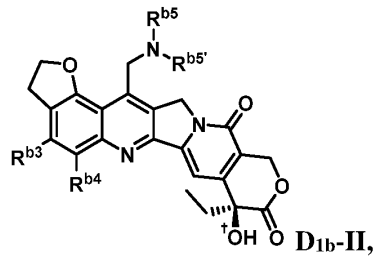
wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

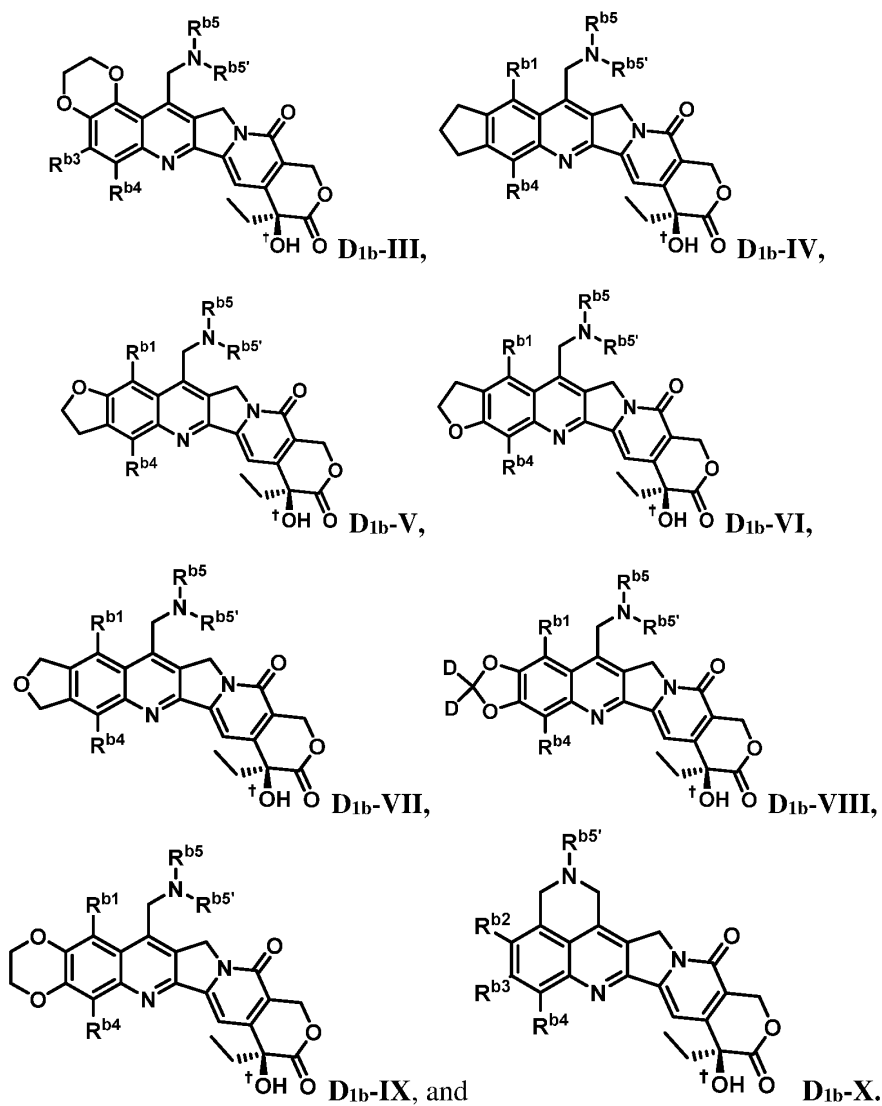
Embodiment 2. The Camptothecin Conjugate of embodiment 1, wherein D has a formula selected from the group consisting of



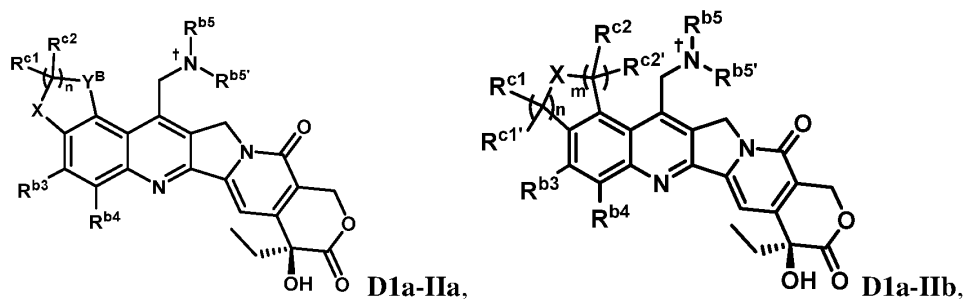
or a salt thereof, wherein the dagger indicates the site of covalent attachment of D to the secondary linker of the drug linker moiety.

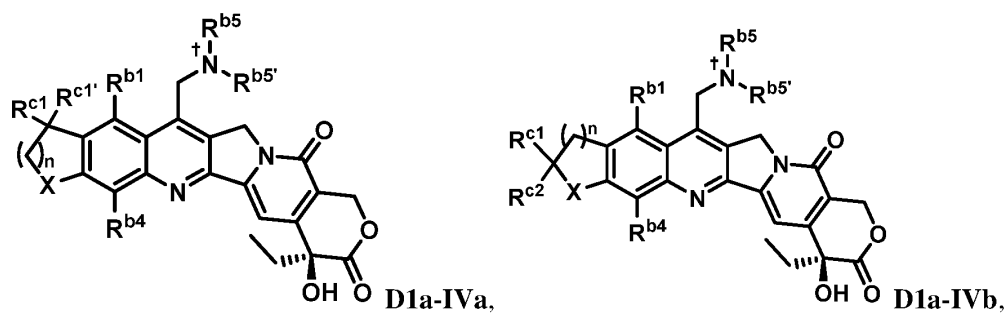
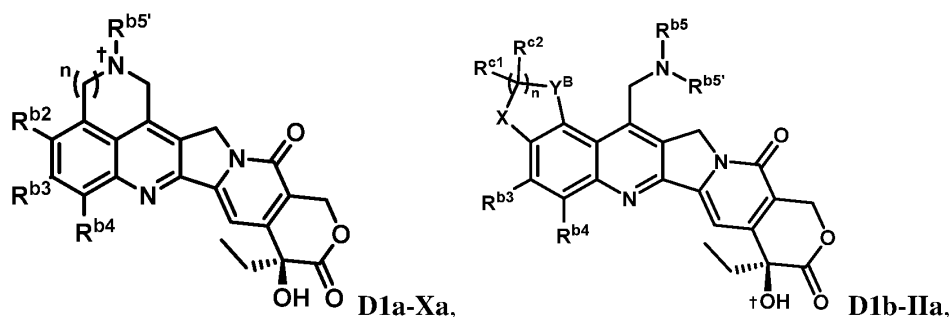
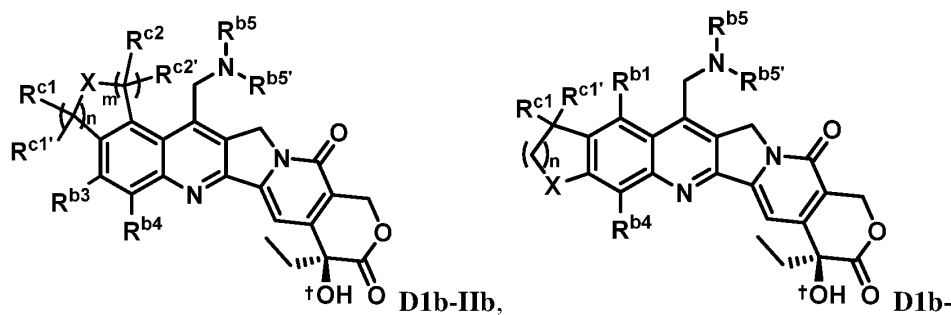
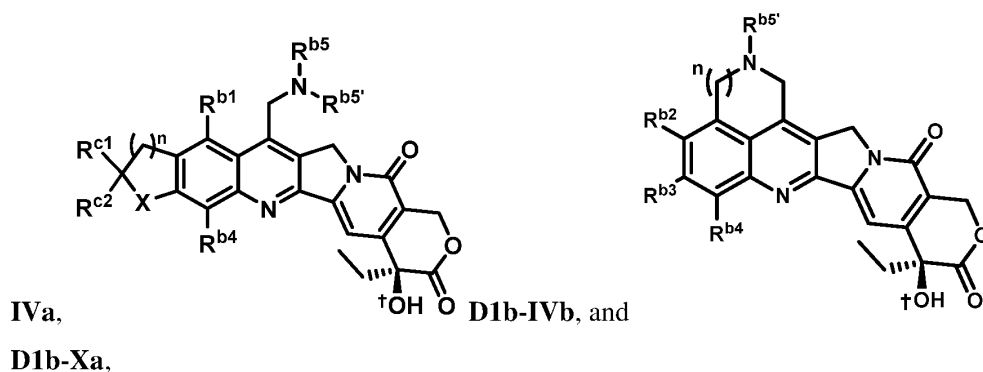
Embodiment 3. The Camptothecin Conjugate of embodiment 2, wherein D has a formula selected from selected from the group consisting of





Embodiment 4. The Camptothecin Conjugate of embodiment 2, wherein D has a formula selected from the group consisting of





wherein

X and Y^B are each independently O, S, S(O)₂, CR^xR^{x'}, or NR^x;

R^x and R^{x'} are each independently selected from the group consisting of H, OH, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ aminoalkyl-C(O)-, C₁-C₆ alkyl-C(O)-, C₁-C₆ hydroxyalkyl-C(O)-, C₁-C₆ alkyl-NH-C(O)-, or C₁-C₆ alkyl-S(O)₂-; and

m and n are each 1 or 2;

each R^{c1} , $R^{c1'}$, R^{c2} , and $R^{c2'}$ is independently

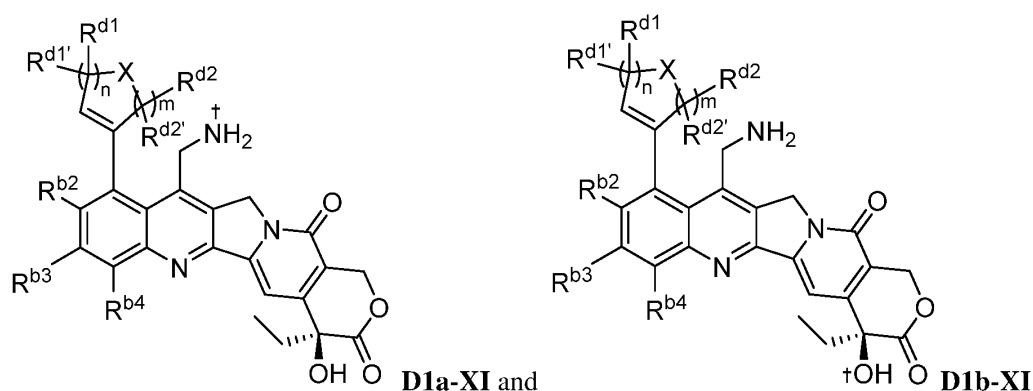
(i) selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, -OR^a, -NR^aR^{a'}, and -SR^a, C₁-C₆ alkyl-C(O)-, C₁-C₆ alkyl-NR^a-C(O)-, and C₁-C₆ alkyl-S(O)₂-; or

(ii) taken together with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; or

(iii) taken together with R^{x'} and the intervening atoms to form a 3 to 6-membered carbocyclo or heterocyclo; and

when m and n are both present, the sum of m + n is 2 or 3.

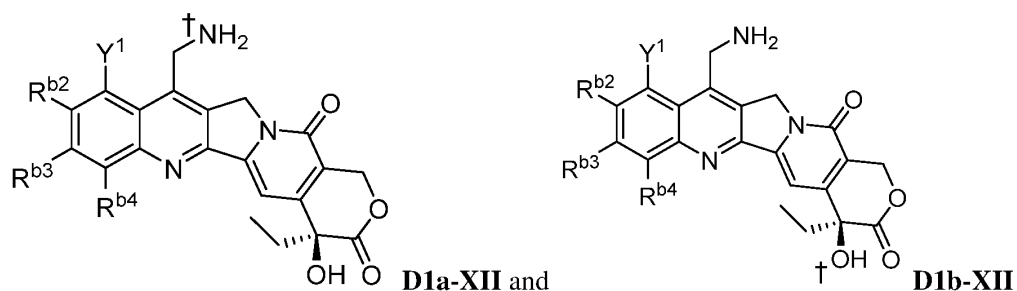
Embodiment 5. The Camptothecin Conjugate of embodiment 2, wherein D has a formula selected from selected from the group consisting of



wherein

R^{d1} , $R^{d1'}$, R^{d2} , and $R^{d2'}$ are each independently selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a, C₁-C₆ alkyl-C(O)-, C₁-C₆ alkyl-NR^a-C(O)-, and C₁-C₆ alkyl-S(O)₂-.

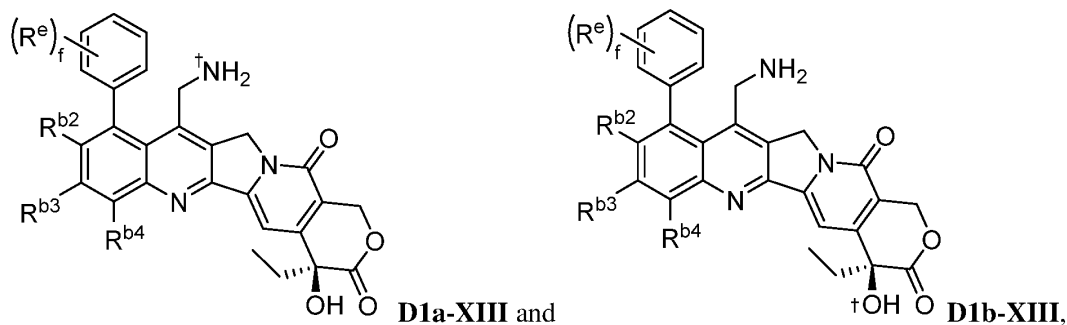
Embodiment 6. The Camptothecin Conjugate of embodiment 2, wherein D has a formula selected from the group consisting of



wherein

Y^1 is a 5- or 6-membered heteroaryl, optionally substituted with halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 aminoalkyl, or C_1 - C_6 alkyl- $S(O)_2$.

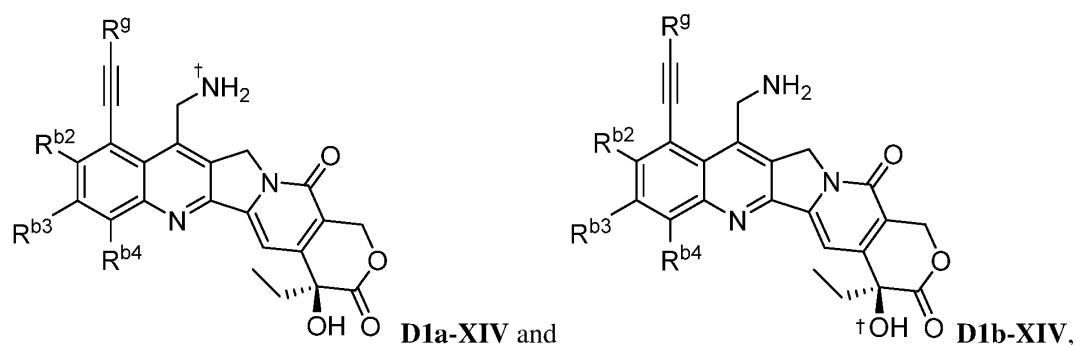
Embodiment 7. The Camptothecin Conjugate of embodiment 2, wherein D has a formula selected from the group consisting of



wherein

each R^e is independently selected from the group consisting of halogen, $-OH$, $-NH_2$, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 alkyl- $S(O)_2$, and C_1 - C_6 alkyl- NR^a - $C(O)-$; and f is 0, 1, 2, 3, 4, or 5.

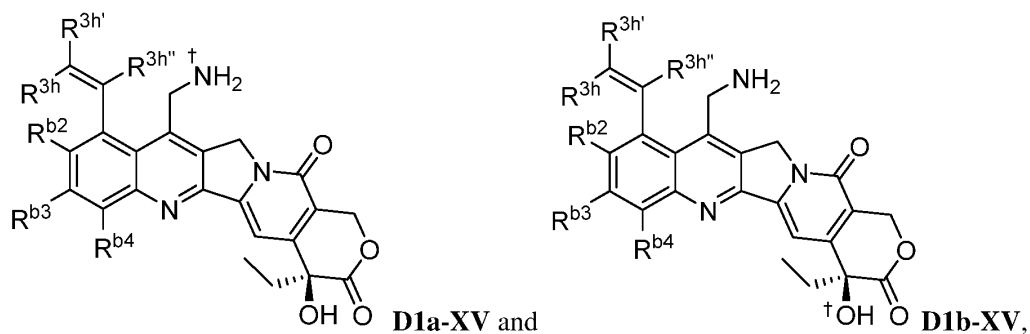
Embodiment 8. The Camptothecin Conjugate of embodiment 2, wherein D has a formula selected from the group consisting of



wherein

R^g is H, C₁-C₆ alkyl, or 3 to 8-membered heterocyclyl.

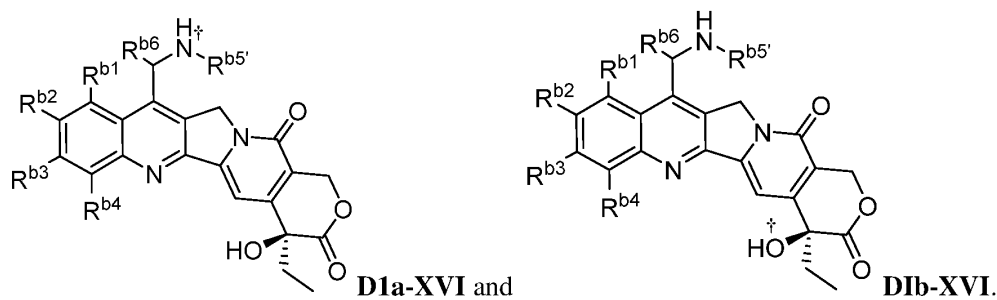
Embodiment 9. The Camptothecin Conjugate of embodiment 2, wherein D has a formula selected from the group consisting of



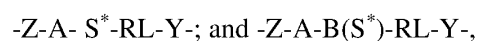
wherein

R^{3h} , $R^{3h'}$, and $R^{3h''}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, -C(O)-C₁-C₆ alkyl, -C(O)O-C₁-C₆ alkyl, -C(O)NH-C₁-C₆ alkyl, C₆-C₁₀ aryl, -C₆-C₁₀ aryl-C₁-C₆ alkyl, and -C₆-C₁₀ aryl-C₁-C₆ alkoxy; each optionally substituted with, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a.

Embodiment 10. The Camptothecin Conjugate of embodiment 2, wherein D has a formula selected from the group consisting of

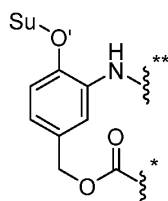


Embodiment 11. The Camptothecin Conjugate of any one of embodiments 1-10, wherein Q is a Linker Unit having the formula selected from the group consisting of:



wherein A is a Connector Unit and RL is a Glycoside (e.g., Glucuronide) Unit.

Embodiment 12. The Camptothecin Conjugate of embodiment 11, wherein the Glycoside (e.g., Glucuronide) Unit has the formula of:



wherein

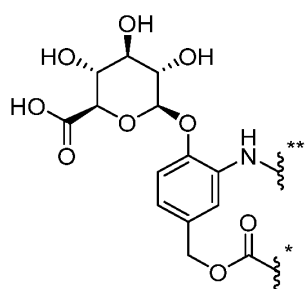
Su is a hexose form of a monosaccharide;

O' represents the oxygen atom of a glycosidic bond that is capable of cleavage by a glycosidase;

the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D; and

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the remainder of Q,

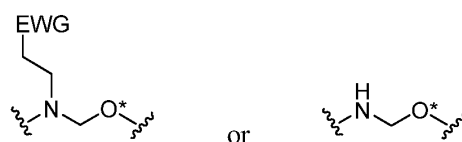
in particular the Glycoside (e.g., Glucuronide) Unit has the formula of:



Embodiment 13. The Camptothecin Conjugate of embodiment 11, wherein

Q is a Linker Unit having the formula of -Z-A-RL-Y-, -Z-A-S*-RL-Y- or -Z-A-B(S*)-RL-Y-; and

Spacer Unit (Y) has the formula of:



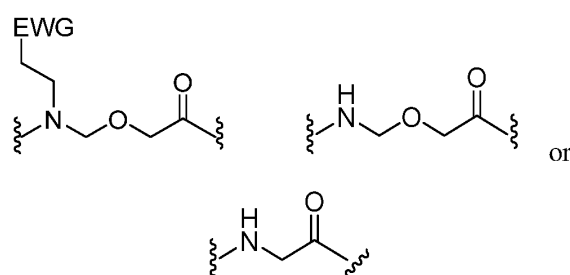
wherein EWG is an electron-withdrawing group;

O* represent the oxygen atom from a hydroxy substituent of D;

the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment to the carbonyl carbon atom of the Glycoside (e.g., Glucuronide) Unit; and

the wavy line adjacent to O* indicates the site of covalent attachment to the remainder of D, or

the Spacer Unit (Y) has the formula of:



wherein

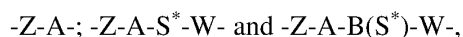
EWG is an electron-withdrawing group;

the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment to the carbonyl carbon atom of the Glycoside (e.g., Glucuronide) Unit; and

the wavy line adjacent to the carbonyl carbon atom indicates the site of covalent attachment to the nitrogen atom of the amino substituent of D.

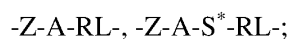
Embodiment 14. The Camptothecin Conjugate of any one of embodiments 1-10, wherein

Q is a Linker Unit having a formula selected from the group consisting of:



wherein A is a Connector Unit, or

Q is a Linker Unit having a formula selected from the group consisting of:

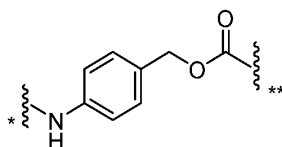


wherein A is a Connector Unit and RL is a Releasable linker other than a Glycoside (e.g., Glucuronide) Unit.

Embodiment 15. The Camptothecin Conjugate of embodiment 14, wherein

Q is a Linker Unit having the formula selected from the group consisting of $-Z-A-RL-$, $-Z-A-S^*-RL-$ and $-Z-A-S^*-W-RL-$, wherein

RL has the formula:



wherein

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to D; and

the wavy line marked with a single asterisk (*) indicates the point of covalent attachment to A, S* or W.

Embodiment 16. The Camptothecin Conjugate of embodiment 14 or 15, wherein

-Q-D has the formula of $-Z-A-S^*-W-RL-D$, wherein

D is covalently attached to Q via the nitrogen atom of an amine functional group of D;

and

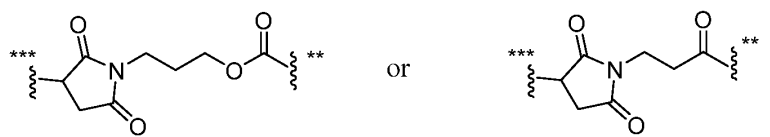
W is an Amino Acid Unit selected from the group consisting of N-methyl-glycine (sarcosine), N-methyl-alanine, N-methyl- β -alanine, valine, N-methyl-valine, or

D is covalently attached to Q via an oxygen atom of the hydroxyl substituent on the lactone ring of D; and

W is an Amino Acid Unit selected from the group consisting glutamic acid or lysine.

Embodiment 17. The Camptothecin Conjugate of embodiment 16, wherein -Z-A- comprises a succinimido-alkanoyl moiety or succinimido and triazole moieties, each optionally having the succinimide ring in hydrolyzed form as a succinic acid amide moiety, or a succinic acid amide moiety derivable from mDPR of a Camptothecin-Linker Compound, or

wherein -Z-A- has the formula of:

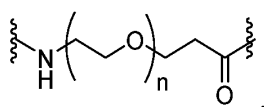


optionally having the succinimide ring in hydrolyzed form as a succinic acid amide moiety, wherein the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to S*; and the wavy line marked with a triple asterisk (***) indicates the point of covalent attachment to a sulfur atom of L.

Embodiment 18. The Camptothecin Conjugate of embodiment 14, wherein

Q is a Linker Unit having the formula selected from the group consisting of -Z-A-S*-RL- and -Z-A-S*-W-RL-, wherein

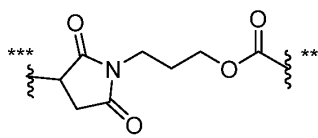
S* has the formula of:



wherein subscript n is an integer ranging from 2 to 36,

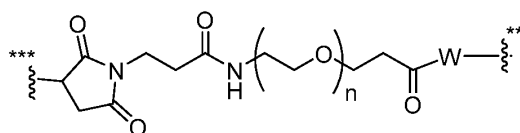
the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment to a carbonyl carbon atom of A, and the wavy adjacent to the carbonyl carbon atom indicates the site of covalent attachment to the nitrogen atom of the amine functional group of RL of -Z-A-S*-RL- or W of -Z-A-S*-W-RL-,

in particular, -Z A- in either formula of Q has the formula of:



wherein the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the nitrogen atom of the amine functional group of S*; and the wavy line marked with a triple asterisk (***) indicates the point of covalent attachment to a sulfur atom of L.

Embodiment 19. The Camptothecin Conjugate of embodiment 14, wherein Q is a Linker Unit of formula $-Z-A-S^*-W-$ or $-Z-A-S-W-RL-$, wherein $-Z-A-S^*-W-$ in either formula has the formula of:



optionally having the succinimide ring in hydrolyzed form as a succinic acid amide moiety, wherein subscript n is an integer ranging from 2 to 10, preferably ranging from 2 to 4; the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to D or RL; and the wavy line marked with a triple asterisk (***) indicates the point of covalent attachment to a sulfur atom of L.

Embodiment 20. A Camptothecin-Linker compound having a formula selected from the group consisting of:

- (i) $Z'-A-RL-D$;
- (ii) $Z'-A-RL-Y-D$;
- (iii) $Z'-A-S^*-RL-D$;
- (iv) $Z'-A-S^*-RL-Y-D$;
- (v) $Z'-A-B(S^*)-RL-D$;
- (vi) $Z'-A-B(S^*)-RL-Y-D$;
- (vii) $Z'-A-D$
- (viii) $Z'-A-S^*-W-D$

(ix) Z'-A-B(S*)-W-D

(x) Z'-A-S*-W-RL-D; and

(xi) Z'-A-B(S*)-W-RL-D

wherein

Z' is a Stretcher Unit precursor;

A is a bond or a Connector Unit;

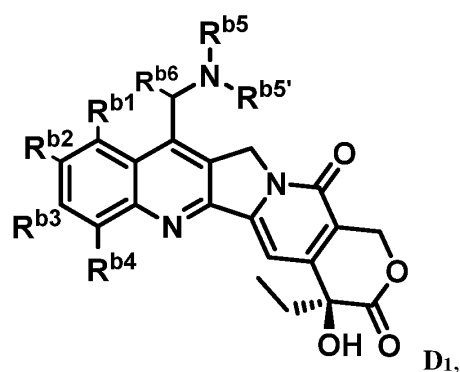
B is a Parallel Connector Unit;

S* is a Partitioning Agent;

RL is a Releasable Linker;

Y is a Spacer Unit; and

D is a Drug Unit D having a formula of



or a salt thereof; wherein

R^{b1} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo; R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-,

C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with -OR^a-, -NR^aR^{a'}-, and -SR^a-, or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a-, -NR^aR^{a'}-, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;
each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, and heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

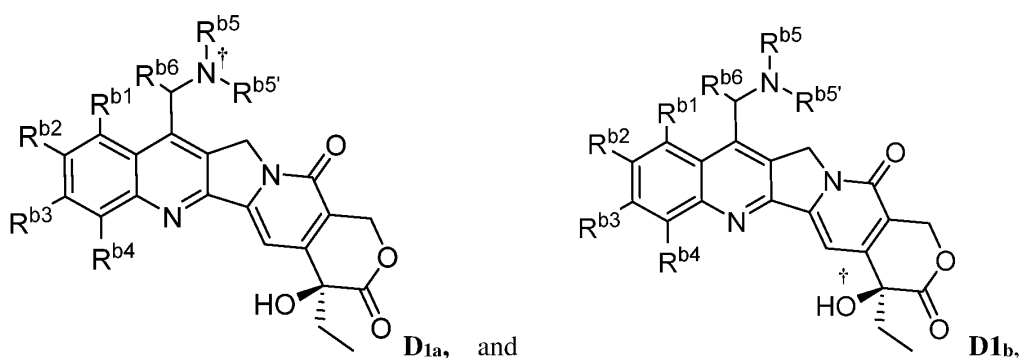
R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and $R^{a'}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

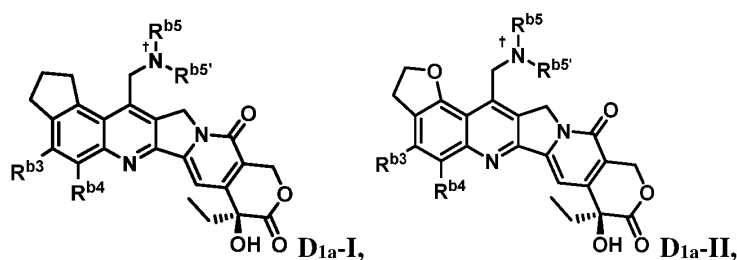
wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

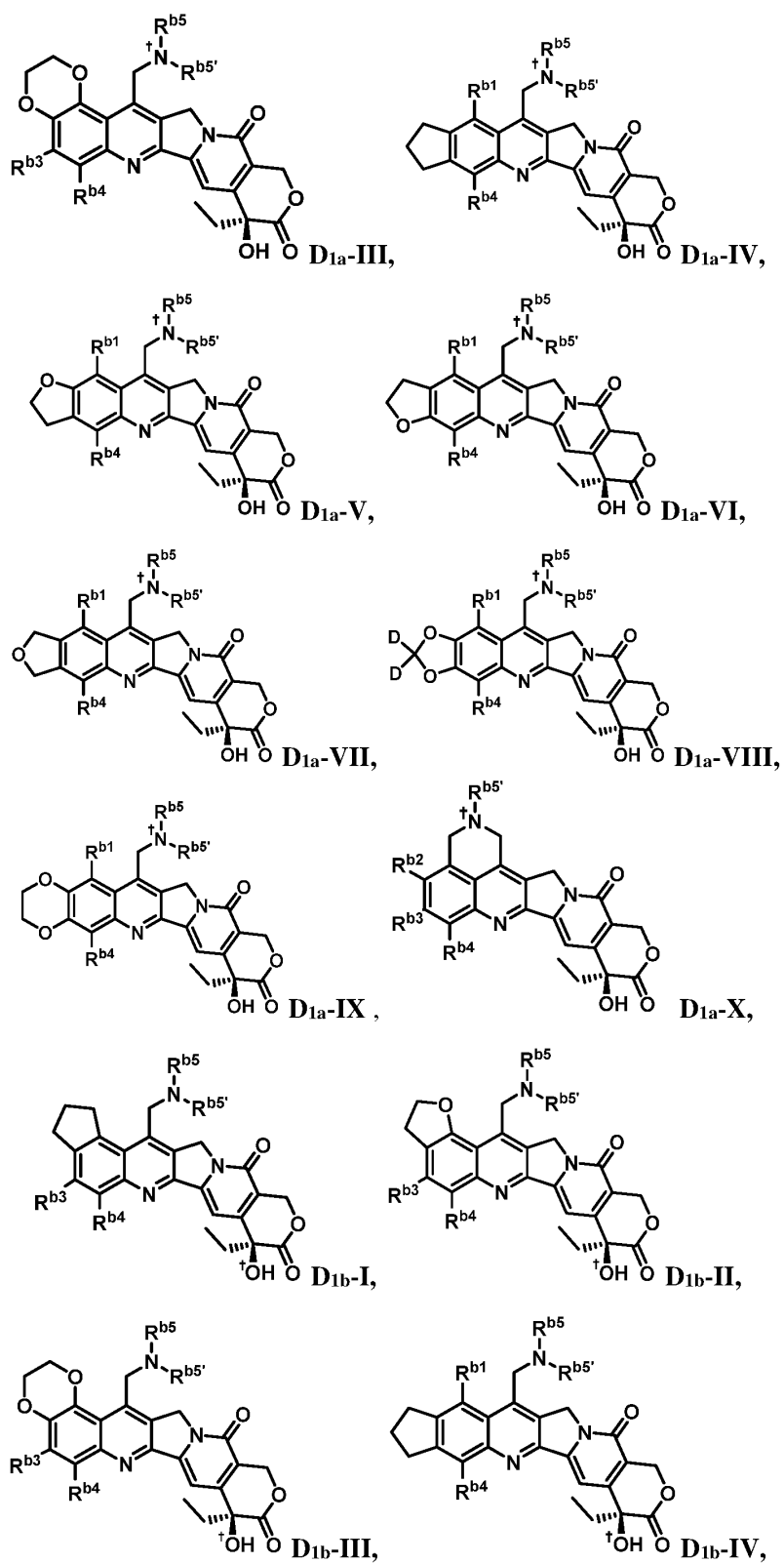
Embodiment 21. The Camptothecin-Linker compound of embodiment 20, wherein D has a formula selected from the group consisting of

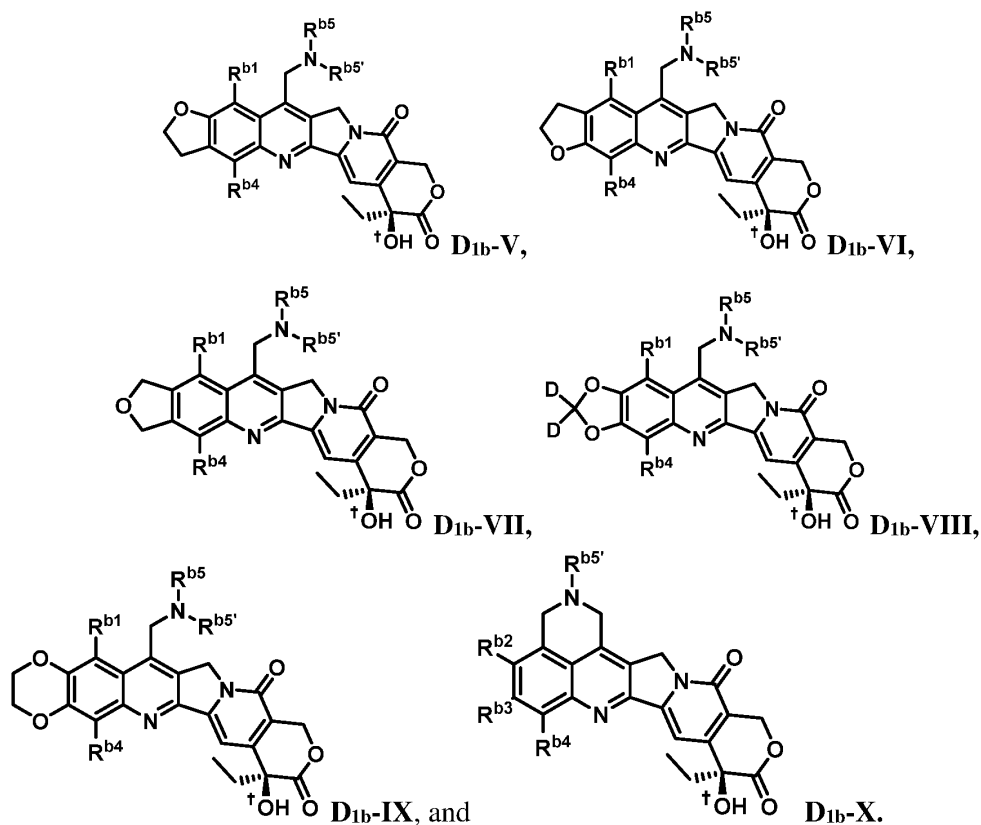


or a salt thereof, wherein the dagger indicates the site of covalent attachment of D to the secondary linker of the drug linker moiety.

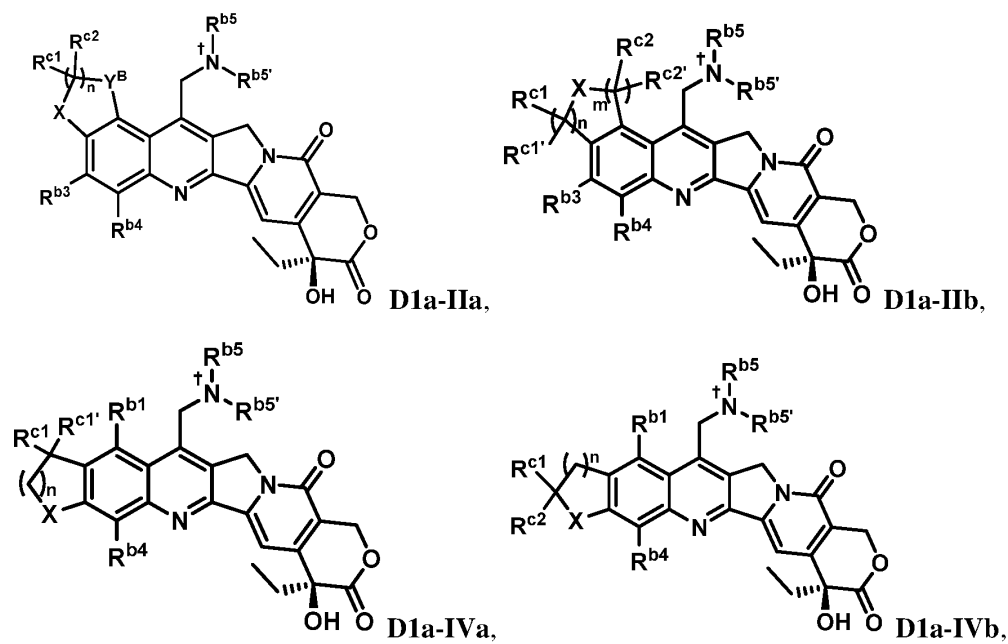
Embodiment 22. The Camptothecin-Linker compound of embodiment 20, wherein D has a formula selected from the group consisting of

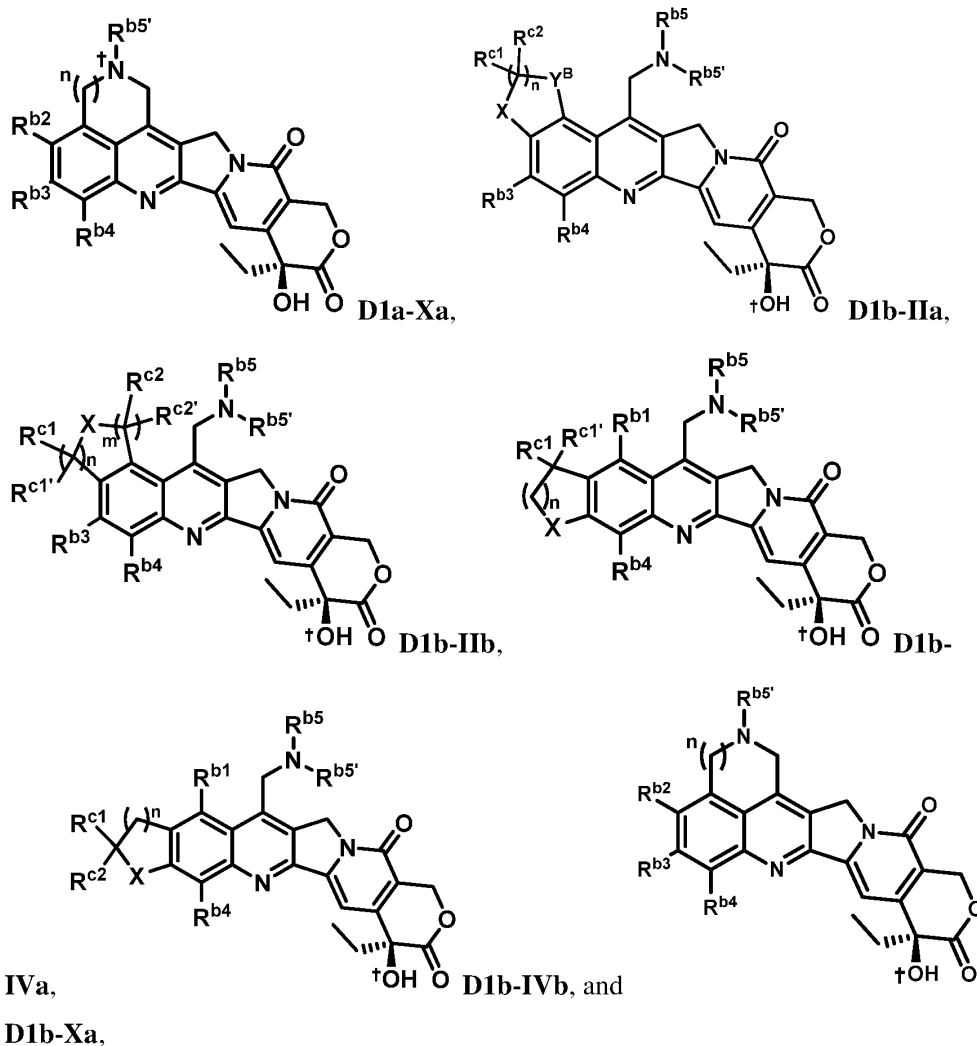






Embodiment 23. The Camptothecin-Linker compound of embodiment 20, wherein D has a formula selected from the group consisting of





wherein

X and Y^B are each independently O, S, S(O)₂, CR^xR^{x'}, or NR^x;

R^x and R^{x'} are each independently selected from the group consisting of H, OH, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ aminoalkyl-C(O)-, C₁-C₆ alkyl-C(O)-, C₁-C₆ hydroxyalkyl-C(O)-, C₁-C₆ alkyl-NH-C(O)-, or C₁-C₆ alkyl-S(O)₂-; and

m and n are each 1 or 2;

each R^{c1}, R^{c1'}, R^{c2}, and R^{c2'} is independently

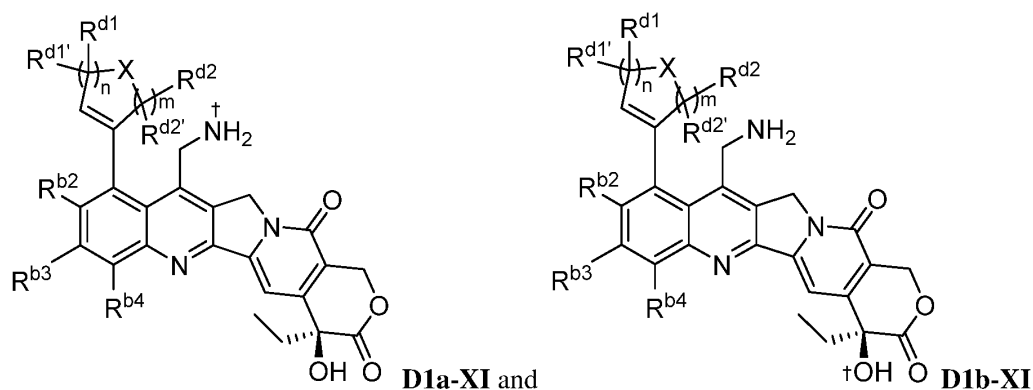
(i) selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, -OR^a, -NR^aR^{a'}, and -SR^a, C₁-C₆ alkyl-C(O)-, C₁-C₆ alkyl-NR^a-C(O)-, and C₁-C₆ alkyl-S(O)₂-; or

(ii) taken together with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; or

(iii) taken together with $R^{x'}$ and the intervening atoms to form a 3 to 6-membered carbocyclo or heterocyclo; and

when m and n are both present, the sum of $m + n$ is 2 or 3.

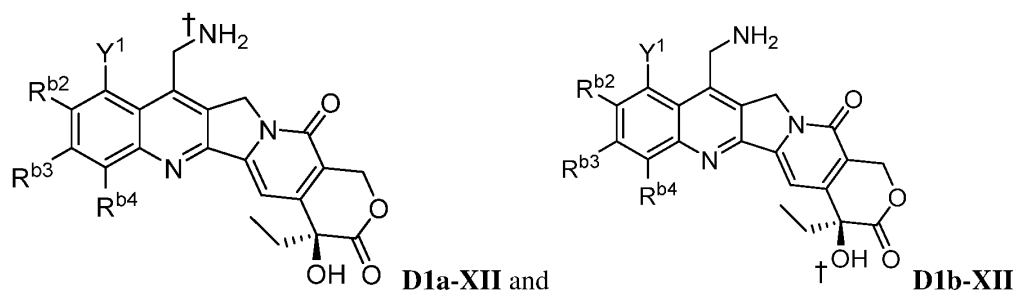
Embodiment 24. The Camptothecin-Linker compound of embodiment 20, wherein D has a formula selected from the group consisting of



wherein

R^{d1} , $R^{d1'}$, R^{d2} , and $R^{d2'}$ are each independently selected from the group consisting of H, halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, $-OR^a$, $-NR^aR^{a'}$, and $-SR^a$, C_1 - C_6 alkyl- $C(O)-$, C_1 - C_6 alkyl- $NR^a-C(O)-$, and C_1 - C_6 alkyl- $S(O)_2-$.

