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(54) IMMUNOMODULATORY ANTIBODY-DRUG CONJUGATES

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WA (US)

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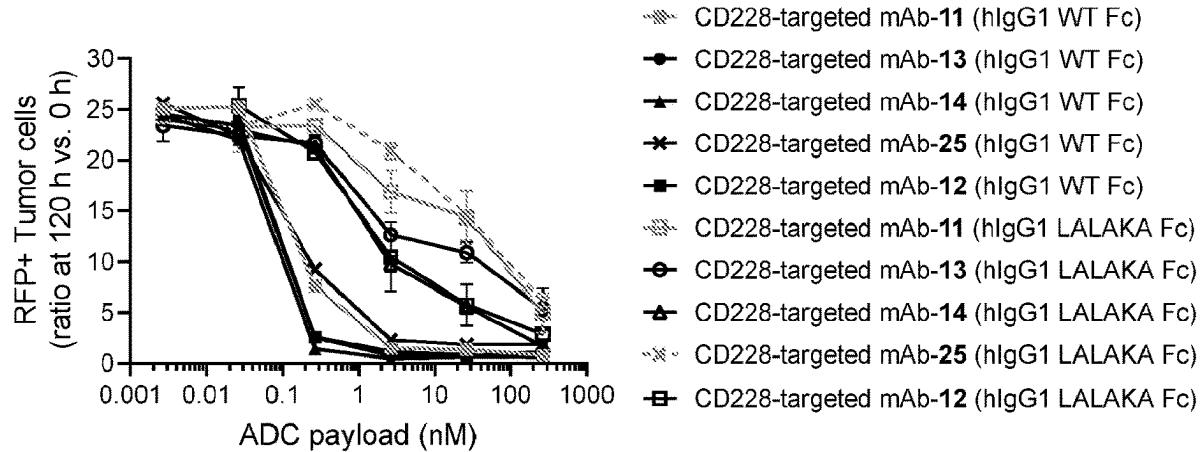
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A61K 47/68 (2017.01)
A61P 35/00 (2006.01)
C07K 16/28 (2006.01)

(52) **U.S. Cl.**
CPC *A61K 47/6851* (2017.08); *A61K 47/68035* (2023.08); *A61P 35/00* (2018.01); *C07K 16/2896* (2013.01)

(57) **ABSTRACT**

The present disclosure provides, inter alia, antibody-drug conjugates that are useful in treating various diseases such as cancer.

Specification includes a Sequence Listing.