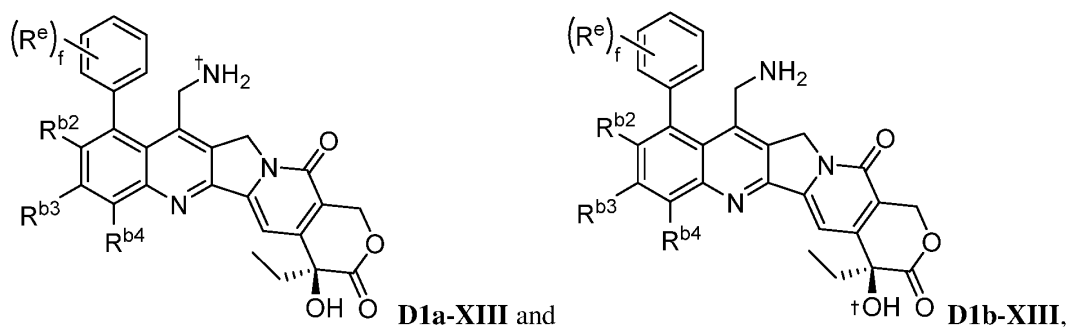
Embodiment 25. The Camptothecin-Linker compound of embodiment 20, wherein D has a formula selected from the group consisting of



wherein

Y^1 is a 5- or 6-membered heteroaryl, optionally substituted with halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 aminoalkyl, or C_1 - C_6 alkyl- $S(O)_2-$.

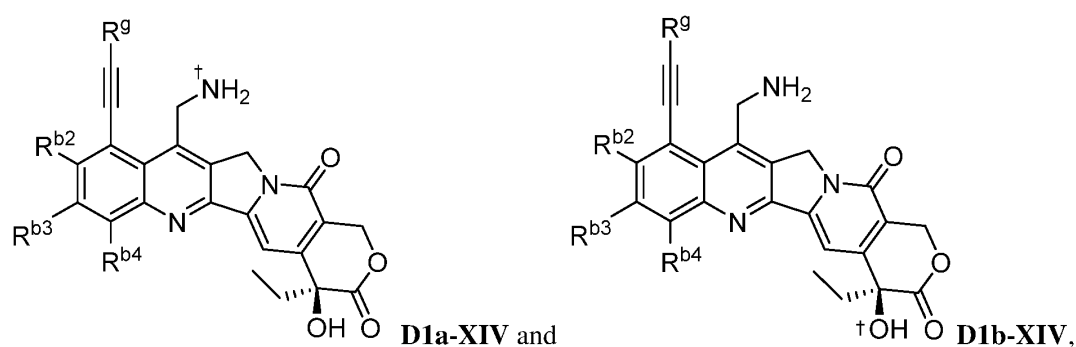
Embodiment 26. The Camptothecin-Linker compound of embodiment 20, wherein D has a formula selected from the group consisting of



wherein

each R^e is independently selected from the group consisting of halogen, -OH, -NH₂, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkyl-S(O)₂-, and C₁-C₆ alkyl-NR^a-C(O)-; and f is 0, 1, 2, 3, 4, or 5.

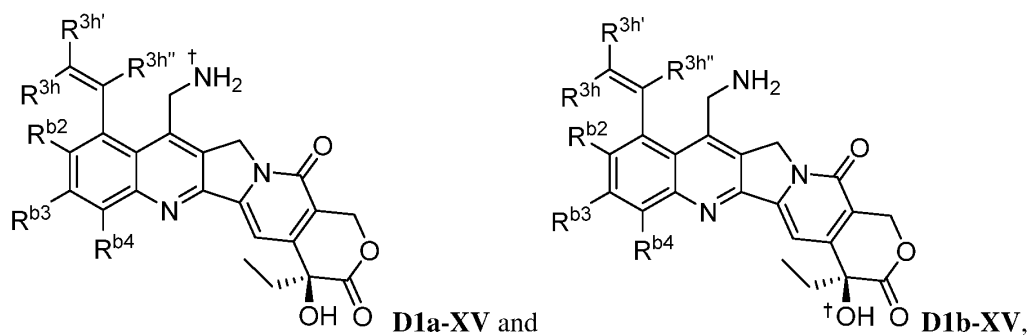
Embodiment 27. The Camptothecin-Linker compound of embodiment 20, wherein D has a formula selected from the group consisting of



wherein

R^g is H, C₁-C₆ alkyl, or 3 to 8-membered heterocyclyl.

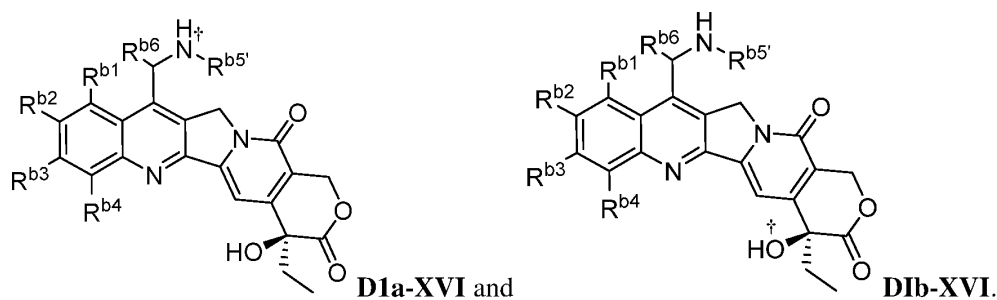
Embodiment 28. The Camptothecin-Linker compound of embodiment 20, wherein D has a formula selected from the group consisting of



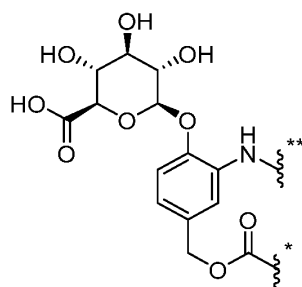
wherein

R^{3h} , $R^{3h'}$, and $R^{3h''}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, -C(O)-C₁-C₆ alkyl, -C(O)O-C₁-C₆ alkyl, -C(O)NH-C₁-C₆ alkyl, C₆-C₁₀ aryl, -C₆-C₁₀ aryl-C₁-C₆ alkyl, and -C₆-C₁₀ aryl-C₁-C₆ alkoxy; each optionally substituted with, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a.

Embodiment 29. The Camptothecin-Linker compound of embodiment 20, wherein D has a formula selected from the group consisting of



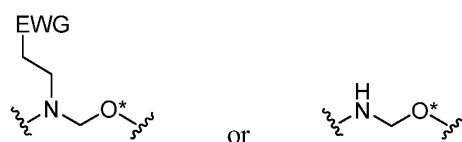
Embodiment 30. The Camptothecin-Linker compound of any one of embodiments 20-29 having the formula selected from the group consisting of formula (i), formula (ii); formula (iii), formula (iv), formula (v) and formula (vi), wherein A is a Connector Unit; and RL is a Glycoside (e.g., Glucuronide) Unit, in particular, having the structure of:



wherein the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D or to a Spacer Unit (Y); and the wavy line marked with a double asterisk (**) indicates the point of covalent attachment to A, B or S*.

Embodiment 31. The Camptothecin-Linker compound of any one of embodiments 20-29 having formula (iii), formula (iv), formula (v) and formula (vi), wherein S* is a PEG group.

Embodiment 32. The Camptothecin-Linker compound of any one of embodiments 20-29 having formula (ii), formula (iv) or formula (vi), wherein the Spacer Unit (Y) has the formula of:



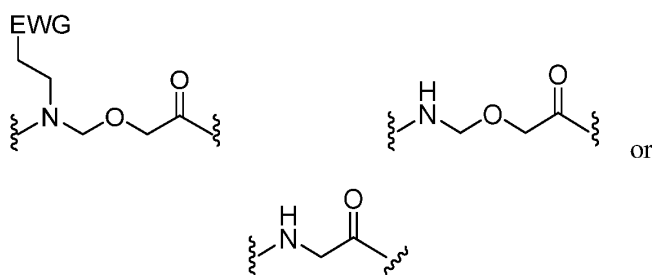
wherein EWG is an electron-withdrawing group;

O* represent the oxygen atom from a hydroxy functional group of D;

the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment to the carbonyl carbon atom of the Glycoside (e.g., Glucuronide) Unit; and

the wavy line adjacent to O* indicates the site of covalent attachment to the remainder of D, or

the Spacer Unit (Y) has the formula of:



wherein

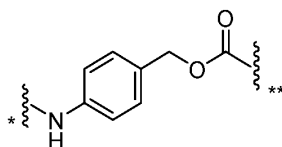
EWG is an electron-withdrawing group;

the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment to the carbonyl carbon atom of the Glycoside (e.g., Glucuronide) Unit; and

the wavy line adjacent to the carbonyl carbon atom indicates the site of covalent attachment to the nitrogen atom of the amine functional group of D.

Embodiment 33. The Camptothecin-Linker Compound of any one of embodiments 20-29 having formula (vii), formula (viii) or formula (ix), wherein A is a Connector Unit, or having formula (i), formula (iii), formula (x) or formula (xi), wherein A is a Connector Unit and RL is a Releasable linker other than a Glycoside (e.g., Glucuronide) Unit.

Embodiment 34. The Camptothecin-Linker Compound of embodiment 33 having formula (i), formula (iii) or formula (x), wherein
RL has the formula:



wherein

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to D; and

the wavy line marked with a single asterisk (*) indicates the point of covalent attachment to A, S* or W.

Embodiment 35. The Camptothecin-Linker Compound of embodiment 34 having formula (x) wherein W is an Amino Acid Unit selected from the group consisting of N-methyl-glycine (sarcosine), N-methyl-alanine, N-methyl-β-alanine, valine and N-methyl-valine.

Embodiment 36. The Camptothecin-Linker Compound of any one of embodiments 33-35 wherein Z'-A- is comprised of a maleimido-alkanoyl moiety or mDPR, the basic nitrogen atom of which is optionally protonated or protected by an acid-labile protecting group.

Embodiment 37. The Camptothecin-Linker Compound of any one of embodiments 33-35 having formula (iii) or formula (x), wherein

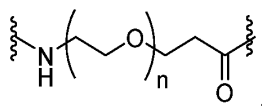
Z'-A- has a formula selected from the group consisting of:



wherein the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to S*.

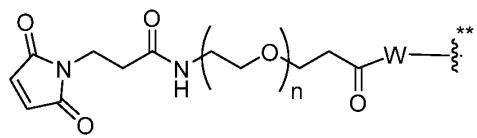
Embodiment 38. The Camptothecin-Linker Compound of any one of embodiments **33-35** having formula (iii) or formula (x), wherein

S* has the formula of:



wherein subscript n is an integer ranging from 2 to 36.

Embodiment 39. The Camptothecin-Linker Compound of embodiment **33** or **34** of formula (viii) or formula (x) in which Z'-A-S*-W- has the formula of:



wherein subscript n is an integer ranging from 2 to 10, preferably ranging from 2 to 4; the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to D or RL.

Embodiment 40. A method of treating cancer in a subject in need thereof, comprising administering to the subject an effective amount of a Camptothecin Conjugate of any one of embodiments 1-19, optionally said cancer is selected from the group consisting of lymphomas, leukemias, and solid tumors, optionally a lymphoma or a leukemia.

Embodiment 41. Use of a Camptothecin Conjugate of any one of embodiments 1-19 in preparation of a medicament for treatment of a cancer in a subject, optionally said

cancer is selected from the group consisting of lymphomas, leukemias, and solid tumors, optionally a lymphoma or a leukemia.

Embodiment 42. A pharmaceutically acceptable composition comprising a Camptothecin Conjugate of any one of embodiments 1-19 and at least one pharmaceutically acceptable excipient.

Embodiment 43. A composition for treatment of a cancer in a subject in need thereof, wherein the composition is comprised of an effective amount of a Camptothecin Conjugate of any one of embodiments 1-19, optionally said cancer is selected from the group consisting of lymphomas, leukemias, and solid tumors, optionally a lymphoma or a leukemia.

SEQ ID NO	Description	Sequence
1	cAC10 CDR-H1	DYYIT
2	cAC10 CDR-H2	WIYPGSGNTKYNEKFKG
3	cAC10 CDR-H3	YGNYWFAY
4	cAC10 CDR-L1	KASQSVDFDGD SYMN
5	cAC10 CDR-L2	AASNLES
6	cAC10 CDR-L3	QQSNE DPWT
7	cAC10 VH	QIQLQQSGPEVVKPGASVKISCKASGYTFTDYYITWVKQKPGQG LEWIGWIYPGSGNTKY NEKFKGKATLTVDTSSTAFMQLSSLTSED TAVYFCANYGNYW FAYWGQGTQVTVSA
8	cAC10 VL	DIVLTQSPASLAVSLGQRATISCKASQSVDFDGD SYMNWYQQKP GQPPKVLIIAASNLES GIPARFSGSGGTDFTLNIHPVEEEDAATYYCQQSNE DPWTFGGG TKLEIK
9	cAC10 HC	QIQLQQSGPEVVKPGASVKISCKASGYTFTDYYITWVKQKPGQG LEWIGWIYPGSGNTKY

		NEKFKGKATLTVDTSSTAFMQLSSLTSEDNAVYFCANYGNYW FAYWGQGTQVTVSAAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSD GSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
10	cAC10 HC v2	QIQQQSGPEVVKPGASVKISCKASGYTFTDYYITWVKQKPGQG LEWIGWIYPGSGNTKY NEKFKGKATLTVDTSSTAFMQLSSLTSEDNAVYFCANYGNYW FAYWGQGTQVTVSAAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSD GSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPG
11	cAC10 LC	DIVLTQSPASLAVSLGQRATISCKASQSVDFDGD SYMNWYQQKP GQPPKVLIIYAASNLES GIPARFSGSGSGTDFTLNIHPVEEEDAATYYCQQSNEDPWTFGGG TKLEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
12	h1F6 VH	QVQLVQSGAEVKKPGASVKVSKASGYTFTNYGMNWVRQAPG QGLKWMGWINTYTGEPTY ADAFKGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARDYGDY GMDYWGQGTITVTVSS
13	h1F6 VL	DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSFMHWYQQKP GQPPKLLIYLASNLES GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQHSREVPWTFGQ GTKVEIK
14	h1F6 HC	QVQLVQSGAEVKKPGASVKVSKASGYTFTNYGMNWVRQAPG QGLKWMGWINTYTGEPTY ADAFKGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARDYGDY GMDYWGQGTITVTVSSAS

		TKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKT HTCPPCPAPELLGGPS VFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ PREPQVYTLPPSRDELT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGS FFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
15	h1F6 LC	DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSFMHWYQQKP GQPPKLLIYLASNLES GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQHSREVPWTFGQ GTKVEIKRTVAAPSVF IFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ ESVTEQDSKDSYSTLS STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
16	TROP2 CDR-H1	NYGMN
17	TROP2 CDR-H2	WINTYTGEPTYTDDFKG
18	TROP2 CDR-H3	GGFGSSYWYFDV
19	TROP2 CDR-L1	KASQDVSIABA
20	TROP2 CDR-L2	SASYRYT
21	TROP2 CDR-L3	QQHYITPLT
22	TROP2 VH	QVQLQQSGSELKKPGASVKVSKASGYTFTNYGMNWKQAPG QGLKWMGWINTYTGEPT YTDDFKGRFAFSLDTSVSTAYLQISSLKADDTAVYFCARGGFGSS YWYFDVWGQGSLVTVSS
23	TROP2 VL	DIQLTQSPSSLSASVGDRAVITCKASQDVSIABAWYQQKPGKAPK LLIYSASYRYTGVP DRFSGSGSGTDFTLTISSLQPEDFAVYYCQQHYITPLTFGAGTKV EIK
24	TROP2 CDR-H1	TAGMQ
25	TROP2 CDR-H2	WINTHSGVPKYAEDFKG
26	TROP2 CDR-H3	SGFGSSYWYFDV
27	TROP2 CDR-L1	KASQDVSTABA

28	TROP2 CDR-L2	SASYRYT
29	TROP2 CDR-L3	QQHYITPLT
30	TROP2 VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTTAGMQWVRQAPG QGLEWMGWINTHSGVPKYAEDFKGRVTISADTSTSTAYLQLSSL KSEDTAVYYCARSGFGSSYWFYFDVWGQGTLVTVSS
31	TROP2 VL	DIQMTQSPSSLSASVGDRVTITCKASQDVSTAVAWYQQKPGKAP KLLIYSASYRYTGVPSPRFGSGSGTDFTLTISLQPEDFAVYYCQQ HYITPLTFGQGTKLEIK
32	MICA CDR- H1	SQNIY
33	MICA CDR- H2	YIEPYNVPMYNPKFKG
34	MICA CDR- H3	SGSSNFDY
35	MICA CDR- L1	SASSSISSHYLH
36	MICA CDR- L2	RTSNLAS
37	MICA CDR- L3	QQGSSLPLT
38	MICA VH	EIQLVQSGAEVKKPGASVKVSCKASGYAFTSQNIYWVRQAPGQ GLEWIGYIEPYNVPMYNPKFKGRATLTVDKSTSTAYLELSSLRS EDTAVYYCARSGSSNFDYWQGQTLVTVSS
39	MICA VL	DIQLTQSPSSLSASVGDRVTITCSASSSISSHYLHWYQQKPGKSPK LLIYRTSNLASGVPSPRFGSGSGTDYTLTISLQPEDFATYYCQQG SSLPLTFGQGTKVEIK
40	MICA CDR- H1	NYAMH
41	MICA CDR- H2	LIWYDGSNKFYGDVSKG
42	MICA CDR- H3	EGSGHY
43	MICA CDR- L1	RASQGISSALA
44	MICA CDR- L2	DASSLES
45	MICA CDR- L3	QQFNSYPIT
46	MICA VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYAMHWVRQAPGE GLEWVALIWYDGSNKFYGDVSKGRFTISRDNKNTLYLQMNSL SAEDTAVYYCAREGSGHYWGQGTLVTVSS
47	MICA VL	AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKVPK SLIYDASSLESGVPSPRFGSGSGTDFTLTISLQPEDFATYYCQQF NSYPITFGQGTREIK

48	MICA CDR-H1	NYAMS
49	MICA CDR-H2	YISPGGDYIYYADSVKG
50	MICA CDR-H3	DRRHYGSYAMDY
51	MICA CDR-L1	RSSKSLLSNLNTYLY
52	MICA CDR-L2	RMSNLAS
53	MICA CDR-L3	MQHLEYPFT
54	MICA VH	QVQLVESGGGLVKPGGSLRLSCAASGFTFSNYAMSWIRQAPGK GLEWVSYISPGGDYIYYADSVKGRFTISRDNKNSLYLQMNSLR AEDTAVYYCTTDRRHYGSYAMDYWGQGTLVTVSS
55	MICA VL	DIVMTQSPLSLPVTPGEPASISCRSSKSLLSNLNTYLYWFLQKPG QSPQILIYRMSNLASGVDPDRFSGSGSGTAFTLKISRVEAEDVGVY YCMQHLEYPFTFGPGTKLEIK
56	MICA CDR-H1	TYAFH
57	MICA CDR-H2	GIVPIFGTLKYAQKFQD
58	MICA CDR-H3	AIQLEGRPFDH
59	MICA CDR-L1	RASQGITSYLA
60	MICA CDR-L2	AASALQS
61	MICA CDR-L3	QQVNRGAAIT
62	MICA VH	QVQLVQSGAEVKKPGSSVRVSCRASGGSSTTYAFHWVRQAPGQ GLEWMGGIVPIFGTLKYAQKFQDRVTLTADKSTGTAYMELNSL RLDDTAVYYCARAIQLEGRPFHDHWGQGTQVTVSA
63	MICA VL	DIQLTQSPSFLSASVGDRVTITCRASQGITSYLAWYQQKPGKAPK LLIYAASALQSGVPSRFSGRSGTEFTLTISLQPEDFATYYCQQV NRGAAITFGHGTRLDIK
64	CD24 CDR-H1	TYAFH
65	CD24 CDR-H2	GIVPIFGTLKYAQKFQD
66	CD24 CDR-H3	AIQLEGRPFDH
67	CD24 CDR-L1	RASQGITSYLA
68	CD24 CDR-L2	AASALQS

69	CD24 CDR-L3	QQVNRGAAIT
70	CD24 VH	QVQLVQSGAEVKKPGSSVRVSCRASGGSSTTYAFHWVRQAPGQ GLEWMGGIVPIFGTLKYAQKFQDRVTLTADKSTGTAYMELNSL RLDDTAVYYCARAIQLEGRPFDPHWGQGTQVTVSA
71	CD24 VL	DIQLTQSPSFLSASVGDRVITICRASQGITSYLAWYQQKPGKAPK LLIYAASALQSGVPS RFSGRGSGTEFTLTISLQPEDFATYYCQQVNRGAAITFGHGTRL DIK
72	ITGav CDR-H1	RYTMH
73	ITGav CDR-H2	VISFDGSNKYYVDSVKG
74	ITGav CDR-H3	EARGSYAFDI
75	ITGav CDR-L1	RASQSVSSYLA
76	ITGav CDR-L2	DASNRAT
77	ITGav CDR-L3	QQRSNWPPFT
78	ITGav VH	QVQLVESGGGVVQPGRSRRLSCAASGFTFSRYTMHWVRQAPGK GLEWVAVISFDGSNKYYVDSVKGKRFITSRDSENTLYLQVNILR AEDTAVYYCAREARGSYAFDIWGQGTMTVTVSS
79	ITGav VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPR LLIYDASNRATGIPARFSGSGSGTDFTLTISLQPEDFAVYYCQQR SNWPPFTFGPGTKVDIK
80	ITGav CDR-H1	SFWMH
81	ITGav CDR-H2	YINPRSGYTEYNEIFRD
82	ITGav CDR-H3	FLGRGAMDY
83	ITGav CDR-L1	RASQDISNYLA
84	ITGav CDR-L2	YTSKIHS
85	ITGav CDR-L3	QQGNTFPYT
86	ITGav VH	QVQLQQSGGELAKPGASVKVSCASGYTFSSFWMHWRQAPG QGLEWIGYINPRSGYTEYNEIFRDKATMTTDTSTSTAYMELSSLR SEDTAVYYCASFLGRGAMDYWGQGTITVTVSS
87	ITGav VL	DIQMTQSPSSLSASVGDRVITICRASQDISNYLAWYQQKPGKAP KLLIYYTSKIHSVPSRFSGSGSGTDYFTISLQPEDATYYCQQ GNTFPYTFGQGTKEIK

88	gpA33 CDR-H1	TSSYYWG
89	gpA33 CDR-H2	TIYYNGSTYYSPSLKS
90	gpA33 CDR-H3	QGYDIKINIDV
91	gpA33 CDR-L1	RASQSVSSYLA
92	gpA33 CDR-L2	VASNRAT
93	gpA33 CDR-L3	QQRSNWPLT
94	gpA33 VH	QLQLQESGPGLVKPSSETLSLTCTVSGGSISTSSYYWGWIRQPPGK GLEWIGTIYYNGSTYYSPSLKSRVSISVDTSKNQFSLKLSSVTAA DTSVYYCARQGYDIKINIDVWGQGTTVTVSS
95	gpA33 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPR LLIYVASNRATGIPARFSGSGSGTDFTLTISSELPEDFAVYYCQQR SNWPLTFGGGTKVEIK
96	IL1Rap CDR-H1	SSWMN
97	IL1Rap CDR-H2	RIYPGDGNTHYAQKFQG
98	IL1Rap CDR-H3	GYLDPMDY
99	IL1Rap CDR-L1	QASQGINNYLN
100	IL1Rap CDR-L2	YTSGLHA
101	IL1Rap CDR-L3	QQYSILPWT
102	IL1Rap VH	QVQLVQSGAEVKKPGSSVKVSKASGYAFTSSWMNWVRQAPG QGLEWMGRIYPGDGNTHYAQKFQGRVTLTADKSTSTAYMELSS LRSEDTAVYYCGEGYLDPM DYWGQGT LVT VSS
103	IL1Rap VL	DIQMTQSPSSLSASVGDRVTITCQASQGINNYLNWYQQKPGKAP KLLIHYTSGLHAGVPSRFSGSGSGTDYTLTISSELPEDVATYYCQ QYSILPWTFGGGTKVEIK
104	EpCAM CDR-H1	SYGMH
105	EpCAM CDR-H2	VISYDGSNKYYADSVKG
106	EpCAM CDR-H3	DMG
107	EpCAM CDR-L1	RTSQSISSYLN
108	EpCAM CDR-L2	WASTRES

109	EpCAM CDR-L3	QQSYDIPYT
110	EpCAM VH	EVQLLESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGK GLEWVAVISYDGSNKYYADSVKGRFTISRDN SKNTLYLQMNSL RAEDTAVYYCAKDMGWGSGWRPYYYYGMDVWGQGTTVTVS S
111	EpCAM VL	ELQMTQSPSSLSASVGDRVITTCRTSQSISSYLNWYQQKPGQPPK LLIYWASTRESGVPDRFSGSGSGTDFTLTISLQPEDSATYYCQQS YDIPYTFGQGKLEIK
112	EpCAM CDR-H1	NYWMS
113	EpCAM CDR-H2	NIKQDGSEKFYADSVKG
114	EpCAM CDR-H3	VGPSWEQDY
115	EpCAM CDR-L1	TGSSSNIGSYYG VH
116	EpCAM CDR-L2	SDTNRPS
117	EpCAM CDR-L3	QSYDKGFGHRV
118	EpCAM VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYWMSWVRQAPGK GLEWVANIKQDGSEKFYADSVKGRFTISRDN AKNSLYLQMNSL RAEDTAVYYCARVGPSWEQDYWGQGLVTVSA
119	EpCAM VL	QSVLTQPPSVSGAPGQRVTISCTGSSSNIGSYYG VHWYQQLPGTA PKLLIYSDTNRPSGVPDRFSGSKSGTSASLAITGLQAEDEADYYC QSYD
120	EpCAM CDR-H1	SYAIS
121	EpCAM CDR-H2	GIPIFGTANYAQKFQG
122	EpCAM CDR-H3	GLLWNY
123	EpCAM CDR-L1	RASQSVSSNLA
124	EpCAM CDR-L2	GASTTAS
125	EpCAM CDR-L3	QQYNNWPPAYT
126	EpCAM VH	QVQLVQSGAEVKKPGSSVKVSKASGGTFSSY AISWVRQAPGQ GLEWMGGIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYYCARGLLWNYWGQGLVTVSS
127	EpCAM VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLA WYQQKPGQAP RLIYGASTTASGIPARFSASGSGTDFTLTISLQSEDFAVYYCQQ YNNWPPAYTFGQGKLEIK
128	EpCAM CDR-H1	NYGMN

129	EpCAM CDR-H2	WINTYTGEPTYGEDFKG
130	EpCAM CDR-H3	FGNYVDY
131	EpCAM CDR-L1	RSSKNLLHSNGITYLY
132	EpCAM CDR-L2	QMSNLAS
133	EpCAM CDR-L3	AQNLEIPRT
134	EpCAM VH	QVQLVQSGPEVKKPGASVKVSCASGYTFTNYGMNWVRQAPG QGLEWMGWINTYTGEPTYGEDFKGRFAFSLDTSASTAYMELSSL RSED TAVYFCARFGNYVDYWGQGSLVTVSS
135	EpCAM VL	DIVMTQSPLSLPVTGPGEPAISCRSSKNLLHSNGITYLYWYLQKP GQSPQLLIYQMSNLASGVPDRFSSSGSGTDFTLKISRVEAEDVGV YYCAQNLEIPRTFGQGTKVEIK
136	EpCAM CDR-H1	KYGMN
137	EpCAM CDR-H2	WINTYTEPTYGDDFKG
138	EpCAM CDR-H3	FGSAVDY
139	EpCAM CDR-L1	RSSKSLLSNGITYLY
140	EpCAM CDR-L2	QMSNRAS
141	EpCAM CDR-L3	AQNLELPRT
142	EpCAM VH	QIQLVQSGPEVKKPGESVKISCKASGYTFTKYGMNWVKQAPGQ GLKWMGWINTYTEPTYGDDFKGRFTFTLDTSTSTAYLEISLRS EDTATYFCARFGSAVDYWGQGTLLTVSS
143	EpCAM VL	DIVMTQSALSNPVTLGESGISCRSSKSLLSNGITYLYWYLQKP GQSPQLLIYQMSNRASGVPDRFSSSGSGTDFTLKISRVEAEDVGV YYCAQNLELPRTFGQGTKLEMKR
144	EpCAM CDR-H1	DYSMH
145	EpCAM CDR-H2	WINTETGEPTYADDFKG
146	EpCAM CDR-H3	TAVY
147	EpCAM CDR-L1	RASQEISVSLS
148	EpCAM CDR-L2	ATSTLDS
149	EpCAM CDR-L3	LQYASYPWT

150	EpCAM VH	QVKLQESGPELKKPGETVKISCKASGYTFTDYSMHVWKQAPGK GLKWMGWINTETGEPTYADDFKGRFAFSLETSASTAYLQINNLIK NEDTATYFCARTAVYWGGQTTVTVSS
151	EpCAM VL	DIQMTQSPSSLSASLGERVSLTCRASQEISVSLSWLQQEPDGTIKR LIYATSTLD SGV PKRFSGSRSGSDYSLTISSLESEDFVDYYCLQYA SYPWTFGGG TKLEIKR
152	CD352 CDR-H1	NYGMN
153	CD352 CDR-H2	WINTYSGEPRYADDFKG
154	CD352 CDR-H3	DYGRWYFDV
155	CD352 CDR-L1	RASSSVSHMH
156	CD352 CDR-L2	ATSNLAS
157	CD352 CDR-L3	QQWSSTPRT
158	CD352 VH	QIQLVQSGSELKKPGASVKVSCASGYTFTNYGMNWVRQAPGQ DLKWMGWINTYSGEPRYADDFKGRFVFSLDKSVNTAYLQISSL KAEDTAVYYCARDYGRWYFDVWGQGTTLTVSS
159	CD352 VL	QIVLSQSPATLSLSPGERATMSCRASSSVSHMHYQQKPGQAPR PWIYATSNLASGVPARFSGSGSGTDYTLTISSLEPEDFAVYYCQQ WSSTPRTFGGG TKVEIKR
160	CS1 CDR- H1	RYWMS
161	CS1 CDR- H2	EINPDSSTINYAPSLKD
162	CS1 CDR- H3	PDGNYWYFDV
163	CS1 CDR- L1	KASQDVGIABA
164	CS1 CDR- L2	WASTRHT
165	CS1 CDR- L3	QQYSSYPYT
166	CS1 VH	EVQLVESGGGLVQPGGSLRLSCAASGFDPSRYWMSWVRQAPGK GLEWIGEINPDSSTINYAPSLKDKFIISRDNANKNSLYLQMNSLRAE DTAVYYCARPDGNYWYFDVWGQGTTLTVSS
167	CS1 VL	DIQMTQSPSSLSASVGDRTITCKASQDVGIABAWYQQKPGKVP KLLIYWASTRHTGVPDRFSGSGSGTDFTLTISLQPEDVATYYCQ QYSSYPYTFGQGT KVEIKR
168	CD38 CDR- H1	SFAMS
169	CD38 CDR- H2	AISGSGGGTYADSVKG

170	CD38 CDR-H3	DKILWFGEPVFDY
171	CD38 CDR-L1	RASQSVSSYLA
172	CD38 CDR-L2	DASNRAT
173	CD38 CDR-L3	QQRSNWPPT
174	CD38 VH	EVQLLESGGGLVQPGGSLRLSCAVSGFTFNSFAMSWVRQAPGK GLEWVSAISGSGGGTYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYFCAKD KILWFGEPVFDYWGQGTLTVSS
175	CD38 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLA WYQQKPGQAPR LLIYDASNRATGIPARFSGSGGTDFLT LTISSLEPEDFAVYYCQQR SNWPPTFGQG TKVEIKR
176	CD25 CDR-H1	SYRMH
177	CD25 CDR-H2	YINPSTGYTEYNQKFKD
178	CD25 CDR-H3	GGGVFDY
179	CD25 CDR-L1	SASSSISYMH
180	CD25 CDR-L2	TTSNLAS
181	CD25 CDR-L3	HQRSTYPLT
182	CD25 VH	QVQLVQSGAEVKKPGSSVKV SCKASGYTFTSYRMHWVRQAPG QGLEWIGYINPSTGYTEYNQKFKDKATITADESTNTAYMELSSL RSED TAVYYCARGGGVFDYWGQGTLTVSS
183	CD25 VL	DIQMTQSPSTLSASVGDRTITCSASSSISYMH WYQQKPGKAPKL LIYTTSNLASGVPARFSGSGSGTEFTLT ISSLQPDDFATYYCHQRS TYPLTFGQG TKVEVK
184	ADAM9 CDR-H1	SYWM
185	ADAM9 CDR-H2	EIIPINGHTNYNEKFKS
186	ADAM9 CDR-H3	GGYYYYGSRDYFDY
187	ADAM9 CDR-L1	KASQSVDDYDGDSYMN
188	ADAM9 CDR-L2	AASDLES
189	ADAM9 CDR-L3	QQSHEDPFT
190	ADAM9 VH	QVQLQQPGAELVKPGASVKLSCKASGYTFTSYWMHWVKQRP QGLEWIGEIIIPINGHTNYNEKFKSKATLTLDKSSSTAYMQLSSLA SEDSAVYYCARGGGYYYYGSRDYFDYWGQGTTTLTVSS

191	ADAM9 VL	DIVLTQSPASLAVSLGQRATISCKASQSVDYDGD SYMNWYQQIP GQPPKLLIYAASDLESGIPARFSGSGSGTDFTLNHPVEEEDAATY YCQQSHEDPFTFGGGTKLEIK
192	ADAM9 CDR-H1	SYWM
193	ADAM9 CDR-H2	EIIPIFGHTNYNEKFKS
194	ADAM9 CDR-H3	GGYYYYPRQGFLDY
195	ADAM9 CDR-L1	KASQSVDYDSGDSYMN
196	ADAM9 CDR-L2	AASDLES
197	ADAM9 CDR-L3	QQSHEDPFT
198	ADAM9 VH	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYWMHWRQAPGK GLEWVGEIPIFGHTNYNEKFKSRFTISLDNSKNTLYLQMGLRA EDTAVYYCARGGGYYYYPRQGFLDYWGQGTTVTSS
199	ADAM9 VL	DIVMTQSPDSLAVSLGERATISCKASQSVDYSGDSYMNWYQQK PGQPPKLLIYAASDLESGIPARFSGSGSGTDFTLTSSLEPEDFATY YCQQSHEDPFTFGQGTKLEIK
200	CD59 CDR- H1	YGMN
201	CD59 CDR- H2	YISSSSSTIYADSVKG
202	CD59 CDR- H3	GPGMDV
203	CD59 CDR- L1	KSSQSVLYSSNNKNYLA
204	CD59 CDR- L2	WASTRES
205	CD59 CDR- L3	QQYYSTPQLT
206	CD59 VH	QVQLQQSGGGVVQPGRSLGLSCAASFTFSSYGMNWVRQAPGKG LEWVSYISSSSSTIYADSVKGRFTISRDN SKNTLYLQMNSLRAED TAVYYCARGPGMDVWGQGTTVTSS
207	CD59 VL	DIVLTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYLA WYQQ KPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTPAISSLQAEDV AVYYCQQYYSTPQLTFGGGKVDIK
208	CD19 CDR- H1	TSGMGVG
209	CD19 CDR- H2	HIWWDDDKRYNPALKS
210	CD19 CDR- H3	MELWSYYFDY

211	CD19 CDR-L1	SASSSVSYMH
212	CD19 CDR-L2	DTSKLAS
213	CD19 CDR-L3	FQGSVYPFT
214	CD19 VH	QVQLQESGPGLVKPSQTLSTCTVSGGSISTSGMGVGVIRQHPG KGLEWIGHIWWDDDKRYNPALKSRVTISVDTSKNQFSLKLSSVT AADTAVYYCARMELWSYYFDYWGQGTLVTVSS
215	CD19 VL	EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGQAPRL LIYDTSKLASGIPARFSGSGSGTDFTLTISSELPEDVAVYYCFQGS VYPFTFGQGTKLEIKR
216	CD70 CDR-H1	NYGMN
217	CD70 CDR-H2	WINTYTGEPTYADAFKG
218	CD70 CDR-H3	DYGDYGM DY
219	CD70 CDR-L1	RASKSVSTSGYSFMH
220	CD70 CDR-L2	LASNLES
221	CD70 CDR-L3	QHSREVPWT
222	CD70 VH	QVQLVQSGAEVKKPGASVKVSCASGYTFTNYGMNWVRQAPG QGLKWMGWINTYTGEPTYADAFKGRVTMTRDTSISTAYMELSR LRSDDTAVYYCARDYGDYGM DYWGQGTTVTVSS
223	CD70 VL	DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSFMHWYQQKP GQPPKLLIYASNLES GVPDRFSGSGSGTDFTLTISLQAEDVAVY YCQHSREVPWTFGQGTKVEIK
224	B7H4 CDR-H1	SGYSWH
225	B7H4 CDR-H2	YIHSSGSTNYPNPSLKS
226	B7H4 CDR-H3	YDDYFEY
227	B7H4 CDR-L1	KASQNVGFNVA
228	B7H4 CDR-L2	SASYRYS
229	B7H4 CDR-L3	QQYNWYPFT
230	B7H4 VH	EVQLQESGPGLVKPSSETLSLTCAVTGYSITSGYSWHWIRQFPGNG LEWMGYIHSSGSTNYPNPSLKSRISSRDTSKNQFFLKLSSVTAADT AVYYCAGYDDYFEYWGQGTTVTVSS

231	B7H4 VL	DIQMTQSPSSLSASVGDRVITITCKASQNVGFNVAWYQQKPGKSP KALIYSASYRYSVPSRFRSGSGSGTDFTLTISLQPEDFAEYFCQQ YNWYPFTFGQGTKLEIK
232	CD138 CDR-H1	NYWIE
233	CD138 CDR-H2	EILPGTGRTIYNEKFKG
234	CD138 CDR-H3	RDYYGNFYAMDY
235	CD138 CDR-L1	SASQGINNYLN
236	CD138 CDR-L2	YTSTLQS
237	CD138 CDR-L3	QQYSKLPRT
238	CD138 VH	QVQLQQSGSELMMPGASVKISCKATGYTFSNYWIEWVKQRPGH GLEWIGEILPGTGRTIY NEKFKGKATFTADISSNTVQMQLSSLTSEDSAVYYCARRDYYGN FYYAMDYWGQGTSTVTVSS
239	CD138 VL	DIQMTQSTSSLSASLGDRVITISCSASQGINNYLNWYQQKPDGTV ELLIYYTSTLQSGVP SRFSGSGSGTDYSLTISNLEPEDIGTYYCQQYSKLPRTFGGGTKLE IK
240	CD166 CDR-H1	TYGMGVG
241	CD166 CDR-H2	NIWWSEDKHYSPSLKS
242	CD166 CDR-H3	IDYGNDYAFTY
243	CD166 CDR-L1	RSSKSLLSHNGITYLY
244	CD166 CDR-L2	QMSNLAS
245	CD166 CDR-L3	AQNLELPYT
246	CD166 VH	QITLKESGPTLVKPTQTLTLTCTFSGFSLSTYGMGVGWIRQPPGK ALEWLANIWWSEDKHYSPSLKSRLTITKDTSKNQVVLITNVDP VDATYYCVQIDYGNDYAFTYWGQGTSLTVTVSS
247	CD166 VL	DIVMTQSPLSLPVTGPGEPAISCRSSKSLLSHNGITYLYWYLQKPG QSPQLLIYQMSNLASGVDPDRFSGSGSGTDFTLKISRVEAEDVGVY YCAQNLELPYTFGQGTKLEIK
248	CD51 CDR- H1	RYTMH
249	CD51 CDR- H2	VISFDGSNKYYVDSVKG
250	CD51 CDR- H3	EARGSYAFDI

251	CD51 CDR-L1	RASQSVSSYLA
252	CD51 CDR-L2	DASNRAT
253	CD51 CDR-L3	QQRSNWPPFT
254	CD51 VH	QVQLVESGGGVVQPGRSRRLSCAASGFTFSRYTMHWVRQAPGK GLEWVAVISFDGSNKYYVDSVKGRFTISRDNSENTLYLQVNILR AEDTAVYYCAREARGSYAFDIWGQGTMTVTVSS
255	CD51 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPR LLIYDASNRATGIPARFSGSGSGTDFTLTISSELPEDFAVYYCQQR SNWPPFTFGPGTKVDIK
256	CD56 CDR-H1	SFGMH
257	CD56 CDR-H2	YISSGSFTIYYADSVKG
258	CD56 CDR-H3	MRKGYAMDY
259	CD56 CDR-L1	RSSQIIIHSDGNTYLE
260	CD56 CDR-L2	KVSNRFS
261	CD56 CDR-L3	FQGSHVPHT
262	CD56 VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSFGMHWVRQAPGK GLEWVAYISSGSFTIYYADSVKGRFTISRDN SKNTLYLQMNSLRA EDTAVYYCARMRKGYAMDYWGQGTSLTVTVSS
263	CD56 VL	DVVMTQSPSLPVTLGQPASISCRSSQIIIHSDGNTYLEWVFQRP QSPRRLIYKVS NRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVY YCFQGSHPHTFGQGTKVEIK
264	CD74 CDR-H1	NYGVN
265	CD74 CDR-H2	WINPNTGEPTFDDDFKG
266	CD74 CDR-H3	SRGKNEAWFAY
267	CD74 CDR-L1	RSSQSLVHRNGNTYLH
268	CD74 CDR-L2	TVSNRFS
269	CD74 CDR-L3	SQSSHVPPT
270	CD74 VH	QVQLQQSGSELKKPGASVKVSKASGYTFTNYGVNWIQAPGQ GLQWMGWNPNTGEPTFDDDFKGRFAFSLDTSVSTAYLQISL ADDTAVYFCRSRGKNEAWFAYWGQGTSLTVTVSS

271	CD74 VL	DIQLTQSPLSLPVTLGQPASISCRSSQSLVHRNGNTYLHWFQQRPGQSPRLLIYTVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSSHVPPTFGAGTRLEIK
272	CEACAM5 CDR-H1	TYWMS
273	CEACAM5 CDR-H2	EIHPDSSTINYAPSLKD
274	CEACAM5 CDR-H3	LYFGFPWFAY
275	CEACAM5 CDR-L1	KASQDVGTSVA
276	CEACAM5 CDR-L2	WTSTRHT
277	CEACAM5 CDR-L3	QQYSLYRS
278	CEACAM5 VH	EVQLVESGGGVVQPGRSLRLSCSASGFDFTTYWMSWVRQAPGKGLEWIGEIHDPDSSTINYAPSLKDRFTISRDNKNTLFLQMDSLRPEDTGVIYFCASLYFGFPWFAYWGQGTPVTVSS
279	CEACAM5 VL	DIQLTQSPSSLSASVGDRVITCKASQDVGTSVAWYQQKPGKAPKLLIYWTSTRHTGVPSRFSGSGSGTDFTFTISSLPEDIATYYCQQYSLYRSFGQGTKVEIK
280	CanAg CDR-H1	YYGMN
281	CanAg CDR-H2	WIDTTTGEPTYAQKFQG
282	CanAg CDR-H3	RGPYNWYFDV
283	CanAg CDR-L1	RSSKSLHNSNGNTYLY
284	CanAg CDR-L2	RMSNLVS
285	CanAg CDR-L3	LQHLEYPFT
286	CanAg VH	QVQLVQSGAEVKKPGETVKISCKASDYFTFTYYGMNWVKQAPGQGLKWMGWIDTTTGEPTYAQKFQGRIAFSLETSASTAYLQIKSLKSEDTATYFCARRGPYNWYFDVWGQGTTVTVSS
287	CanAg VL	DIVMTQSPLSVPVTPGEPVSISCRSSKSLHNSNGNTYLYWFLQRP GQSPQLLIYRMSNLVSGVPDRFSGSGSGTAFTLRISRVEAEDVGVYYCLQHLEYPFTFGPGTKLELK
288	DLL-3 CDR-H1	NYGMN
289	DLL-3 CDR-H2	WINTYTGEPTYADDFKG
290	DLL-3 CDR-H3	IGDSSPSDY
291	DLL-3 CDR-L1	KASQSVSNDVV

292	DLL-3 CDR-L2	YASNRYT
293	DLL-3 CDR-L3	QQDYTSPWT
294	DLL-3 VH	QVQLVQSGAEVKKPGASVKVSCASGYTFTNYGMNWVRQAPG QGLEWMGWINTYTGEPTY ADDFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARIGDSSP SDYWGGQGTLLTVSS
295	DLL-3 VL	EIVMTQSPATLSVSPGERATLSCKASQSVSNDVVWYQQKPGQAP RLLIYYASNRYTGIPA RFSGSGSGTEFTLTISLQSEDFAVYYCQQDYTSPWTFGQGKLE IK
296	DPEP-3 CDR-H1	SYWIE
297	DPEP-3 CDR-H2	EILPGSGNTYYNERFKD
298	DPEP-3 CDR-H3	RAAAYYSNPEWFAY
299	DPEP-3 CDR-L1	TASSSVNSFY LH
300	DPEP-3 CDR-L2	STSNLAS
301	DPEP-3 CDR-L3	HQYHRSPYT
302	DPEP-3 VH	QVQLVQSGAEVKKPGSSVKVSCASGGTFSSYWIEWVRQAPGQ GLEWMGEILPGSGNTYYNERFKDRVITADESTSTAYMELSSLR SEDTAVYYCARRAAAYYSNPEWFAYWGQGTLLTVSS
303	DPEP-3 VL	EIVLTQSPATLSLSPGERATLSCTASSSVNSFY LHWYQQKPLAP RLLIYSTSNLASGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCHQ YHRSPYTFGQGKLEIK
304	EGFR CDR-H1	SYWMQ
305	EGFR CDR-H2	TIYPGDGDTTYTQKFQG
306	EGFR CDR-H3	YDAPGYAMDY
307	EGFR CDR-L1	RASQDINNYLA
308	EGFR CDR-L2	YTSTLHP
309	EGFR CDR-L3	LQYDNLLYT
310	EGFR VH	QVQLVQSGAEVAKPGASVKLSCKASGYTFTSYWMQWVKQRP QGLECIGTIYPGDGDTTYTQKFQGKATLTADKSSSTAYMQLSSL RSEDSAVYYCARYDAPGYAMDYWGQGTLLTVSS

311	EGFR VL	DIQMTQSPSSLSASVGDRVITTCRASQDINNYLAWYQHKPGKGP KLLIHYTSTLHPGIPSRFSGSGSGRDYSFSISSLEPEDIATYYCLQY DNLLYTFGQGTKLEIK
312	EGFR CDR- H1	RDFAWN
313	EGFR CDR- H2	YISYNGNTRYQPSLKS
314	EGFR CDR- H3	ASRGFPY
315	EGFR CDR- L1	HSSQDINSNIG
316	EGFR CDR- L2	HGTNLDD
317	EGFR CDR- L3	VQYAQFPWT
318	EGFR VH	EVQLQESGPGLVKPSQTLSTCTVSGYSISRDFAWNWIRQPPGKG LEWMGYISYNGNTRYQPSLKSRTISRDTSKNQFFLKLNSVTAAD TATYYCVTASRGFPYWGQGTLLTVSS
319	EGFR VL	DIQMTQSPSSMSVSVGDRVITITCHSSQDINSNIGWLQQKPGKSFK GLIYHGTNLDDGVPSRFSGSGSGTDYTLTISSLQPEDFATYYCVQ YAQFPWTFGGGTKLEIK
320	EGFR CDR- H1	RDFAWN
321	EGFR CDR- H2	YISYNGNTRYQPSLKS
322	EGFR CDR- H3	ASRGFPY
323	EGFR CDR- L1	HSSQDINSNIG
324	EGFR CDR- L2	HGTNLDD
325	EGFR CDR- L3	VQYAQFPWT
326	EGFR VH	EVQLQESGPGLVKPSQTLSTCTVSGYSISRDFAWNWIRQPPGKG LEWMGYISYNGNTRYQPSLKSRTISRDTSKNQFFLKLNSVTAAD TATYYCVTASRGFPYWGQGTLLTVSS
327	EGFR VL	DIQMTQSPSSMSVSVGDRVITITCHSSQDINSNIGWLQQKPGKSFK GLIYHGTNLDDGVPSRFSGSGSGTDYTLTISSLQPEDFATYYCVQ YAQFPWTFGGGTKLEIK
328	EGFR CDR- H1	NYGVH
329	EGFR CDR- H2	VIWSGGNTDYNTPFST
330	EGFR CDR- H3	ALTYDYEFAY
331	EGFR CDR- L1	RASQSIGTNIH

332	EGFR CDR-L2	YASESIS
333	EGFR CDR-L3	QQNNNWPTT
334	EGFR VH	QVQLKQSGPGLVQPSQSL SITCTVSGFSLTNYGVHWVRQSPGKG LEWLGVIWSSGNTDYNTPFTSRLSINKDNSKSQVFFKMNSLQSN DTAIYYCARALTYDYEFAYWGQGT LVTVSA
335	EGFR VL	DILLTQSPVILSVSPGERVSFSCRASQSIGTNIHWYQQRTNGSPRL LIKYASESISGIPSRFSGSGSGTDFTLSINSVESEDIADYYCQQNNN WPTTFGAGTKLELK
336	FRa CDR-H1	GYFMN
337	FRa CDR-H2	RIHPYDGDTFYNQKFQG
338	FRa CDR-H3	YDGSRAMDY
339	FRa CDR-L1	KASQSVSFAGTSLMH
340	FRa CDR-L2	RASNLEA
341	FRa CDR-L3	QQSREYPYT
342	FRa VH	QVQLVQSGAEVVKPGASVKISCKASGYTFTGYFMNWVKQSPGQ SLEWIGRIHPYDGDTFY NQKFQGKATLTVDKSSNTAHMELLSLTSEDFAVYYCTRYDGSR AMDYWGQGT TTVTVSS
343	FRa VL	DIVLTQSPLSLAVSLGQPAISCKASQSVSFAGTSLMHWYHQKPG QQPRLLIYRASNLEAGVPDRFSGSGSKTDFTLTISPVEAEDAATY YCQQSREYPYTFGGG TKLEIK
344	FRa CDR-H1	GYGLS
345	FRa CDR-H2	MISSGGSYTTYADSVKG
346	FRa CDR-H3	HGDDPAWFAY
347	FRa CDR-L1	SVSSSISSNNLH
348	FRa CDR-L2	GTSNLAS
349	FRa CDR-L3	QQWSSYPMYT
350	FRa VH	EVQLVESGGGVVQPGRSLRLSCSASGFTFSGYGLSWVRQAPGKG LEWVAMISSGGSYTTY ADSVKGRFAISRDNKNTLFLQMDSL RPEDTGVYFCARHGDDP AWFAYWGQGT PTVTVSS
351	FRa VL	DIQLTQSPSSLSASVGDRVITITCSVSSSISSNNLHWYQQKPGKAPK PWIYGTSNLASGVPSRFSGSGSGTDYFTFTISLQPEDATYYCQQ WSSYPMYTFTGQGTKVEIK
352	MUC-1 CDR-H1	NYWMN
353	MUC-1 CDR-H2	EIRLKSNNYTTHYAESVKG

354	MUC-1 CDR-H3	HYYFDY
355	MUC-1 CDR-L1	RSSKSLLSNGITYFF
356	MUC-1 CDR-L2	QMSNLAS
357	MUC-1 CDR-L3	AQNLELPPT
358	MUC-1 VH	EVQLVESGGGLVQPGGSMRLSCVASGFPSNYWMNWVRQAPG KGLEWVGEIRLKSNNYTHYAESVKGRFTISRDDSKNSLYLQMN SLKTEDTAVYYCTRHYYFDYWGQGTLVTVSS
359	MUC-1 VL	DIVMTQSPLSNPVTGPGEASISCRSSKSLLSNGITYFFWYLQKPG QSPQLLIYQMSNLASGVDPDRFSGSGSGTDFTLRISRVEAEDVGVY YCAQNLELPPTFGQGTKVEIK
360	Mesothelin CDR-H1	SYWIG
361	Mesothelin CDR-H2	IIDPGDSRTRYSPSFQG
362	Mesothelin CDR-H3	GQLYGGTYMDG
363	Mesothelin CDR-L1	TGTSSDIGGYNSVS
364	Mesothelin CDR-L2	GVNNRPS
365	Mesothelin CDR-L3	SSYDIESATPV
366	Mesothelin VH	QVELVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQAPGKG LEWMGIIDPGDSRTRYSPSFQGQVTISADKSISTAYLQWSSLKAS DTAMYYCARGQLYGGTYMDGWGQGTLVTVSS
367	Mesothelin VL	DIALTPASVSGSPGQSITISCTGTSSDIGGYNSVSWYQQHPGKAP KLMIYGVNNRPSGV SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYDIESATPVFGGG TKLTVL
368	ROR-1 CDR-H1	AYNIH
369	ROR-1 CDR-H2	SFDPYDGGSSYNQKFKD
370	ROR-1 CDR-H3	GWYYFDY
371	ROR-1 CDR-L1	RASKSISKYLA
372	ROR-1 CDR-L2	SGSTLQS
373	ROR-1 CDR-L3	QQHDESPYT

374	ROR-1 VH	QVQLQESGPGLVKPSQTLSTCTVSGYAFTAYNIHWVRQAPGQG LEWMGSFDPYDGGSSYNQKFKDRLTISKDTSKNQVLTMTNMD PVDATATYYCARGWYYFDYWGHGTLTVSS
375	ROR-1 VL	DIVMTQTPLSLPVTGPGEPAISCRASKSISKYLAWYQQKPGQAPR LLIYSGSTLQSGIPPRFSGSGYGTDFTLTINNIESEDAAYYFCQQH DESPYTFGEGTKVEIK
376	B7H4 CDR- H1	GSIKSGSYWYG
377	B7H4 CDR- H2	NIYYSGSTYYNPSLRS
378	B7H4 CDR- H3	AREGSYPNQFDP
379	B7H4 CDR- L1	RASQSVSSNLA
380	B7H4 CDR- L2	GASTRAT
381	B7H4 CDR- L3	QQYHSFPFT
382	B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGSGSIKSGSYWGWIRQPPGK GLEWIGNIYYSGSTY YNPSLRSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPN QFDPWGQGTLTVSS
383	B7H4 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPA RFGSGSGTEFTLTISLQSEDAVYYCQQYHSFPFTFGGGTKVEI K
384	B7-H3 CDR- H1	SFGMH
385	B7-H3 CDR- H2	YISSDSSAIYY
386	B7-H3 CDR- H3	GRENIYYGSRLD
387	B7-H3 CDR- L1	KASQNVD
388	B7-H3 CDR- L2	SASYRYSGVPD
389	B7-H3 CDR- L3	QQYNNYPFTFGS
390	B7-H3 VH	DVQLVESGGGLVQPGGSRKLSAASGFTFSSFGMHWVRQAPEK GLEWVAYISSDSSAIYY ADTVKGRFTISRDNPKNTLFLQMTSLRSEDAMYYCGRGRENIY YGSRLDYWGQGTTTLTVSS
391	B7-H3 VL	DIAMTQSQKFMSTSVGDRVSVTCKASQNVDNTNVAWYQQKPGQ SPKALIYSASYRYSGVPD RFTGSGSGTDFTLTINNVSQEDLAIEYFCQQYNNYPFTFGSGTKLE IK

392	B7-H3 CDR-H1	SYWMQWVRQA
393	B7-H3 CDR-H2	TIYPGDGDTRY
394	B7-H3 CDR-H3	RGIPRLWYFDVM
395	B7-H3 CDR-L1	ITCRASQDIS
396	B7-H3 CDR-L2	YTSRLHSGVPS
397	B7-H3 CDR-L3	QQGNTLPPFTGG
398	B7-H3 VH	DVQLVESGGGLVQPGGSRKLSCAASGFTFSSFGMHWVRQAPEK GLEWVAYISSDSSAIYY ADTVKGRFTISRDNPKNTLFLQMTSLRSEDAMYYCGRGRENIY YGSRLDYWGQGTTTLTVSS
399	B7-H3 VL	DIAMTQSQKFMSTSVGDRVSVTCKASQNVDTNVAWYQQKPGQ SPKALIYSASYRYSVGPDP RFTGSGSGTDFTLTINNVSQEDLAEIFCQQYNNYPFTFGSGTKLE IK
400	B7-H3 CDR-H1	SYGMSWVRQA
401	B7-H3 CDR-H2	INSGGSNTYY
402	B7-H3 CDR-H3	HDGGAMDYW
403	B7-H3 CDR-L1	ITCRASESIYSYLA
404	B7-H3 CDR-L2	NTKTLPE
405	B7-H3 CDR-L3	HHYGTPPWTFG
406	B7-H3 VH	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYGMSWVRQAPGK GLEWVATINSGGSNTYY PDSLKGRFTISRDNKNSLYLQMNSLRAEDTAVYYCARHDGGA MDYWGQGTTVTVSS
407	B7-H3 VL	DIQMTQSPSSLSASVGDRVTITCRASESIYSYLAWYQQKPGKAPK LLVYNTKTLPEGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQH HYGTPPWTFGQGRLEIK
408	B7-H3 CDR-H1	SFGMHWVRQA
409	B7-H3 CDR-H2	ISSGSGTIYYADTVKGRFTI
410	B7-H3 CDR-H3	HGYRYEGFDYWG
411	B7-H3 CDR-L1	ITCKASQNVDTNVA

412	B7-H3 CDR-L2	SASYRYSGVPS
413	B7-H3 CDR-L3	QQYNNYPFTFGQ
414	B7-H3 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSFGMHWVRQAPGK GLEWVAYISSGSGTIY YADTVKGRFTISRDNANKNSLYLQMNSLRAEDTAVYYCARHGYR YEGFDYWGQGTTVTVSS
415	B7-H3 VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDTNVAWYQQKPGKA PKALIYSASYRYSGVPSRFSGSGSGTDFTLTISLQPEDFAEYFCQ QYNNYPFTFGQGKLEIK
416	B7-H3 CDR-H1	NYVMH
417	B7-H3 CDR-H2	YINPYNDDVKYNEKFKG
418	B7-H3 CDR-H3	WGYYGSPLYFFDY
419	B7-H3 CDR-L1	RASSRLIYMH
420	B7-H3 CDR-L2	ATSNLAS
421	B7-H3 CDR-L3	QQWNSNPPT
422	B7-H3 VH	EVQLQQSGPELVKPGASVKMSCKASGYTFTNYVMHWVKQKPG QGLEWIGYINPYNDDVKYNEKFKGKATQTSDKSSSTAYMELSSL TSEDSAVYYCARWGYYGSPLYFFDYWGQGTTTLTVSS
423	B7-H3 VL	QIVLSQSPTILSASPGEKVTMTCRASSRLIYMHWYQQKPGSSPKP WIYATSNLASGVPAR FSGSGGTSYSLTISRVEAEDAATYYCQQWNSNPPTFGTGKLEL K
424	B7-H3 CDR-H1	NYVMH
425	B7-H3 CDR-H2	YINPYNDDVKYNEKFKG
426	B7-H3 CDR-H3	WGYYGSPLYFFDY
427	B7-H3 CDR-L1	RASSRLIYMH
428	B7-H3 CDR-L2	ATSNLAS
429	B7-H3 CDR-L3	QQWNSNPPT
430	B7-H3 VH	QVQLVQSGAEVKKPGSSVKVSCASGYTFTNYVMHWVRQAPG QGLEWMGYINPYNDDVKYNE KFKGRVTITADESTAYMELSSLRSEDTAVYYCARWGYYGSPL YYFDYWGQGTLLTVSS

431	B7-H3 VL	EIVLTQSPATLSLSPGERATLSCRASSRLIYMHWYQQKPGQAPRP LIYATSNLASGIPARFSGSGSGTDFTLTISSELPEDFAVYYCQQWN SNPPTFGQGTKVEIK
432	B7-H3 CDR- H1	GYSFTSYTIH
433	B7-H3 CDR- H2	YINPNSRNTDYAQKFQG
434	B7-H3 CDR- H3	YSGSTPYWYFDV
435	B7-H3 CDR- L1	RASSSVSYMN
436	B7-H3 CDR- L2	ATSNLAS
437	B7-H3 CDR- L3	QQWSSNPLT
438	B7-H3 VH	EVQLVQSGAEVKKPGSSVKVSCASGYSTSYTIHWVRQAPGQ GLEWMGYINPNSRNTDYAQKFQGRVTLTADKSTSTAYMELSSL RSEDTAVYYCARYSGSTPYWYFDVWGQGTTVTVSS
439	B7-H3 VL	DIQMTQSPSSLSASVGDRVTITCKASQNVGFNAWYQQKPGKSP KALIYSASYRYSVPSRFSGSGSGTDFTLTISLQPEDFAEYFCQQ YNWYPFTFGQGTKLEIK
440	B7-H3 CDR- H1	GYTFSSYWMH
441	B7-H3 CDR- H2	LIHPDSGSTNYNEMFKN
442	B7-H3 CDR- H3	GGRLYFD
443	B7-H3 CDR- L1	RSSQSLVHSNGDTYLR
444	B7-H3 CDR- L2	KVSNRFS
445	B7-H3 CDR- L3	SQSTHVPYT
446	B7-H3 VH	EVQLVQSGAEVKKPGSSVKVSCASGYTFSSYWMHWVRQAPG QGLEWIGLIHPDSGSTNYNEMFKNRATLTVDRTSTAYVELSSLR SEDTAVYFCAGGGRLYFDYWGQGTTVTVSS
447	B7-H3 VL	DVVMQTQSPLSLPVTGPASISCRSSQSLVHSNGDTYLRWYLQKP GQSPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGV YYCSQSTHVPYTFGGGTKVEIK
448	B7-H3 CDR- H1	GYTFSSYWMH
449	B7-H3 CDR- H2	LIHPESGSTNYNEMFKN
450	B7-H3 CDR- H3	GGRLYFDY
451	B7-H3 CDR- L1	RSSQSLVHSNQDTYLR

452	B7-H3 CDR-L2	KVSNRFS
453	B7-H3 CDR-L3	SQSTHVPYT
454	B7-H3 VH	EVQLVQSGAEVKKPGSSVKVSCKASGYTFSSYWMHWVRQAPG QGLEWIGLIHPESGSTNY NEMFKNRATLTVDIRSTSTAYMELSSLRSEDNAVYYCAGGGRLY FDYWGGQGTTVTVSS
455	B7-H3 VL	DIVMTQSPSLPVTGPGEPAISCRSSQSLVHSNQDTYLRWYLQKP GQSPQLLIYKVS NRF SGVPDRFSGSGSGTDFTLKKISRVEAEDVGVYYCSQSTHVPYTFG GGTKVEIK
456	B7-H3 CDR-H1	TGYSITSGYSWH
457	B7-H3 CDR-H2	YIHSSGSTNYPNPSLKS
458	B7-H3 CDR-H3	YDDYFEY
459	B7-H3 CDR-L1	KASQNVGFNVAW
460	B7-H3 CDR-L2	SASYRYS
461	B7-H3 CDR-L3	QQYNWYPFT
462	B7-H3 VH	EVQLQESGPGLVKPSSETLSLTCAVTGYSITSGYSWHWIRQFPGNG LEWMGYIHSSGSTNY NPSLKSRISSRDTSKNQFFLKLSSVTAADNAVYYCAGYDDYFEY WGQGTFTVTVSS
463	B7-H3 VL	DIQMTQSPSSLSASVGDRVTITCKASQNVGGFNVAWYQQKPGKS PKALIYSASYRYS PSRFGSGSGSGTDFTLTISLQPEDFAEYFCQQYNWYPFTFGQGTK LEIK
464	B7-H3 CDR-H1	NYDIN
465	B7-H3 CDR-H2	WIGWIFPGDDSTQYNEKFKG
466	B7-H3 CDR-H3	QTTGTWFAY
467	B7-H3 CDR-L1	RASQSIDYLY
468	B7-H3 CDR-L2	YASQSIG
469	B7-H3 CDR-L3	CQNGHSFPL
470	B7-H3 VH	QVQLVQSGAEVVKPGASVKLSCKTSGYTFTNYDINWVRQRPQG GLEWIGWIFPGDDSTQY

		NEKFKGKATLTTDTSTSTAYMELSSLRSEDNAVYFCARQTTGTW FAYWQGQTLVTVSS
471	B7-H3 VL	EIVMTQSPATLSVSPGERVTLSRASQSDYLYWYQQKSHESPR LLIKYASQSIGIPA RFSGSGSGSEFTLTINSVEPEDVGVYYCQNGHSFPLTFGQGTKLE LK
472	B7-H3 VH	QVQLQQSGAEVKKPGSSVKVSCASGGTFSSYAISWVRQAPGQ GLEWMGGIIPILGIAN YAQKFQGRVTITADESTSTAYMELSSLRSEDNAVYYCARGGSGS YHMDVWGKGTTVTVSS
473	B7-H3 VL	EIVLTQSPATLSLSPGERATLSRASQSVSSYLAWYQQKPGQAPR LLIYDASNRATGIP ARFSGSGSGTDFTLTISLEPEDFAVYYCQQRSNWPPRITFGQGT RLEIK
474	B7-H3 CDR- H1	IYNVH
475	B7-H3 CDR- H2	TIFPGNGDTSYNQKFKD
476	B7-H3 CDR- H3	WDDGNVGFAH
477	B7-H3 CDR- L1	RASENINNYLT
478	B7-H3 CDR- L2	HAKTLAE
479	B7-H3 CDR- L3	QHHYGTPPT
480	B7-H3 VH	QVQLQQPGAELVKPGASVKMSCKASGYTFTIYNVHWIKQTPGQ GLEWMGTIFPGNGDTSY NQKFKDKATLTTDKSKTAYMQLNSLTSEDSAVYYCARWDDG NVGFAHWGQGTTLTVSA
481	B7-H3 VL	DIQMTQSPASLSASVGETVTITCRASENINNYLTFWQQKQGKSPQ LLVYHAKTLAEGVPS RFSGSGSGTQFSLKINSLPEDFGSYQCQHHYGTPPTFGGGTKLEI K
482	B7-H3 VH	EVQLVQSGAEVKKPGASVKVSCASGYTFTIYNVHWVRQAPGQ GLEWMGTIFPGNGDTS YNQKFKDKVTMTTDTSTSTAYMELSSLRSEDNAVYYCARWDD GNVGFAHWGQGTTLTVSS
483	B7-H3 VL	DIQMTQSPSSLSASVGDRVITITCRASENINNYLTFWQQKQGKSPQ LLIYHAKTLAEGVP SRFSGSGSGTDFTLTISLQPEDFATYYCQHHYGTPPTFGGGTKV EIK
484	B7-H3 VH	EVQLVQSGAEVKKPGASVKVSCASGYTFTIYNVHWIRQAPGQ GLEWMGTIFPGNGDTSY NQKFKDRATLTTDKSTKTAYMELRSLRSDDTAVYYCARWDDG NVGFAHWGQGTTLTVSS

485	B7-H3 VL	DIQMTQSPSSLSASVGDRTITCRASENINNYLTWFQQKPGKAPK LLVYHAKTLAEGVPS RFGSGSGTQFTLTISSLQPEDFATYYCQHHYGPPTFGQGTKLEI K
486	HER3 H	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWSWIRQPPGK GLEWIGEINHSGSTNYN PSLKSRVTISVETSKNQFSLKLSSVTAADTAVYYCARDKWTWYF DLWGRGTLVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGL YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKT HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL DSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSL SLSPGK
487	HER3 L	DIEMTQSPDSLAVSLGERATINCRSSQSVLYSSSNRNYLAWYQQ NPGQPPKLLIYWASTRESGVDPDRFSGSGSGTDFTLTISSLQAEDV AVYYCQYYSTPRTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSG TASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDS TYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
488	HER3 H	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYVMAWVRQAPGK GLEWVSSISSSGGWTLY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCTRGLKMA TIFDYWGQGT LVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSG LYSLSSVVTVPSSNFGTQTYTCNV DHKPSNTKVDKTVERKCCVE CPPCPAPPVAGPSVFL FPPKPKDTLMISRTPEVTCVVDVSHEDPEVQFNWYVDGVEVH NAKTKPREEQFNSTFRV VSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREP QVYTLPPSREEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPMLDSDGSFFL YSKLTVDKSRWQQGNV FCSVMHEALHNHYTQKSLSLSPGK
489	HER3 L	QSALTQPASVSGSPGQSITISCTGTSSDVGSYNVVS WYQQHPGKA PKLIIEVSQRPSGVSNRFGSGSKSGNTASLTISGLQTEDEADYYCC SYAGSSIFVIFGGGTKVTVLGQPKAAPSVTLFPPSSEELQANKATL VCLVSDFYPGA VTVAWKADGSPVKVGVETTKPSKQSN NKYAAS SYLSLTPEQWKSHRSYSCRVTHEGSTVEKTVAPAEC S
490	HER3 H	EVQLLESGGGLVQPGGSLRLSCAASGFTFSYAMSWVRQAPGK GLEWVSAINSQGKSTYYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCARWGDEGFDIWGQGT LVTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSC DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVD

		VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP PSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP VLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQK SLSLSPGK
491	HER3 L	DIQMTQSPSSLSASVGDRVTITCRASQGISNWLAWYQQKPGKAP KLLIYGASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ YSSFPTTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
492	HER3 H	QVQLVQSGAEVKKPGASVKVSCKASGYTRSSYSISWVRQAPGQ GLEWMGWYIYAGTGPSYNQKLQGRVTMTTDTSTSTAYMELRSL RSDDTAVYYCARHRDYYSNSLTWYWGQGLTVTVSSASTKGPSVF PLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKV EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHN HYTQKSLSLSPG
493	HER3 L	DIVMTQSPDSLAVSLGERATINCKSSQSVLNSGNQKNYLTWYQQ KPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDV AVYYCQSDYSYPYTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSG TASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDS TYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
494	PTK7 CDR- H1	TSNMGVG
495	PTK7 CDR- H2	HIWWDDDKYYSPSLKS
496	PTK7 CDR- H3	SNYGYAWFAY
497	PTK7 CDR- L1	KASQDIYPYLN
498	PTK7 CDR- L2	RTNRLLD
499	PTK7 CDR- L3	LQYDEFPLT
500	PTK7 VH	QITLKESGPTLVKPTQTLTLCTFSGFSLSTSNMGVGWIRQPPGK ALEWLAHIWWDDDKYYSPSLKSRLTITKDTSKNQVLTMTNMD PVDATYYCVRSNYGYAWFAYWGQGLTVTVSS
501	PTK7 VL	DIQMTQSPSSLSASVGDRVTITCKASQDIYPYLNWFQQKPGKAP KTLIYRTNRLLDGVPS RFSGSGSGTDFTFTISSLQPEDATYYCLQYDEFPLTFGAGTKLEI K
502	PTK7 CDR- H1	DYAVH

503	PTK7 CDR-H2	VISTYNDYTYNNQDFKG
504	PTK7 CDR-H3	GNSYFYALDY
505	PTK7 CDR-L1	RASESVDSYGKSFMH
506	PTK7 CDR-L2	RASNLES
507	PTK7 CDR-L3	QQSNEPWT
508	PTK7 VH	QVQLVQSGPEVKKPGASVKVSCASGYTFTDYAVHWVRQAPG KRLEWIGVISTYNDYTY NNQDFKGRVTMTRDTSASTAYMELSRLRSEDNAVYYCARGNSY FYALDYWGQGTSTVTVSS
509	PTK7 VL	EIVLTQSPATLSLSPGERATLSCRASESVDSYGKSFMHWYQQKP GQAPRLLIYRASNLES GIPARFSGSGGTDFLTITSSLEPEDFAVYYCQQSNEDPWTFGGG TKLEIK
510	PTK7 CDR-H1	RYWMS
511	PTK7 CDR-H2	DLNPDSSAINYVDSVKG
512	PTK7 CDR-H3	ITTLVPYTMDF
513	PTK7 CDR-L1	ITNTDIDDDMN
514	PTK7 CDR-L2	EGNGLRP
515	PTK7 CDR-L3	LQSDNLPLT
516	PTK7 VH	EVQLVESGGGLVQPGGSLRLSCAASGFDPSRYWMSWVRQAPGK GLEWIGDLNPDSSAINY VDSVKGRFTISRDNKNSLYLQMNSLRAEDNAVYYCTLITLVP YTMDFWGQGTSTVTVSS
517	PTK7 VL	ETTLTQSPAFMSATPGDKVNISCITNTDIDDDMNWYQQKPGEAA ILLISEGNGLRPGIPPRFSGSGYGTDFLTINNIESEDAAYYFCLQS DNLPLTFGSGTKLEIK
518	LIV1 CDR-H1	DYYMH
519	LIV1 CDR-H2	WIDPENGDEYGPKEQG
520	LIV1 CDR-H3	HNAHYGTWFAY
521	LIV1 CDR-L1	RSSQSLLHSSGNTYLE
522	LIV1 CDR-L2	KISTRFS

523	LIV1 CDR-L3	FQGSHPYPT
524	LIV1 VH	QVQLVQSGAEVKKPGASVKVSCASGLTIEDYYMHWVRQAPG QGLEWMGWIDPENGDT GPKFQGRVTMTRDTSINTAYMELSRLSDDTAVYYCAVHNAHY GTWFAYWGQGTLLTVSS
525	LIV1 VL	DVVMTQSPSLPVTLGQPASISCRSSQSLLHSSGNTYLEWYQQR GQSPRPLIYKISTRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVY YCFQGSHPYPTFGGGTKVEIK
526	avb6 CDR-H1	DYNVN
527	avb6 CDR-H2	VINPKYGTTRYNQKFKG
528	avb6 CDR-H3	GLNAWDY
529	avb6 CDR-L1	GASENIYGALN
530	avb6 CDR-L2	GATNLED
531	avb6 CDR-L3	QNVLTTPYT
532	avb6 VH	QFQLVQSGAEVKKPGASVKVSCASGYSFTDYNVNWVRQAPG QGLEWIGVINPKYGTTRY NQKFKGRATLTVDKSTSTAYMELSSLRSEDVAVYYCTRGLNAW DYWGQGTLLTVSS
533	avb6 VL	DIQMTQSPSSLSASVGRVTITCGASENIYGALNWWYQKPGKAP KLLIYGATNLEDGVP RFSGSGSGRDYFTISSLPEDIATYYCQNVLTTPYTFGQGTKLEIK
534	avb6 CDR-H1	GYFMN
535	avb6 CDR-H2	LINPYNGDSFYNQKFKG
536	avb6 CDR-H3	GLRRDFDY
537	avb6 CDR-L1	KSSQSLLSDGKTYLN
538	avb6 CDR-L2	LVSELD
539	avb6 CDR-L3	WQGTHFPRT
540	avb6 VH	QVQLVQSGAEVKKPGASVKVSCASGYSFSGYFMNWVRQAPG QGLEWMGLINPYNGDSFY NQKFKGRVTMTRQTSTSTVYMELSSLRSEDVAVYYCVRGLRRD FDYWGQGTLLTVSS
541	avb6 VL	DVVMTQSPSLPVTLGQPASISCKSSQSLLSDGKTYLNWLFQRP GQSPRRLIYLVSELD

		SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCWQGTHFPRTFG GGTKLEIK
542	CD48 CDR- H1	DFGMN
543	CD48 CDR- H2	WINTFTGEPsyGNVFKG
544	CD48 CDR- H3	RHGNGNVFDS
545	CD48 CDR- L1	RASQSIGSNIH
546	CD48 CDR- L2	YTSESIS
547	CD48 CDR- L3	QQSNSWPLT
548	CD48 VH	QVQLVQSGSELKKPGASVKVSCASGYTFTDFGMNWVRQAPG QGLEWMGWINTFTGEPsyGNVFKGRFVFSLDTSVSTAYLQISSL KAEDTAVYYCARRHGNGNVFDSWGQGTLTVSS
549	CD48 VL	EIVLTQSPDFQSVTPKEKVITCRASQSIGSNIHWYQQKPDQSPKL LIKYTSESISGVPSRFSGSGSGTDFTLTINSLEAEDAATYYCQQSN SWPLTFGGGTKVEIKR
550	PD-L1 CDR- H1	TAAIS
551	PD-L1 CDR- H2	GIPIFGKAHYAQKFQG
552	PD-L1 CDR- H3	KHFVSGSPFGMDV
553	PD-L1 CDR- L1	RASQSVSSYLA
554	PD-L1 CDR- L2	DASNRAT
555	PD-L1 CDR- L3	QQRSNWPT
556	PD-L1 VH	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKHFVSGSPFGMDVWGQGTTTVTVSS
557	PD-L1 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPR LLIYDASNRATGIPARFSGSGSGTDFTLTISLEPEDFAVYYCQQR SNWPTFGQGTKVEIK
558	IGF-1R CDR-H1	SYAIS
559	IGF-1R CDR-H2	GIPIFGTANYAQKFQG
560	IGF-1R CDR-H3	APLRFLEWSTQDHYYYYYMDV
561	IGF-1R CDR-L1	QGDSLRSYYAT

562	IGF-1R CDR-L2	GENKRPS
563	IGF-1R CDR-L3	KSRDGSQGHLV
564	IGF-1R VH	EVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQ GLEWMGGIPIFGTANY AQKFQGRVTITADKSTSTAYMELSSLRSEDVAVYYCARAPLRFL EWSTQDHYYYYYMDVWGKGTITVTVSS
565	IGF-1R VL	SSELTQDPAVSVALGQTVRITCQGDSLRSYYATWYQQKPGQAPI LVIYGENKRPSGIPDR FSGSSSGNTASLTITGAQAEDADYYCKSRDGSQGHLVFGGGTK LTVL
566	Claudin-18.2 CDR-H1	SYWIN
567	Claudin-18.2 CDR-H2	NIYPSDSYTNYNQKFKD
568	Claudin-18.2 CDR-H3	SWRGNSFDY
569	Claudin-18.2 CDR-L1	KSSQSLLNSGNQKNYLT
570	Claudin-18.2 CDR-L2	WASTRES
571	Claudin-18.2 CDR-L3	QNDYSYPFT
572	Claudin-18.2 VH	QVQLQQPGAELVRPGASVKLSCKASGYTFTSYWINWVKQRPGQ GLEWIGNIYPSDSYTN YNQKFKDKATLTVDKSSSTAYMQLSSPTSEDSAVYYCTRSWRG NSFDYWGQGTTTLTVSS
573	Claudin-18.2 VL	DIVMTQSPSSLTVTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQ QKPGQPPKLLIYWASTR ESGVPDRFTGSGSGTDFLTISVQAEDLAVYYCQNDYSYPFTFG SGTKLEIK
574	Claudin-18.2 CDR-H1	NYGMN
575	Claudin-18.2 CDR-H2	WINTNTGEPTYAEEFKG
576	Claudin-18.2 CDR-H3	LGFGNAMDY
577	Claudin-18.2 CDR-L1	KSSQSLLNSGNQKNYLT
578	Claudin-18.2 CDR-L2	WASTRES
579	Claudin-18.2 CDR-L3	QNDYSYPLT
580	Claudin-18.2 VH	QIQLVQSGPELKKPGETVKISCKASGYTFTNYGMNWVKQAPGK GLKWMGWINTNTGEPTY

		AEEFKGRFAFSLETSASTAYLQINNLNKNE DTATYFCARLGFGNA MDYWGQGTSTVTVSS
581	Claudin-18.2 VL	DIVMTQSPSSLT VTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQ QKPGQPPKLLIYWASTR ESGVPDRFTGSGSGTDFTLTISSVQAEDLAVYYCQNDYSYPLTFG AGTKLELK
582	Nectin-4 CDR-H1	SYNMN
583	Nectin-4 CDR-H2	YISSSSSTIYYADSVKG
584	Nectin-4 CDR-H3	AYYYGMDV
585	Nectin-4 CDR-L1	RASQGISGWL A
586	Nectin-4 CDR-L2	AASTLQS
587	Nectin-4 CDR-L3	QQANSFPPT
588	Nectin-4 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYNMNWVRQAPGK GLEWVSYISSSSSTIYY ADSVKGRFTISRDN AKNSLSLQMNSLRDEDTAVYYCARAYYYG MDVWGQGTTVTVSS
589	Nectin-4 VL	DIQMTQSPSSVSASVGDRTITCRASQGISGWLAWYQQKPGKAP KFLIYAASTLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQANSFPPTFGGGTKVEI K
590	SLTRK6 CDR-H1	SYGMH
591	SLTRK6 CDR-H2	VIWYDGSNQYYADSVKG
592	SLTRK6 CDR-H3	GLTSGRYGMDV
593	SLTRK6 CDR-L1	RSSQSLLLSHGFNYLD
594	SLTRK6 CDR-L2	LGSSRAS
595	SLTRK6 CDR-L3	MQPLQIPWT
596	SLTRK6 VH	QVQLVESGGGVVQPGRSRLSCAASGFTFSSYGMHWVRQAPGK GLEWVAVIWYDGSNQYY ADSVKGRFTISRDN SKNTLFLQMHSRAEDTAVYYCARGLTSGR YGMDVWGQGTTVTVSS
597	SLTRK6 VL	DIVMTQSPLSLPVT PGEPASISCRSSQSLLLSHGFNYLDWYLQKP GQSPQLLIYLGSSRASGVPDRFSGSGSGTDFTLKISRVEAEDVGL YYCMQPLQIPWTFGQG TKVEIK
598	CD228 CDR-H1	SGYWN

599	CD228 CDR-H2	YISDSGITYYNPSLKS
600	CD228 CDR-H3	RTLATYYAMDY
601	CD228 CDR-L1	RASQSLVHSDGNTYLH
602	CD228 CDR-L2	RVSNRFS
603	CD228 CDR-L3	SQSTHVPPT
604	CD228 VH	QVQLQESGPGLVKPSSETLSLTCTVSGDSITSGYWNWIRQPPGKGL EYIGYISDSGITYYN PSLKSRVTISRDTSKNQYSLKLSSVTAADTAVYYCARRTLATYY AMDYWGQGTLVTVSS
605	CD228 VL	DFVMTQSPLSLPVTLGQPASISCRASQSLVHSDGNTYLHWYQQR PGQSPRLLIYRVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCSQSTHVPPTFGQGTKLEIKR
606	CD142 (TF) CDR-H1	NYAMS
607	CD142 (TF) CDR-H2	SISGSGDYTYTDSVKG
608	CD142 (TF) CDR-H3	SPWGYYLDS
609	CD142 (TF) CDR-L1	RASQGISSRLA
610	CD142 (TF) CDR-L2	AASSLQS
611	CD142 (TF) CDR-L3	QQYNSYPYT
612	CD142 (TF) VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSNYAMSWVRQAPGK GLEWVSSISGSGDYTY YTDSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCARSPWG YYLDSWGQGTLVTVSS
613	CD142 (TF) VL	DIQMTQSPPSLASAGDRVITITCRASQGISSRLAWYQQKPEKAPK SLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSYPYTFGQGTKLEI K
614	STn CDR- H1	DHAIH
615	STn CDR- H2	YFSPGNDDIKYNEKFRG
616	STn CDR- H3	SLSTPY
617	STn CDR-L1	KSSQSLLNRGNHKNYLT
618	STn CDR-L2	WASTRES
619	STn CDR-L3	QNDYTYPYT

620	STn VH	EVQLVQSGAEVKKPGASVKVSCKASGYTFTDHAHWVRQAPGQ GLEWMGYFSPGNDDIKY NEKFRGRVTMTADKSSSTAYMELRSLRSDDTAVYFCKRSLSTPY WGQGTLLTVSS
621	STn VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNRGNHKNYLTWYQQ KPGQPPKLLIYWAST RESGVDPDRFSGSGSGTDFTLTISLQAEDVAVYYCQNDYTYPYTF GQGTKVEIK
622	CD20 CDR-H1	SYNMH
623	CD20 CDR-H2	AIYPGNGDTSYNQKFKG
624	CD20 CDR-H3	STYYGGDWYFNV
625	CD20 CDR-L1	RASSSVSYIH
626	CD20 CDR-L2	ATSNLAS
627	CD20 CDR-L3	QQWTSNPPT
628	CD20 VH	QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPG RGLIEWIGAIYPGNGDTSY NQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYG GDWYFNVWGAGTTVTVSA
629	CD20 VL	QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWVQQKPGSSPKP WIYATSNLASGVPVR FSGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEI K
630	HER2 CDR-H1	DTYIH
631	HER2 CDR-H2	RIYPTNGYTRYADSVKG
632	HER2 CDR-H3	WGGDGFYAMDY
633	HER2 CDR-L1	RASQDVNTAVA
634	HER2 CDR-L2	SASFLYS
635	HER2 CDR-L3	QQHYTTPPT
636	HER2 VH	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKG LEWVARIYPTNGYTRY ADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDG FYAMDYWGQGTLLTVSS
637	HER2 VL	DIQMTQSPSSLSASVGDRTITCRASQDVNTAVAWYQQKPGKAP KLLIYSASFLYSGVPS

		RFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGKTKVEIK
638	CD79b CDR-H1	SYWIE
639	CD79b CDR-H2	EILPGGGDTNYNEIFKG
640	CD79b CDR-H3	RVPIRLDY
641	CD79b CDR-L1	KASQSVDYEGDSFLN
642	CD79b CDR-L2	AASNLES
643	CD79b CDR-L3	QQSNEDPLT
644	CD79b VH	EVQLVESGGGLVQPGGSLRLSCAASGYTFSSYWIEWVRQAPGK GLEWIGEILPGGGDTNYNEIFKGRATFSADTSKNTAYLQMNSLR AEDTAVYYCTRRVPIRLDYWGQGTLVTVSS
645	CD79b VL	DIQLTQSPSSLSASVGDRVTITCKASQSVDYEGDSFLNWKYQQKP GKAPKLLIYAASNLES GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPLTFGQGT KVEIK
646	NaPi2B CDR-H1	DFAMS
647	NaPi2B CDR-H2	TIGRVAFTHTYYPDSMKG
648	NaPi2B CDR-H3	HRGFDVGHFDF
649	NaPi2B CDR-L1	RSSETLVHSSGNTYLE
650	NaPi2B CDR-L2	RVSNRFS
651	NaPi2B CDR-L3	FQGSFNPLT
652	NaPi2B VH	EVQLVESGGGLVQPGGSLRLSCAASGFSFSDFAMSWVRQAPGK GLEWVATIGRVAFTHTYY PDSMKGRFTISRDNSTNTLYLQMNSLRAEDTAVYYCARHRGFD VGHFDFWGQGTLVTVSS
653	NaPi2B VL	DIQMTQSPSSLSASVGDRVTITCRSSETLVHSSGNTYLEWYQQKP GKAPKLLIYRVSNRF SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCFQGSFNPLTFGQG TKVEIK
654	Muc16 CDR-H1	NDYAWN
655	Muc16 CDR-H2	YISYSGYTTYNPSLKS
656	Muc16 CDR-H3	WTSGLDY

657	Muc16 CDR-L1	KASDLIHNWLA
658	Muc16 CDR-L2	GATSLET
659	Muc16 CDR-L3	QQYWTTTPFT
660	Muc16 VH	EVQLVESGGGLVQPGGSLRLSCAASGYSITNDYAWN WVRQAPG KGLEWVGYISYSGYTTY NPSLKS RFTISRDT SKNTLYLQMNSLRAEDTAVYYCAR WTSGLD YWGQGT LTVSS
661	Muc16 VL	DIQMTQSPSSLSASVGDRVTITCKASDLIHNWLAWYQQKPGKAP KLLIYGATSLETGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQ YWTTPTFGQGTKVEIK
662	STEAP1 CDR-H1	SDYAWN
663	STEAP1 CDR-H2	YISNSGSTSYNPSLKS
664	STEAP1 CDR-H3	ERNYDYDDYYYAMDY
665	STEAP1 CDR-L1	KSSQSLLYRSNQKNYLA
666	STEAP1 CDR-L2	WASTRES
667	STEAP1 CDR-L3	QQYYNYPRT
668	STEAP1 VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWN WVRQAPG KGLEWVGYISNSGSTSYNPSLKS RFTISRDT SKNTLYLQMNSLRA EDTAVYYCARERNYDYDDYYYAMDYWGQGT LTVSS
669	STEAP1 VL	DIQMTQSPSSLSASVGDRVTITCKSSQSLLYRSNQKNYLAWYQQ KPGKAPKLLIYWASTRESGVPSRFSGSGSGTDFTLTISLQPEDFA TYYCQQYYNYPRTFGQGTKVEIK
670	BCMA CDR-H1	NYWMH
671	BCMA CDR-H2	ATYRGHSDTYYNQKFKG
672	BCMA CDR-H3	GAIYDGYDVLDN
673	BCMA CDR-L1	SASQDISNYLN
674	BCMA CDR-L2	YTSNLHS
675	BCMA CDR-L3	QQYRKLPWT
676	BCMA VH	QVQLVQSGAEVKKPGSSVKVSCASGGTFSNYWMHWVRQAPG QGLEWMGATYRGHSDTYYNQKFKGRVTITADKSTSTAYMELSS LRSED TAVYYCARGAIYDGYDVLDN WGQGT LTVSS