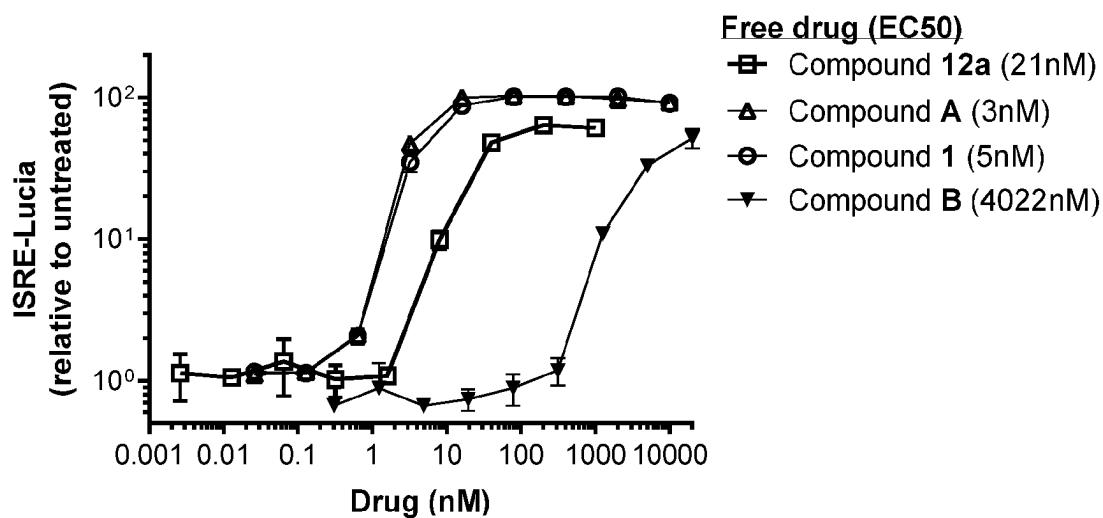


FIG. 1

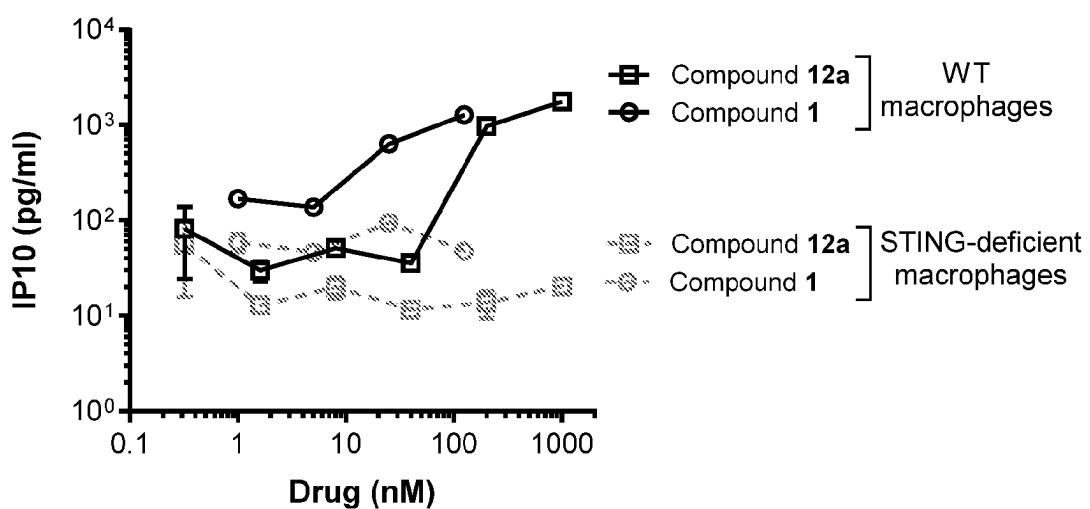


FIG. 2

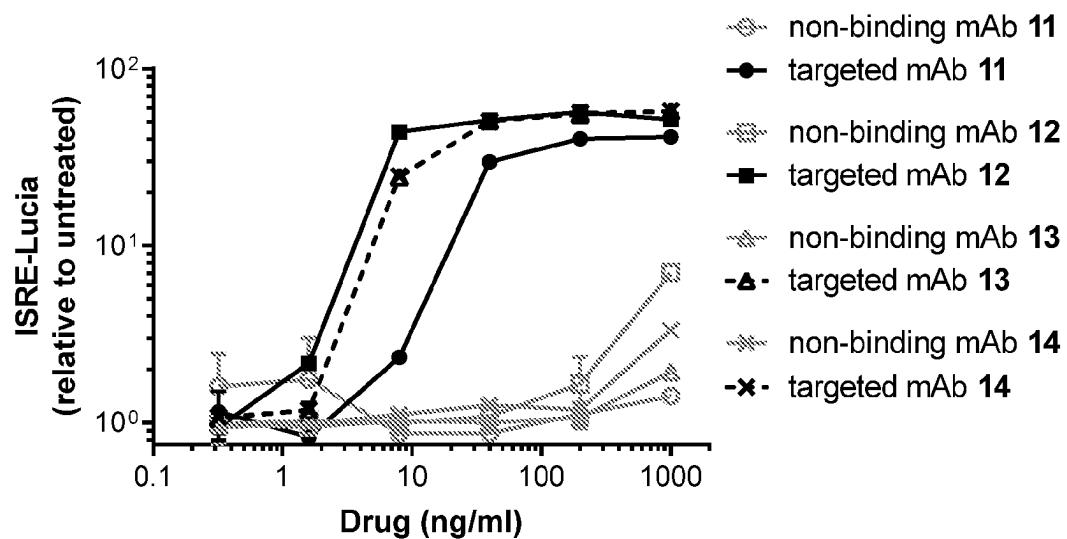


FIG. 3

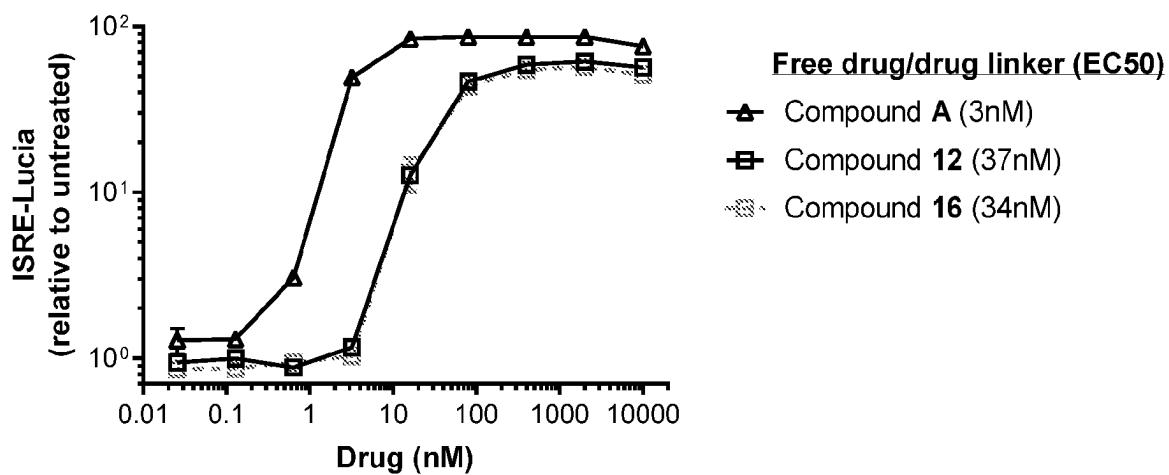


FIG. 4

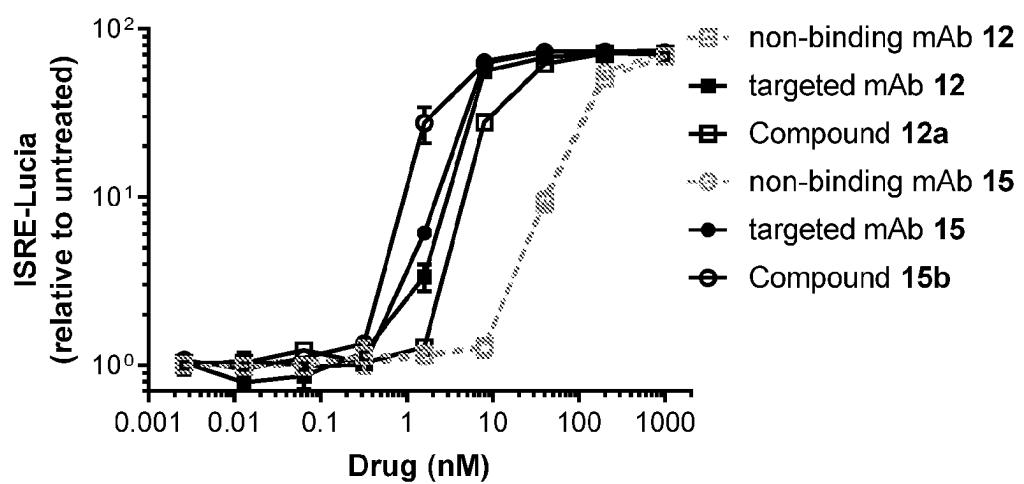


FIG. 5