677	BCMA VL	DIQMTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQKPGKAP KLLIYYTSNLHSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ YRKLPWTFGQGTKLEIK
678	c-Met CDR- H1	AYTMH
679	c-Met CDR- H2	WIKPNNGLANYAQKFQG
680	c-Met CDR- H3	SEITTEFDY
681	c-Met CDR- L1	KSSESVDSYANSFLH
682	c-Met CDR- L2	RASTRES
683	c-Met CDR- L3	QQSKEDPLT
684	c-Met VH	QVQLVQSGAEVKKPGASVKVSKASGYIFTAYTMHWVRQAPG QGLEWMGWIKPNNGLAN Y AQKFQGRVTMTRDTSISTAYMELSRRLSDDTAVYYCARSEITT EFDYWGQGTLLTVSS
685	c-Met VL	DIVMTQSPDSLAVSLGERATINCKSSESVDSYANSFLHWYQQKP GQPPKLLIYRASTRE SGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQSKEDPLTFGG GTKVEIK
686	EGFR CDR- H1	SDFAWN
687	EGFR CDR- H2	YISYSGNTRYQPSLKS
688	EGFR CDR- H3	AGRGFPY
689	EGFR CDR- L1	HSSQDINSNIG
690	EGFR CDR- L2	HGTNLDD
691	EGFR CDR- L3	VQYAQFPWT
692	EGFR VH	QVQLQESGPGLVKPSQTLSTCTVSGYISSDFAWNWIRQPPGKG LEWMGYISYSGNTRY QPSLKSRTISRDTSKNQFFLKLNSVTAADTATYYCVTAGRGFPY WGQGTLLTVSS
693	EGFR VL	DIQMTQSPSSMSVSVGDRVTITCHSSQDINSNIGWLQQKPGKSFK GLIYHGTNLDDGVPS RFSGSGSGTDYTLTISSLQPEDFATYYCVQYAQFPWTFGGGTKLE IK
694	SLAMF7 CDR-H1	DYYMA
695	SLAMF7 CDR-H2	SINYDGSSTYYVDSVKG

696	SLAMF7 CDR-H3	DRGYFDY
697	SLAMF7 CDR-L1	RSSQSLVHSNGNTYLH
698	SLAMF7 CDR-L2	KVSNRFS
699	SLAMF7 CDR-L3	SQSTHVPPFT
700	SLAMF7 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMAWVRQAPGK GLEWVASINYDGSSTY YVDSVKGRFTISRDNANKNSLYLQMNSLRAEDTAVYYCARDRGY YFDYWGQGTTVTVSS
701	SLAMF7 VL	DVVMTQTPLSLSVTPGQPASISCRSSQSLVHSNGNTYLHWYLQK PGQSPQLLIYKVSNR SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPPFTFG GGTKVEIK
702	SLITRK6 CDR-H1	SYGMH
703	SLITRK6 CDR-H2	VIWYDGSNQYYADSVKG
704	SLITRK6 CDR-H3	GLTSGRYGMDV
705	SLITRK6 CDR-L1	RSSQSLLLSHGFNYLD
706	SLITRK6 CDR-L2	LGSSRAS
707	SLITRK6 CDR-L3	MQPLQIPWT
708	SLITRK6 VH	QVQLVESGGGVVQGRSLRLSCAASGFTFSSYGMHWVRQAPGK GLEWVAWIWYDGSNQYY ADSVKGRFTISRDNANKNTLFLQMNSLRAEDTAVYYCARGLTSGR YGMDVWGQGTTVTVSS
709	SLITRK6 VL	DIVMTQSPLSLPVTPGEPASISCRSSQSLLLSHGFNYLDWYLQKP GQSPQLLIYLGSSRA SGVPDRFSGSGSGTDFTLKISRVEAEDVGLYYCMQPLQIPWTFG QGTKVEIK
710	C4.4a CDR- H1	NAWMS
711	C4.4a CDR- H2	YISSSGSTIYYADSVKG
712	C4.4a CDR- H3	EGLWAFDY
713	C4.4a CDR- L1	TGSSSNIGAGYVVH
714	C4.4a CDR- L2	DNNKRPS

715	C4.4a CDR-L3	AAWDDRLNGPV
716	C4.4a VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSNAWMSWVRQAPGK GLEWVSYISSSGSTIYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAREGLWA FDYWGQGTLVTVSS
717	C4.4a VL	ESVLTQPPSVSGAPGQRVTISCTGSSSNIGAGYVVHWYQQLPGT APKLLIYDNNKRPSGV PDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDDRLNGPVFVG GTKLTVL
718	GCC CDR-H1	GYYS
719	GCC CDR-H2	EINHRGNTNDNPSLKS
720	GCC CDR-H3	ERGYTYGNFDH
721	GCC CDR-L1	RASQSVSRNLA
722	GCC CDR-L2	GASTRAT
723	GCC CDR-L3	QQYKTWPRT
724	GCC VH	QVQLQQWGAGLLKPSETLSLTCVFGGSFSGYYWSWIRQPPGK GLEWIGEINHRGNTNDN PSLKSRTISVDTSKNQFALKLSSVTAADTAVYYCARERGYTYG NFDHWGQGT LTVSS
725	GCC VL	EIVMTQSPATLSVSPGERATLSCRASQSVSRNLAWYQQKPGQAP RLLIYGASTRATGIP ARFSGSGSGTEFTLTIGSLQSEDFAVYYCQQYKTWPRTFGQGTN VEIK
726	AxI CDR-H1	SYAMN
727	AxI CDR-H2	TTSGSGASTYYADSVKG
728	AxI CDR-H3	IWIAFDI
729	AxI CDR-L1	RASQSVSSSYLA
730	AxI CDR-L2	GASSRAT
731	AxI CDR-L3	QQYGSSPYT
732	AxI VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSYAMNWVRQAPGK GLEWVSTTSGSGASTYY ADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKIWIAFD IWGQGTMTVTVSS
733	AxI VL	EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWYQQKPGQAP RLLIYGASSRATGIP DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPYTFGQGTKL EIK
734	gpNMB CDR-H1	SFNYYWS

735	gpNMB CDR-H2	YIYYSGSTYSNPSLKS
736	gpNMB CDR-H3	GYNWNYFDY
737	gpNMB CDR-L1	RASQSVDNNLV
738	gpNMB CDR-L2	GASTRAT
739	gpNMB CDR-L3	QQYNNWPPWT
740	gpNMB VH	QVQLQESGPGLVKPSQTLSTCTVSGGSISSEFNYYWSWIRHHPGK GLEWIGYIYYSGSTY SNPSLKS RVTISVDTSKNQFSLTLSSVTAADTAVYYCARGYNWN YFDYWGGQGLTVTVSS
741	gpNMB VL	EIVMTQSPATLSVSPGERATLSCRASQSVDNNLVWYQQKPGQAP RLLIYGASTRATGIPA RFGSGSGTEFTLTISSLQSEDFAVYYCQQYNNWPPWTFGQGTEK VEIK
742	Prolactin receptor CDR-H1	TYWMH
743	Prolactin receptor CDR-H2	EIDPSDSYSNQNQKFKD
744	Prolactin receptor CDR-H3	NGGLGPAWFSY
745	Prolactin receptor CDR-L1	KASQYVGTAVA
746	Prolactin receptor CDR-L2	SASNRYT
747	Prolactin receptor CDR-L3	QQYSSYPWT
748	Prolactin receptor VH	EVQLVQSGAEVKKPGSSVKVSCKASGYTFTTYWMHWVRQAPG QGLEWIGEIDPSDSYSNY NQKFKDRATLTVDKSTSTAYMELSSLRSED TAVYYCARNGLG PAWFSYWGQGLTVTVSS
749	Prolactin receptor VL	DIQMTQSPSSVSASVGDRVTITCKASQYVGTAVAWYQQKPGKSP KLLIYSASNRYTGVP SFSDSGSGTDFTLTISSLQPEDFATYFCQQYSSYPWTFGGGTEK K
750	FGFR2 CDR-H1	SYAMS

751	FGFR2 CDR-H2	AISGSGTSTYYADSVKG
752	FGFR2 CDR-H3	VRYNWNHGDWFD
753	FGFR2 CDR-L1	SGSSSNIGNNYVS
754	FGFR2 CDR-L2	ENYNRPA
755	FGFR2 CDR-L3	SSWDDSLNYWV
756	FGFR2 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK GLEWVSAISGSGTSTYYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCARVRYNWNHGDWFD PWGQGT LVT VSS
757	FGFR2 VL	QSVLTQPPSASGTPGQRTISCSGSSSNIGNNYVSWYQQLPGTAP KLLIYENYNRPAGVP DRFSGSKSGTSASLAISGLRSEDEADYYCSSWDDSLNYWVFGGG TKLTVL
758	CDCP1 CDR-H1	SYGMS
759	CDCP1 CDR-H2	TISSGGSYKYYVDSVKG
760	CDCP1 CDR-H3	HPDYDGVWFAY
761	CDCP1 CDR-L1	SVSSSVFYVH
762	CDCP1 CDR-L2	DTSKLAS
763	CDCP1 CDR-L3	QQWNSNPPT
764	CDCP1 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFNSYGMWSVRQAPGK GLEWVATISSGGSYKYY VDSVKGRFTISRDN AKNSLYLQMNSLRAEDTAVYYCARHPDYD GVWFAYWGQGT LVT VSS
765	CDCP1 VL	DIQMTQSPSSLSASVGDRVTITCSVSSSVFYVHWYQQKPGKAPK LLIYDTSKLASSGVPS RFSGSGSGTDFTFTISSLPEDIAITYYCQQWNSNPPTFGGGTKVEI K
766	CDCP1 CDR-H1	SYGMS
767	CDCP1 CDR-H2	TISSGGSYTYYPDSVKG
768	CDCP1 CDR-H3	HPDYDGVWFAY
769	CDCP1 CDR-L1	SVSSSVFYVH
770	CDCP1 CDR-L2	DTSKLAS

771	CDCP1 CDR-L3	QQWNSNPPT
772	CDCP1 VH	EVQLVESGGDLVKPGGSLKLSAASGFTFNSYGMSWVRQTPDK RLEWVATISSGGSYTTY PDSVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHPDYD GVWFAYWGQGLTVTVSA
773	CDCP1 VL	QIVLTQSPAIMASPGKVTMTCSVSSSVFYVHWYQQKSGTSPKR WIYDTSKLASGVPARF SGSGSGTSYSLTISSMEAEDAATYYCQQWNSNPPTFGGGTKLEIK
774	CDCP1 CDR-H1	SYMH
775	CDCP1 CDR-H2	IINPSGGSTSYAQKFQG
776	CDCP1 CDR-H3	DGVLRIFYDWLLDYHYY
777	CDCP1 CDR-L1	RASQSVGSYLA
778	CDCP1 CDR-L2	DASNRAT
779	CDCP1 CDR-L3	QQRANVFT
780	CDCP1 VH	EVQLVQSGAEVKKPGASVKVSCASGYTFTSYMHVVRQAPG QGLEWMGIINPSGGSTSY AQKFQGRVTMTTRDTSTSTVYMESSLRSEDTAVYYCARDGVLR YFDWLLDYHYYMDVWGKG TTVTVSS
781	CDCP1 VL	EIVLTQSPATLSLSPGERATLSCRASQSVGSYLAWYQQRPGQAPR LLIYDASNRATGIPA RFSGSGSGTDFTLTISLEPEDFAVYYCQQRANVFTFGGQGTKVEI K
782	CDCP1 CDR-H1	SYMH
783	CDCP1 CDR-H2	IINPSGGSTSYAQKFQG
784	CDCP1 CDR-H3	DAELRHFDHLLDYHYYMDV
785	CDCP1 CDR-L1	RASQSVGSYLA
786	CDCP1 CDR-L2	DASNRAT
787	CDCP1 CDR-L3	QQRAQEFT
788	CDCP1 VH	EVQLVQSGAEVKKPGASVKVSCASGYTFTSYMHVVRQAPG QGLEWMGIINPSGGSTSYAQKFQGRVTMTTRDTSTSTVYMESSL RSEDTAVYYCARDAELRHFDHLLDYHYYMDVWGQGTITVTVSS
789	CDCP1 VL	EIVMTQSPATLSLSPGERATLSCRASQSVGSYLAWYQQKPGQAP RLIYDASNRATGIPA

		RFSGSGSGTDFTLTISLQPEDFAVYYCQQRAQEFTFGQGTKVEIK
790	ASCT2 VH	QVQLVQSGSELKKPGAPVKVSKASGYTFSTFGMSWVRQAPGQGLKWMGWIHTYAGVPIYGDDFKGRFVFSLDTSVSTAYLQISSLK AEDTAVYFCARRSDNYRYFFDYWGQGTTVTVSS
791	ASCT2 VL	DIQMTQSPSSLSASLGDRVTITCRASQDIRNYLNWYQQKPGKAP KLLIYYTSRLHSGVPSRFSGSGSGTDYTLTISLQPEDFATYFCQQGHTLPPTFGQGTKLEIK
792	ASCT2 VH	QIQLVQSGPELKKPGAPVKISCKASGYTFTTFGMSWVKQAPGQG LKWMGWIHTYAGVPIYGDDFKGRFVFSLDTSVSTAYLQISSVKA EDTATYFCARRSDNYRYFFDYWGQGTTTLTVSS
793	ASCT2 VL	DIQMTQSPSSLSASLGDRVTITCRASQDIRNYLNWYQQKPGKAP KLLIYYTSRLHSGVPS RFSGSGSGTDYTLTISLQPEDFATYFCQQGHTLPPTFGQGTKLEIK
794	ASCT2 CDR-H1	NYYYMA
795	ASCT2 CDR-H2	SITKGGGNTYYRDSVKG
796	ASCT2 CDR-H3	QVTIAAVSTSYFDS
797	ASCT2 CDR-L1	KTNQKVDYYGNSYVY
798	ASCT2 CDR-L2	LASNLAS
799	ASCT2 CDR-L3	QQSRNLPYT
800	ASCT2 VH	EVQLVESGGGLVQSGRSIRLSCAASGFSFSNYMAWVRQAPSKG LEWVASITKGGGNTYYRDSVKGRFTFSRDNAKSTLYLQMDSLRS EDTATYYCARQVTIAAVSTSYFDSWGQGVMVTVSS
801	ASCT2 VL	DIVLTQSPALAVSLGQRATISCKTNQKVDYYGNSYVYVYQQKP GQQPKLLIYLASNLASGIPARFSGRSGTDFTLTIDPVEADDTAT YYCQQSRNLPYTFGAGTKLELK
802	CD123 CDR-H1	DYYMK
803	CD123 CDR-H2	DIIPSNGATFYNQKFKG
804	CD123 CDR-H3	SHLLRASWFAY
805	CD123 CDR-L1	KSSQSLLNSGNQKNYLT
806	CD123 CDR-L2	WASTRES
807	CD123 CDR-L3	QNDYSYPYT

808	CD123 VH	QVQLVQSGAEVKKPGASVKMSCKASGYTFTDYMKWVKQAP GQGLEWIGDIIPSNNGATFYNQKFKGKATLTVDRSISTAYMHLNR LRSDDTAVYYCTRSHLLRASWFAYWGQGTLLTVSS
809	CD123 VL	DFVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLTWYLQ KPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISLQAEDV AVYYCQNDYSYPYTFGQGTKLEIK
810	GPC3 CDR- H1	DYEMH
811	GPC3 CDR- H2	WIGGIDPETGGTAYNQKFKG
812	GPC3 CDR- H3	YYSFAY
813	GPC3 CDR- L1	RSSQSIVHSNGNTYLQ
814	GPC3 CDR- L2	KVSNRFS
815	GPC3 CDR- L3	FQVSHVPYT
816	GPC3 VH	EVQLVQSGAEVKKPGATVKISCKVSGYTFTDYEMHWVQQAPG KGLEWMGGIDPETGGTAYNQKFKGRVTLTADKSTDTAYMELSS LRSEDTAVYYCGRYYSFAYWGQGTLLTVSS
817	GPC3 VL	DVVMTQSPSLPVTLGQPASISCRSSQSIVHSNANTYLQWFQQR GQSPRLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGV YYCFQVSHVPYTFGQGTKLEIK
818	B6A CDR- H1	DYNVN
819	B6A CDR- H2	VINPKYGTTRYNQKFKG
820	B6A CDR- H3	GLNAWDY
821	B6A CDR- L1	GASENIYGALN
822	B6A CDR- L2	GATNLED
823	B6A CDR- L3	QNVLTTPYT
824	B6A VH	QFQLVQSGAEVKKPGASVKVSCASGYSFTDYNVNWVRQAPG QGLEWIGVINPKYGTTRYNQKFKGRATLTVDKSTSTAYMELSSL RSEDTAVYYCTRGLNAWDYWGQGTLLTVSS
825	B6A VL	DIQMTQSPSSLSASVGDRVTITCGASENIYGALNHWYQQKPGKAP KLLIYGATNLEDGVPSRFSGSGSGRDYFTFTISLQPEDIATYYCQN VLTTPYTFGQGTKLEIK
826	B6A CDR- H1	GYFMN
827	B6A CDR- H2	linpyngdsfynqkfk

828	B6A CDR-H3	glrrdfdy
829	B6A CDR-L1	kssqslldsdgktyln
830	B6A CDR-L2	lvselds
831	B6A CDR-L3	wqgthfprt
832	B6A VH	QVQLVQSGAEVKKPGASVKVSCKASGYSFSGYFMNWVRQAPG QGLEWMGLINPYNGDSFYNQKFKGRVTMTRQTSTSTVYMELSS LRSEDTAVYYCVRGLRRDFDYWGQGTLLTVSS
833	B6A VL	DVVMTQSPSLPVTLGQPASISCKSSQSLLSDGKTYLNWLFQRP GQSPRRLIYLVSELDGVPDRFSGSGSGTDFTLKISRVEAEDVGV YYCWQGTHFPRTFGGGTKLEIK
834	PD-L1 CDR-H1	TAAIS
835	PD-L1 CDR-H2	GIPIFGKAHYAQKFQG
836	PD-L1 CDR-H3	KFHVSGSPFGMDV
837	PD-L1 CDR-L1	RASQSVSSYLA
838	PD-L1 CDR-L2	DASNRAT
839	PD-L1 CDR-L3	QQRSNWPT
840	PD-L1 VH	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKFHVSGSPFGMDVWGQGTLLTVSS
841	PD-L1 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPR LLIYDASNRATGIPARFSGSGSGTDFTLTSSLEPEDFAVYYCQQR SNWPTFGQGTKVEIK
842	TIGIT CDR-H1	GTFSSY AIS
843	TIGIT CDR-H2	SIPIFGTANYAQKFQG
844	TIGIT CDR-H3	ARGPSEVGAILGYVWFDP
845	TIGIT CDR-L1	RSSQSLLHSNGYNYLD
846	TIGIT CDR-L2	LGSNRAS
847	TIGIT CDR-L3	MQARRIPIT
848	TIGIT VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSY AISWVRQAPGQ GLEWMGSIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYYCARGPSEVGAILGYVWFDPWGQGTLLTVSS

849	TIGIT VL	DIVMTQSPSLPVPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKP GQSPQLLIYLGSNRASGVDPDRFSGSGSGTDFTLKISRVEAEDVGV YYCMQARRIPITFGGGTKVEIK
850	STN CDR- H1	GYTFTDHAIHWV
851	STN CDR- H2	FSPGNDDIKY
852	STN CDR- H3	KRSLSTPY
853	STN CDR- L1	QSLNLRGNHKNY
854	STN CDR- L2	WASTRES
855	STN CDR- L3	QNDYTYPYT
856	STN VH	EVQLVQSGAEVKKPGASVKVSCKASGYTFTDHAIHWVRQAPGQ GLEWMGYFSPGNDDIKYNEKFRGRVTMTADKSSSTAYMELRSL RSDDTAVYFCRSLSTPYWGQGLVTVSS
857	STN VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNRGNHKNYLTWYQQ KPGQPPKLLIYWASTRESGVDPDRFSGSGSGTDFTLTISSLQAEDV AVYYCQNDYTYPYTFGQGTKVEIK
858	CD33 CDR- H1	NYDIN
859	CD33 CDR- H2	WIYPGDGSTKYNEKFKA
860	CD33 CDR- H3	GYEDAMDY
861	CD33 CDR- L1	KASQDINSYLS
862	CD33 CDR- L2	RANRLVD
863	CD33 CDR- L3	LQYDEFPLT
864	CD33 VH	QVQLVQSGAE VKKPGASVKV SCKASGYTFT NYDINWVRQA PGQGLEWIGW IYPGDGSTKY NEKFKAATL TADTSTSTAY MELRSLRSDD TAVYYCASGY EDAMDYWGQG TTVTVSS
865	CD33 VL	DIQMTQSPS SLSASVGDRT INCKASQDINSYLSWFQQKPGKAPKTL IYRANRLVDGVPS RFSGSGSGQDYTLT ISSLPEDFATYYCLQYDEFPLTFGGGTKVE
866	NTBA CDR- H1	NYGMN
867	NTBA CDR- H2	WINTYSGEPRYADDFKG
868	NTBA CDR- H3	DYGRWYFDV
869	NTBA CDR- L1	RASSSVSHMH

870	NTBA CDR-L2	ATSNLAS
871	NTBA CDR-L3	QQWSSTPRT
872	NTBA VH	QIQLVQSGSELKKPGASVKVSCKASGYTFTNYGMNWVRQAPGQ DLKWMGWINTYSGEPRYADDFKGRFVFSLDKSVNTAYLQISSL KAEDTAVYYCARDYGRWYFDVWGQGTTVTVSS
873	NTBA VL	QIVLSQSPATLSLSPGERATMSCRASSSVSHMHWYQQKPGQAPR PWIYATSNLASGVPARFSGSGSGTDYTLTISSLEPEDFAVYYCQQ WSSTPRTFGGGTKVEIK
874	BCMA CDR-H1	DYYIH
875	BCMA CDR-H2	YINPNSGYTNYAQKFQG
876	BCMA CDR-H3	YMWERTGFFDF
877	BCMA CDR-L1	LASEDISDDLA
878	BCMA CDR-L2	TTSSLQS
879	BCMA CDR-L3	QQTYKFPPT
880	BCMA VH	QVQLVQSGAEVKKPGASVKLSCKASGYTFTDYYIHWVRQAPGQ GLEWIGYINPNSGYTNYAQKFQGRATMTADKSINTAYVELSRLR SDDTAVYFCTRYMWERTGFFDFWVGQGTMTVTVSS
881	BCMA VL	DIQMTQSPSSVSASVGDRTITCLASEDISDDLAWYQQKPGKAP KVLVYTTSSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYFCQQ TYKFPPTFGGGTKVEIK
882	TF CDR-H1	GFTFSNYA
883	TF CDR-H2	ISGSGDYT
884	TF CDR-H3	ARSPWGYLDS
885	TF CDR-L1	QGISSR
886	TF CDR-L2	AAS
887	TF CDR-L3	QQYNSYPYT
888	TF VH	EVQLLESGLLVQPGGSLRLSCAASGFTFSNYAMSWVRQAPGK GLEWVSSISGSGDYTYTDSVKGRFTISRDNKNTLYLQMNSLR AEDTAVYYCARSPWGYLDSWGQGTTLTVTVSS
889	TF VL	DIQMTQSPPSLSASAGDRVTITCRASQGISSRLAWYQQKPEKAPK SLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQY NSYPYTFGQGTKLEIK
890	Anti-PD-L1 HC	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTA AISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLR EDTAVYFCARKFHFVSGSPFGMDVWGQGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKK VEPKSCDKHTHTCPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV

		VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPGK
891	Anti-PD-L1 HC v2	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKFHFVSGSPFGMDVWGQGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKK VEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPG
892	Anti-PD-L1 LALA HC	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKFHFVSGSPFGMDVWGQGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKK VEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPGK
893	Anti-PD-L1 LALA HC v2	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKFHFVSGSPFGMDVWGQGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKK VEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPG
894	Anti-PD-L1 LC	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPR LLIYDASNRTGIPARFSGSGSGTDFTLTISSELPEDFAVYYCQQR SNWPTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLN NFYPREAKVQWKVDNALQSGNSQESVTEQDSKIDSTYLSSTLTLS SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
895	Anti-PD-L1 (engineered cysteines) LALA HC	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKFHFVSGSPFGMDVWGQGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKK VEPKSCDKTHTCPPCPAPEAAGGPCVFLFPPKPKDTLMISRTPEV

		TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVELTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEAL HNHYTQKSLSLSPGK
896	Anti-PD-L1 (engineered cysteines) LALA HC v2	QVQLVQSGAEVKKPGSSVKVCSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKFHFVSGSPFGMDVWGQGTITVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKK VEPKSCDKTHHTCPPCAPEAAGGPCVFLFPPKPKDTLMISRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVELTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEAL HNHYTQKSLSLSPG
897	Anti-PD-L1 mIgG2a LALA HC	QVQLVQSGAEVKKPGSSVKVCSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKFHFVSGSPFGMDVWGQGTITVTVSSAKTTAPSV YPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHT FPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIE PRGPTIKPCPPCKCPAPNAAGGPSVFIFPPKIKDVLMSISPIVTCV VVDVSEDDPDVQISWVFNNEVHTAQTQTHREDYNSTLRVVS LPIQHQQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVY VLPPPEEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYK NTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHEGLHNH HTTKSFSRTPGK
898	Anti-PD-L1 mIgG2a LALA HC v2	QVQLVQSGAEVKKPGSSVKVCSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKFHFVSGSPFGMDVWGQGTITVTVSSAKTTAPSV YPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHT FPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIE PRGPTIKPCPPCKCPAPNAAGGPSVFIFPPKIKDVLMSISPIVTCV VVDVSEDDPDVQISWVFNNEVHTAQTQTHREDYNSTLRVVS LPIQHQQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVY VLPPPEEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYK NTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHEGLHNH HTTKSFSRTPG
899	Anti-PD-L1 mK LC	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPR LLIYDASNRATGIPARFSGSGGTDFLTITISLEPEDFAVYYCQQR SNWPTFGQGTKVEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLN NFYPKDINVKWKIDGSRQNGVLNSWTDQDSKDYSTYSMSSTLT TKDEYERHNSYTCEATHKTSTSPIVKSFNRECE
900	Anti-PD-L1 mIgG2a (engineered cysteines) LALA HC	QVQLVQSGAEVKKPGSSVKVCSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKFHFVSGSPFGMDVWGQGTITVTVSSAKTTAPSV YPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHT FPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIE

		PRGPTIKPCPPCKCPAPNAAGGPCVFIFPPKIKDVLMSLSPIVTCV VVDVSEDDPDVQISWVFNVEVHTAQTQTHREDYNSTLRVVSA LPIQHQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVY VLPPPEEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYK NTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHEGLHNH HTTKSFSRTPGK
901	Anti-PD-L1 mIgG2a (engineered cysteines) LALA HC v2	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKFHFVSGSPFGMDVWGQGTTVTVSSAKTTAPSV YPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHT FPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKIE PRGPTIKPCPPCKCPAPNAAGGPCVFIFPPKIKDVLMSLSPIVTCV VVDVSEDDPDVQISWVFNVEVHTAQTQTHREDYNSTLRVVSA LPIQHQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVY VLPPPEEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYK NTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHEGLHNH HTTKSFSRTPG
902	Anti-PD-L1 CDR-H1	TAAIS
903	Anti-PD-L1 CDR-H2	GIPIFGKAHYAQKFQG
904	Anti-PD-L1 CDR-H3	KFHFVSGSPFGMDV
905	Anti-PD-L1 CDR-L1	RASQSVSSYLA
906	Anti-PD-L1 CDR-L2	DASNRAT
907	Anti-PD-L1 CDR-L3	QQRSNWPT
908	Anti-PD-L1 VH	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQ GLEWMGGIPIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYFCARKFHFVSGSPFGMDVWGQGTTVTVSS
909	Anti-PD-L1 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPR LLIYDASNRATGIPARFSGSGSGTDFTLTISSELEPEDFAVYYCQQR SNWPTFGQGTKVEIK
910	Anti-EphA2 CDR-H1	HYMMA
911	Anti-EphA2 CDR-H2	RIGPSGGPTHYADSVKG
912	Anti-EphA2 CDR-H3	YDSGYDYVAVAGPAEYFQH
913	Anti-EphA2 CDR-L1	RASQSISTWLA
914	Anti-EphA2 CDR-L2	KASNLHT
915	Anti-EphA2 CDR-L3	QQYNSYSRT

916	Anti-EphA2 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGK GLEWVSRIGPSGGPTHYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQGTLVTVSS
917	Anti-EphA2 VL	DIQMTQSPSSLSASVGDRVTITCRASQSISTWLAWYQQKPGKAP KLLIYKASNLHTGVPSRFSGSGSGTEFSLTISGLQPDDFATYYCQ QYNSYSRTFGQGTKVEIK
918	Anti-EphA2 HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGK GLEWVSRIGPSGGPTHYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQGTLVTVSSA STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSN TKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
919	Anti-EphA2 HC v2	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGK GLEWVSRIGPSGGPTHYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQGTLVTVSSA STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSN TKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPG
920	Anti-EphA2 LC	DIQMTQSPSSLSASVGDRVTITCRASQSISTWLAWYQQKPGKAP KLLIYKASNLHTGVPSRFSGSGSGTEFSLTISGLQPDDFATYYCQ QYNSYSRTFGQGTKVEIKRTVAAPS VFIFPPSDEQLKSGTASVVC LLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS KDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
921	Anti-EphA2 mIgG2a HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGK GLEWVSRIGPSGGPTHYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQGTLVTVSSA KTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGS LSSGVHTFPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASST KVDKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKDVLMI SPIVTCVVDVSEDDPDVQISWVFNNEVHTAQTQTHREDYNST LRVVSALPIQHQQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSV RAPQVYVLPPEEEMTKKQVTLTCMVTD FMPEDIYVEWTNNGK TELNYKNTEPVLDSGSYFMYSKLRVEKKNWVERNSYSCSVVH EGLHNHHTTKSFSRTPGK
922	Anti-EphA2 mIgG2a HC v2	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGK GLEWVSRIGPSGGPTHYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQGTLVTVSSA

		KTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGS LSSGVHTFPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASST KVDKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKDVLMLSL SPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQTQTHREDYNST LRVVSALPIQHQQDWMMSGKEFKCKVNNKDLGAPIERTISKPKGSV RAPQVYVLPPEEEMTKKQVTLTCMVTDMPEDIYVEWTNNGK TELNYKNTEPVLDSGSGYFMYSKLRVEKKNWVERNSYSCSVVH EGLHNHHTTKSFSRTPG
923	Anti-EphA2 mIgG2a LC	DIQMTQSPSSLSASVGDRVTITCRASQSISTWLAWYQQKPGKAP KLLIYKASNLHTGVPSRFSGSGSGTEFSLTISGLQPDDFATYYCQ QYNSYSRTFGQGTKVEIKRADAAPTVSIFPPSSEQLTSGGASVVC FLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSS TLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRECE
924	Anti-EphA2 mIgG2a LALAPG HC	EVQLLESQGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGK GLEWVSRIGPSGGPHTHYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQGT LVTVSSA KTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGS LSSGVHTFPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASST KVDKKIEPRGPTIKPCPPCKCPAPNAAGGPSVFIFPPKIKDVLMLSL SPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQTQTHREDYNST LRVVSALPIQHQQDWMMSGKEFKCKVNNKDLGAPIERTISKPKGSV RAPQVYVLPPEEEMTKKQVTLTCMVTDMPEDIYVEWTNNGK TELNYKNTEPVLDSGSGYFMYSKLRVEKKNWVERNSYSCSVVH EGLHNHHTTKSFSRTPGK
925	Anti-EphA2 mIgG2a LALAPG HC v2	EVQLLESQGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGK GLEWVSRIGPSGGPHTHYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQGT LVTVSSA KTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGS LSSGVHTFPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASST KVDKKIEPRGPTIKPCPPCKCPAPNAAGGPSVFIFPPKIKDVLMLSL SPIVTCVVVDVSEDDPDVQISWVFNNEVHTAQTQTHREDYNST LRVVSALPIQHQQDWMMSGKEFKCKVNNKDLGAPIERTISKPKGSV RAPQVYVLPPEEEMTKKQVTLTCMVTDMPEDIYVEWTNNGK TELNYKNTEPVLDSGSGYFMYSKLRVEKKNWVERNSYSCSVVH EGLHNHHTTKSFSRTPG
926	Anti-EphA2 mIgG2a LALAPG LC	DIQMTQSPSSLSASVGDRVTITCRASQSISTWLAWYQQKPGKAP KLLIYKASNLHTGVPSRFSGSGSGTEFSLTISGLQPDDFATYYCQ QYNSYSRTFGQGTKVEIKRADAAPTVSIFPPSSEQLTSGGASVVC FLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSS TLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRECE
927	Anti-CD228 CDR-H1	SGYWN
928	Anti-CD228 CDR-H2	YISDSGITYYNPSLKS
929	Anti-CD228 CDR-H3	RTLATYYAMDY
930	Anti-CD228 CDR-L1	RASQSLVHSDGNTYLH

931	Anti-CD228 CDR-L2	RVSNRFS
932	Anti-CD228 CDR-L3	SQSTHVPPT
933	Anti-CD228 VH	QVQLQESGPGLVKPSSETLSLTCTVSGDSITSGYWNWIRQPPGKGL EYIGYISDSGITYYNPSLKSRTISRDTSKNQYSLKLSSVTAADTA VYYCARRTLATYYAMDYWGQGTLLTVSS
934	Anti-CD228 VL	DFVMTQSPLSLPVTLGQPASISCRASQSLVHSDGNTYLHWYQQR PGQSPRLLIYRVSNRFSQVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCSQSTHVPPTFGQGTKEIK
935	Anti-CD228 HC	QVQLQESGPGLVKPSSETLSLTCTVSGDSITSGYWNWIRQPPGKGL EYIGYISDSGITYYNPSLKSRTISRDTSKNQYSLKLSSVTAADTA VYYCARRTLATYYAMDYWGQGTLLTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPV LSDSGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKS LSLSPGK
936	Anti-CD228 HC v2	QVQLQESGPGLVKPSSETLSLTCTVSGDSITSGYWNWIRQPPGKGL EYIGYISDSGITYYNPSLKSRTISRDTSKNQYSLKLSSVTAADTA VYYCARRTLATYYAMDYWGQGTLLTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPV LSDSGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKS LSLSPG
937	Anti-CD228 LC	DFVMTQSPLSLPVTLGQPASISCRASQSLVHSDGNTYLHWYQQR PGQSPRLLIYRVSNRFSQVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCSQSTHVPPTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTA SVVCLLNFFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTY SLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
938	Anti-CD228 LALAKA HC	QVQLQESGPGLVKPSSETLSLTCTVSGDSITSGYWNWIRQPPGKGL EYIGYISDSGITYYNPSLKSRTISRDTSKNQYSLKLSSVTAADTA VYYCARRTLATYYAMDYWGQGTLLTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLPP SRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPV LSDSGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKS LSLSPGK

939	Anti-CD228 LALAKA HC v2	QVQLQESGPGLVKPSSETLSLTCTVSGDSITSGYWNWIRQPPGKGL EYIGYISDSGITYYNPSLKSRTISRDTSKNQYSLKLSSVTAADTA VYYCARRTLATYYAMDYWGQGTLLTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSKVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLPP SRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPV LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPG
940	Anti-CD228 LALAKA LC	DFVMTQSPLSLPVTLGQPASISCRASQSLVHSDGNTYLHWYQQR PGQSPRLLIYRVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCSQSTHVPPTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTA SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTY SLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
941	Anti-avB6 HC CDR-H1	DYNVN
942	Anti-AvB6 HC CDR-H2	VINPKYGTTRYNQKFKG
943	Anti-AvB6 HC CDR-H3	GLNAWDY
944	Anti-AvB6 LG CDR-L1	GASENIYGALN
945	Anti-AvB6 LG CDR-L2	GATNLED
946	Anti-AvB6 LG CDR-L3	QNVLTTPYT
947	Anti-AvB6 HC VH	QFQLVQSGAEVKKPGASVKVSCKASGYSFTDYNVNWVRQAPG QGLEWIGVINPKYGTTRYNQKFKGRATLTVDKSTSTAYMELSSL RSEDТАVYYCTRGLNAWDYWGQGTLLTVSS
948	Anti-AvB6 LG VL	DIQMTQSPSSLSASVGDRTITCGASENIYGALNHWYQQKPGKAP KLLIYGATNLEDGVPSTRFSGSGSGRDYFTISSLQPEDATYYCQN VLTTPYTFGQGTKLEIK
949	Anti-AvB6 HC	QFQLVQSGAEVKKPGASVKVSCKASGYSFTDYNVNWVRQAPG QGLEWIGVINPKYGTTRYNQKFKGRATLTVDKSTSTAYMELSSL RSEDТАVYYCTRGLNAWDYWGQGTLLTVSSASTKGPSVFPLAP SSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSKVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP VLSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
950	Anti-AvB6 HC v2	QFQLVQSGAEVKKPGASVKVSCKASGYSFTDYNVNWVRQAPG QGLEWIGVINPKYGTTRYNQKFKGRATLTVDKSTSTAYMELSSL RSEDТАVYYCTRGLNAWDYWGQGTLLTVSSASTKGPSVFPLAP

		SSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVTV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQK SLSLSPG
951	Anti-AvB6 LG LC	DIQMTQSPSSLSASVGDRVTITCGASENIYGALNWKYQQKPGKAP KLLIYGATNLEDGVPSRFGSGSGRDTFTISSSLQPEDATYYCQN VLTPPYTFGGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPRFAKVKWVDNALQSGNSQESVTEQDSKDSSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
952	Anti-AvB6 LALAKA HC	QFQLVQSGAEVKKPGASVKVSCKASGYSTFDYNNVWVRQAPG QGLEWIGVINPKYGTTRYNQKFKGRATLTVDKSTSTAYMELSSL RSEDVAVYYCTRGLNAWDYWGQGTLLTVSSASTKGPSVFPLAP SSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVTV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQK SLSLSPGK
953	Anti-AvB6 LALAKA HC v2	QFQLVQSGAEVKKPGASVKVSCKASGYSTFDYNNVWVRQAPG QGLEWIGVINPKYGTTRYNQKFKGRATLTVDKSTSTAYMELSSL RSEDVAVYYCTRGLNAWDYWGQGTLLTVSSASTKGPSVFPLAP SSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVTV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQK SLSLSPG
954	Anti-AvB6 LG LALAKA LC	DIQMTQSPSSLSASVGDRVTITCGASENIYGALNWKYQQKPGKAP KLLIYGATNLEDGVPSRFGSGSGRDTFTISSSLQPEDATYYCQN VLTPPYTFGGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPRFAKVKWVDNALQSGNSQESVTEQDSKDSSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
955	Anti-B7H4 CDR-H1	SGSYWYG
956	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLRS
957	Anti-B7H4 CDR-H3	EGSYPNQFDP
958	Anti-B7H4 CDR-L1	RASQSVSSNLA

959	Anti-B7H4 CDR-L2	GASTRAT
960	Anti-B7H4 CDR-L3	QQYHSFPFT
961	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGWIRQPPGK GLEWIGNIYYSGSTYYNPSLRSRVTISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYPNQFDPWGQGTLLTVSS
962	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIK
963	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGWIRQPPGK GLEWIGNIYYSGSTYYNPSLRSRVTISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYPNQFDPWGQGTLLTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGGEVHNAAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLTP PSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP VLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
964	Anti-B7H4 HC v2	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGWIRQPPGK GLEWIGNIYYSGSTYYNPSLRSRVTISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYPNQFDPWGQGTLLTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGGEVHNAAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLTP PSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP VLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPG
965	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKIDSTYLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
966	Anti-B7H4 LALAKA HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGWIRQPPGK GLEWIGNIYYSGSTYYNPSLRSRVTISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYPNQFDPWGQGTLLTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGGEVHNAAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLTP PSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP VLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK

967	Anti-B7H4 LALAKA HC v2	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGWIRQPPGK GLEWIGNIYYSGSTYYNPSLRSRVTISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYPNQFDPWQGQTLVTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLP PSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQK SLSLSPG
968	Anti-B7H4 LALAKA LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLT LSKADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC
969	Anti-B7H4 CDR-H1	GSISSSSYWGW
970	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
971	Anti-B7H4 CDR-H3	AREGSYPNWFDPP
972	Anti-B7H4 CDR-L1	RASQSVSSNLA
973	Anti-B7H4 CDR-L2	GASTRAT
974	Anti-B7H4 CDR-L3	QQYHSFPFT
975	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSSYWGWIRQPPGK GLEWIGNIYYSGSTYYNPSLKS RV TISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYPNWFDPPWQGQTLVTVSS
976	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIK
977	Anti-B7H4 CDR-H1	GSIKSGSHYWG
978	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLRS
979	Anti-B7H4 CDR-H3	AREGSYPNWFDPP
980	Anti-B7H4 CDR-L1	RASQSVSSNLA
981	Anti-B7H4 CDR-L2	GASTRAT
982	Anti-B7H4 CDR-L3	QQYHSFPFT

983	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWG WIRQPPGK GLEWIGNIYYSGSTYYNPSLRSRV TISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYPNWFD PWGQGT LTVSS
984	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSC RASQSVSSNLAWYQQKPGQAP RLLIYG ASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIK
985	Anti-B7H4 CDR-H1	GSIKSGSHYWG
986	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
987	Anti-B7H4 CDR-H3	AREGSYPNWLD
988	Anti-B7H4 CDR-L1	RASQSVSSNLA
989	Anti-B7H4 CDR-L2	GASTRAT
990	Anti-B7H4 CDR-L3	QQYHSFPFT
991	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWG WIRQPPGK GLEWIGNIYYSGSTYYNPSLKS RV TISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYPNWLD PWGQGT LTVSS
992	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSC RASQSVSSNLAWYQQKPGQAP RLLIYG ASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIK
993	Anti-B7H4 CDR-H1	GSIKSGSYWG
994	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
995	Anti-B7H4 CDR-H3	AREGSYPNQFD
996	Anti-B7H4 CDR-L1	RASQSVSSNLA
997	Anti-B7H4 CDR-L2	GASTRAT
998	Anti-B7H4 CDR-L3	QQYHSFPFT
999	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWG WIRQPPGK GLEWIGNIYYSGSTYYNPSLKS RV TISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYPNQF DPWGQ GILVTVSS
1000	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSC RASQSVSSNLAWYQQKPGQAP RLLIYG ASTRATGIPARFSGSGSGTEFTL TISSLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIK
1001	Anti-B7H4 CDR-H1	GSIKSGSHYWG
1002	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS

1003	Anti-B7H4 CDR-H3	AREGSYPNWFDP
1004	Anti-B7H4 CDR-L1	RASQSVSTNLA
1005	Anti-B7H4 CDR-L2	DASARVT
1006	Anti-B7H4 CDR-L3	QQYHSFPFT
1007	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWG WIRQPPGK GLEWIGNIYYSGSTYYNPSLKS SRVTMSVDTSKNQFSLKLSSVTA ADTAVYYCAREGSYPNWFDPWGQGT LTVSS
1008	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSTNLA WYQQKPGQAP RLLIYDASARVTGIPARFSGSGSGTEFTLTI SSLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIK
1009	Anti-B7H4 CDR-H1	GSISSSSYWG
1010	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
1011	Anti-B7H4 CDR-H3	AREGSYTTVLNV
1012	Anti-B7H4 CDR-L1	RASQSVSSSYLA
1013	Anti-B7H4 CDR-L2	GASSRAT
1014	Anti-B7H4 CDR-L3	QQAASYPLT
1015	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYWG WIRQPPGK GLEWIGNIYYSGSTYYNPSLKS SRVTISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYTTVLNVWGQGT MVTSS
1016	Anti-B7H4 VL	EIVLTQSPGTLSPGERATLSCRASQSVSSSYLA WYQQKPGQAP RLLIYGASSRATGIPDRFSGSGSGTDFTLTIS RLEPEDFAVYYCQQ AASYPLTFGGGTKVEIK
1017	Anti-B7H4 CDR-H1	GSIGRGSYYWG
1018	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
1019	Anti-B7H4 CDR-H3	AREGSYTTVLNV
1020	Anti-B7H4 CDR-L1	RASQSVASSHLA
1021	Anti-B7H4 CDR-L2	DAVSRAT
1022	Anti-B7H4 CDR-L3	QQAASYPLT
1023	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSI GRGSYYWG WIRQPPGK GLEWIGNIYYSGSTYYNPSLKS SRVTISVDTSKNQFSLKLSSVTA ADTAVYYCAREGSYTTVLNVWGQGT MVTSS