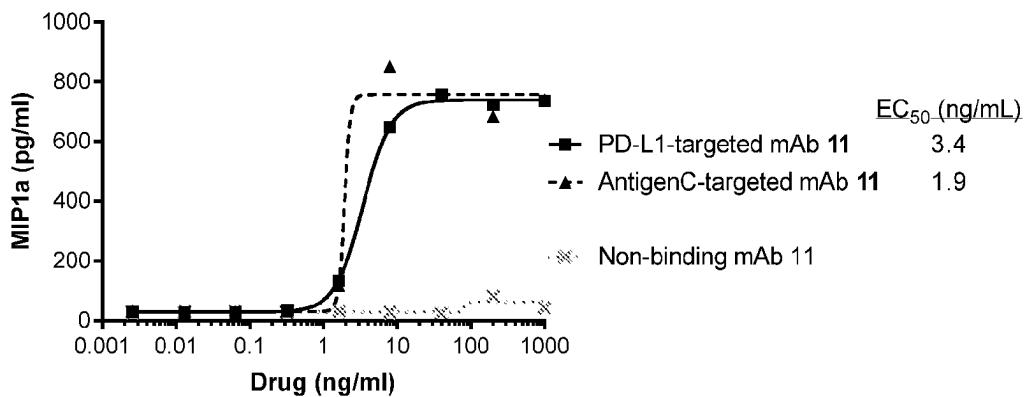


FIG. 6A

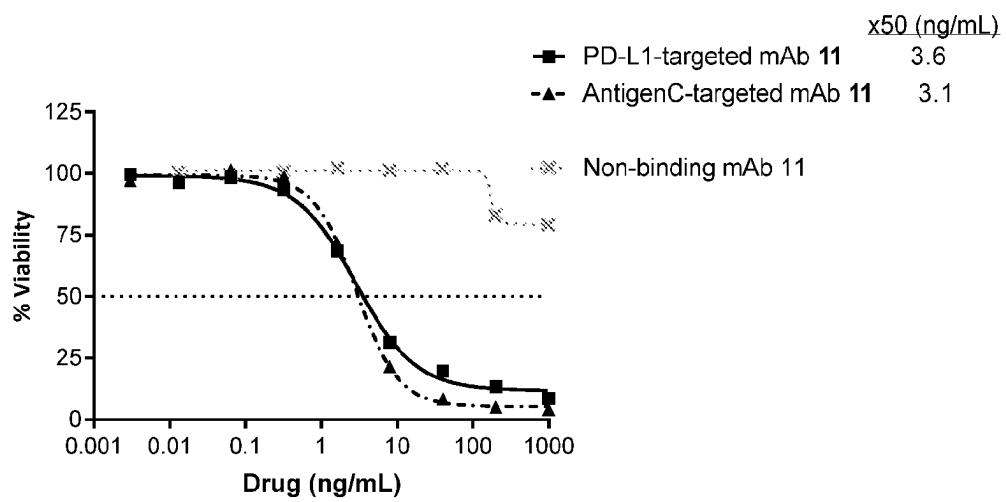


FIG. 6B

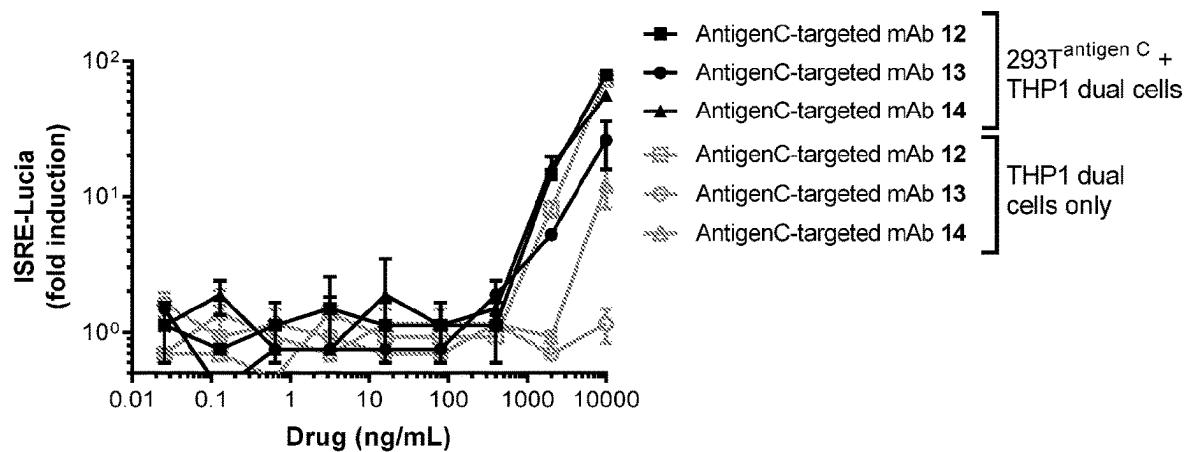


FIG. 7

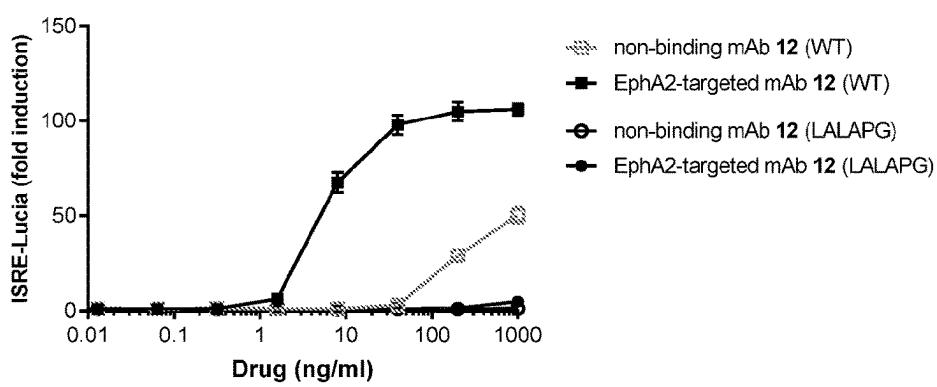


FIG. 8

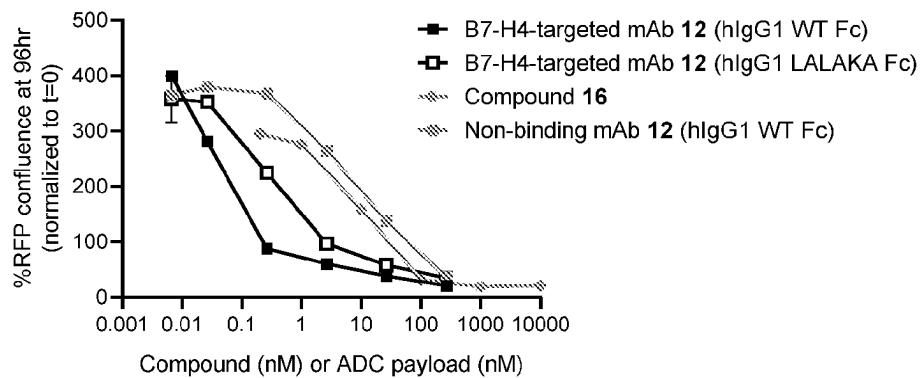


FIG. 9A

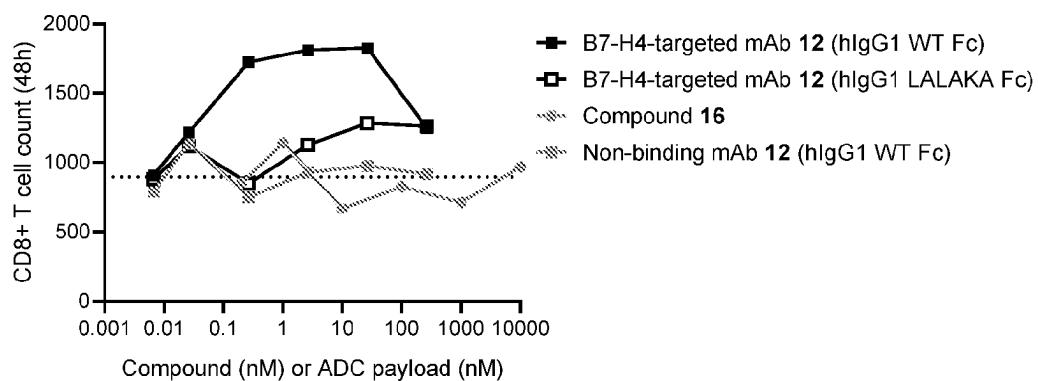


FIG. 9B

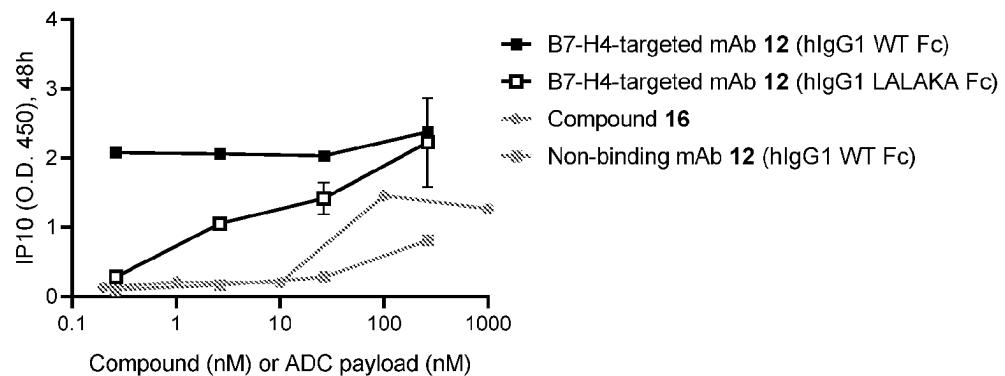


FIG. 9C

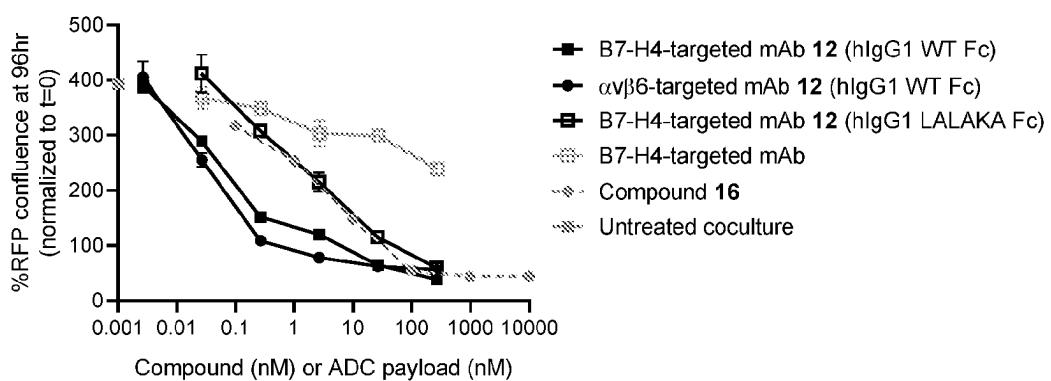


FIG. 10

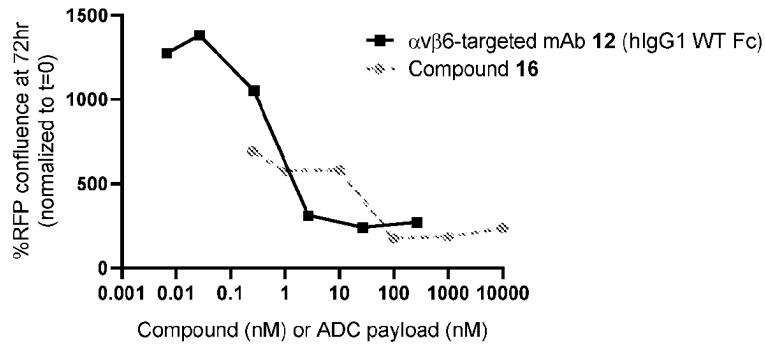


FIG. 11

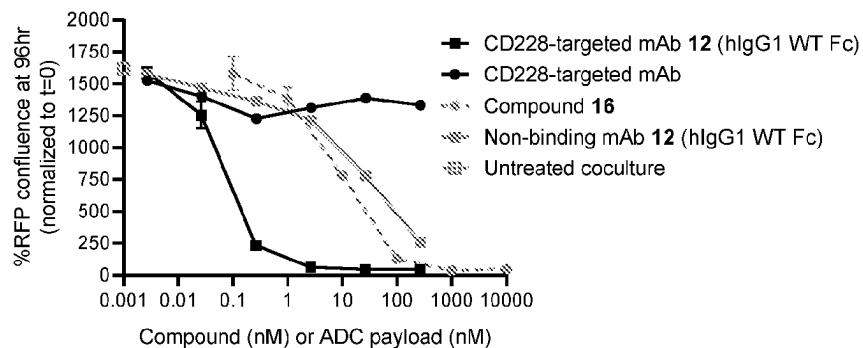


FIG. 12

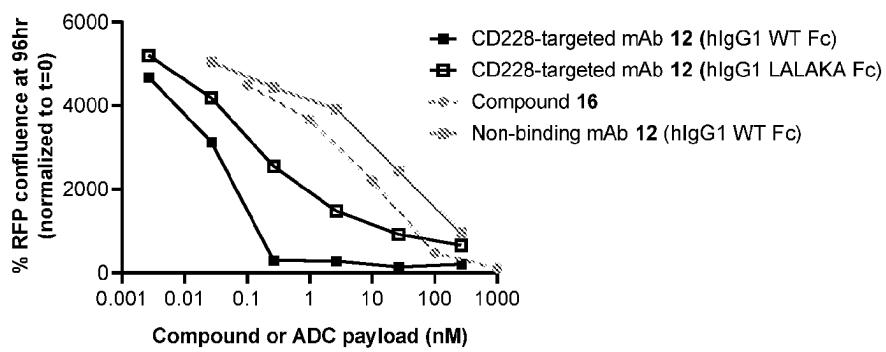