1024	Anti-B7H4 VL	EIVLTQSPGTLSPGERATLSCRASQSVASSHLAWYQQKPGQAP RLLIYDAVSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQ AASYPLTFGGGTKVEIK
1025	Anti-B7H4 CDR-H1	GSISSGGYYWS
1026	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
1027	Anti-B7H4 CDR-H3	ARESSTISADFDL
1028	Anti-B7H4 CDR-L1	RASQGISRWLA
1029	Anti-B7H4 CDR-L2	AASSLQS
1030	Anti-B7H4 CDR-L3	QQAHTFPYT
1031	Anti-B7H4 VH	QVQLQESGPGLVKPSQTLSTCTVSGSGSISSGGYYWSWIRQHPG KGLEWIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTA ADTAVYYCARESSTISADFDLWGRGTLVTVSS
1032	Anti-B7H4 VL	DIQMTQSPSSVSASVGDRVTITCRASQGISRWLAWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQ AHTFPYTFGGGTKVEIK
1033	Anti-B7H4 CDR-H1	GSISHGGYYWS
1034	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
1035	Anti-B7H4 CDR-H3	ARESSTISADFDL
1036	Anti-B7H4 CDR-L1	RASQGISRWLA
1037	Anti-B7H4 CDR-L2	AASSLQS
1038	Anti-B7H4 CDR-L3	QQAHTFPYT
1039	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTASGSGSISHGGYYWSWIRQHPG KGLEWIGNIYYSGSTYYNPSLKSRTVMSVDTSKNQFSLKLSSVT AADTAVYYCARESSTISADFDLWGRGTLVTVSS
1040	Anti-B7H4 VL	DIQMTQSPSSVSASVGDRVTITCRASQGISRWLAWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQ AHTFPYTFGGGTKVEIK
1041	Anti-B7H4 CDR-H1	GSISSGGYYWS
1042	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
1043	Anti-B7H4 CDR-H3	ARGLSTIDEAFDP
1044	Anti-B7H4 CDR-L1	RASQSISSWLA

1045	Anti-B7H4 CDR-L2	KASSLES
1046	Anti-B7H4 CDR-L3	QQDNSYPYT
1047	Anti-B7H4 VH	QVQLQESGPGLVKPSQTLSTCTVSGGSISSGGYYWSWIRQHPG KGLEWIGNIYYSGSTYYNPSLRSRVTISVDTSKNQFSLKLSSVTA ADTAVYYCARGLSTIDEAFDPWGQGTLVTVSS
1048	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAP KLLIYKASSLESGVPSRFSGSGSGTEFTLTISLQPDFFATYYCQQ DNSYPYTFGGGTKVEIK
1049	Anti-B7H4 CDR-H1	GSISDGSYYWS
1050	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLRS
1051	Anti-B7H4 CDR-H3	ARGLSTIDEAFDP
1052	Anti-B7H4 CDR-L1	RASQSISSWLA
1053	Anti-B7H4 CDR-L2	KASSLES
1054	Anti-B7H4 CDR-L3	QQDNSYPYT
1055	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISDGSYYWSWIRQHPGK GLEWIGNIYYSGSTYYNPSLRSRVTMSVDTSKNQFSLKLSSVTA ADTAVYYCARGLSTIDEAFDPWGQGTLVTVSS
1056	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAP KLLIYKASSLESGVPSRFSGSGSGTEFTLTISLQPDFFATYYCQQ DNSYPYTFGGGTKVEIK
1057	Anti-B7H4 CDR-H1	GSISDGSYYWS
1058	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLRS
1059	Anti-B7H4 CDR-H3	ARGLSTIDEAFDP
1060	Anti-B7H4 CDR-L1	RASKSISSWLA
1061	Anti-B7H4 CDR-L2	EASSLHS
1062	Anti-B7H4 CDR-L3	QQDNSYPYT
1063	Anti-B7H4 VH	QVQLQESGPGLVKPSQTLSTCTVSGGSISDGSYYWSWIRQHPG KGLEWIGNIYYSGSTYYNPSLRSRVTMSVDTSKNQFSLKLSSVTA ADTAVYYCARGLSTIDEAFDPWGQGTLVTVSS
1064	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASKSISSWLAWYQQKPGKAP KLLIYEASSLHSGVPSRFSGSGSGTEFTLTISLQPDFFATYYCQQ DNSYPYTFGGGTKVEIK

1065	Anti-B7H4 CDR-H1	GSISSYYWS
1066	Anti-B7H4 CDR-H2	YIYSSGSTNYPNPSLKS
1067	Anti-B7H4 CDR-H3	ARGSGQYAAPDYGMD
1068	Anti-B7H4 CDR-L1	RASQSISSWLA
1069	Anti-B7H4 CDR-L2	KASSLES
1070	Anti-B7H4 CDR-L3	QQDNSFPFT
1071	Anti-B7H4 VH	QVQLQESGPGLVKPSSETLSLTCTVSGGSISSYYWSWIRQPPGKGL EWIGYIYSSGSTNYPNPSLKSRTVISVDTSKNQFSLKLSSVTAADT AVYYCARGSGQYAAPDYGMDVWGQGTTVTVSS
1072	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRTITCRASQSISSWLAWYQQKPGKAP KLLIYKASSLESQVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQ DNSFPFTFGGGTKVEIK
1073	Anti-B7H4 CDR-H1	GSIISSYYWG
1074	Anti-B7H4 CDR-H2	YIYSSGSTSYNPSLKS
1075	Anti-B7H4 CDR-H3	ARGSGLYAAPDYGLDV
1076	Anti-B7H4 CDR-L1	RASQSISSWLA
1077	Anti-B7H4 CDR-L2	KASSLES
1078	Anti-B7H4 CDR-L3	QQDNSFPFT
1079	Anti-B7H4 VH	QVQLQESGPGLVKPSSETLSLTCTVSGGSIISYYWGWIRQPPGKGL EWIGYIYSSGSTSYNPSLKSRTVISVDTSKNQFSLKLSSVTAADTA VYYCARGSGLYAAPDYGLDVWGQGTTVTVSS
1080	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRTITCRASQSISSWLAWYQQKPGKAP KLLIYKASSLESQVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQ DNSFPFTFGGGTKVEIK
1081	Anti-B7H4 CDR-H1	FTFSSYAMS
1082	Anti-B7H4 CDR-H2	TISGSGGSTYYADSVKG
1083	Anti-B7H4 CDR-H3	ARGAGHYDLVGRY
1084	Anti-B7H4 CDR-L1	RASQSISSYLN
1085	Anti-B7H4 CDR-L2	AASSLQS

1086	Anti-B7H4 CDR-L3	QQLYSLPPT
1087	Anti-B7H4 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK GLEWVSTISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCARGAGHYDLVGRYWGGQGLTVTVSS
1088	Anti-B7H4 VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPK LLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQL YSLPPTFGGGTKVEIK
1089	Anti-B7H4 CDR-H1	FTFSSYAMS
1090	Anti-B7H4 CDR-H2	AISGSGGSTYYADSVKG
1091	Anti-B7H4 CDR-H3	ARVGFRALNY
1092	Anti-B7H4 CDR-L1	RASQDISSWLA
1093	Anti-B7H4 CDR-L2	AASSLQS
1094	Anti-B7H4 CDR-L3	QQATSYPPWT
1095	Anti-B7H4 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK GLEWVSAISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCARVGFRALNYWGGQGLTVTVSS
1096	Anti-B7H4 VL	DIQLTQSPSSVSASVGDRVTITCRASQDISSWLAWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQ ATSYPPWTFGGGTKEIK
1097	Anti-B7H4 CDR-H1	GTFSSYAIS
1098	Anti-B7H4 CDR-H2	GIPIFGTASYAQKFQG
1099	Anti-B7H4 CDR-H3	ARQQYDGRRYFGL
1100	Anti-B7H4 CDR-L1	RASQSVSSNLA
1101	Anti-B7H4 CDR-L2	SASTRAT
1102	Anti-B7H4 CDR-L3	QQVNVWPPT
1103	Anti-B7H4 VH	QVQLVQSGAEVKKPGSSVKVSCASGGTFSSYAIWVRQAPGQ GLEWMGGIPIFGTASYAQKFQGRVTITADESTSTAYMELSSLR EDTAVYYCARQQYDGRRYFGLWGRGTLTVTVSS
1104	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYASTRATGIPARFSGSGSGTEFTLTISLQSEDFAVYYCQQ VNVWPPTFGGGTKVEIK
1105	Anti-B7H4 CDR-H1	GTFSSYAIS

1106	Anti-B7H4 CDR-H2	GIPIFGTANYAQKFQG
1107	Anti-B7H4 CDR-H3	ARGGPWFDP
1108	Anti-B7H4 CDR-L1	RASQSISSWLA
1109	Anti-B7H4 CDR-L2	KASSLES
1110	Anti-B7H4 CDR-L3	QQYNSYPPFT
1111	Anti-B7H4 VH	QVQLVQSGAEVKKPGSSVKVSCASGGTFSSYAISWVRQAPGQ GLEWMGGIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYYCARGGPWFDPWGQGTLVTVSS
1112	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAP KLLIYKASSLESGVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQQ YNSYPPFTFGGGTKVEIK
1113	Anti-B7H4 CDR-H1	FTFSSYAMS
1114	Anti-B7H4 CDR-H2	AISGSGGSTSYADSVKG
1115	Anti-B7H4 CDR-H3	AKPSLATMLAFDI
1116	Anti-B7H4 CDR-L1	RASQSISSWLA
1117	Anti-B7H4 CDR-L2	DASSLES
1118	Anti-B7H4 CDR-L3	QQSKSYPR
1119	Anti-B7H4 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK GLEWVSAISGSGGSTSYADSVKGRFTISRDNKNTLYLQMNSLR AEDTAVYYCAKPSLATMLAFDIWGQGTMTVTVSS
1120	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAP KLLIYDASSLESGVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQQ SKSYPRFTFGGGTKVEIK
1121	Anti-B7H4 CDR-H1	GSISSSVYYWS
1122	Anti-B7H4 CDR-H2	SILVSGSTYYNPSLKS
1123	Anti-B7H4 CDR-H3	ARAVSFLDV
1124	Anti-B7H4 CDR-L1	RASQSISSYLN
1125	Anti-B7H4 CDR-L2	GASSLQS
1126	Anti-B7H4 CDR-L3	QQSYDPPWT

1127	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSVYYWSWIRQPPGK GLEWIGSILVSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAAD TAVYYCARAVSFLDVWGQGTMTIVSS
1128	Anti-B7H4 VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPK LLIYGASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQS YDPPWTFGGGTKEIK
1129	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSVYYWGWIWIRQPPGK GLEWIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAAD DTAVYYCAREGSPYNWFDWPWGQGTLLTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLTP PSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP VLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
1130	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTISLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1131	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIWIRQPPGK GLEWIGNIYYSGSTYYNPSLRSRTISVDTSKNQFSLKLSSVTAAD DTAVYYCAREGSPYNWFDWPWGQGTLLTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLTP PSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP VLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
1132	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTISLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1133	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIWIRQPPGK GLEWIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAAD DTAVYYCAREGSPYNWLDWPWGQGTLLTVSSASTKGPSVFPLAP SSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVD DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPP

		VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
1134	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1135	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGWIRQPPGK GLEWIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYPNQFDPWGQGLVTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
1136	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1137	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIRQPPGK GLEWIGNIYYSGSTYYNPSLKSRTMSVDTSKNQFSLKLSSVTA ADTAVYYCAREGSYPNWFDPWGQGLVTVSSASTKGPSVFPLA PSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPK SCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
1138	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSTNLAWYQQKPGQAP RLLIYDASARVTGIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQ YHSFPFTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1139	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSYWGWIRQPPGK GLEWIGNIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAA DTAVYYCAREGSYTTVLNVWGQGTMTVSSASTKGPSVFPLAP SSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP

		VLDS DGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQK SLSLSPGK
1140	Anti-B7H4 LC	EIVLTQSPGTL SLSPGERATL SCRASQSVSSSYLAWYQQKPGQAP RLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQ AASYPLTFGGGT KVEIKRTVAAPS VFIFPPSDEQLKSGTASVVCL LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTL TL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1141	Anti-B7H4 HC	QLQLQESGPGLVKPS ETLSLTCTVSGGSI GRGSSYYWG WIRQPPG KGLEWIGNIYYSGSTYYNPSLKSRVTISVDT SKNQFSLKLSSVTA ADTAVYYCAREGSYTTVLNVWGQGTMTVSSASTKGPSVFPLA PSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPK SCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDS DGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQK SLSLSPGK
1142	Anti-B7H4 LC	EIVLTQSPGTL SLSPGERATL SCRASQSVASSHLAWYQQKPGQAP RLLIYDAVSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQ AASYPLTFGGGT KVEIKRTVAAPS VFIFPPSDEQLKSGTASVVCL LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTL TL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1143	Anti-B7H4 HC	QVQLQESGPGLVKPSQTL SLTCTVSGGSISSGGYYWSWIRQHPG KGLEWIGNIYYSGSTYYNPSLKSRVTISVDT SKNQFSLKLSSVTA ADTAVYYCARESSTISADFDLWGRGTLTVTSSASTKGPSVFPLAP SSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDS DGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQK SLSLSPGK
1144	Anti-B7H4 LC	DIQMTQSPSSVSASVGD RVTITCRASQGISRWLAWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQ AHTFPYTFGGGT KVEIKRTVAAPS VFIFPPSDEQLKSGTASVVCL LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTL TL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1145	Anti-B7H4 HC	QLQLQESGPGLVKPS ETLSLTCTASGGSI SHGGYYWSWIRQHPG KGLEWIGNIYYSGSTYYNPSLKSRVTMSVDT SKNQFSLKLSSVT AADTAVYYCARESSTISADFDLWGRGTLTVTSSASTKGPSVFPL APSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY TL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT

		TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK
1146	Anti-B7H4 LC	DIQMTQSPSSVSASVGDRVITITCRASQGISRWLAWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ AHTFPYTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCL LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYLSSTL TLISKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1147	Anti-B7H4 HC	QVQLQESGPGLVKPSQTLSTCTVSGGSISGGYYWSWIRQHPG KGLEWIGNIYYSGSTYYNPSLKRVTISVDTSKNQFSLKLSSVTA ADTAVYYCARGLSTIDEAFDPWGQGTLLTVSSASTKGPSVFPLA PSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPK SCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
1148	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVITITCRASQSISSWLAWYQQKPGKAP KLLIYKASSLESQVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQQ DNSYPYTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCL LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYLSSTL TLISKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1149	Anti-B7H4 HC	QLQLQESGPGLVKPSSETLSLTCTVSGGSISDGSYYSWIRQHPGK GLEWIGNIYYSGSTYYNPSLRSRVTMSVDTSKNQFSLKLSSVTA ADTAVYYCARGLSTIDEAFDPWGQGTLLTVSSASTKGPSVFPLA PSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
1150	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVITITCRASQSISSWLAWYQQKPGKAP KLLIYKASSLESQVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQQ DNSYPYTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCL LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYLSSTL TLISKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1151	Anti-B7H4 HC	QVQLQESGPGLVKPSQTLSTCTVSGGSISDGSYYSWIRQHPG KGLEWIGNIYYSGSTYYNPSLRSRVTMSVDTSKNQFSLKLSSVTA ADTAVYYCARGLSTIDEAFDPWGQGTLLTVSSASTKGPSVFPLA PSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPK SCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP

		VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
1152	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVITITCRASKSISSWLAWYQQKPGKAP KLLIYEASSLHSGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQ DNSYPYTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCL LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1153	Anti-B7H4 HC	QVQLQESGPGLVKPSSETLSLTCTVSGGSISSYYWSWIRQPPGKGL EWIGYIYSSGSTNYPNPSLKSRVTISVDTSKNQFSLKLSSVTAADT AVYYCARGSGQYAAPDYGMDVWGQGTITVTVSSASTKGPSVF LAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF AVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKV EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPGK
1154	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVITITCRASQSISSWLAWYQQKPGKAP KLLIYKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQ DNSFPFTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1155	Anti-B7H4 HC	QVQLQESGPGLVKPSSETLSLTCTVSGGSISSYYWGWIRQPPGKGL EWIGYIYSSGSTSYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTA VYYCARGSGLYAAPDYGLDVWGQGTITVTVSSASTKGPSVFPLA PSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPK SCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
1156	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVITITCRASQSISSWLAWYQQKPGKAP KLLIYKASSLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQ DNSFPFTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1157	Anti-B7H4 HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK GLEWVSTISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLR AEDTAVYYCARGAGHYDLVGRYWGQGTITVTVSSASTKGPSVF LAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF AVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKV EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY

		KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPGK
1158	Anti-B7H4 LC	DIQMTQSPSSLSASVGDRVITITCRASQSISSYLNWYQQKPGKAPK LLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQL YSLPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLN NFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLT SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1159	Anti-B7H4 HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK GLEWVSAISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCARVGFALNYWGQGTITVTVSSASTKGPSVFPLAP SSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVTV DVSHPEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPGK
1160	Anti-B7H4 LC	DIQLTQSPSSVSASVGDRVITITCRASQDISSWLAWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQ ATSYPPWTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVC LLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSST LTLKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1161	Anti-B7H4 HC	QVQLVQSGAEVKKPGSSVKVSCASGGTFSSYAISWVRQAPGQ GLEWMGGIPIFGTASYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYYCARQQYDGRRYFGLWGRGTLTVTVSSASTKGPSVFPL APSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK
1162	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYSASTRATGIPARFSGSGSGTEFTLTISLQSEDFAVYYCQQ VNVWPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCL LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTL TLKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1163	Anti-B7H4 HC	QVQLVQSGAEVKKPGSSVKVSCASGGTFSSYAISWVRQAPGQ GLEWMGGIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRS EDTAVYYCARGGPWFDPWGQGTITVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVTV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV

		LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK
1164	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVITTCRASQSISSWLAWYQQKPGKAP KLLIYKASSLESGVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQQ YNSYPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCL LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1165	Anti-B7H4 HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK GLEWVSAISGSGGSTSYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYYCAKPSLATMLAFDIWGQGTMTVTVSSASTKGPSVF LAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF AVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKVK EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPGK
1166	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVITTCRASQSISSWLAWYQQKPGKAP KLLIYDASSLESGVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQQ SKSYPRTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1167	Anti-B7H4 HC	QLQLQESGPGLVKPSSETLSLTCTVSGGSISSSVYYWSWIRQPPGK GLEWIGSILVSGSTYYNPSLKRVTISVDTSKNQFSLKLSSVTAAD TAVYYCARAVSFLDVWGQGTMTVIVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKEPKSCDKT HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPV LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK
1168	Anti-B7H4 LC	DIQMTQSPSSLSASVGDRVITTCRASQSISSYLNWYQQKPGKAPK LLIYGASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQS YDPPWTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1169	Anti-CD70 CDR-H1	NYGMN
1170	Anti- CD70CDR- H2	WINTYTGEPTYADAFKG
1171	Anti-CD70 CDR-H3	DYGDYGM DY
1172	Anti-CD70 CDR-L1	RASKSVSTSGYSFMH

1173	Anti-CD70 CDR-L2	LASNLES
1174	Anti-CD70 CDR-L3	QHSREVPWT
1175	Anti-CD19 (hBU12) HC	QVQLQESGPGLVKPSQTLSTCTVSGGSISTSGMGVGVIRQHPG KGLEWIGHIWWDDDKRYNPALKSRVTISVDTSKNQFSLKLSSVT AADTAVYYCARMELWSYFYFDYWGQGTLLTVSSASTKGPSVFPL APSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK
1176	Anti-CD19 (hBU12) LC	EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGQAPRL LIYDTSKLASGIPARFSGSGSGTDFTLTISLEPEDVAVYYCFQGS VYPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLN NFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLS SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1177	Anti-ZIP6 HC	QVQLVQSGAEVKKPGASVKVSCKASGLTIEDYYMHWVRQAPG QGLEWMGWIDPENGDEYGPKEFQGRVTMTRDTSINTAYMELSR LRSDDTAVYYCAVHNAHYGTWFAFYWGQGTLLTVSSASTKGPS VFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK KVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPG
1178	Anti-ZIP6 LC	DVVMTQSPSLPVTTLGQPASISCRSSQSLHSSGNTYLEWYQQR GQSPRPLIYKISTRFGVPDRFSGSGSGTDFTLKISRVEAEDVGVY YCFQGSHPYTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTAS VVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYS LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
1179	Anti-gpNMB HC	QVQLQESGPGLVKPSQTLSTCTVSGGSISFNYYWSWIRHHPGK GLEWIGYIYYSGSTYSNP SLKSRVTISVDTSKNQFSLTLSSVTAAD TAVYYCARGYNWNYFDYWGQGTLLTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPV LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK

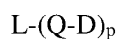
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1181	Anti- EpCAM CDR-H3	DMGWGSGWRPYYYYGMDV
1182	Anti- EpCAM VL	QSVLTQPPSVSGAPGQRVTISCTGSSSNIGSYYGVHWYQQLPGTA PKLLIYSDTNRPSGVPDRFSGSKSGTSASLAITGLQAEDEADYYC QSYDKGFGHRVFGGGTKLTVL
1183	Anti- ADAM9 CDR-H1	SYWMH
1184	Anti- ADAM9 CDR-H1	SYWMH
1185	Anti- ADAM9 CDR-L1	KASQSDYSGDSYMN
1186	Anti-CD59 CDR-H1	SYGMN
1187	Anti-CD59 CDR-H2	YISSSSSTIYYADSVKG
1188	Anti-CD59 VH	QVQLQQSGGGVVQPGRSLGLSCAASGFTFSSYGMNWVRQAPGK GLEWVSYISSSSSTIYYADSVKGRFTISRDNKNTLYLQMNSLRA EDTAVYYCARGPGMDVWGQGTITVTS
1189	Anti-B7-H3 CDR-H2	YISSDSSAIYYADTVKG
1190	Anti-B7-H3 CDR-H3	GRENIYYGSRLDY
1191	Anti-B7-H3 CDR-L1	KASQNVDTNVA
1192	Anti-B7-H3 CDR-L2	SASYRYS
1193	Anti-B7-H3 CDR-L3	QQYNNYPFT
1194	Anti-B7-H3 CDR-H1	SYGMS
1195	Anti-B7-H3 CDR-H2	TINSGGSNTYYPDSLKG
1196	Anti-B7-H3 CDR-H3	HDGGAMDY
1197	Anti-B7-H3 CDR-L1	RASESIYSYLA
1198	Anti-B7-H3 CDR-L3	QHGYGTPPWT

1199	Anti-B7-H3 CDR-H1	SFGMH
1200	Anti-B7-H3 CDR-H2	YISSGSGTIYYADTVKG
1201	Anti-B7-H3 CDR-H3	HGYRYEGFDY
1202	Anti-B7-H3 CDR-L1	KASQNVDTNVA
1203	Anti-B7-H3 CDR-L2	SASYRYS
1204	Anti-B7-H3 CDR-L3	QQYNNYPFT
1205	Anti-B7-H3 CDR-H1	SYTIH
1206	Anti-B7-H3 VL	DIQLTQSPSFLSASVGDRVTITCRASSSVSYMNWYQQKPGKSPKP WIYATSNLASGVPSRFSVSVSGTEHTLTISLQPEDFATYYCQQW SSNPLTFGQGTKLEIK
1207	Anti-B7-H3 CDR-H1	SYWMH
1208	Anti-B7-H3 CDR-H3	GGRLYFDY
1209	Anti-B7-H3 CDR-H1	SYWMH
1210	Anti-B7-H3 VL	DIVMTQSPLSLPVTGPGEPAISCRSSQSLVHSNQDTYLRWYLQKP GQSPQLLIYKVSNRFSGVDPDRFSGSGSGTDFTLKISRVEAEDVGV YYCSQSTHVPYTFGGGTKVEIK
1211	Anti-B7-H3 CDR-H1	SGYSWH
1212	Anti-B7-H3 VL	DIQMTQSPSSLSASVGDRVTITCKASQNVGFNVAWYQQKPGKSP KALIYSASYRSGVPSRFSGSGSGTDFTLTISLQPEDFAEYFCQQ YNWYPFTFGQGTKLEIK
1213	Anti-B7-H3 CDR-H2	WIFPGDDSTQYNEKFKG
1214	Anti-B7-H3 CDR-L3	QNGHSFPLT
1215	Anti-CDCP1 VL	DIQMTQSPSSLSASVGDRVTITCSVSSSVFYVHWYQQKPGKAPK LLIYDTSKLASGVPSRFSGSGSGTDFTFTISLQPEDATYYCQQW NSNPPTFGGGGTKVEIK
1216	Anti-CDCP1 VL	QIVLTQSPAIMSASPGEKVTMTCSVSSSVFYVHWYQQKSGTSPK RWIYDTSKLASGVPARFSGSGSGTSYSLTISSMEAEDAATYYCQ QWNSNPPTFGGGGTKLEIK
1217	Anti-CDCP1 CDR-H3	DGVLR YFDWLLDY YY YMDV
1218	Anti-GPC3 CDR-H2	GIDPETGGTAYNQKFKG
1219	Anti-GPC3 CDR-L1	RSSQSIVHSNANTYLQ

1220	Anti-TIGIT CDR-H3	GPSEVGAILGYVWFDP
1221	Anti-CD33 VL	DIQMTQSPSSLSASVGDRVTINCKASQDINSYLSWFQQKPGKAPK TLIYRANRVDGVPSRFSGSGSGQDYTLT ISSLPEDFATYYCLQYDEFPLTFGGGTKVEIK

WHAT IS CLAIMED IS:

1. A Camptothecin Conjugate having the formula of

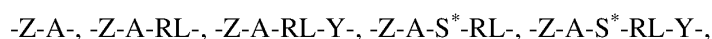
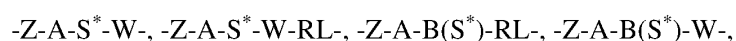
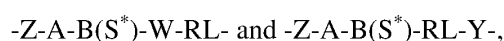


or a salt thereof, wherein

L is a Ligand Unit from a targeting agent, in particular from an antibody that selectively binds to a cancer cell antigen;

subscript p is an integer ranging from 1 to 16;

Q is a Linker Unit having a formula selected from the group consisting of:



wherein Z is a Stretcher Unit;

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

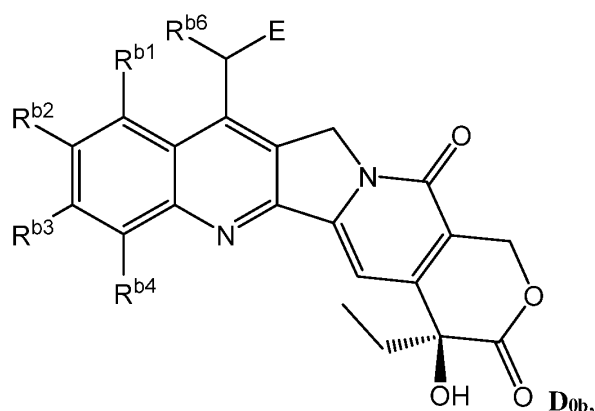
S* is a Partitioning Agent;

RL is a Releasable Linker;

W is a Amino Acid Unit;

Y is a Spacer Unit; and

D is a Drug Unit D having a formula of **D_{0b}**,



or a salt thereof, wherein;

E is $-OR^{b5}$ or $-NR^{b5}R^{b5'}$;

R^{b1} is selected from the group consisting of H, halogen, -CN, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered

heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with C₁-C₃ alkyl, -OR^a-, -NR^aR^{a'}-, -C(O)R^a-, and -SR^a-, or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with -OR^a-, -NR^aR^{a'}-, and -SR^a-, or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a-, -NR^aR^{a'}-, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;

each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, C₁-C₆ hydroxyalkyl-heteroaryl-, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀

heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and R^{a'} are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

wherein a) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane and E is -NR^{b5}R^{b5'}, then each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-N-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -

NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

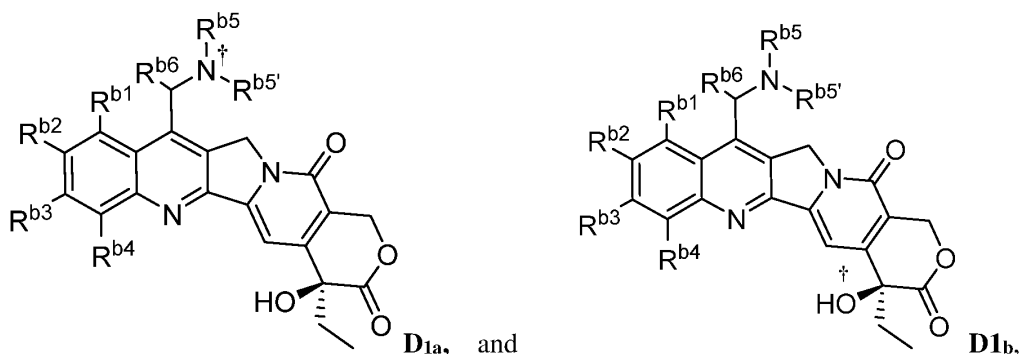
b) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, E is not -OH; and

c) when R^{b2} is methyl and R^{b3} is F, then R^{b1} does not come together with R^{b6} and the intervening atoms to form a ring, and

d) D is not (*S*)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(7*H*)-dione or (*S*)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(7*H*)-dione, or a salt of any of the foregoing;

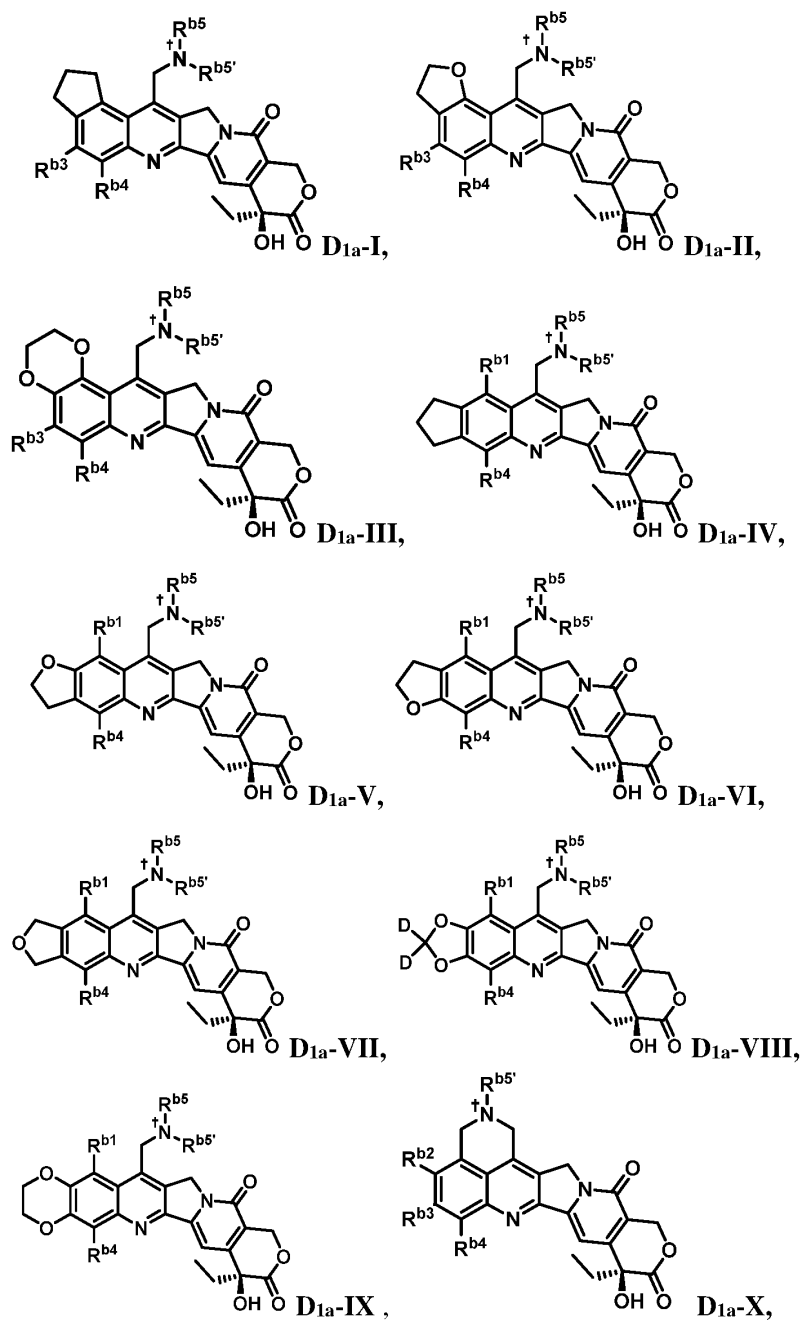
wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

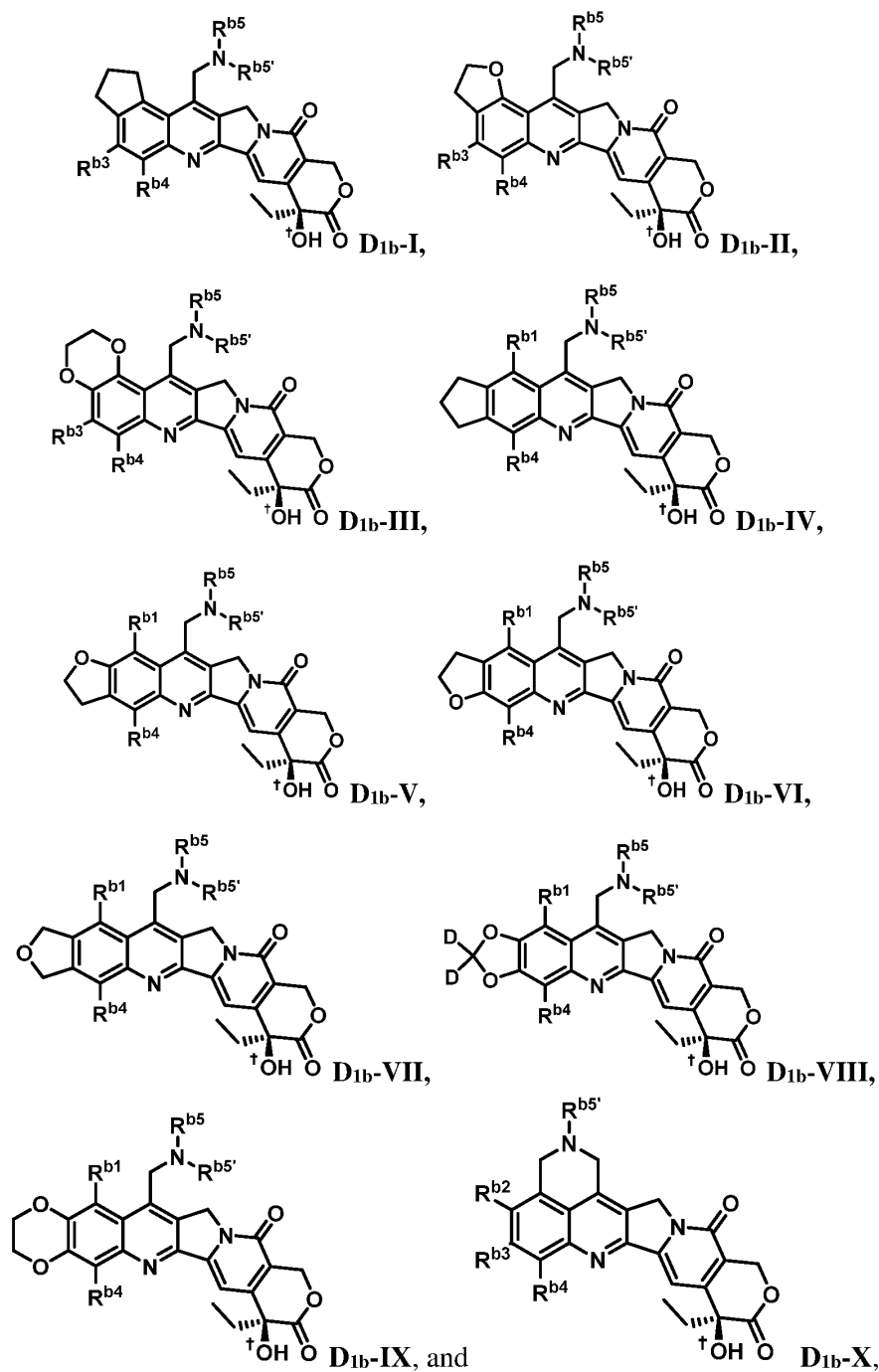
2. The Camptothecin Conjugate of claim 1, wherein D has a formula selected from the group consisting of



or a salt thereof, wherein the dagger indicates the site of covalent attachment of D to Q, or wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of R^{b5} is replaced with a bond to Q or a tertiary amine of R^{b5} is quaternized to form a bond to Q.

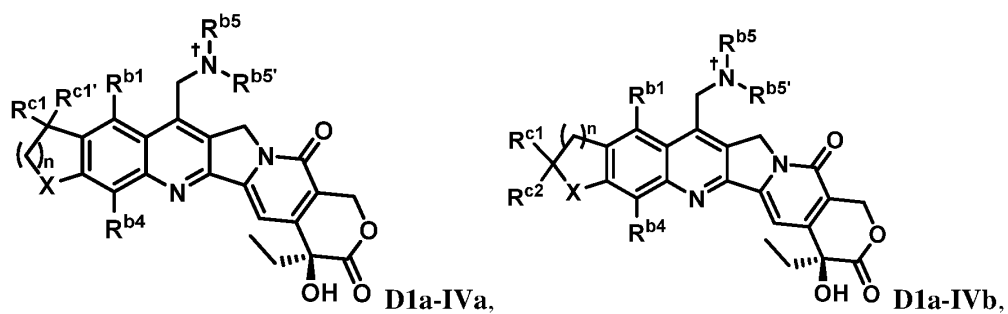
3. The Camptothecin Conjugate of claim 2, wherein D has a formula selected from the group consisting of

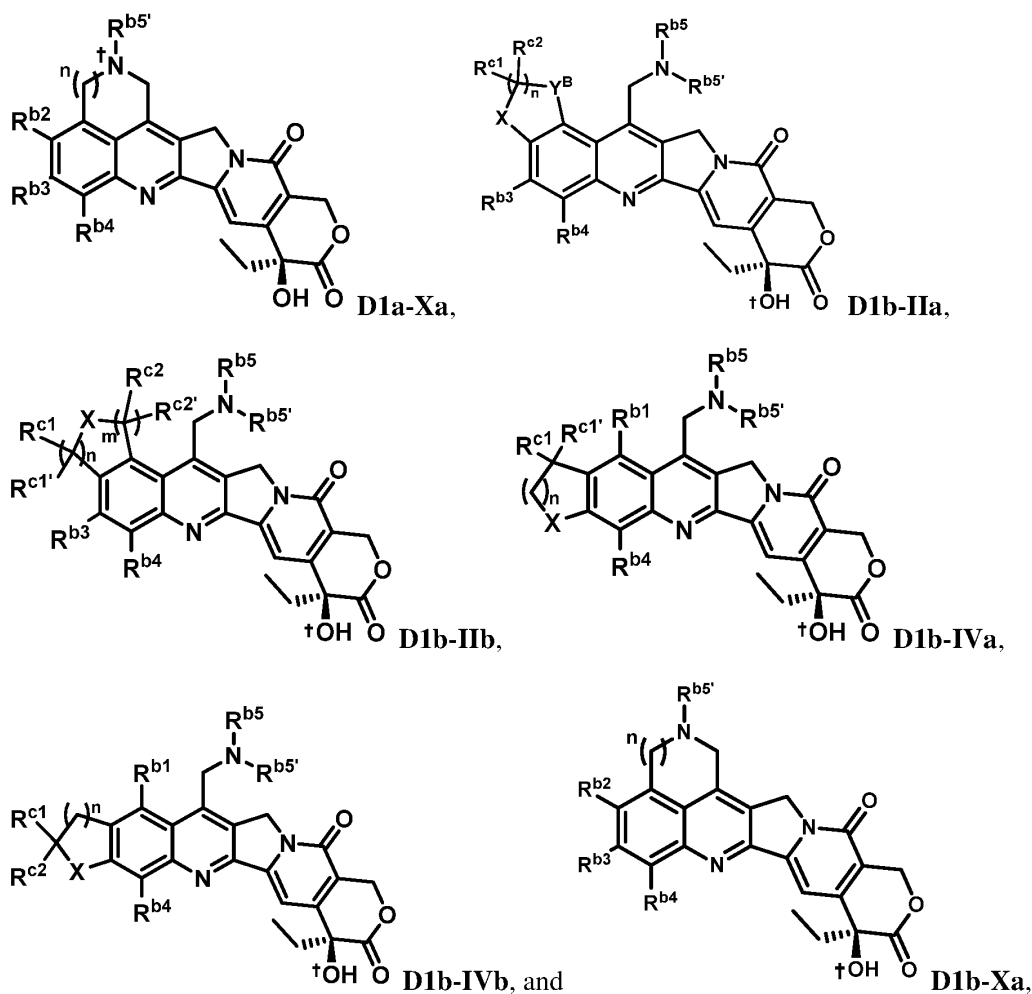




or a salt thereof, wherein the dagger indicates the site of covalent attachment of D to Q, or wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of R^{b5} is replaced with a bond to Q or a tertiary amine of R^{b5} is quaternized to form a bond to Q.

-
- D1a-IIa,**
- D1a-IIb,**





or a salt thereof, wherein

X and Y^B are each independently O, S, S(O)₂, CR^xR^{x'}, or NR^x;

R^x and R^{x'} are each independently selected from the group consisting of H, OH, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ aminoalkyl-C(O)-, C₁-C₆ alkyl-C(O)-, C₁-C₆ hydroxyalkyl-C(O)-, C₁-C₆ alkyl-NH-C(O)-, or C₁-C₆ alkyl-S(O)₂-; and

m and n are each 1 or 2;

each R^{c1}, R^{c1'}, R^{c2}, and R^{c2'} is independently

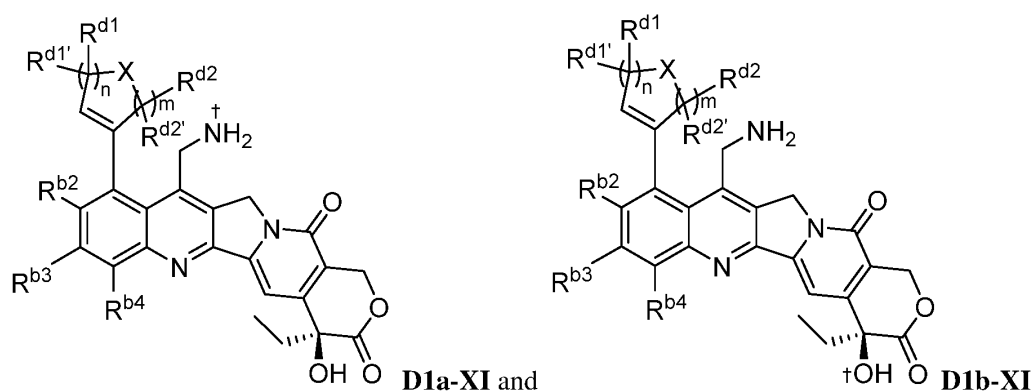
- (i) selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, -OR^a, -NR^aR^{a'}, and -SR^a, C₁-C₆ alkyl-C(O)-, C₁-C₆ alkyl-NR^a-C(O)-, and C₁-C₆ alkyl-S(O)₂-; or
- (ii) taken together with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocycle or heterocycle; or

(iii) taken together with $R^{x'}$ and the intervening atoms to form a 3 to 6-membered carbocyclo or heterocyclo; and

when m and n are both present, the sum of $m + n$ is 2 or 3;

wherein the dagger indicates the site of covalent attachment of D to Q, or wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of R^{b5} is replaced with a bond to Q or a tertiary amine of R^{b5} is quaternized to form a bond to Q.

5. The Camptothecin Conjugate of claim 2, wherein D has a formula selected from the group consisting of

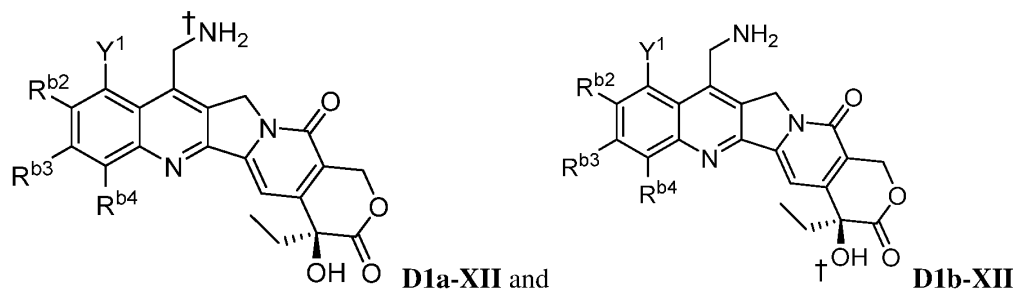


or a salt thereof, wherein

R^{d1} , $R^{d1'}$, R^{d2} , and $R^{d2'}$ are each independently selected from the group consisting of H, halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, $-OR^a$, $-NR^aR^{a'}$, and $-SR^a$, C_1 - C_6 alkyl- $C(O)-$, C_1 - C_6 alkyl- $NR^a-C(O)-$, and C_1 - C_6 alkyl- $S(O)_2-$;

wherein the dagger indicates the site of covalent attachment of D to Q.

6. The Camptothecin Conjugate of claim 2, wherein D has a formula selected from the group consisting of

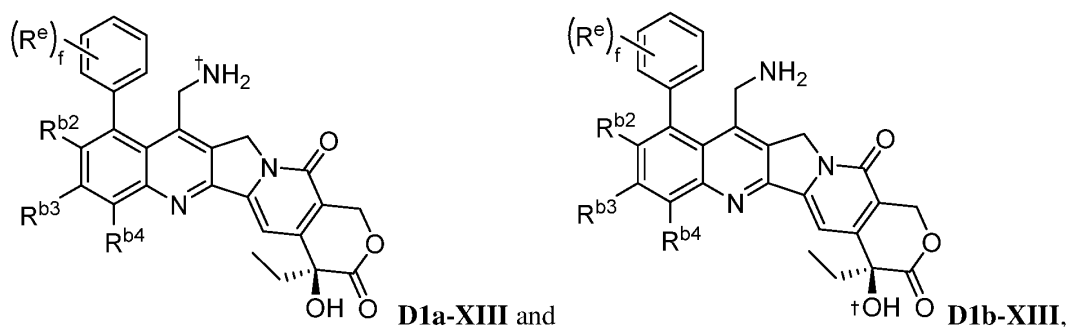


or a salt thereof, wherein

Y^1 is a 5- or 6-membered heteroaryl, optionally substituted with halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 aminoalkyl, or C_1 - C_6 alkyl-S(O)₂-;

wherein the dagger indicates the site of covalent attachment of D to Q.

7. The Camptothecin Conjugate of claim 2, wherein D has a formula selected from the group consisting of

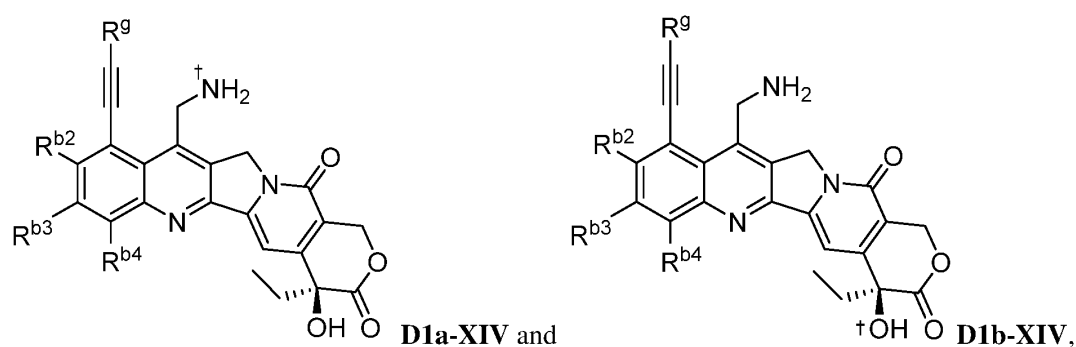


or a salt thereof, wherein

each R^e is independently selected from the group consisting of halogen, -OH, -NH₂, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 alkyl-S(O)₂-, and C_1 - C_6 alkyl-NR^a-C(O)-; and f is 0, 1, 2, 3, 4, or 5;

wherein the dagger indicates the site of covalent attachment of D to Q.

8. The Camptothecin Conjugate of claim 2, wherein D has a formula selected from the group consisting of

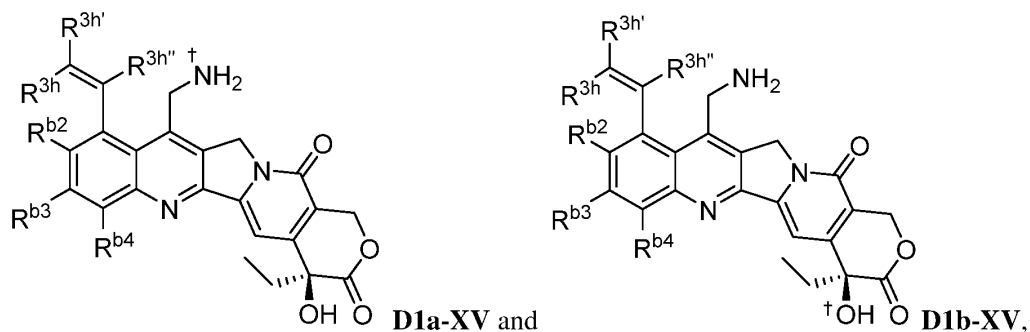


or a salt thereof, wherein

R^g is H, C_1 - C_6 alkyl, or 3 to 8-membered heterocycle;

wherein the dagger indicates the site of covalent attachment of D to Q.

9. The Camptothecin Conjugate of claim 2, wherein D has a formula selected from the group consisting of

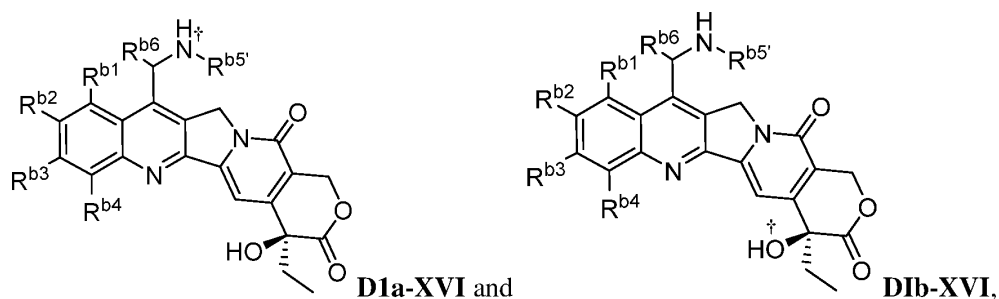


or a salt thereof, wherein

R^{3h} , $R^{3h'}$, and $R^{3h''}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, -C(O)-C₁-C₆ alkyl, -C(O)O-C₁-C₆ alkyl, -C(O)NH-C₁-C₆ alkyl, C₆-C₁₀ aryl, -C₆-C₁₀ aryl-C₁-C₆ alkyl, and -C₆-C₁₀ aryl-C₁-C₆ alkoxy; each optionally substituted with, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a;

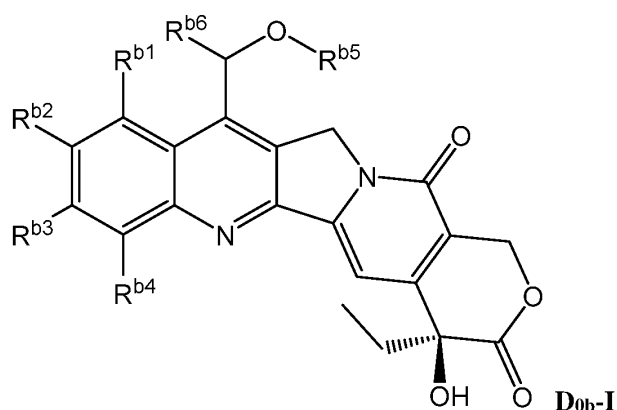
wherein the dagger indicates the site of covalent attachment of D to Q.

10. The Camptothecin Conjugate of claim 2, wherein D has a formula selected from the group consisting of



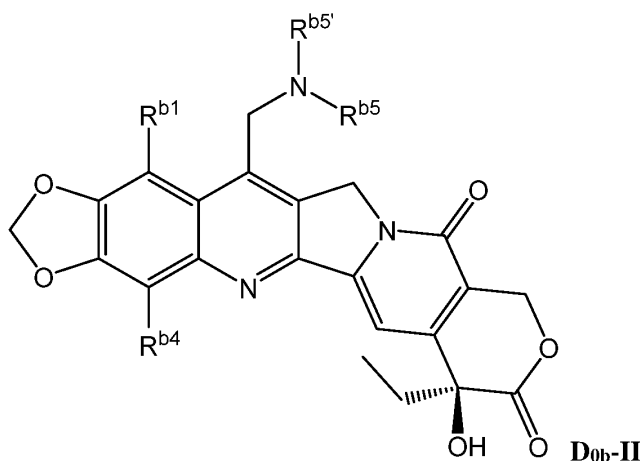
or a salt thereof; wherein the dagger indicates the site of covalent attachment of D to Q.

11. The Camptothecin Conjugate of claim 1, wherein D has the formula of **D0b-I**



or a salt thereof; wherein when R^{b2} is combined with R^{b3} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle, the heterocycle has no more than one O.

12. The Camptothecin Conjugate of claim 1, wherein D has the formula of **D_{0b-II}**



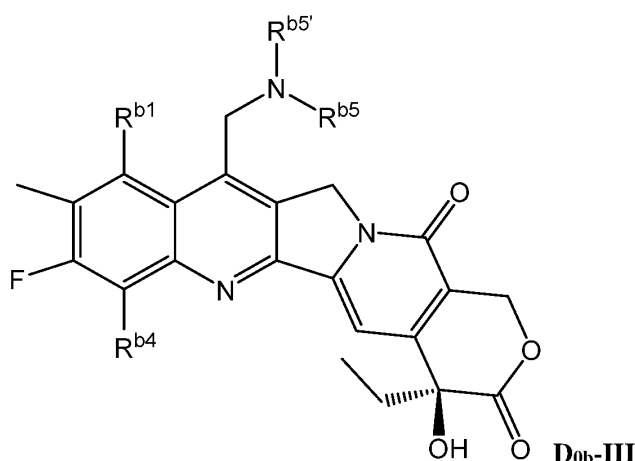
or a salt thereof, wherein;

R^{b5} is H and $R^{b5'}$ is selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-N-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group

consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

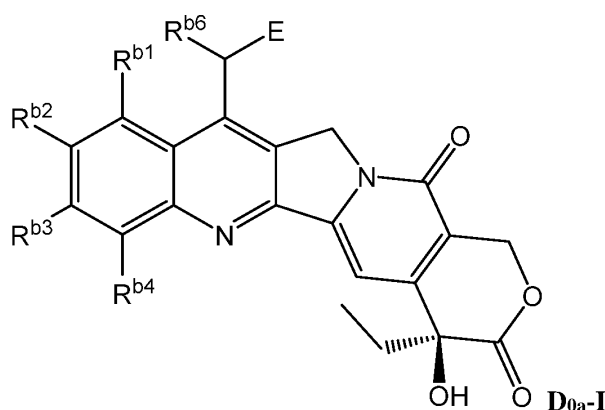
R^{b5'} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂, provided that D is not (*S*)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(7*H*)-dione or (*S*)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(7*H*)-dione, or a salt of any of the foregoing.

13. The Camptothecin Conjugate of claim 1, wherein D has the formula of **D_{0b}-III**



or a salt thereof.

14. The Camptothecin Conjugate of claim 1, wherein D has the formula of **D_{0a}-I**



or a salt thereof, wherein;

E is -OR^{b5} or -NR^{b5}R^{b5'};

R^{b1} is selected from the group consisting of H, halogen, -CN, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with C₁-C₃ alkyl, -OR^a, -NR^aR^{a'}, -C(O)R^a, and -SR^a; or

R^{b1} is combined with R^{b2}, R^{b5}, or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^a-, and -SR^a-, each optionally substituted with -OR^a-, -NR^aR^a-, and -SR^a-, or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; ,or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b3} is combined with R^{b2} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo or a 5-membered heterocyclo fused with 6-membered aryl;

R^{b4} is selected from the group consisting of H and halogen;

each R^{b5} and $R^{b5'}$ are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-O-C₁-C₈ alkyl, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ hydroxyalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, heteroaryl-C₁-C₆ hydroxyalkyl, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

$R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

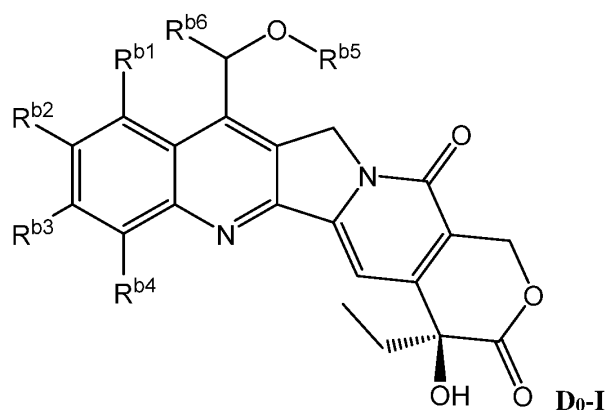
R^a and $R^{a'}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

wherein a) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, and E is -NR^{b5}R^{b5'}, then each R^{b5} and $R^{b5'}$ are independently selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-

- C₄ alkyl-, phenyl-C(O)-, and phenyl-SO₂-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocycle or heterocycle; wherein the cycloalkyl, carbocycle, heterocycloalkyl, heterocycle, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;
- b) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, E is not -OH;
- c) when E is NH₂, R^{b1} is selected from the group consisting of -CN, 5- to 12-membered heteroaryl with at least one annular N, 3- to 10-membered heterocycloalkyl with at least one annular N, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with C₁-C₃ alkyl, -OR^a-, -NR^aR^{a'}-, -C(O)R^a-, and -SR^a-, or R^{b1} is combined with R^{b2} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle with at least one annular N, or 5-membered heterocycle fused with 6-membered aryl; R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with -OR^a-, -NR^aR^{a'}-, and -SR^a-, or R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered heterocycle with at least one annular N, or R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocycle fused with 6-membered aryl; and
- d) when R^{b2} is -OH or methyl and R^{b3} is F, then R^{b1} does not come together with R^{b5}, R^{b5'} or R^{b6} and the intervening atoms to form a ring; and

- e) D is not selected from the group consisting of (S)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, (S)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, (S)-14-((4-(2-aminoethyl)piperazin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, (S)-14-((4-aminopiperidin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, and *tert*-butyl (S)-(1-((7-ethyl-7-hydroxy-8,11-dioxo-7,8,11,13-tetrahydro-10*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-14-yl)methyl)piperidin-4-yl)carbamate, or a salt of any of the foregoing

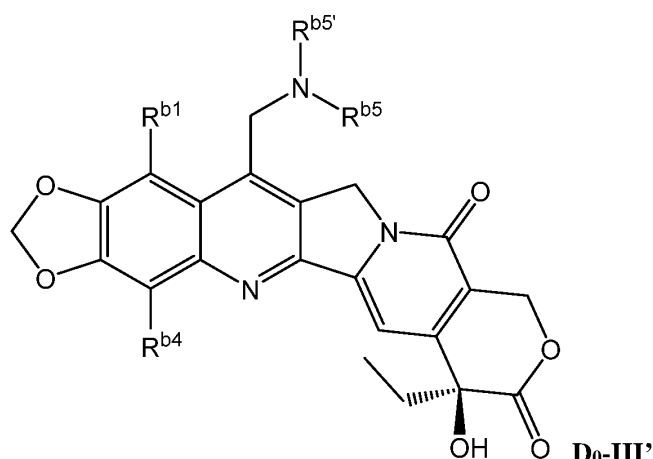
15. The Camptothecin Conjugate of claim 1, wherein D has the formula of **D₀-I'**



or a salt thereof,

wherein when R^{b2} is combined with R^{b3} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle, the heterocycle has no more than one O.

16. The Camptothecin Conjugate of claim 1, wherein D has the formula of **D₀-III'**



or a salt thereof, wherein;

R^{b1} is selected from the group consisting of H, halogen, -CN, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with C₁-C₃ alkyl, -OR^a-, -NR^aR^{a'}-, -C(O)R^a-, and -SR^a-, or R^{b1} is combined with R^{b5} or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b4} is selected from the group consisting of H or halogen;

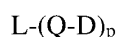
R^{b5} is H and $R^{b5'}$ is C₁-C₈ alkyl-O-C₁-C₈ alkyl, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl-; or

$R^{b5'}$ is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and R^{a'} are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-, provided that D is not selected from the group consisting of (S)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-14-((4-(2-aminoethyl)piperazin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-14-((4-aminopiperidin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, and *tert*-butyl (S)-(1-((7-ethyl-7-hydroxy-8,11-dioxo-7,8,11,13-tetrahydro-10H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-14-yl)methyl)piperidin-4-yl)carbamate, or a salt of any of the foregoing

17. A Camptothecin Conjugate having the formula of

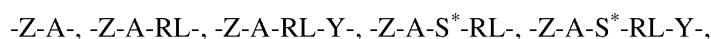
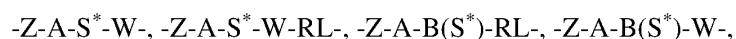
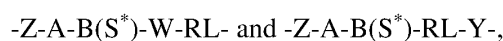


or a salt thereof, wherein

L is a Ligand Unit from a targeting agent, in particular from an antibody that selectively binds to a cancer cell antigen;

subscript p is an integer ranging from 1 to 16;

Q is a Linker Unit having a formula selected from the group consisting of:



wherein Z is a Stretcher Unit;

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

S^{*} is a Partitioning Agent;

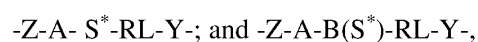
RL is a Releasable Linker;

W is a Amino Acid Unit;

Y is a Spacer Unit; and

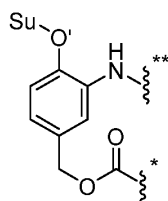
D is a Drug Unit D, wherein D comprises a compound selected from Table I, or a salt thereof, wherein D is covalently attached to Q via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to Q or a tertiary amine of D is quaternized to form a bond to Q.

18. The Camptothecin Conjugate of any one of claims 1-17, wherein Q is a Linker Unit having the formula selected from the group consisting of:



wherein A is a Connector Unit and RL is a Glycoside (e.g., Glucuronide) Unit.

19. The Camptothecin Conjugate of claim 18, wherein the Glycoside (e.g., Glucuronide) Unit has the formula of:



wherein

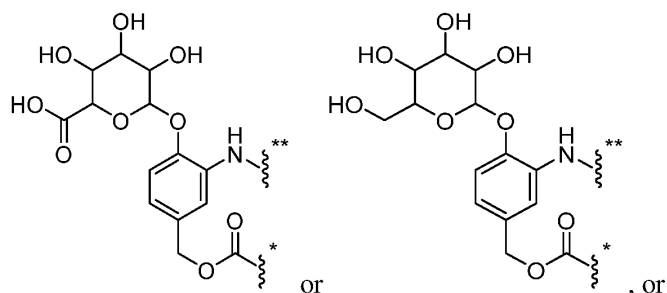
Su is a hexose form of a monosaccharide;

O' represents the oxygen atom of a glycosidic bond that is capable of cleavage by a glycosidase;

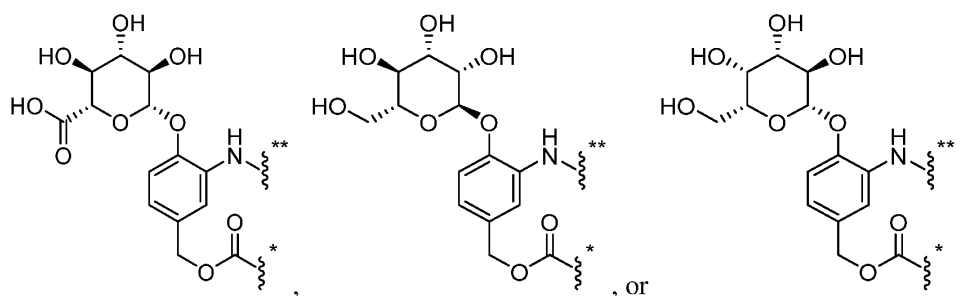
the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D; and

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the remainder of Q,

optionally wherein the Glycoside (e.g., Glucuronide) Unit has the formula of:



optionally wherein the Glycoside (e.g., Glucuronide) Unit has the formula of:



20. The Camptothecin Conjugate of claims 1-16, wherein RL is present and is a peptide comprising from 2 to 8 amino acids.

21. The Camptothecin Conjugate of claim 20, wherein RL is a dipeptide.

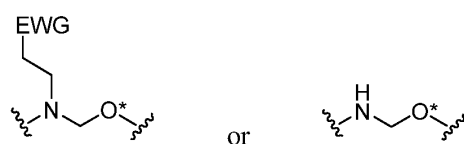
22. The Camptothecin Conjugate of claim 20 or 21, wherein RL is val-ala, val-cit, or val-lys.

23. The Camptothecin Conjugate of claim 18, wherein

Q is a Linker Unit having the formula of -Z-A-RL-Y-, -Z-A-S*-RL-Y- or -Z-A-

B(S*)-RL-Y-; and

Spacer Unit (Y) has the formula of:



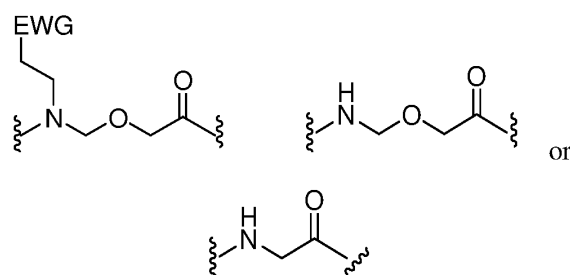
wherein EWG is an electron-withdrawing group;

O* represent the oxygen atom from a hydroxy substituent of D;

the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment to the carbonyl carbon atom of the Glycoside (e.g., Glucuronide) Unit; and

the wavy line adjacent to O* indicates the site of covalent attachment to the remainder of D, or

the Spacer Unit (Y) has the formula of:



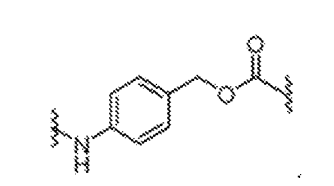
wherein

EWG is an electron-withdrawing group;

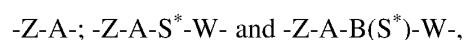
the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment to the carbonyl carbon atom of the Glycoside (e.g., Glucuronide) Unit; and

the wavy line adjacent to the carbonyl carbon atom indicates the site of covalent attachment to a nitrogen atom of an amino substituent of D.

24. The Camptothecin Conjugate of claim 1-17 or 20-22, wherein
Y is present and has the formula of:

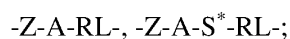


25. The Camptothecin Conjugate of any one of claims 1-17, wherein
Q is a Linker Unit having a formula selected from the group consisting of:



wherein A is a Connector Unit, or

Q is a Linker Unit having a formula selected from the group consisting of:

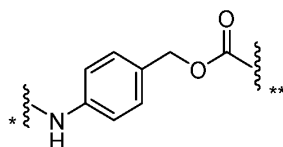


wherein A is a Connector Unit and RL is a Releasable linker other than a Glycoside (e.g., Glucuronide) Unit.

26. The Camptothecin Conjugate of claim 25, wherein

Q is a Linker Unit having the formula selected from the group consisting of $-Z-A-RL-$, $-Z-A-S^*-RL-$ and $-Z-A-S^*-W-RL-$, wherein

RL has the formula:



wherein

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to D; and

the wavy line marked with a single asterisk (*) indicates the point of covalent attachment to A, S* or W.

27. The Camptothecin Conjugate of claim 25 or 26, wherein

-Q-D has the formula of $-Z-A-S^*-W-RL-D$, wherein

D is covalently attached to Q via the nitrogen atom of an amine functional group of D; and

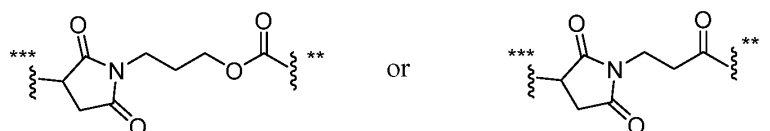
W is an Amino Acid Unit selected from the group consisting of N-methyl-glycine (sarcosine), N-methyl-alanine, N-methyl- β -alanine, valine, N-methyl-valine, or

D is covalently attached to Q via an oxygen atom of the hydroxyl substituent on the lactone ring of D; and

W is an Amino Acid Unit selected from the group consisting glutamic acid or lysine.

28. The Camptothecin Conjugate of claim 27, wherein $-Z-A-$ comprises a succinimido-alkanoyl moiety or succinimido and triazole moieties, each optionally having the succinimide ring in hydrolyzed form as a succinic acid amide moiety, or a succinic acid amide moiety derivable from mDPR of a Camptothecin-Linker Compound, or

wherein $-Z-A-$ has the formula of:

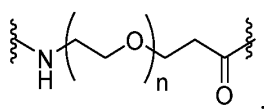


optionally having the succinimide ring in hydrolyzed form as a succinic acid amide moiety, wherein the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to S*; and the wavy line marked with a triple asterisk (***) indicates the point of covalent attachment to a sulfur atom of L.

29. The Camptothecin Conjugate of claim 15, wherein

Q is a Linker Unit having the formula selected from the group consisting of -Z-A-S*-RL- and -Z-A-S*-W-RL-, wherein

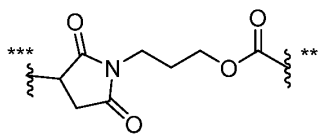
S* has the formula of:



wherein subscript n is an integer ranging from 1 to 36,

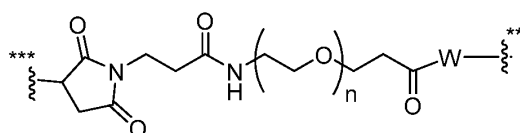
the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment to a carbonyl carbon atom of A, and the wavy line adjacent to the carbonyl carbon atom indicates the site of covalent attachment to the nitrogen atom of the amine functional group of RL of -Z-A-S*-RL- or W of -Z-A-S*-W-RL-,

in particular, -Z A- in either formula of Q has the formula of:



wherein the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the nitrogen atom of the amine functional group of S*; and the wavy line marked with a triple asterisk (***) indicates the point of covalent attachment to a sulfur atom of L.

30. The Camptothecin Conjugate of claim 25, wherein Q is a Linker Unit of formula -Z-A-S*-W- or -Z-A-S-W-RL-, wherein -Z-A-S*-W- in either formula has the formula of:



optionally having the succinimide ring in hydrolyzed form as a succinic acid amide moiety, wherein subscript n is an integer ranging from 2 to 10, preferably ranging from 2 to 4; the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to D or RL; and the wavy line marked with a triple asterisk (***) indicates the point of covalent attachment to a sulfur atom of L.

31. A Camptothecin-Linker compound having a formula selected from the group consisting of:

- (i) Z'-A-RL-D;
- (ii) Z'-A-RL-Y-D;
- (iii) Z'-A-S*-RL-D;
- (iv) Z'-A-S*-RL-Y-D;
- (v) Z'-A-B(S*)-RL-D;
- (vi) Z'-A-B(S*)-RL-Y-D;
- (vii) Z'-A-D
- (viii) Z'-A-S*-W-D
- (ix) Z'-A-B(S*)-W-D
- (x) Z'-A-S*-W-RL-D; and
- (xi) Z'-A-B(S*)-W-RL-D

wherein

Z' is a Stretcher Unit precursor;

A is a bond or a Connector Unit;

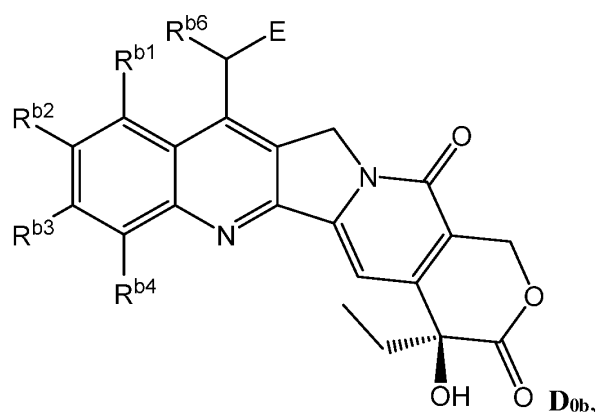
B is a Parallel Connector Unit;

S* is a Partitioning Agent;

RL is a Releasable Linker;

Y is a Spacer Unit; and

D is a Drug Unit D having a formula of D_{0b}



or a salt thereof; wherein;

E is $-\text{OR}^{\text{b5}}$ or $-\text{NR}^{\text{b5}}\text{R}^{\text{b5'}}$;

R^{b1} is selected from the group consisting of H, halogen, $-\text{CN}$, $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_1\text{-C}_8$ haloalkyl, $\text{C}_2\text{-C}_8$ alkenyl, $\text{C}_2\text{-C}_8$ alkynyl, $\text{C}_6\text{-C}_{12}$ aryl, 5- to 12-membered heteroaryl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, 3- to 10-membered heterocycloalkyl, $(\text{C}_6\text{-C}_{12} \text{ aryl})\text{-C}_2\text{-C}_8$ alkenyl-, $\text{C}_1\text{-C}_8$ hydroxyalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ aminoalkyl-, $\text{C}_1\text{-C}_8$ aminoalkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ alkyl-, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{C}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{O-C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-O-}$, $-\text{COOR}^{\text{a}}$, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; each optionally substituted with $\text{C}_1\text{-C}_3$ alkyl, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, $-\text{C}(\text{O})\text{R}^{\text{a}}$, and $-\text{SR}^{\text{a}}$; or

R^{b1} is combined with R^{b2} , R^{b5} , or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_2\text{-C}_8$ alkynyl, $\text{C}_6\text{-C}_{12}$ aryl, 5- to 12-membered heteroaryl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, 3- to 10-membered heterocycloalkyl, $\text{C}_1\text{-C}_8$ haloalkyl, $\text{C}_1\text{-C}_8$ hydroxyalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{S}(\text{O})_2\text{-}$, $\text{C}_1\text{-C}_8$ aminoalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ aminoalkyl-, $\text{C}_1\text{-C}_8$ aminolalkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ alkyl-, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{O-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{C}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{O-C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-O-}$, $-\text{COOR}^{\text{a}}$, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; each optionally substituted with $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;

each R^{b5} and $R^{b5'}$ are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, C₁-C₆ hydroxyalkyl-heteroaryl-, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

$R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and R^a' are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

wherein a) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane and E is $-NR^{b5}R^{b5'}$, then each R^{b5} and $R^{b5'}$ are independently selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-N-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

$R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

b) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, E is not -OH; and

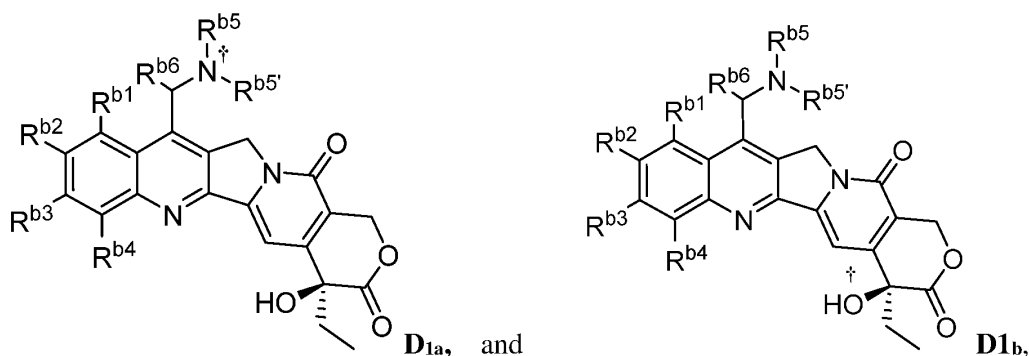
c) when R^{b2} is methyl and R^{b3} is F, then R^{b1} does not come together with R^{b6} and the intervening atoms to form a ring, and

d) D is not (S)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione or (S)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-

11*H*-[1,3]dioxolo[4,5-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(7*H*)-dione, or a salt of any of the foregoing;

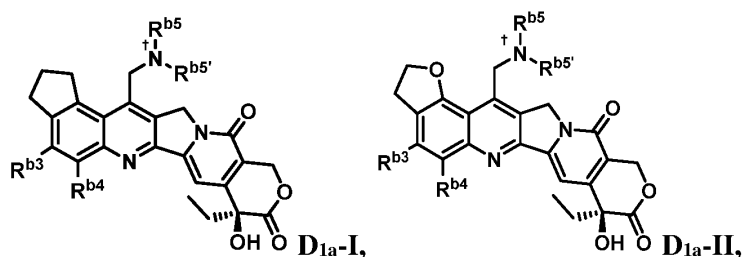
wherein D is covalently attached to the remainder of the Camptothecin-Linker compound via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to the remainder of the Camptothecin-Linker compound or a tertiary amine of D is quaternized to form a bond to the remainder of the Camptothecin-Linker compound.

32. The Camptothecin-Linker compound of claim 31, wherein D has a formula selected from the group consisting of

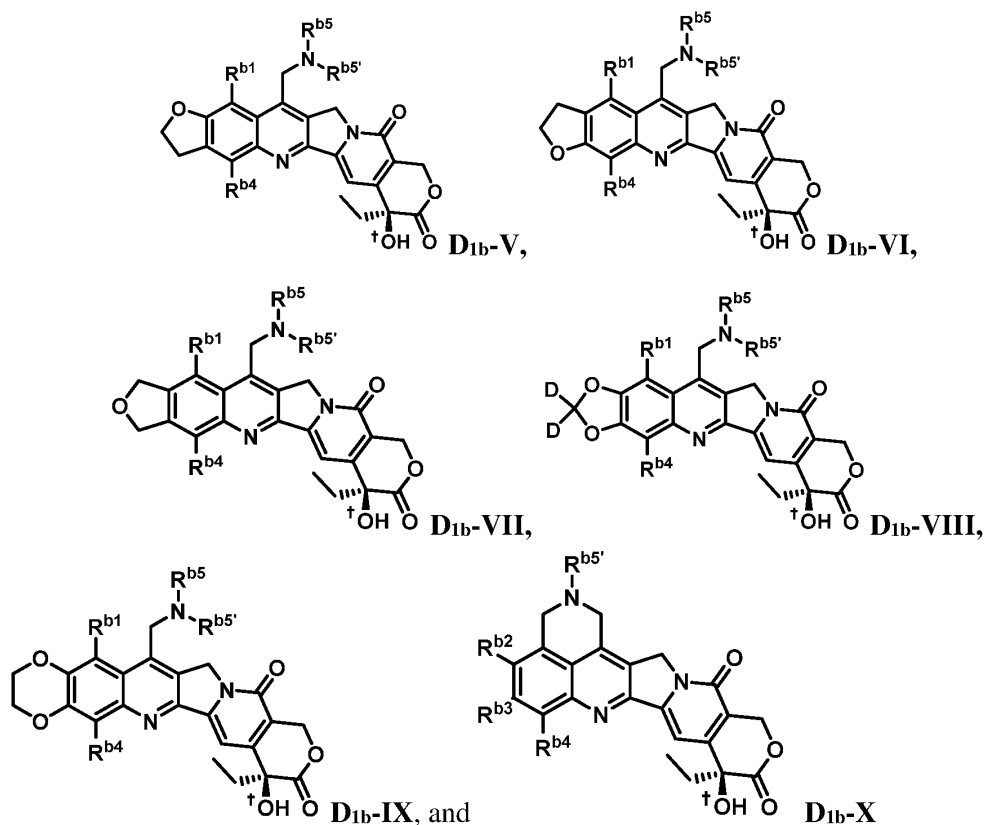


or a salt thereof, wherein the dagger indicates the site of covalent attachment of D to the remainder of the Camptothecin-Linker compound, or wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of R^{b5} is replaced with a bond to the remainder of the Camptothecin-Linker compound or a tertiary amine of R^{b5} is quaternized to form a bond to the remainder of the Camptothecin-Linker compound.

33. The Camptothecin-Linker compound of claim 32, wherein D has a formula selected from the group consisting of

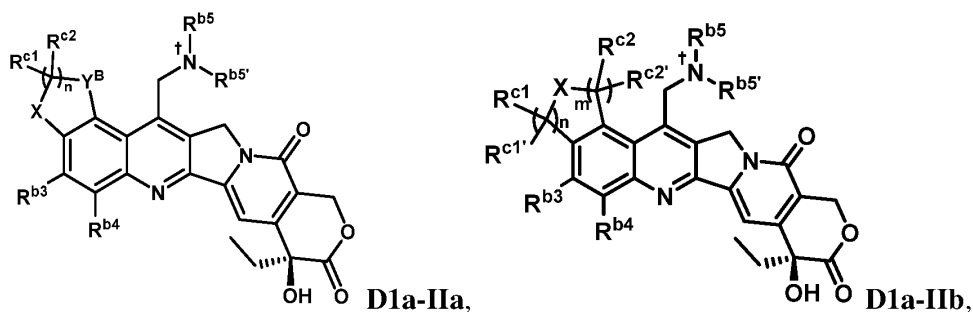


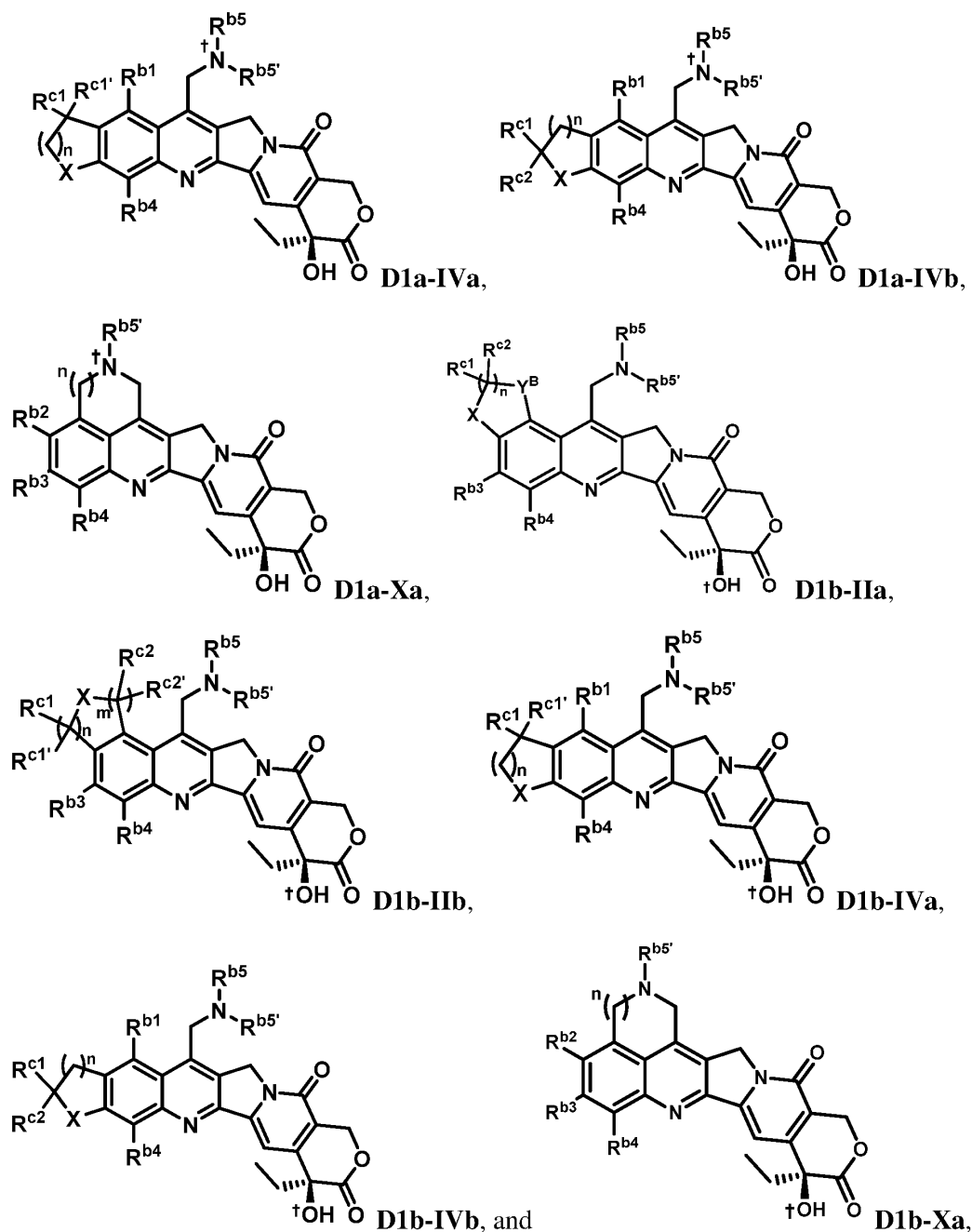




or a salt thereof; wherein the dagger indicates the site of covalent attachment of D to the remainder of the Camptothecin-Linker compound, or wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of R^{b5} is replaced with a bond to the remainder of the Camptothecin-Linker compound or a tertiary amine of R^{b5} is quaternized to form a bond to the remainder of the Camptothecin-Linker compound.

34. The Camptothecin-Linker compound of claim 32, wherein D has a formula selected from the group consisting of





or a salt thereof, wherein

X and Y^B are each independently O, S, S(O)₂, CR^xR^{x'}, or NR^x;

R^x and R^{x'} are each independently selected from the group consisting of H, OH, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ aminoalkyl-C(O)-, C₁-C₆ alkyl-C(O)-, C₁-C₆ hydroxyalkyl-C(O)-, C₁-C₆ alkyl-NH-C(O)-, or C₁-C₆ alkyl-S(O)₂-; and

m and n are each 1 or 2;

each R^{c1} , $R^{c1'}$, R^{c2} , and $R^{c2'}$ is independently

(i) selected from the group consisting of H, halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 hydroxyalkyl, C_1 - C_6 aminoalkyl, $-OR^a$, $-NR^aR^{a'}$, and $-SR^a$, C_1 - C_6 alkyl- $C(O)-$, C_1 - C_6 alkyl- $NR^a-C(O)-$, and C_1 - C_6 alkyl- $S(O)_2-$; or

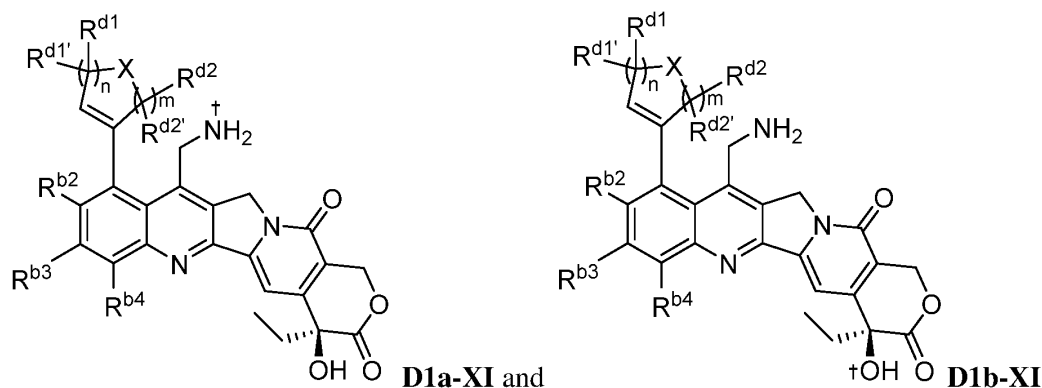
(ii) taken together with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; or

(iii) taken together with $R^{x'}$ and the intervening atoms to form a 3 to 6-membered carbocyclo or heterocyclo; and

when m and n are both present, the sum of m + n is 2 or 3;

wherein the dagger indicates the site of covalent attachment of D to the remainder of the Camptothecin-Linker compound, or wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of R^{b5} is replaced with a bond to the remainder of the Camptothecin-Linker compound or a tertiary amine of R^{b5} is quaternized to form a bond to the remainder of the Camptothecin-Linker compound.