FIG. 13

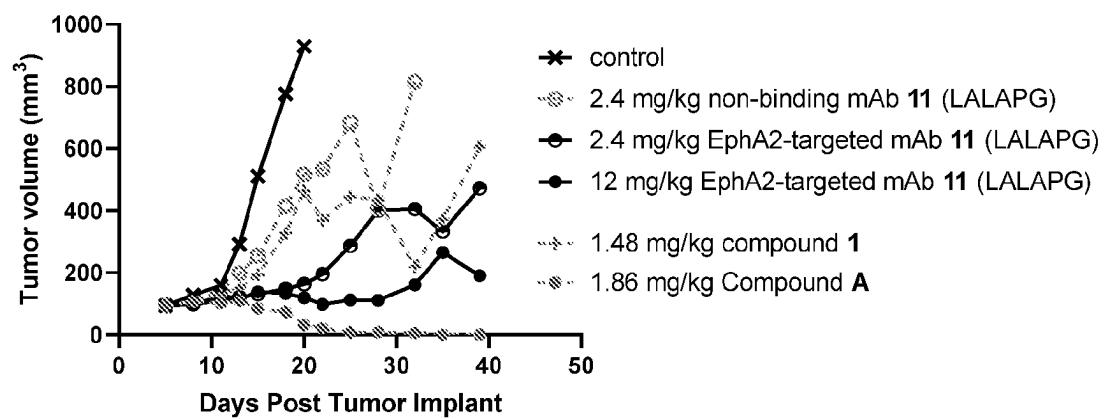


FIG. 14A

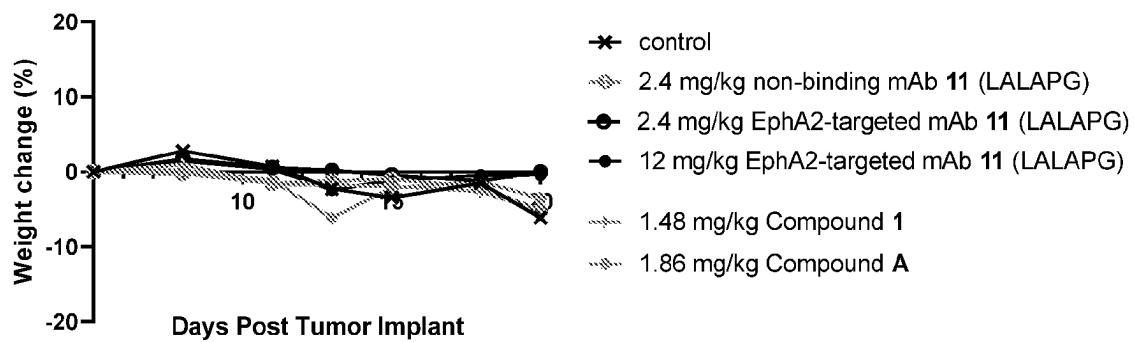


FIG. 14B

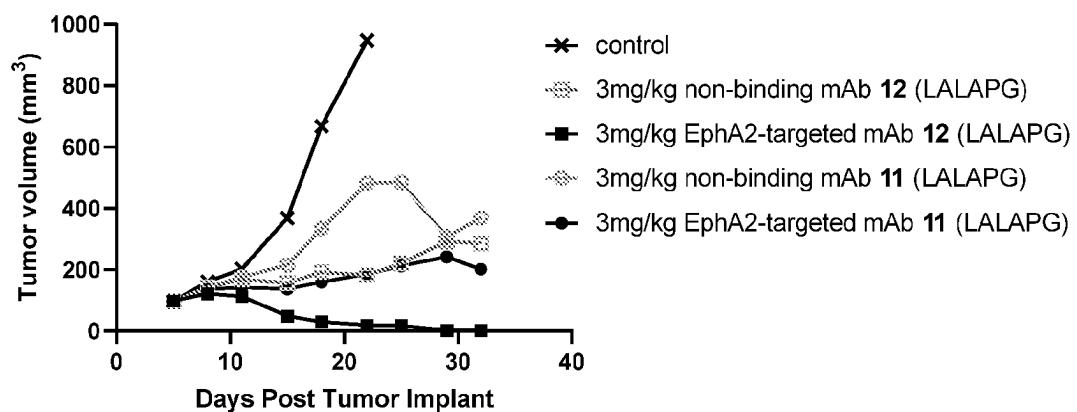


FIG. 15A

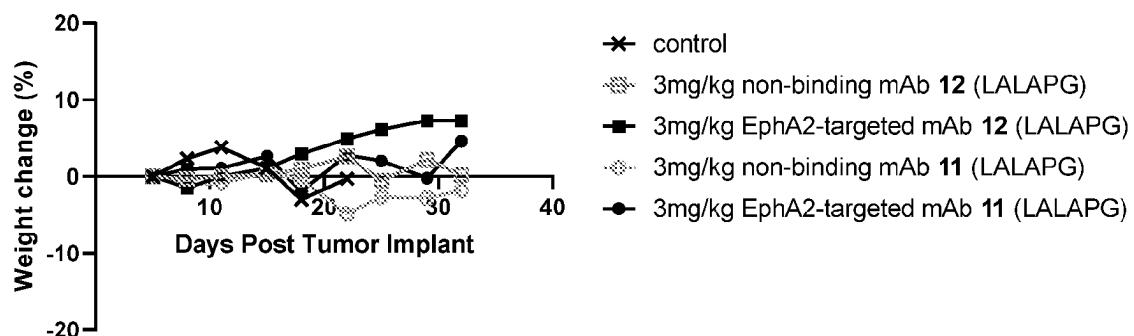


FIG. 15B

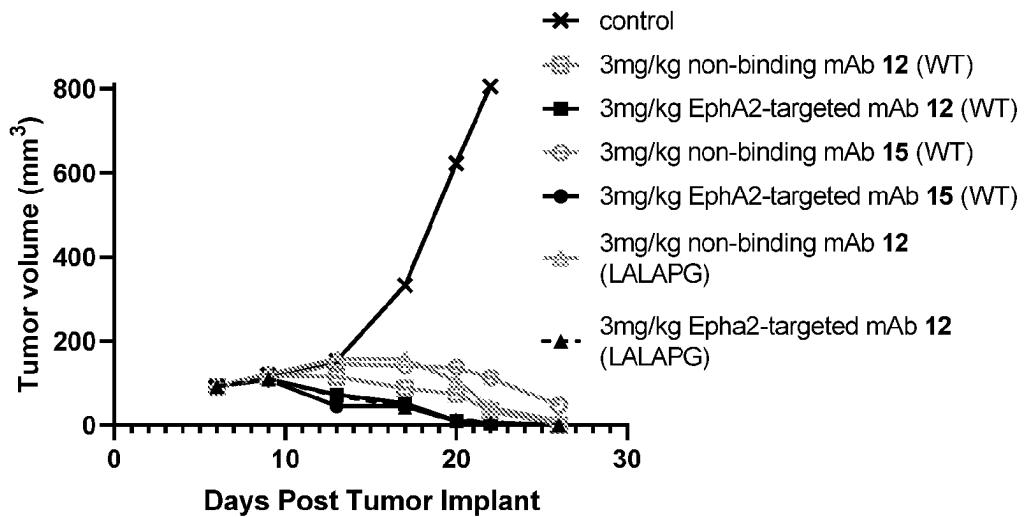