35. The Camptothecin-Linker compound of claim 32, wherein D has a formula selected from selected from the group consisting of

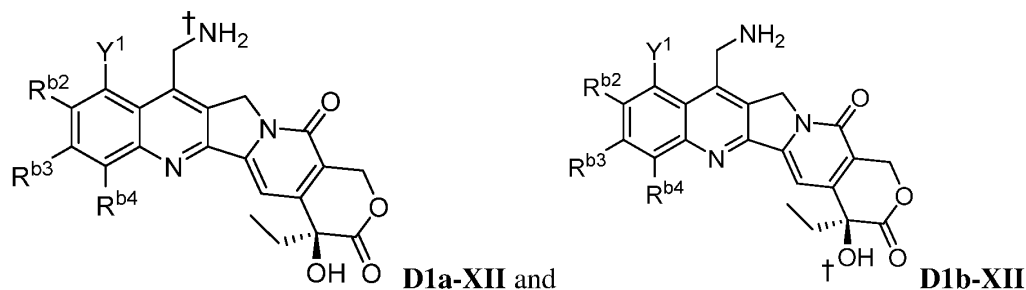


or a salt thereof, wherein

R^{d1} , $R^{d1'}$, R^{d2} , and $R^{d2'}$ are each independently selected from the group consisting of H, halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, $-OR^a$, $-NR^aR^{a'}$, and $-SR^a$, C_1 - C_6 alkyl- $C(O)-$, C_1 - C_6 alkyl- $NR^a-C(O)-$, and C_1 - C_6 alkyl- $S(O)_2-$;

wherein the dagger indicates the site of covalent attachment of D to the remainder of the Camptothecin-Linker compound.

36. The Camptothecin-Linker compound of claim 32, wherein D has a formula selected from the group consisting of

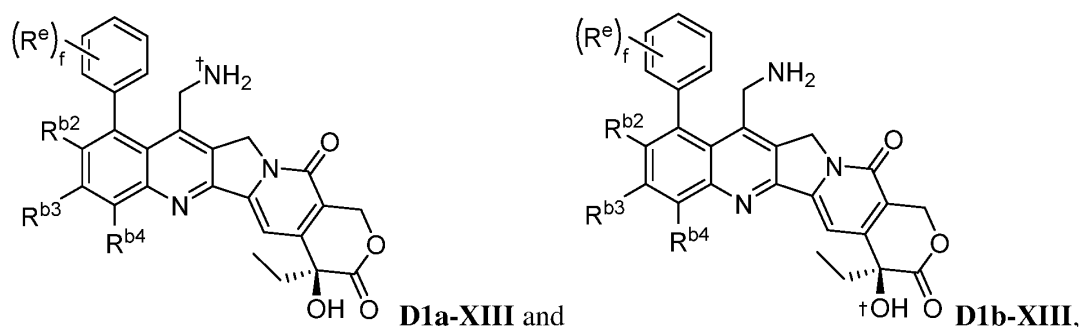


or a salt thereof, wherein

Y¹ is a 5- or 6-membered heteroaryl, optionally substituted with halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, or C₁-C₆ alkyl-S(O)₂;

wherein the dagger indicates the site of covalent attachment of D to the remainder of the Camptothecin-Linker compound.

37. The Camptothecin-Linker compound of claim 31, wherein D has a formula selected from the group consisting of

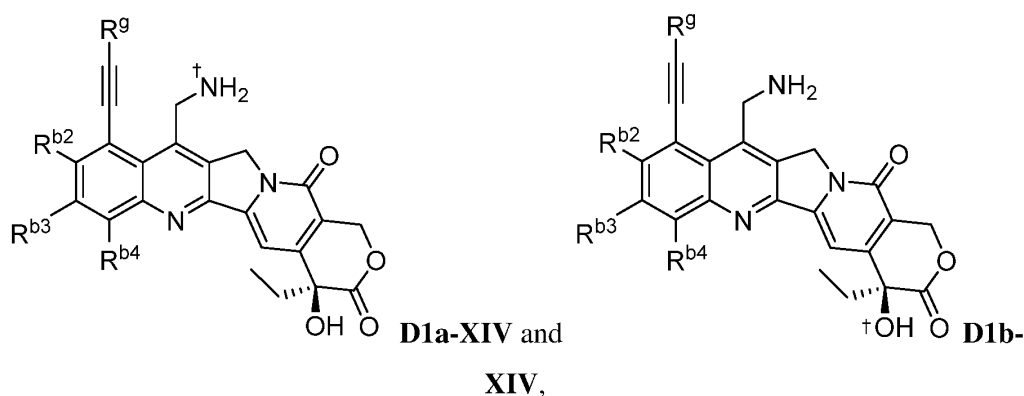


or a salt thereof, wherein

each R^e is independently selected from the group consisting of halogen, -OH, -NH₂, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ alkyl-S(O)₂-, and C₁-C₆ alkyl-NR^a-C(O)-; and f is 0, 1, 2, 3, 4, or 5;

wherein the dagger indicates the site of covalent attachment of D to the remainder of the Camptothecin-Linker compound.

38. The Camptothecin-Linker compound of claim 32, wherein D has a formula selected from the group consisting of

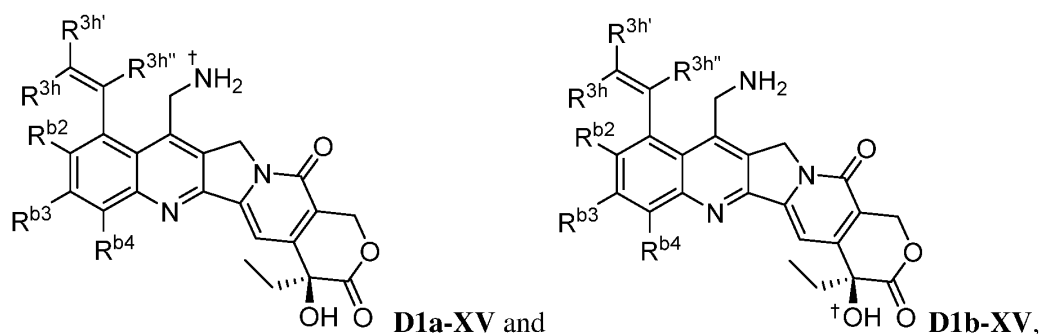


or a salt thereof, wherein

R^g is H, C₁-C₆ alkyl, or 3 to 8-membered heterocyclyl;

wherein the dagger indicates the site of covalent attachment of D to the remainder of the Camptothecin-Linker compound.

39. The Camptothecin-Linker compound of claim 32, wherein D has a formula selected from the group consisting of

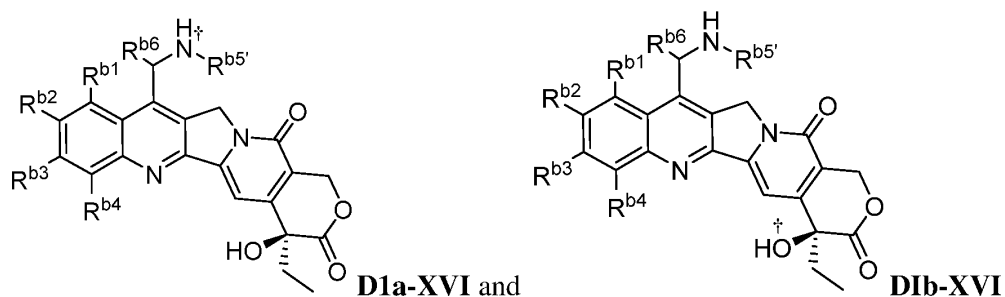


or a salt thereof, wherein

R^{3h} , $R^{3h'}$, and $R^{3h''}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, C₁-C₆ aminoalkyl, -C(O)-C₁-C₆ alkyl, -C(O)O-C₁-C₆ alkyl, -C(O)NH-C₁-C₆ alkyl, C₆-C₁₀ aryl, -C₆-C₁₀ aryl-C₁-C₆ alkyl, and -C₆-C₁₀ aryl-C₁-C₆ alkoxy; each optionally substituted with, C₁-C₆ alkyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a;

wherein the dagger indicates the site of covalent attachment of D to the remainder of the Camptothecin-Linker compound.

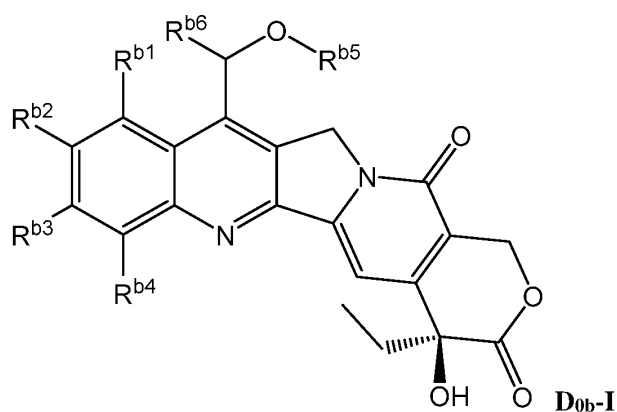
40. The Camptothecin-Linker compound of claim 32, wherein D has a formula selected from the group consisting of



or a salt thereof;

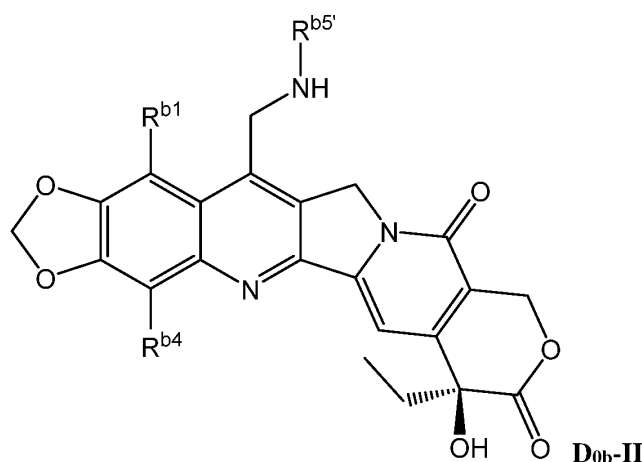
wherein the dagger indicates the site of covalent attachment of D to the remainder of the Camptothecin-Linker compound.

41. The Camptothecin-Linker compound of claim 31, wherein D has the formula of **D0b-I**



or a salt thereof,; and wherein when R^{b2} is combined with R^{b3} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle, the heterocycle has no more than one O.

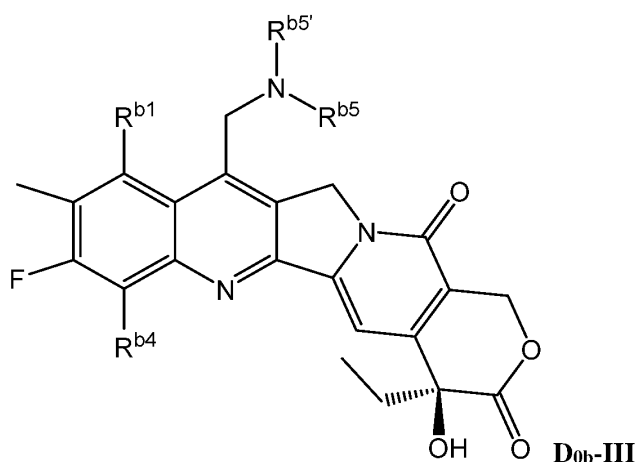
42. The Camptothecin-Linker compound of claim 31, wherein D has the formula of **D0b-II**



or a salt thereof, wherein;

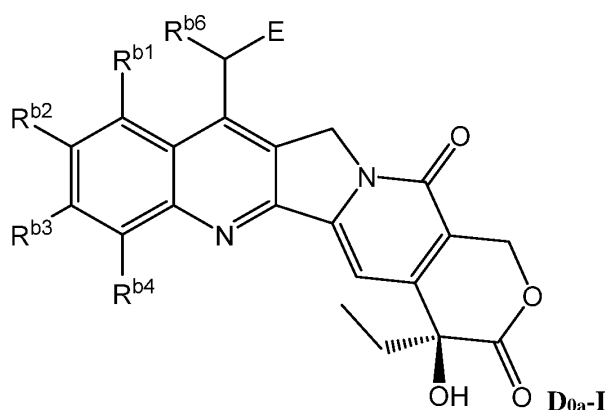
$R^{b5'}$ is selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-N-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or $R^{b5'}$ and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or $R^{b5'}$ is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocycle or heterocycle; wherein the cycloalkyl, carbocycle, heterocycloalkyl, heterocycle, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂, provided that D is not (S)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione or (S)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, or a salt of any of the foregoing.

43. The Camptothecin-Linker compound of claim 31, wherein D has the formula of **D_{0b}-III**



or a salt thereof.

44. The Camptothecin-Linker compound of claim 31, wherein D has the formula of **D_{0a}-I**



or a salt thereof, wherein;

E is -OR^{b5} or -NR^{b5}R^{b5'};

R^{b1} is selected from the group consisting of H, halogen, -CN, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with C₁-C₃ alkyl, -OR^a, -NR^aR^{a'}, -C(O)R^a, and -SR^a; or

- R^{b1} is combined with R^{b2} , R^{b5} , or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;
- R^{b2} is selected from the group consisting of H, halogen, C_1 - C_8 alkyl, C_2 - C_8 alkynyl, C_6 - C_{12} aryl, 5- to 12-membered heteroaryl, C_3 - C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, C_1 - C_8 haloalkyl, C_1 - C_8 hydroxyalkyl, C_1 - C_8 alkyl-S(O)₂-, C_1 - C_8 aminoalkyl, C_1 - C_8 alkyl-C(O)- C_1 - C_8 aminoalkyl-, C_1 - C_8 aminolalkyl-C(O)- C_1 - C_8 alkyl-, C_1 - C_8 alkyl-NR^a-C(O)-, C_1 - C_8 alkyl-C(O)-, C_1 - C_8 alkyl-OC(O)-, C_1 - C_8 alkyl-NR^a-C(O)-, C_1 - C_8 alkyl-C(O)-NR^a-, C_1 - C_8 alkyl-NR^a-C(O)O-, C_1 - C_8 alkyl-OC(O)-NR^a-, C_6 - C_{12} aryl-C(O)-, C_6 - C_{12} aryl-O-C(O)-NR^a-, C_6 - C_{12} aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with -OR^a-, -NR^aR^{a'}-, and -SR^a-, or
- R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or
- R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl;
- R^{b3} is selected from the group consisting of H, halogen, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_1 - C_6 haloalkyl, -OR^a-, -NR^aR^{a'}-, and -SR^a-, or
- R^{b3} is combined with R^{b2} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo or a 5-membered heterocyclo fused with 6-membered aryl;
- R^{b4} is selected from the group consisting of H and halogen;
- each R^{b5} and $R^{b5'}$ are independently selected from the group consisting of H, C_1 - C_8 alkyl, C_1 - C_8 hydroxyalkyl, C_1 - C_8 alkyl-O- C_1 - C_8 alkyl, C_1 - C_8 aminoalkyl, (C_1 - C_4 alkylamino)- C_1 - C_8 alkyl-, *N,N*-(C_1 - C_4 hydroxyalkyl)(C_1 - C_4 alkyl)amino- C_1 - C_8 alkyl-, *N,N*-di(C_1 - C_4 alkyl)amino- C_1 - C_8 alkyl-, *N*-(C_1 - C_4 hydroxyalkyl)- C_1 - C_8 aminoalkyl-, C_1 - C_8 hydroxyalkyl-C(O)-, C_3 - C_{10} cycloalkyl, (C_3 - C_{10} cycloalkyl)- C_1 - C_4 alkyl-, C_3 - C_{10} heterocycloalkyl, (C_3 - C_{10} heterocycloalkyl)- C_1 - C_4 alkyl-, heteroaryl- C_1 - C_6 hydroxyalkyl, phenyl, phenyl- C_1 - C_4 alkyl-, diphenyl- C_1 - C_4 alkyl-, heteroaryl, heteroaryl- C_1 - C_4 alkyl-, C_1 - C_6 alkoxy-C(O)- C_1 - C_8 aminoalkyl-, C_1 - C_6 alkoxy-C(O)-*N*-(C_1 - C_4 alkyl)amino- C_1 - C_8 alkyl-, C_1 - C_6 alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C_1 - C_6 alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)- C_1 - C_8 alkyl-, C_1 - C_4 alkyl-SO₂- C_1 - C_8 alkyl-, NH₂-SO₂- C_1 - C_8 alkyl-, (C₃-C₁₀ heterocycloalkyl)- C_1 - C_4 hydroxyalkyl-, C_1 - C_6 alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)- C_1 - C_8 alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C_1 - C_8 hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C_1 - C_4 alkyl, -OH, - C_1 - C_6 hydroxyalkyl, -OC₁- C_4 alkyl, -NH₂,

-NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂; R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and R^{a'} are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

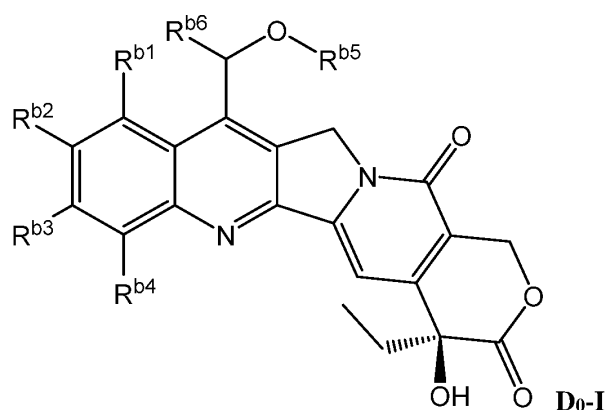
wherein a) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, and E is -NR^{b5}R^{b5'}, then each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, phenyl-C(O)-, and phenyl-SO₂-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

b) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, E is not -OH; c) when E is NH₂, R^{b1} is selected from the group consisting of -CN, 5- to 12-membered heteroaryl with at least one annular N, 3- to 10-membered heterocycloalkyl with at least one annular N, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with C₁-C₃ alkyl, -OR^a, -NR^aR^{a'}, -C(O)R^a, and -SR^a, or R^{b1} is combined with R^{b2} and the intervening atoms to form a 5-, 6-,

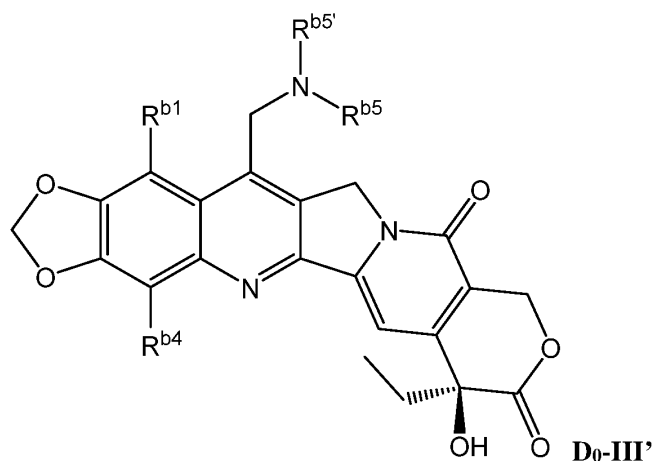
- or 7-membered heterocyclo with at least one annular N, or 5-membered heterocyclo fused with 6-membered aryl; R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with -OR^a-, -NR^aR^{a'}-, and -SR^a-, or
- R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered heterocyclo with at least one annular N, or R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl; and
- d) when R^{b2} is -OH or methyl and R^{b3} is F, then R^{b1} does not come together with R^{b5}, R^{b5'} or R^{b6} and the intervening atoms to form a ring; and
- e) D is not selected from the group consisting of (S)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-14-((4-(2-aminoethyl)piperazin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-14-((4-aminopiperidin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, and *tert*-butyl (S)-(1-((7-ethyl-7-hydroxy-8,11-dioxo-7,8,11,13-tetrahydro-10H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-14-yl)methyl)piperidin-4-yl)carbamate, or a salt of any of the foregoing

45. The Camptothecin-Linker compound of claim 31, wherein D has the formula of **D₀-I'**



or a salt thereof, wherein when R^{b2} is combined with R^{b3} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle, the heterocycle has no more than one O.

45a. The Camptothecin-Linker compound of claim 31, wherein D has the formula of **D0-III'**



or a salt thereof, wherein;

R^{b1} is selected from the group consisting of H, halogen, -CN, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with C₁-C₃ alkyl, -OR^a, -NR^aR^{a'}, -C(O)R^a, and -SR^a; or R^{b1} is combined with R^{b5} or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocycle or heterocycle;

R^{b4} is selected from the group consisting of H or halogen;

$R^{b5'}$ is C_1 - C_8 alkyl- O - C_1 - C_8 alkyl, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C_1 - C_4 alkyl, -OH, - C_1 - C_6 hydroxyalkyl, - OC_1 - C_4 alkyl, - NH_2 , - NH - C_1 - C_4 alkyl, - $N(C_1$ - C_4 alkyl) $_2$, C_1 - C_6 alkoxy- $C(O)$ - NH -, C_1 - C_6 alkoxy- $C(O)$ - C_1 - C_8 aminoalkyl-, and C_1 - C_8 aminoalkyl; or R^{b5} is H and $R^{b5'}$ is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C_1 - C_4 alkyl, -OH, - OC_1 - C_4 alkyl, - NH_2 , - NHC_1 - C_4 alkyl, and - $N(C_1$ - C_4 alkyl) $_2$;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and $R^{a'}$ are each independently selected from the group consisting of H, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 alkyl- $S(O)_2$ -, C_1 - C_6 alkyl- $C(O)$ -, C_1 - C_6 aminoalkyl- $C(O)$ -, and C_1 - C_6 hydroxyalkyl- $C(O)$ -;

provided that D is not selecting from the group consisting of (S)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, (S)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, (S)-14-((4-(2-aminoethyl)piperazin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, (S)-14-((4-aminopiperidin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, and *tert*-butyl (S)-(1-((7-ethyl-7-hydroxy-8,11-dioxo-7,8,11,13-tetrahydro-10*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-14-yl)methyl)piperidin-4-yl)carbamate, or a salt of any of the foregoing

46. A Camptothecin-Linker compound the formula of

- (i) $Z'-A-RL-D$;
- (ii) $Z'-A-RL-Y-D$;
- (iii) $Z'-A-S^*-RL-D$;

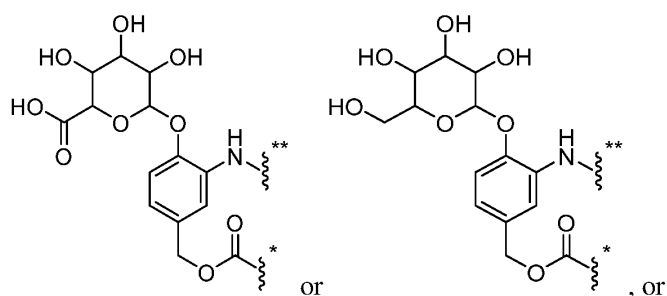
- (iv) Z'-A-S*-RL-Y-D;
- (v) Z'-A-B(S*)-RL-D;
- (vi) Z'-A-B(S*)-RL-Y-D;
- (vii) Z'-A-D
- (viii) Z'-A-S*-W-D
- (ix) Z'-A-B(S*)-W-D
- (x) Z'-A-S*-W-RL-D; and
- (xi) Z'-A-B(S*)-W-RL-D

wherein

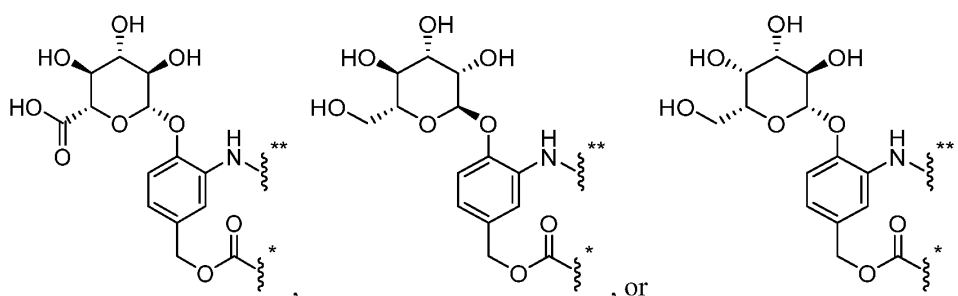
Z' is a Stretcher Unit precursor;
 A is a bond or a Connector Unit;
 B is a Parallel Connector Unit;
 S* is a Partitioning Agent;
 RL is a Releasable Linker;
 Y is a Spacer Unit; and

D is a Drug Unit D, wherein D comprises a compound selected from Table I, or a salt thereof, wherein D is covalently attached to the remainder of Camptothecin-Linker compound via any suitable attachment site on D, optionally wherein a hydrogen atom of a hydroxyl, thiol, primary amine, or secondary amine of D is replaced with a bond to the remainder of the Camptothecin-Linker compound or a tertiary amine of D is quaternized to form a bond to the remainder of the Camptothecin-Linker compound.

47. The Camptothecin-Linker compound of any one of claims 31-46, having the formula selected from the group consisting of formula (i), formula (ii); formula (iii), formula (iv), formula (v) and formula (vi), wherein A is a Connector Unit; and RL is a Glycoside (e.g., Glucuronide) Unit, optionally wherein the Glycoside Unit has the formula of:

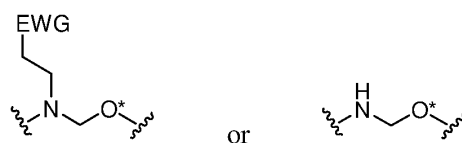


optionally wherein the Glycoside Unit has the formula of:



wherein the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D or to a Spacer Unit (Y); and the wavy line marked with a double asterisk (**) indicates the point of covalent attachment to A, B or S*.

48. The Camptothecin-Linker compound of claims 31-46, wherein RL is present and is a peptide comprising from 2 to 8 amino acids.
49. The Camptothecin-Linker compound of claim 48, wherein RL is a dipeptide.
50. The Camptothecin-Linker compound of claim 48 or 49, wherein RL is val-ala, val-cit, or val-lys.
51. The Camptothecin-Linker compound of any one of claims 31-46 having formula (iii), formula (iv), formula (v) and formula (vi), wherein S* is a PEG group.
52. The Camptothecin-Linker compound of any one of claims 31-46 having formula (ii), formula (iv) or formula (vi), wherein
the Spacer Unit (Y) has the formula of:



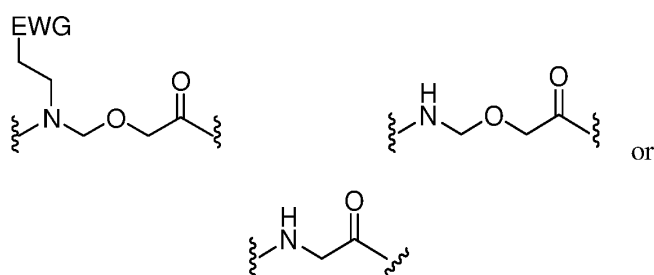
wherein EWG is an electron-withdrawing group;

O* represent the oxygen atom from a hydroxy functional group of D;

the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment to the carbonyl carbon atom of the Glycoside (e.g., Glucuronide) Unit; and

the wavy line adjacent to O* indicates the site of covalent attachment to the remainder of D, or

the Spacer Unit (Y) has the formula of:



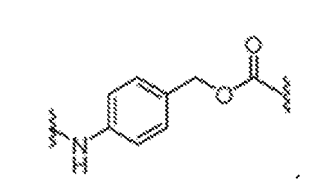
wherein

EWG is an electron-withdrawing group;

the wavy line adjacent to the nitrogen atom indicates the site of covalent attachment to the carbonyl carbon atom of the Glycoside (e.g., Glucuronide) Unit; and

the wavy line adjacent to the carbonyl carbon atom indicates the site of covalent attachment to the nitrogen atom of the amine functional group of D.

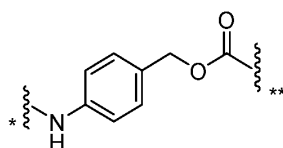
53. The Camptothecin-Linker compound of any one of claims 31-46 or 48-50, wherein Y is present and has the formula of:



54. The Camptothecin-Linker Compound of any one of claims 31-46 having formula (vii), formula (viii) or formula (ix), wherein A is a Connector Unit, or having formula (i), formula (iii), formula (x) or formula (xi), wherein A is a Connector Unit and RL is a Releasable linker other than a Glycoside (e.g., Glucuronide) Unit.

55. The Camptothecin-Linker Compound of claim 54 having formula (i), formula (iii) or formula (x), wherein

RL has the formula:



wherein

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to D; and

the wavy line marked with a single asterisk (*) indicates the point of covalent attachment to A, S* or W.

56. The Camptothecin-Linker Compound of claim 55 having formula (x) wherein W is an Amino Acid Unit selected from the group consisting of N-methyl-glycine (sarcosine), N-methyl-alanine, N-methyl-β-alanine, valine and N-methyl-valine.

57. The Camptothecin-Linker Compound of any one of claims 54-56 wherein Z'-A- is comprised of a maleimido-alkanoyl moiety or mDPR, the basic nitrogen atom of which is optionally protonated or protected by an acid-labile protecting group.

58. The Camptothecin-Linker Compound of any one of claims 54-56 having formula (iii) or formula (x), wherein

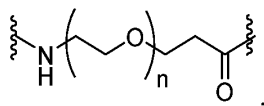
Z'-A- has a formula selected from the group consisting of:



wherein the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to S*.

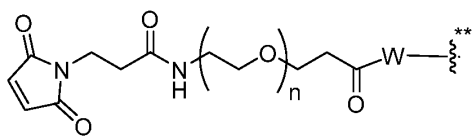
59. The Camptothecin-Linker Compound of any one of claims 54-56 having formula (iii) or formula (x), wherein

S* has the formula of:



wherein subscript n is an integer ranging from 1 to 36.

60. The Camptothecin-Linker Compound of claim 54 or 55 of formula (viii) or formula (x) in which Z'-A-S*-W- has the formula of:



wherein subscript n is an integer ranging from 2 to 10, preferably ranging from 2 to 4; the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to D or RL.

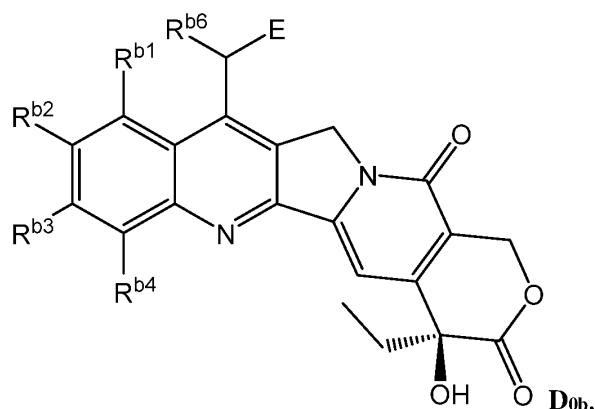
61. A method of treating cancer in a subject in need thereof, comprising administering to the subject an effective amount of a Camptothecin Conjugate of any one of claims 1-30, optionally said cancer is selected from the group consisting of lymphomas, leukemias, and solid tumors, optionally a lymphoma or a leukemia.

62. Use of a Camptothecin Conjugate of any one of claims 1-30 in preparation of a medicament for treatment of a cancer in a subject, optionally said cancer is selected from the group consisting of lymphomas, leukemias, and solid tumors, optionally a lymphoma or a leukemia.

63. A pharmaceutically acceptable composition comprising a Camptothecin Conjugate of any one of claims 1-30 and at least one pharmaceutically acceptable excipient.

64. A composition for treatment of a cancer in a subject in need thereof, wherein the composition is comprised of an effective amount of a Camptothecin Conjugate of any one of claims 1-30, optionally said cancer is selected from the group consisting of lymphomas, leukemias, and solid tumors, optionally a lymphoma or a leukemia.

65. A compound of Formula **D0b**



or a salt thereof, wherein;

E is $-OR^{b5}$ or $-NR^{b5}R^{b5'}$;

R^{b1} is selected from the group consisting of H, halogen, $-CN$, C_1 - C_8 alkyl, C_1 - C_8 haloalkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, C_6 - C_{12} aryl, 5- to 12-membered heteroaryl, C_3 - C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, $(C_6$ - C_{12} aryl)- C_2 - C_8 alkenyl-, C_1 - C_8 hydroxyalkyl, C_1 - C_8 alkyl- $C(O)$ - C_1 - C_8 aminoalkyl-, C_1 - C_8 aminoalkyl- $C(O)$ - C_1 - C_8 alkyl-, C_1 - C_8 alkyl- NR^a - $C(O)$ -, C_1 - C_8 alkyl- $C(O)$ -, C_1 - C_8 alkyl- $OC(O)$ -, C_6 - C_{12} aryl- $C(O)$ -, C_6 - C_{12} aryl- O - $C(O)$ - NR^a -, C_6 - C_{12} aryl- NR^a - $C(O)$ - O -, $-COOR^a$, $-OR^a$, $-NR^aR^{a'}$, and $-SR^a$; each optionally substituted with C_1 - C_3 alkyl, $-OR^a$, $-NR^aR^{a'}$, $-C(O)R^a$, and $-SR^a$; or

R^{b1} is combined with R^{b2} , R^{b5} , or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, C_1 - C_8 alkyl, C_2 - C_8 alkynyl, C_6 - C_{12} aryl, 5- to 12-membered heteroaryl, C_3 - C_{10} cycloalkyl, 3- to 10-membered heterocycloalkyl, C_1 - C_8 haloalkyl, C_1 - C_8 hydroxyalkyl, C_1 - C_8 alkyl- $S(O)_2$ -, C_1 - C_8 aminoalkyl, C_1 - C_8 alkyl- $C(O)$ - C_1 - C_8 aminoalkyl-, C_1 - C_8 aminoalkyl- $C(O)$ - C_1 - C_8 alkyl-, C_1 - C_8 alkyl- NR^a - $C(O)$ -, C_1 - C_8 alkyl- $C(O)$ -, C_1 - C_8 alkyl- $OC(O)$ -, C_1 - C_8 alkyl- NR^a - $C(O)$ -, C_1 - C_8 alkyl- $C(O)$ - NR^a -, C_1 - C_8 alkyl- NR^a - $C(O)O$ -, C_1 - C_8 alkyl- $OC(O)$ - NR^a -, C_6 - C_{12} aryl- $C(O)$ -, C_6 - C_{12} aryl- O - $C(O)$ - NR^a -, C_6 - C_{12} aryl- NR^a -

C(O)-O-, -COOR^a, -OR^a, -NR^aR^{a'}, and -SR^a; each optionally substituted with -OR^a, -NR^aR^{a'}, and -SR^a; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b3} is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, -OR^a, -NR^aR^{a'}, and -SR^a;

R^{b4} is selected from the group consisting of H or halogen;

each R^{b5} and R^{b5'} are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ alkyl-C(O)-, C₁-C₈ hydroxyalkyl-C(O)-, C₁-C₈ aminoalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, C₁-C₆ hydroxyalkyl-heteroaryl-, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and $R^{a'}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

wherein a) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane and E is -NR^{b5}R^{b5'}, then each R^{b5} and $R^{b5'}$ are independently selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-N-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

$R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

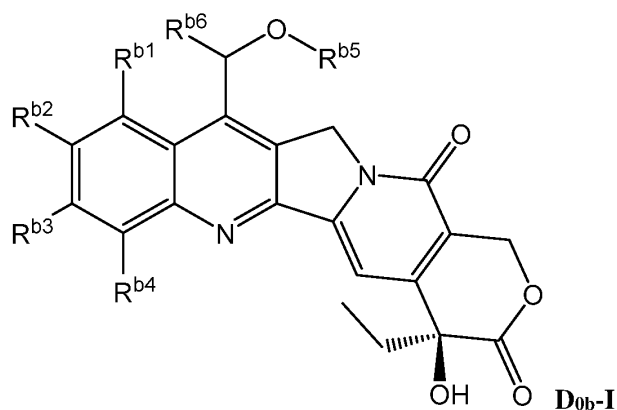
b) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, E is not -OH; and

c) when R^{b2} is methyl and R^{b3} is F, then R^{b1} does not come together with R^{b6} and the intervening atoms to form a ring; and

d) D is not (S)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione or (S)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-

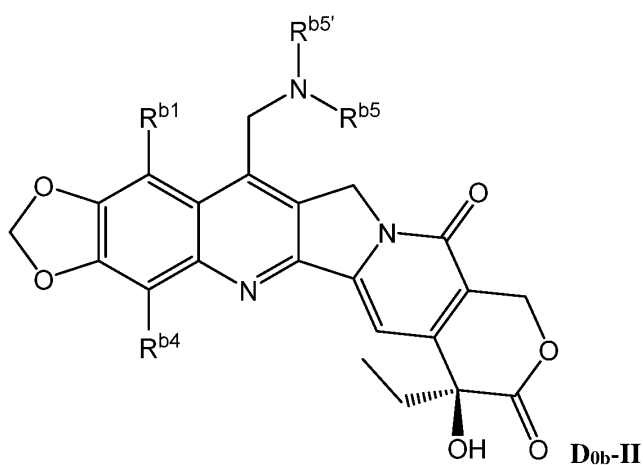
g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, or a salt of any of the foregoing.

66. The compound of claim 65, wherein the compound has formula of **D_{0b-I}**



or a salt thereof; and wherein when R^{b2} is combined with R^{b3} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle, the heterocycle has no more than one O.

67. The compound of claim 65, wherein D has the formula of **D_{0b-II}**



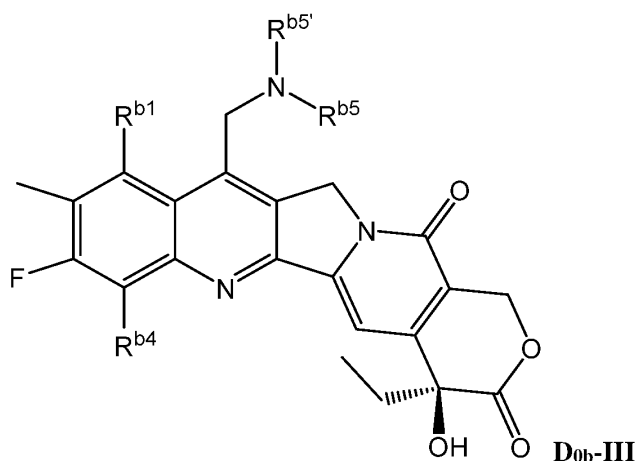
or a salt thereof, wherein;

R^{b5} is H and R^{b5'} is selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄

hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

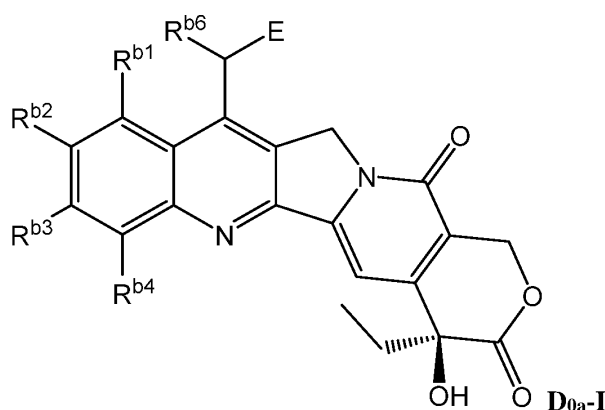
R^{b5'} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂; provided that D is not (*S*)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(7*H*)-dione or (*S*)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-*g*]pyrano[3',4':6,7]indolizino[1,2-*b*]quinoline-8,11(7*H*)-dione, or a salt of any of the foregoing.

68. The compound of claim 65, wherein the compound has the formula of **D_{0b}-III**



or a salt thereof.

69. The compound of claim 65, wherein the compound has the formula of **D_{0a}-I**



or a salt thereof, wherein;

E is $-\text{OR}^{\text{b5}}$ or $-\text{NR}^{\text{b5}}\text{R}^{\text{b5'}}$;

R^{b1} is selected from the group consisting of H, halogen, $-\text{CN}$, $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_1\text{-C}_8$ haloalkyl, $\text{C}_2\text{-C}_8$ alkenyl, $\text{C}_2\text{-C}_8$ alkynyl, $\text{C}_6\text{-C}_{12}$ aryl, 5- to 12-membered heteroaryl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, 3- to 10-membered heterocycloalkyl, $(\text{C}_6\text{-C}_{12} \text{ aryl})\text{-C}_2\text{-C}_8$ alkenyl-, $\text{C}_1\text{-C}_8$ hydroxyalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ aminoalkyl-, $\text{C}_1\text{-C}_8$ aminoalkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ alkyl-, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{C}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{O-C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-O-}$, $-\text{COOR}^{\text{a}}$, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; each optionally substituted with $\text{C}_1\text{-C}_3$ alkyl, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, $-\text{C}(\text{O})\text{R}^{\text{a}}$, and $-\text{SR}^{\text{a}}$; or

R^{b1} is combined with R^{b2} , R^{b5} , or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b2} is selected from the group consisting of H, halogen, $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_2\text{-C}_8$ alkynyl, $\text{C}_6\text{-C}_{12}$ aryl, 5- to 12-membered heteroaryl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, 3- to 10-membered heterocycloalkyl, $\text{C}_1\text{-C}_8$ haloalkyl, $\text{C}_1\text{-C}_8$ hydroxyalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{S}(\text{O})_2\text{-}$, $\text{C}_1\text{-C}_8$ aminoalkyl, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ aminoalkyl-, $\text{C}_1\text{-C}_8$ aminoalkyl- $\text{C}(\text{O})\text{-C}_1\text{-C}_8$ alkyl-, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-O-}$, $\text{C}_1\text{-C}_8$ alkyl- $\text{OC}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{C}(\text{O})\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{O-C}(\text{O})\text{-NR}^{\text{a}}\text{-}$, $\text{C}_6\text{-C}_{12}$ aryl- $\text{NR}^{\text{a}}\text{-C}(\text{O})\text{-O-}$, $-\text{COOR}^{\text{a}}$, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; each optionally substituted with $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo; or

R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocyclo fused with 6-membered aryl;

R^{b3} is selected from the group consisting of H, halogen, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_1\text{-C}_6$ haloalkyl, $-\text{OR}^{\text{a}}$, $-\text{NR}^{\text{a}}\text{R}^{\text{a'}}$, and $-\text{SR}^{\text{a}}$; or

R^{b3} is combined with R^{b2} and the intervening atoms to form a 5- or 6-membered carbocyclo or heterocyclo or a 5-membered heterocyclo fused with 6-membered aryl;

R^{b4} is selected from the group consisting of H and halogen;

each R^{b5} and $R^{b5'}$ are independently selected from the group consisting of H, C₁-C₈ alkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-O-C₁-C₈ alkyl, C₁-C₈ aminoalkyl, (C₁-C₄ alkylamino)-C₁-C₈ alkyl-, *N,N*-(C₁-C₄ hydroxyalkyl)(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N,N*-di(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, *N*-(C₁-C₄ hydroxyalkyl)-C₁-C₈ aminoalkyl-, C₁-C₈ hydroxyalkyl-C(O)-, C₃-C₁₀ cycloalkyl, (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ alkyl-, heteroaryl-C₁-C₆ hydroxyalkyl, phenyl, phenyl-C₁-C₄ alkyl-, diphenyl-C₁-C₄ alkyl-, heteroaryl, heteroaryl-C₁-C₄ alkyl-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, C₁-C₆ alkoxy-C(O)-*N*-(C₁-C₄ alkyl)amino-C₁-C₈ alkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, C₁-C₄ alkyl-SO₂-C₁-C₈ alkyl-, NH₂-SO₂-C₁-C₈ alkyl-, (C₃-C₁₀ heterocycloalkyl)-C₁-C₄ hydroxyalkyl-, C₁-C₆ alkoxy-C(O)-(C₃-C₁₀ heterocycloalkyl)-C₁-C₈ alkyl-, phenyl-C(O)-, phenyl-SO₂-, and C₁-C₈ hydroxyalkyl-C₃-C₁₀ heterocycloalkyl-, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered ring having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or

$R^{b5'}$ is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

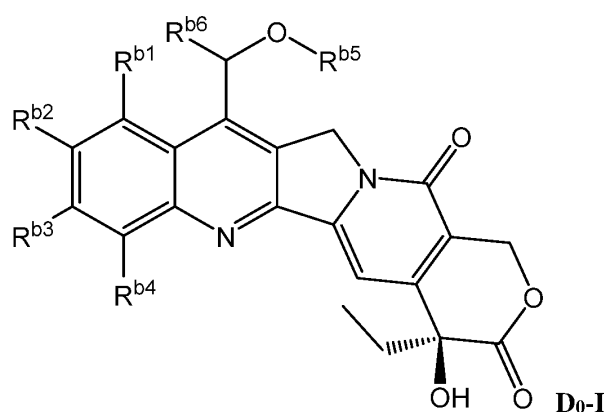
R^a and $R^{a'}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-,

wherein a) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, and E is -NR^{b5}R^{b5'}, then each R^{b5} and $R^{b5'}$ are independently selected from the group consisting of H, C₁-C₈ alkyl-O-C₁-C₈ alkyl-, C₁-C₈ alkyl-C(O) (C₃-C₁₀ cycloalkyl)-C₁-C₄ alkyl-, C₃-C₁₀ heterocycloalkyl, C₁-C₆ hydroxyalkyl-heteroaryl-, heteroaryl, heteroaryl-C₁-

- C₄ alkyl-, phenyl-C(O)-, and phenyl-SO₂-, or R^{b5} and R^{b5'} are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl; or R^{b5'} is H and R^{b5} is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocycle or heterocycle; wherein the cycloalkyl, carbocycle, heterocycloalkyl, heterocycle, phenyl and heteroaryl portions of R^{b1}, R^{b2}, R^{b3}, R^{b4}, R^{b5} and R^{b5'} are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;
- b) when R^{b2} is combined with R^{b3} and the intervening atoms to form a 1,3-dioxolane, E is not -OH; c) when E is NH₂, R^{b1} is selected from the group consisting of -CN, 5- to 12-membered heteroaryl with at least one annular N, 3- to 10-membered heterocycloalkyl with at least one annular N, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with C₁-C₃ alkyl, -OR^a-, -NR^aR^{a'}-, -C(O)R^a-, and -SR^a-, or R^{b1} is combined with R^{b2} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle with at least one annular N, or 5-membered heterocycle fused with 6-membered aryl; R^{b2} is selected from the group consisting of H, halogen, C₁-C₈ alkyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, C₁-C₈ haloalkyl, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-S(O)₂-, C₁-C₈ aminoalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminolalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-NR^a-, C₁-C₈ alkyl-NR^a-C(O)O-, C₁-C₈ alkyl-OC(O)-NR^a-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^{a'}-, and -SR^a-, each optionally substituted with -OR^a-, -NR^aR^{a'}-, and -SR^a-, or R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form a 5- or 6-membered heterocycle with at least one annular N, or R^{b2} is combined with R^{b1} or R^{b3} and the intervening atoms to form 5- or 6-membered heterocycle fused with 6-membered aryl; and
- d) when R^{b2} is -OH or methyl and R^{b3} is F, then R^{b1} does not come together with R^{b5}, R^{b5'} or R^{b6} and the intervening atoms to form a ring; and
- e) D is not selected from the group consisting of (S)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-

g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, (*S*)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, (*S*)-14-((4-(2-aminoethyl)piperazin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, (*S*)-14-((4-aminopiperidin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7*H*)-dione, and *tert*-butyl (*S*)-(1-((7-ethyl-7-hydroxy-8,11-dioxo-7,8,11,13-tetrahydro-10*H*-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-14-yl)methyl)piperidin-4-yl)carbamate, or a salt of any of the foregoing

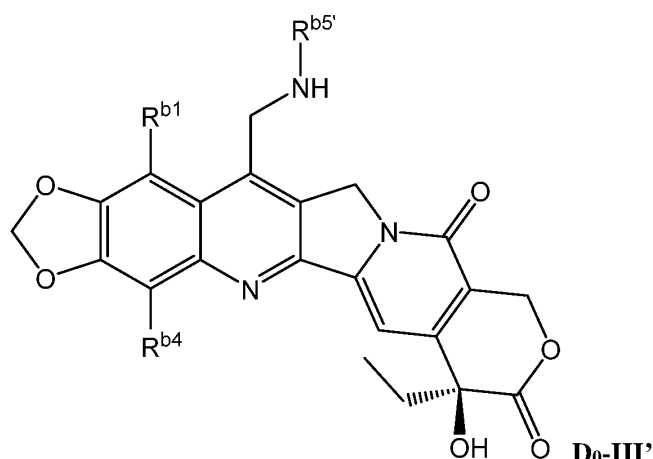
70. The compound of claim 65, wherein the compound has the formula of **D₀-I'**



or a salt thereof,

wherein when R^{b2} is combined with R^{b3} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle, the heterocycle has no more than one O.

71. The compound of claim 65, wherein the compound has the formula of **D₀-III'**



or a salt thereof, wherein;

R^{b1} is selected from the group consisting of H, halogen, -CN, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₆-C₁₂ aryl, 5- to 12-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, (C₆-C₁₂ aryl)-C₂-C₈ alkenyl-, C₁-C₈ hydroxyalkyl, C₁-C₈ alkyl-C(O)-C₁-C₈ aminoalkyl-, C₁-C₈ aminoalkyl-C(O)-C₁-C₈ alkyl-, C₁-C₈ alkyl-NR^a-C(O)-, C₁-C₈ alkyl-C(O)-, C₁-C₈ alkyl-OC(O)-, C₆-C₁₂ aryl-C(O)-, C₆-C₁₂ aryl-O-C(O)-NR^a-, C₆-C₁₂ aryl-NR^a-C(O)-O-, -COOR^a-, -OR^a-, -NR^aR^a-, and -SR^a-, each optionally substituted with C₁-C₃ alkyl, -OR^a-, -NR^aR^a-, -C(O)R^a-, and -SR^a-, or R^{b1} is combined with R^{b5} or R^{b6} and the intervening atoms to form a 5-, 6-, or 7-membered carbocyclo or heterocyclo;

R^{b4} is selected from the group consisting of H or halogen;

$R^{b5'}$ is C₁-C₈ alkyl-O-C₁-C₈ alkyl, or R^{b5} and $R^{b5'}$ are combined with the nitrogen atom to which they are attached to form a 5-, 6- or 7-membered heterocycle having 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -C₁-C₆ hydroxyalkyl, -OC₁-C₄ alkyl, -NH₂, -NH-C₁-C₄ alkyl, -N(C₁-C₄ alkyl)₂, C₁-C₆ alkoxy-C(O)-NH-, C₁-C₆ alkoxy-C(O)-C₁-C₈ aminoalkyl-, and C₁-C₈ aminoalkyl-; or

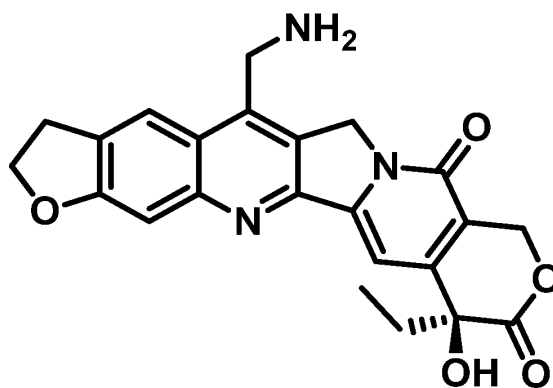
$R^{b5'}$ is combined with R^{b1} and the intervening atoms to form a 5- to 7-membered carbocyclo or heterocyclo; wherein the cycloalkyl, carbocyclo, heterocycloalkyl, heterocyclo, phenyl and heteroaryl portions of R^{b1} , R^{b2} , R^{b3} , R^{b4} , R^{b5} and $R^{b5'}$ are substituted with from 0 to 3 substituents independently selected from the group consisting of halogen, C₁-C₄ alkyl, -OH, -OC₁-C₄ alkyl, -NH₂, -NHC₁-C₄ alkyl, and -N(C₁-C₄ alkyl)₂;

R^{b6} is H, or is taken together with R^{b1} and the intervening atoms to form a carbocyclo or heterocyclo; and

R^a and $R^{a'}$ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkyl-S(O)₂-, C₁-C₆ alkyl-C(O)-, C₁-C₆ aminoalkyl-C(O)-, and C₁-C₆ hydroxyalkyl-C(O)-, provide that D is not selected from the group consisting of (S)-7-ethyl-7-hydroxy-14-((4-methylpiperazin-1-yl)methyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-7-ethyl-7-hydroxy-14-(morpholinomethyl)-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-14-((4-(2-aminoethyl)piperazin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, (S)-14-((4-aminopiperidin-1-yl)methyl)-7-ethyl-7-hydroxy-10,13-dihydro-11H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-8,11(7H)-dione, and *tert*-butyl (S)-1-((7-ethyl-7-hydroxy-8,11-dioxo-7,8,11,13-tetrahydro-10H-[1,3]dioxolo[4,5-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-14-yl)methyl)piperidin-4-yl)carbamate, or a salt of any of the foregoing

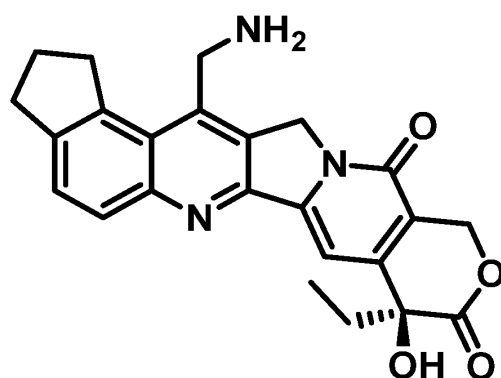
72. A compound selected from the compounds of Table I or a salt thereof.

73. A compound of Formula:



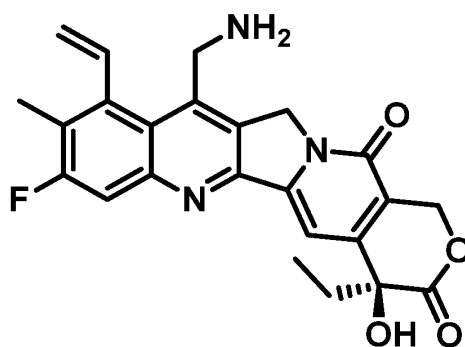
or a salt thereof.

74. A compound of Formula



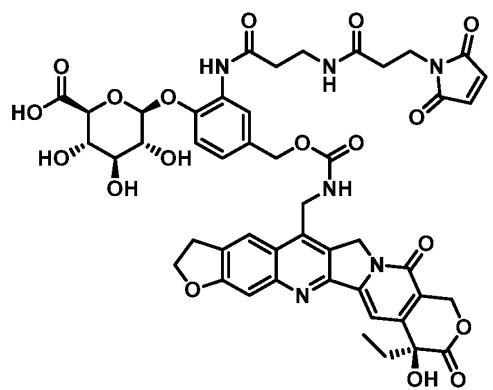
or salt thereof.

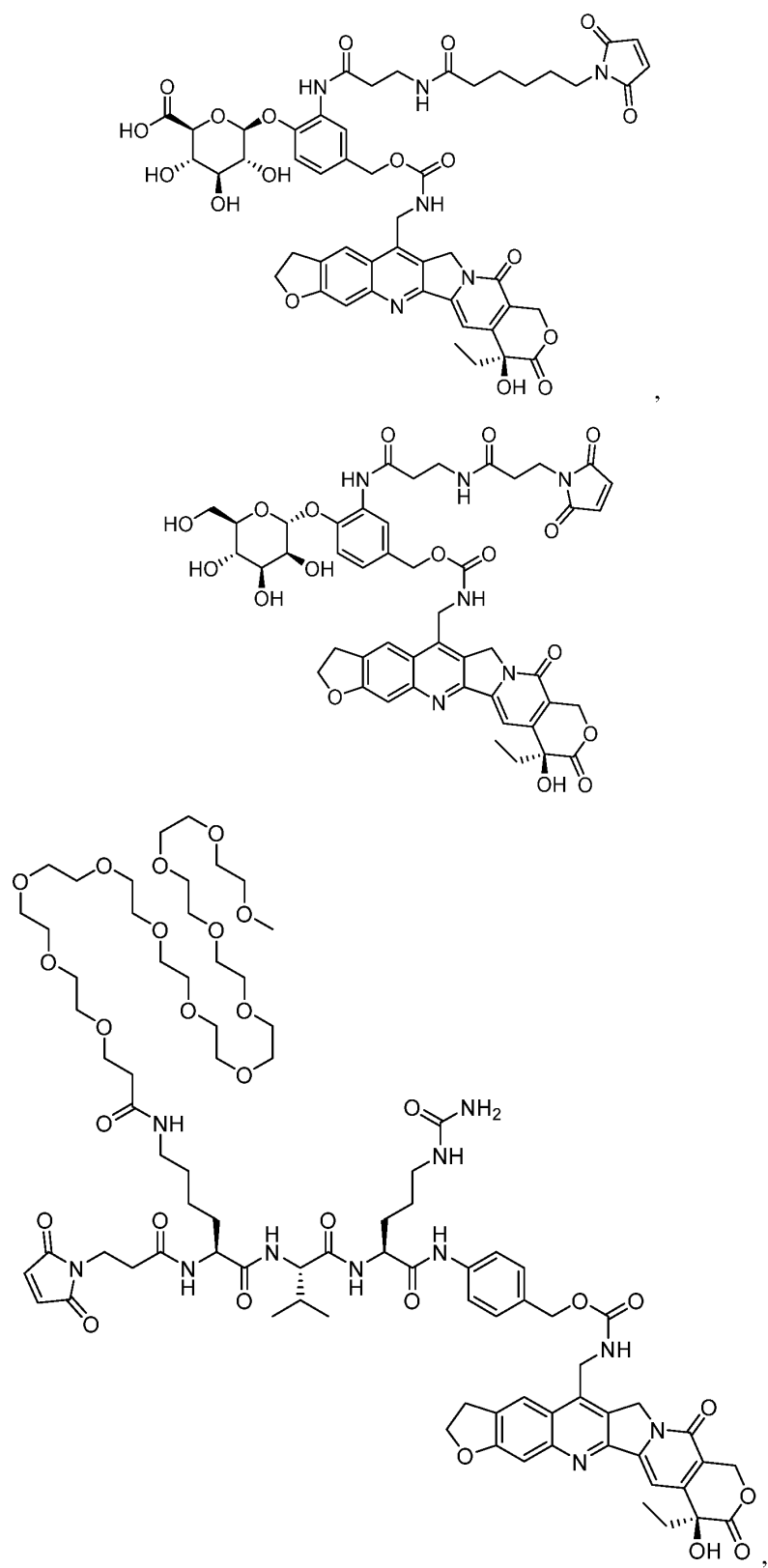
75. A compound of Formula

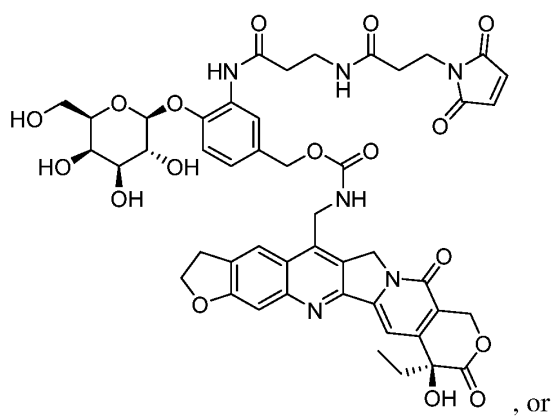


or a salt thereof.

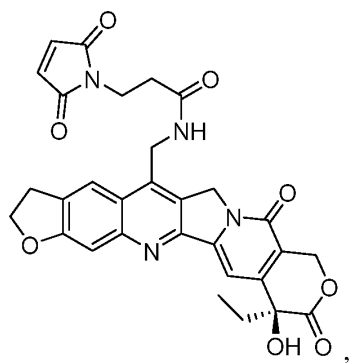
76. A Camptothecin-Linker compound of Formula





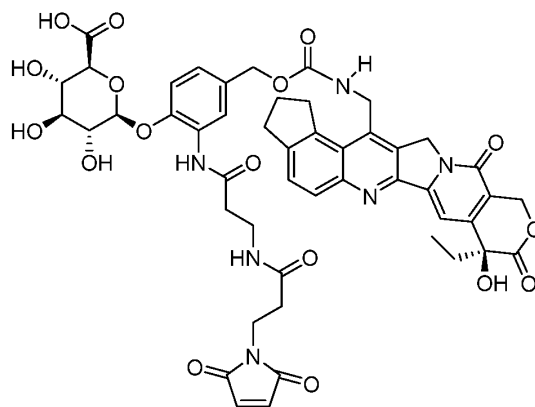


, or



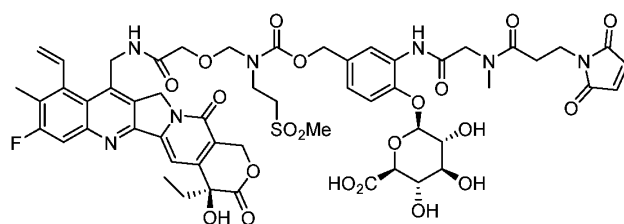
or a salt thereof.

77. A compound of Formula



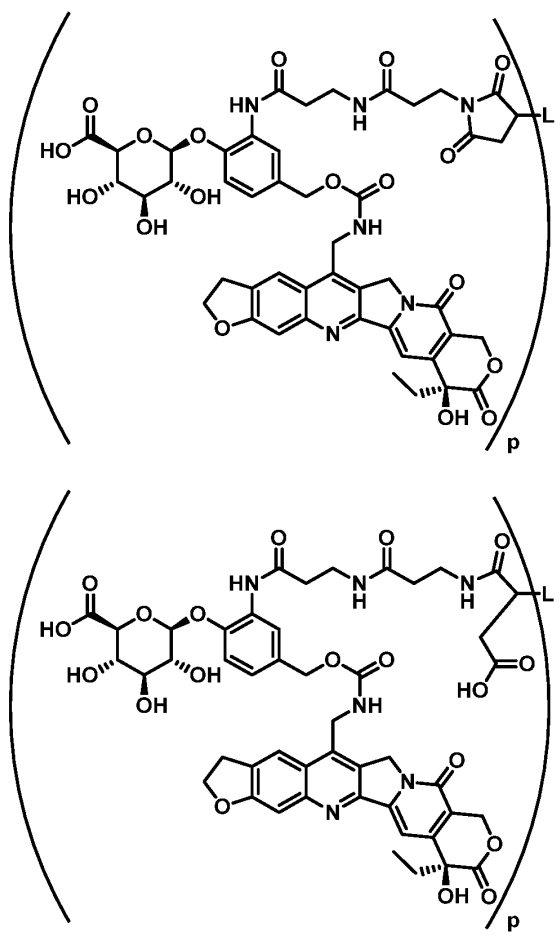
or a salt thereof.

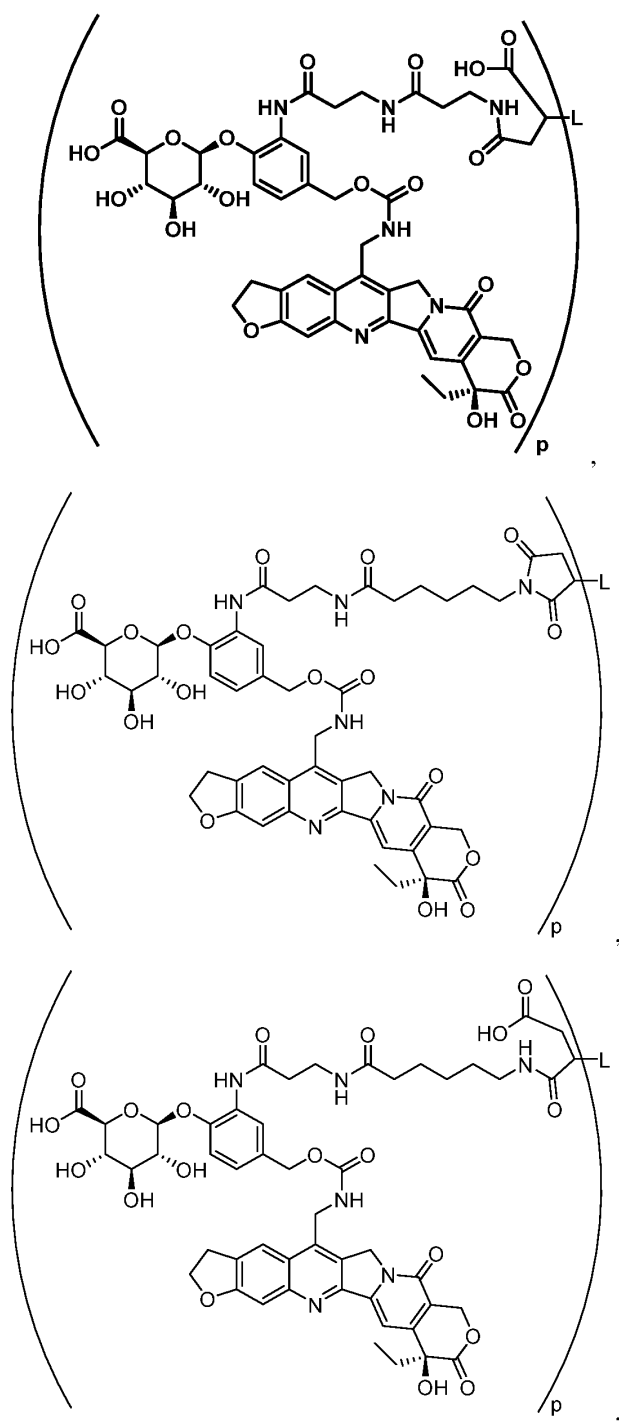
78. A compound of Formula

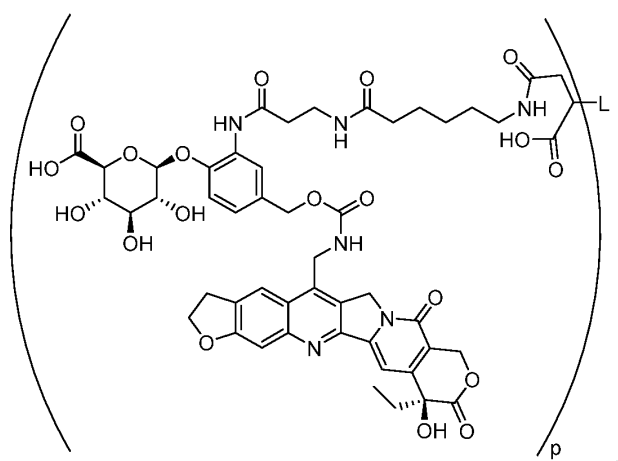
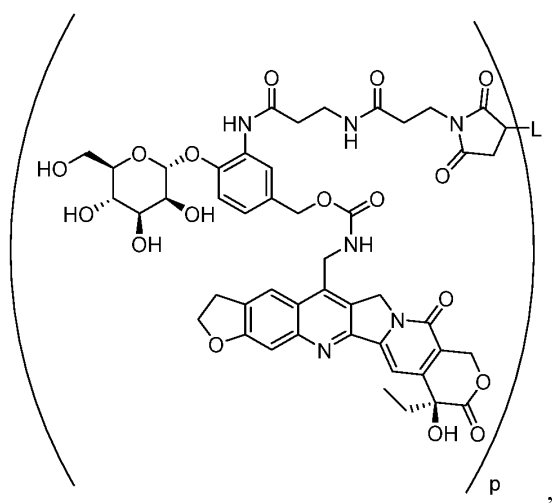
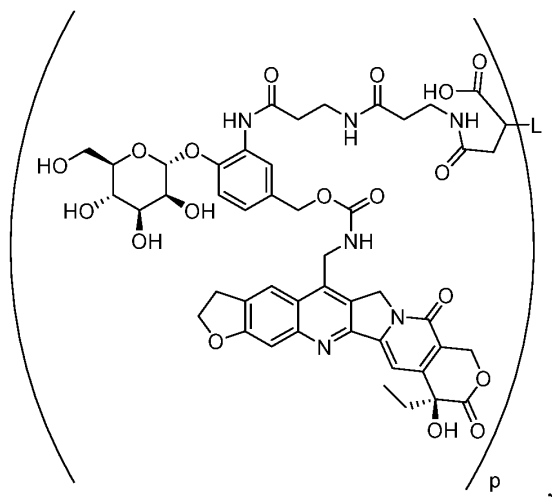


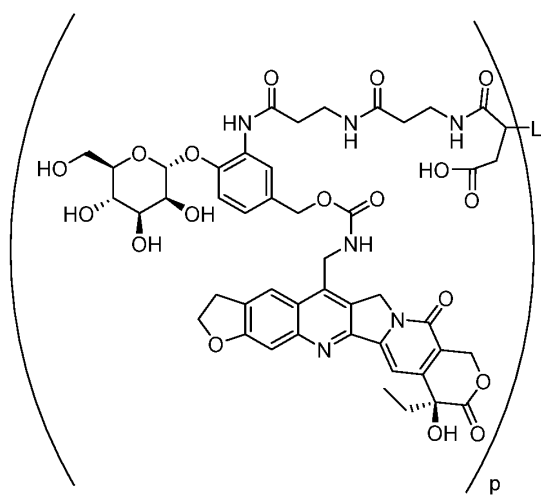
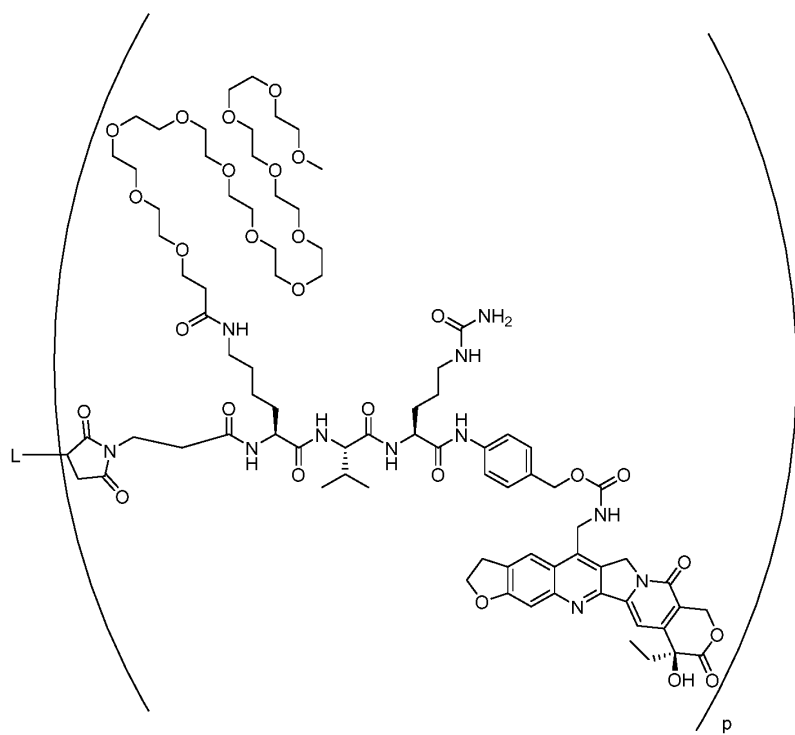
or a salt thereof.

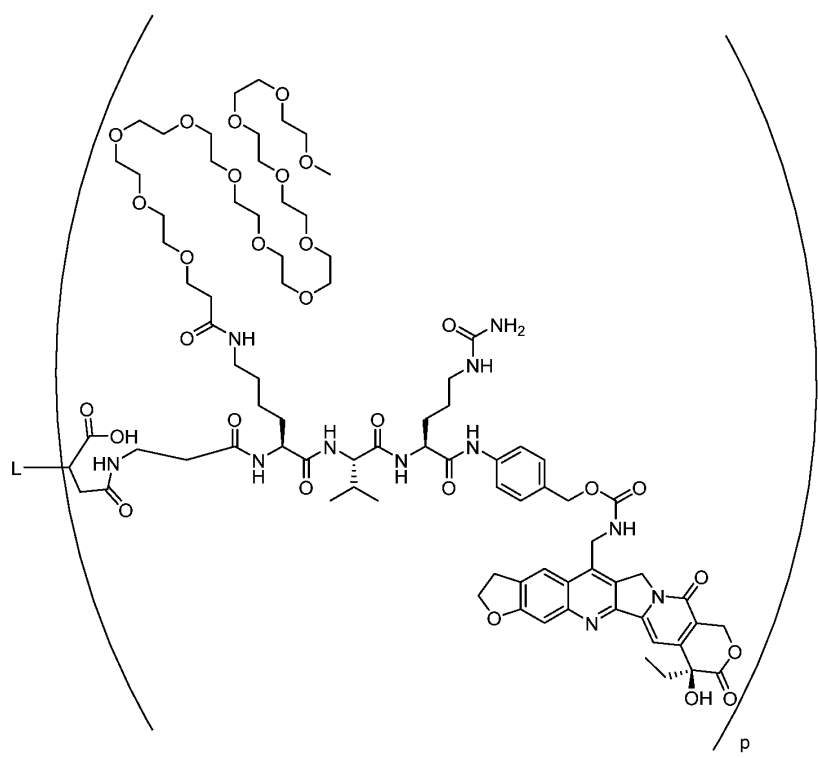
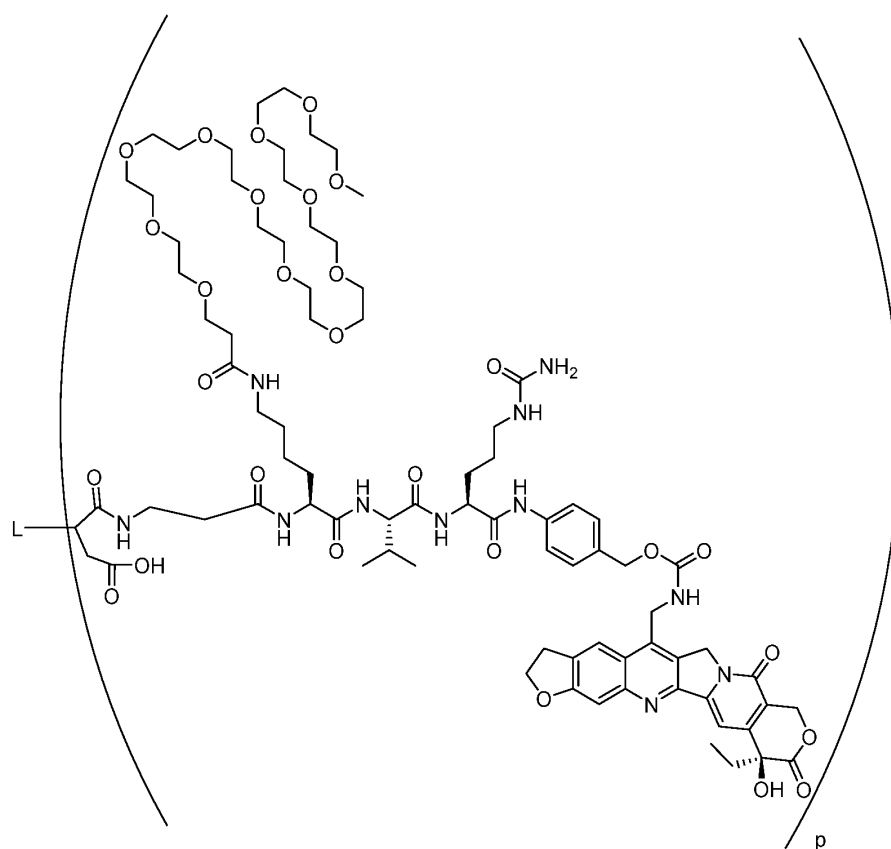
79. A compound of Formula

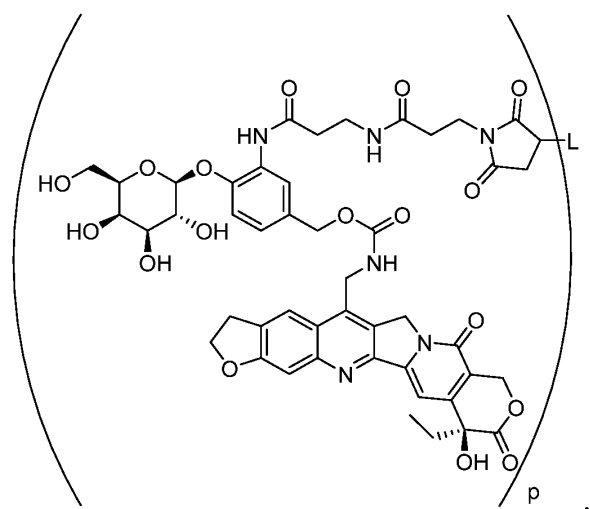
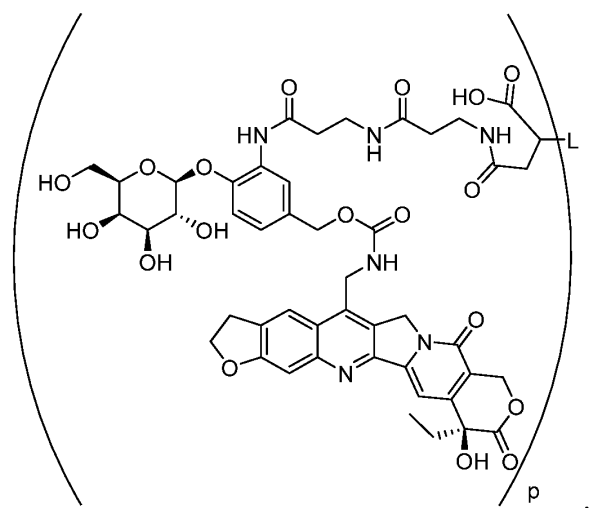
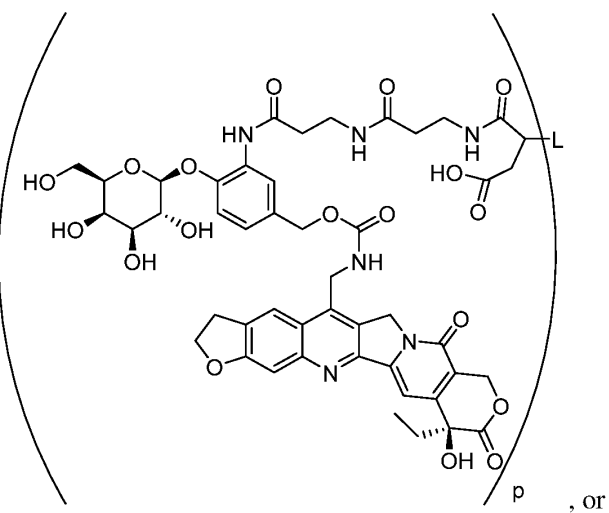


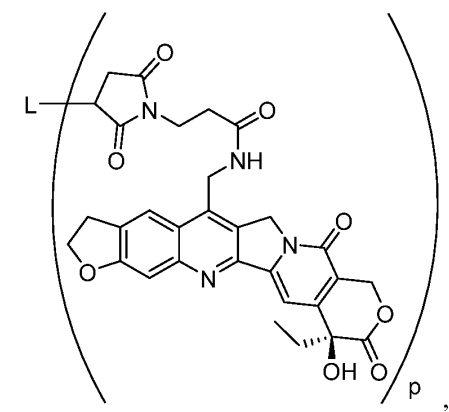
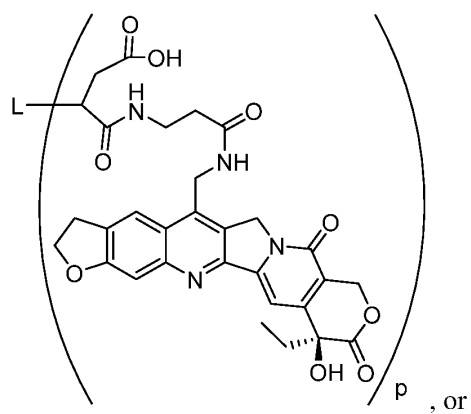
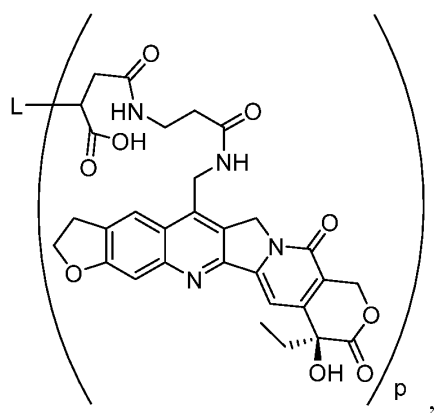






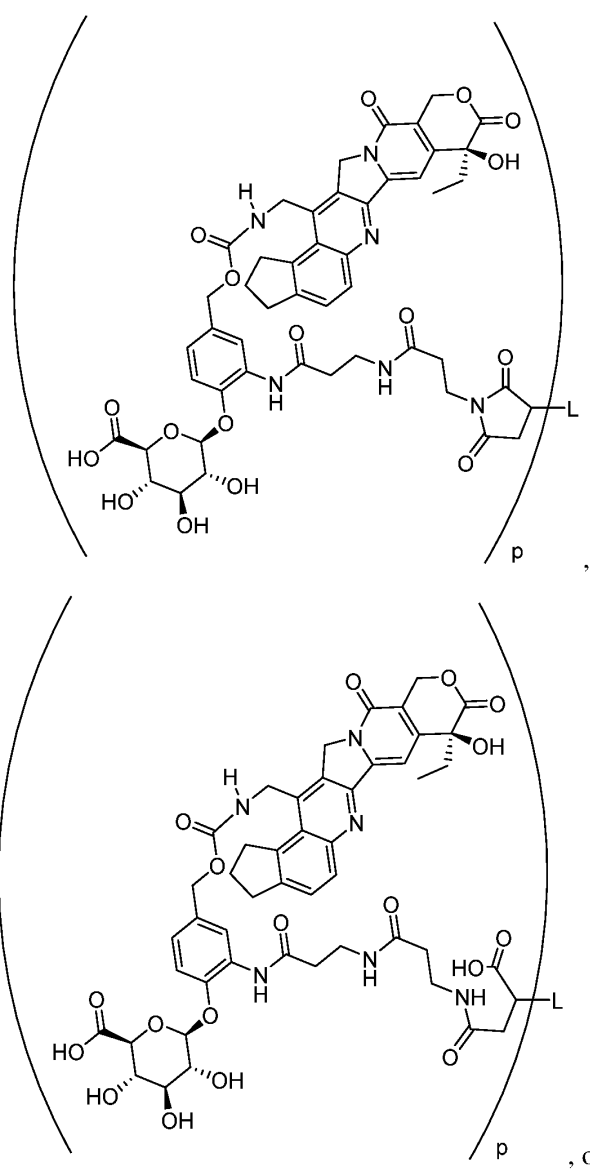


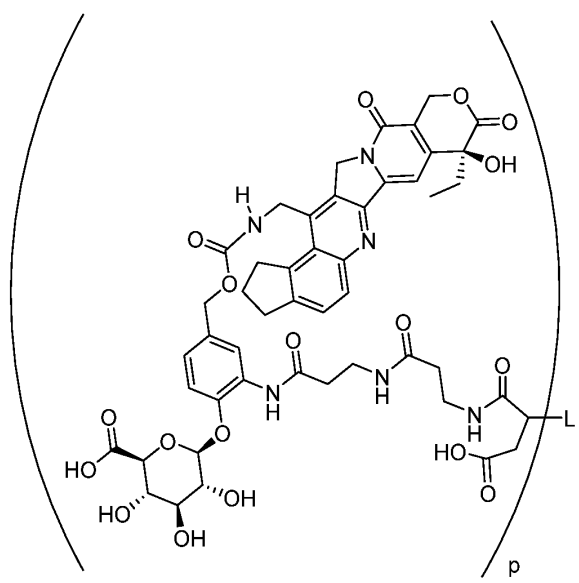




or a salt thereof.

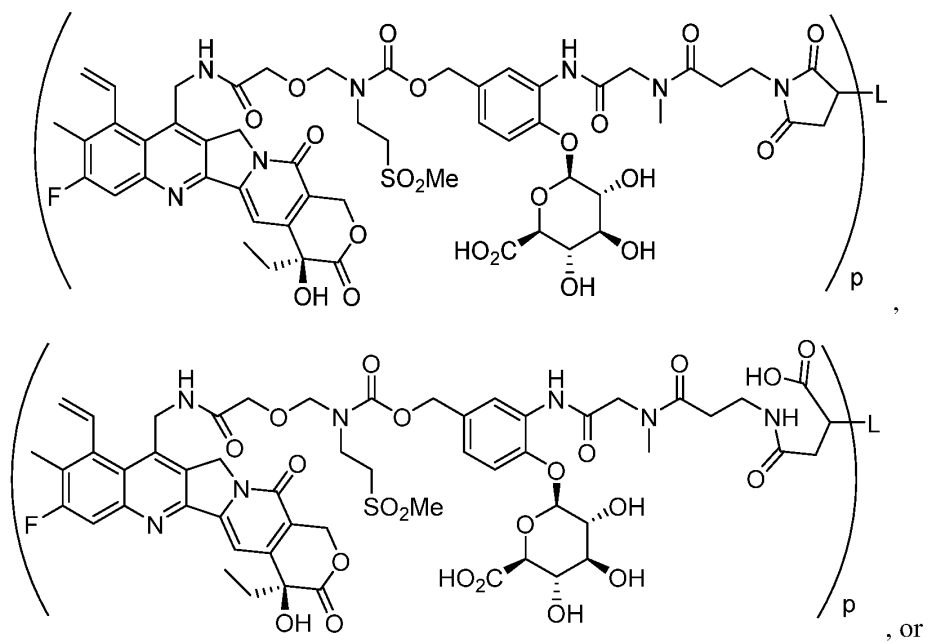
80. A compound of Formula

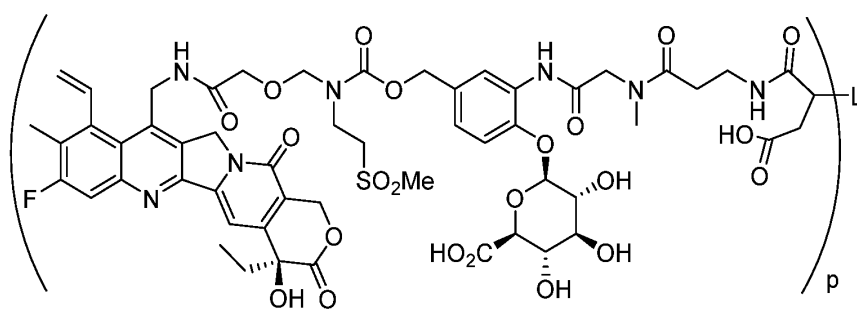




or a salt thereof.

81. A compound of Formula



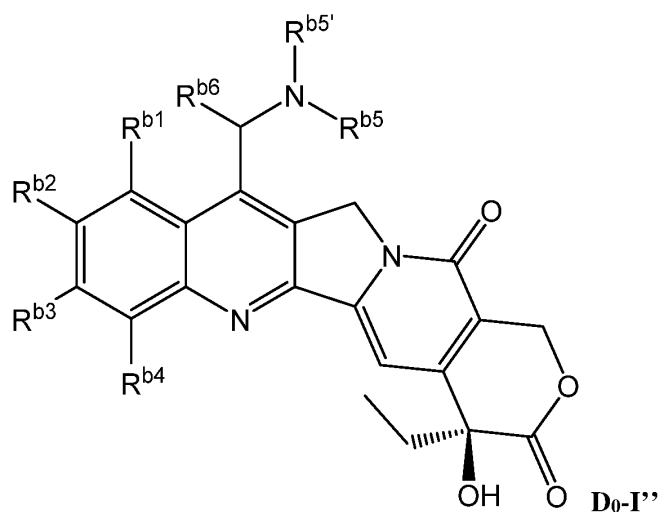


or a salt thereof.

82. A Camptothecin-Linker compound, wherein the compound is a compound of Table II or a salt thereof.

83. A Camptothecin Conjugate, wherein the Conjugate comprises a Ligand attached to a succinimide moiety or a succinic acid-amide moiety of a Camptothecin-Linker moiety, wherein the Camptothecin-Linker moiety comprises a compound of Table II, wherein a maleimide moiety of the Camptothecin-Linker moiety is replaced by the succinimide or succinic acid-amide moiety.

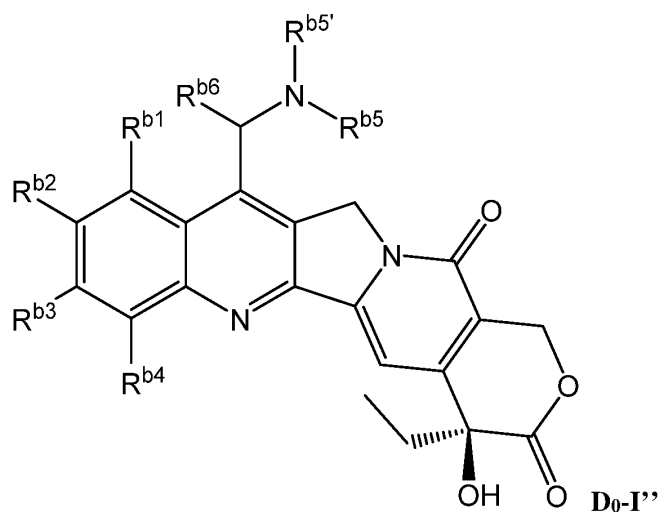
84. The compound of claim 65, wherein the compound has the formula of **D₀-I''**



or a salt thereof,

wherein when R^{b2} is combined with R^{b3} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle, the heterocycle has no more than one O.

85. The Camptothecin Conjugate of claim 1, wherein D has the formula of **D₀-I''**



or a salt thereof,

wherein when R^{b2} is combined with R^{b3} and the intervening atoms to form a 5-, 6-, or 7-membered heterocycle, the heterocycle has no more than one O.