FIG. 16A

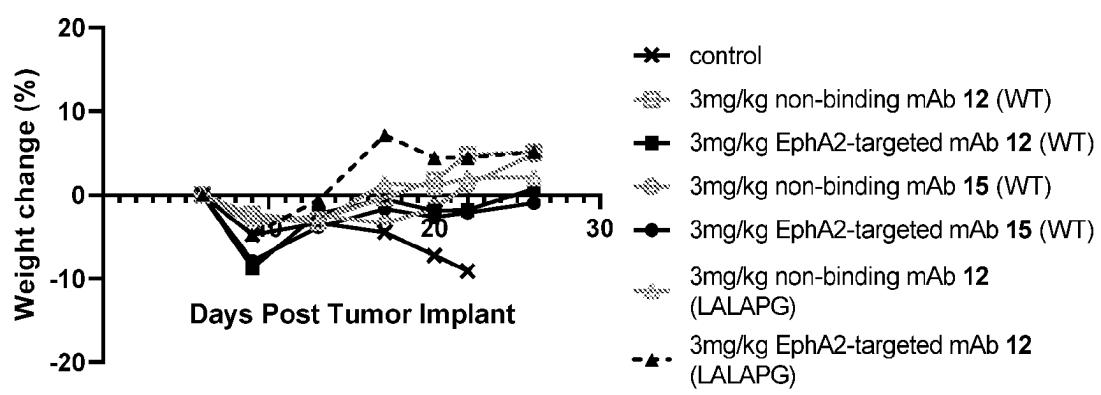


FIG. 16B

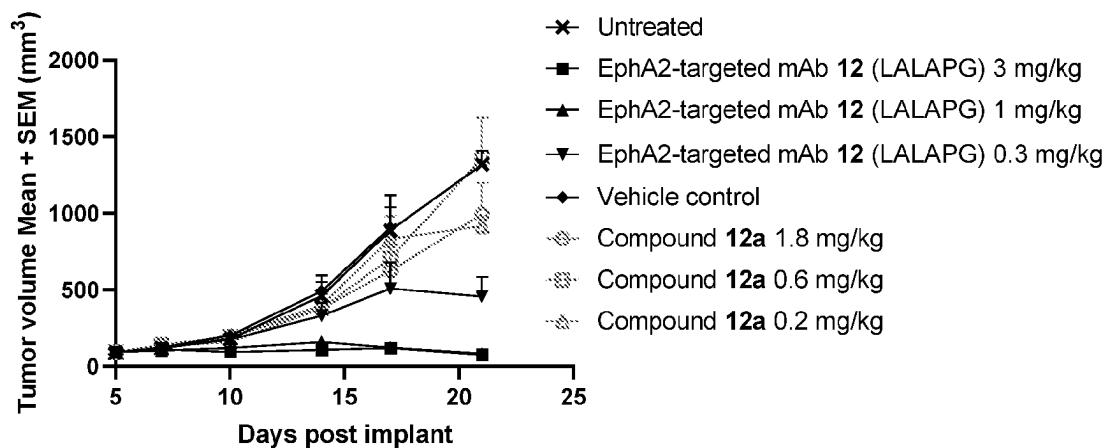


FIG. 17

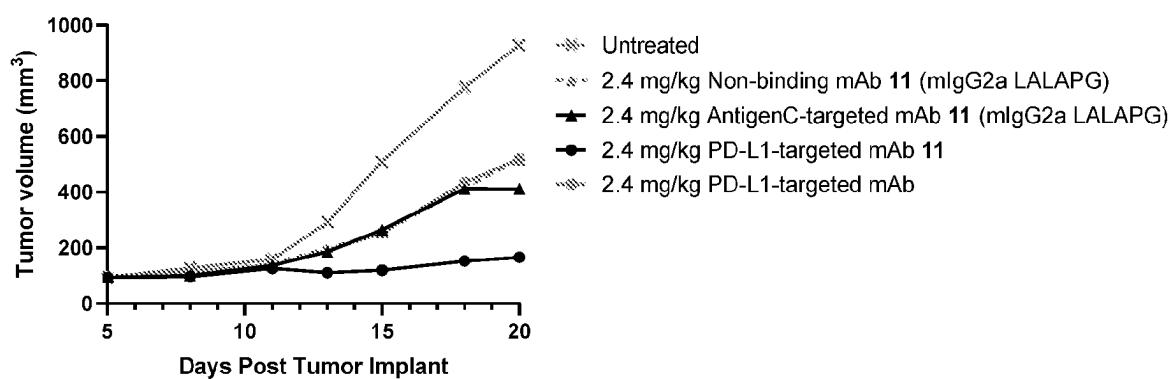


FIG. 18

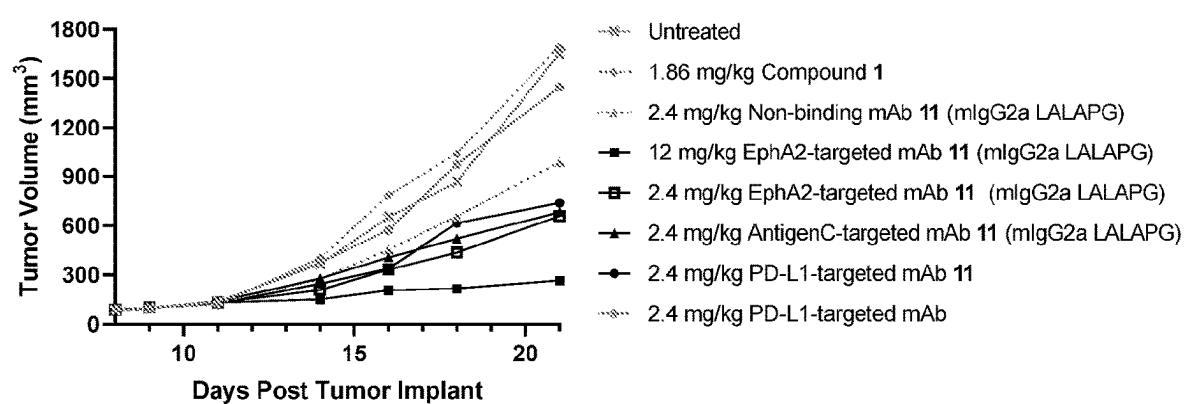


FIG. 19

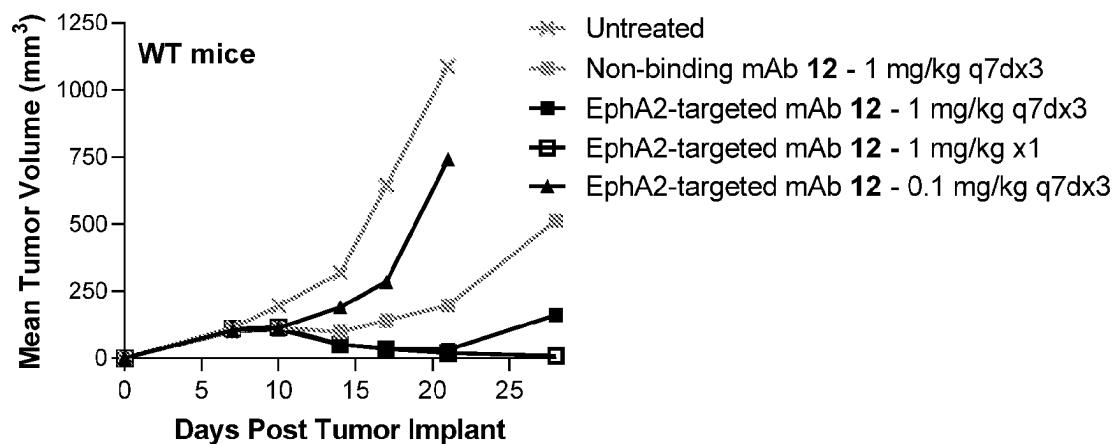


FIG. 20A

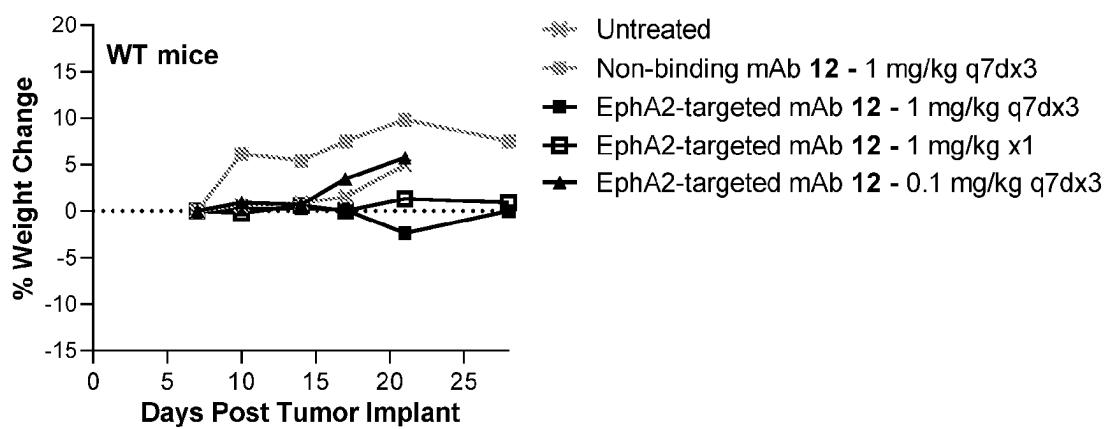


FIG. 20B

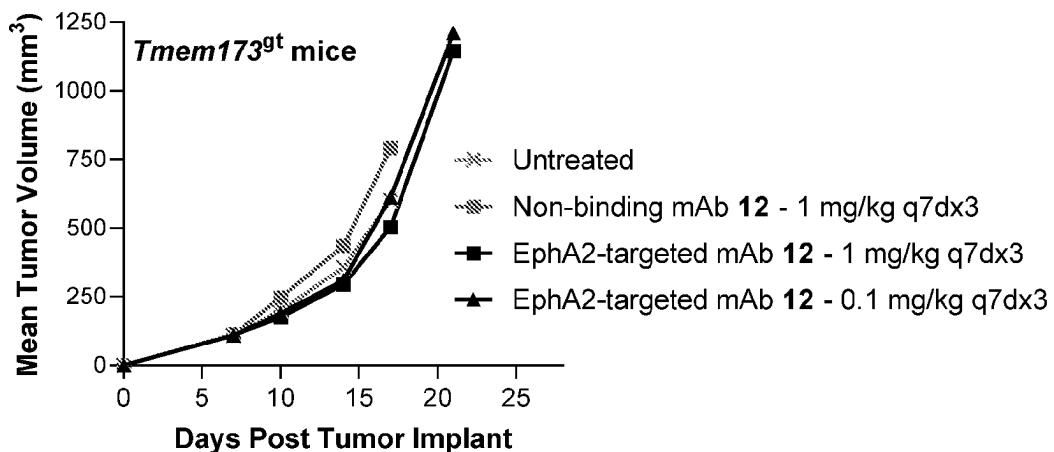


FIG. 20C

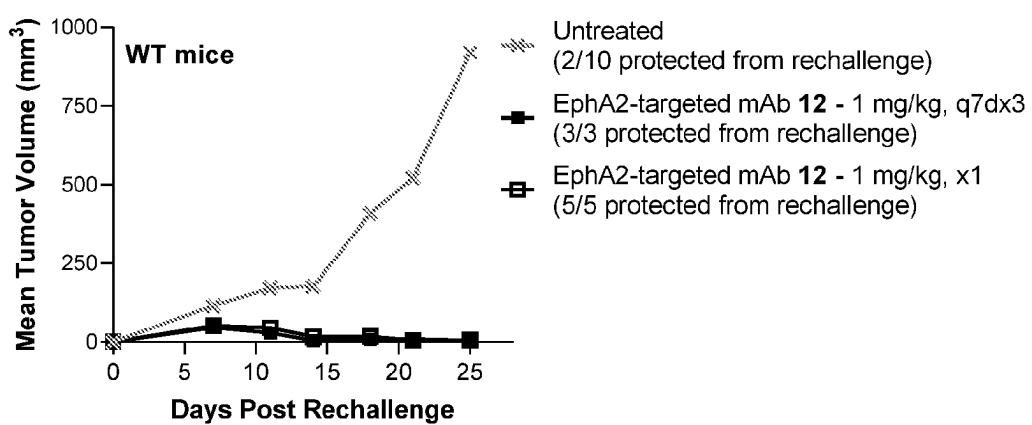


FIG. 20D

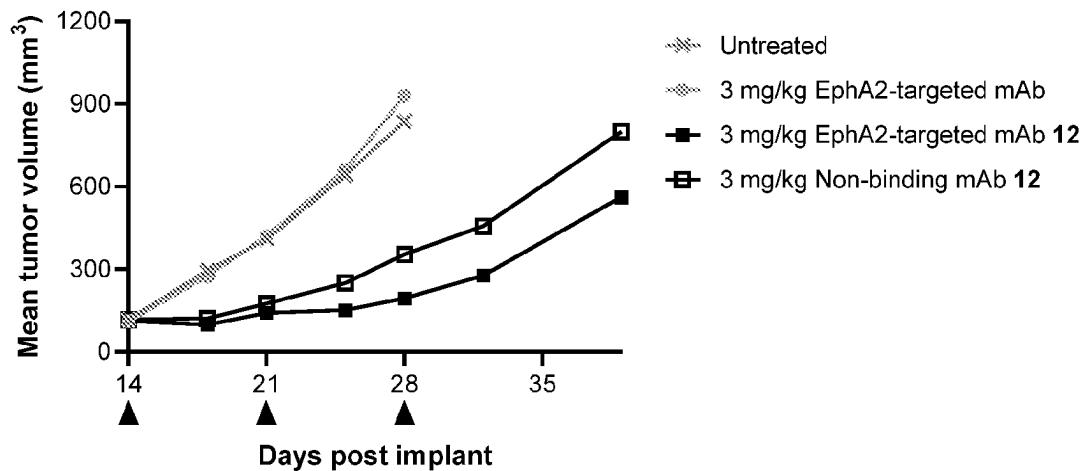


FIG. 21A

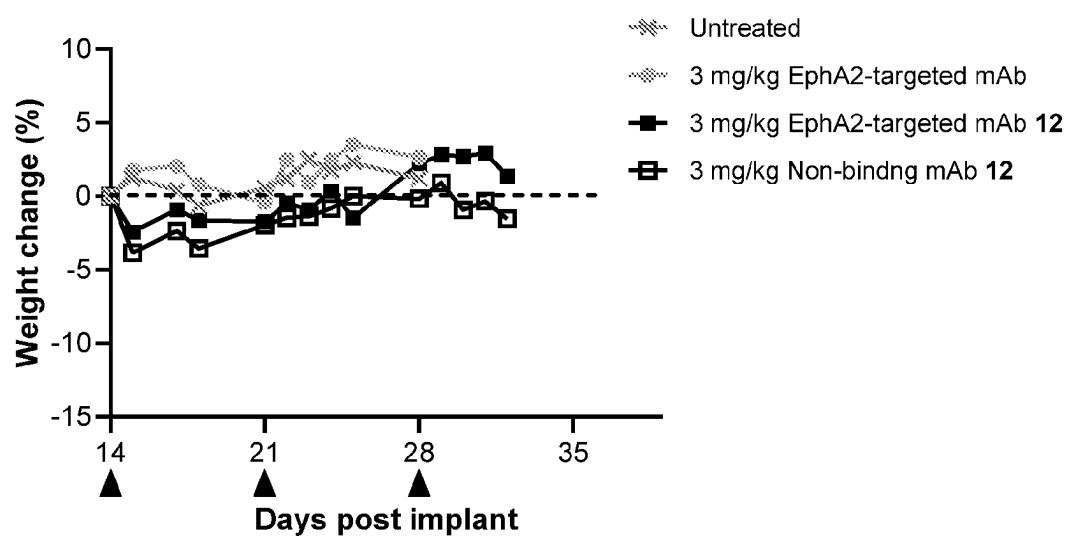


FIG. 21B

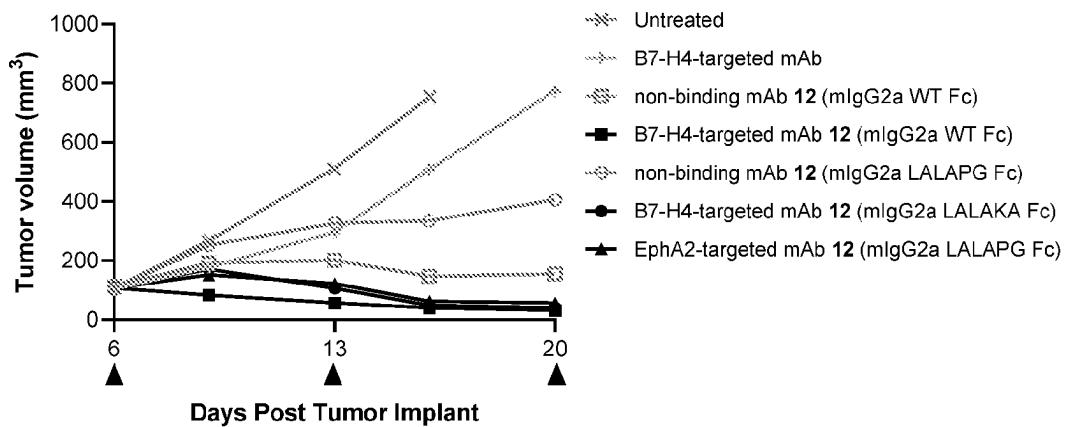


FIG. 22A

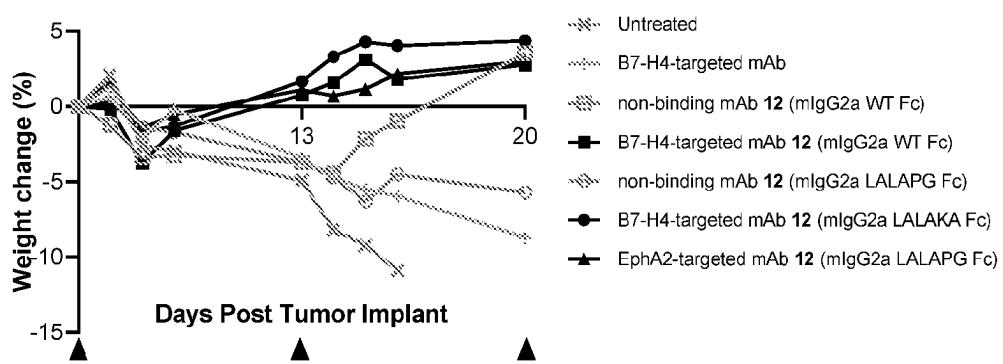


FIG. 22B

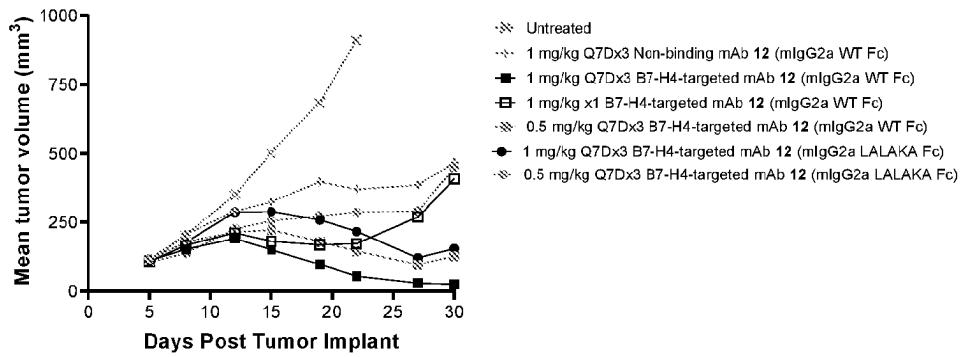


FIG. 23A

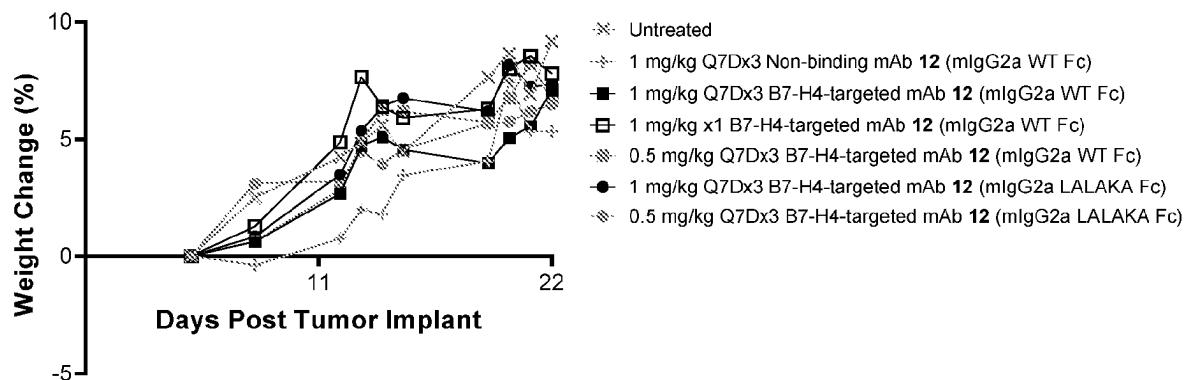


FIG. 23B

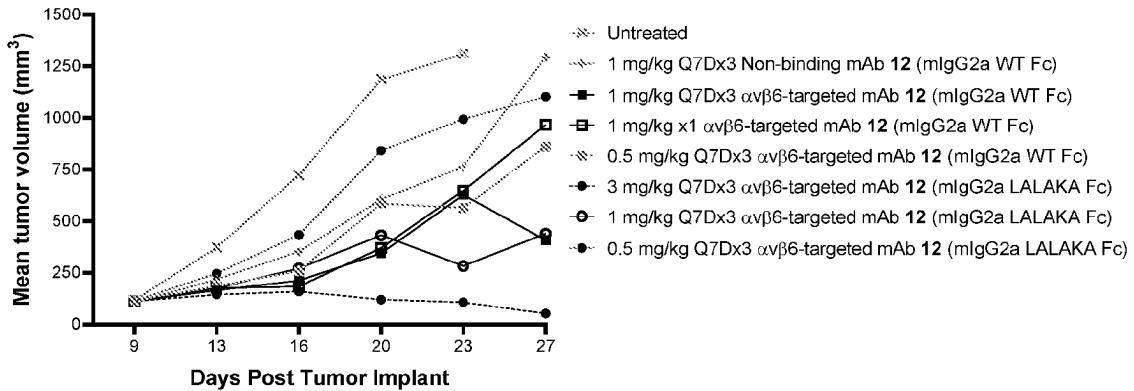


FIG. 24

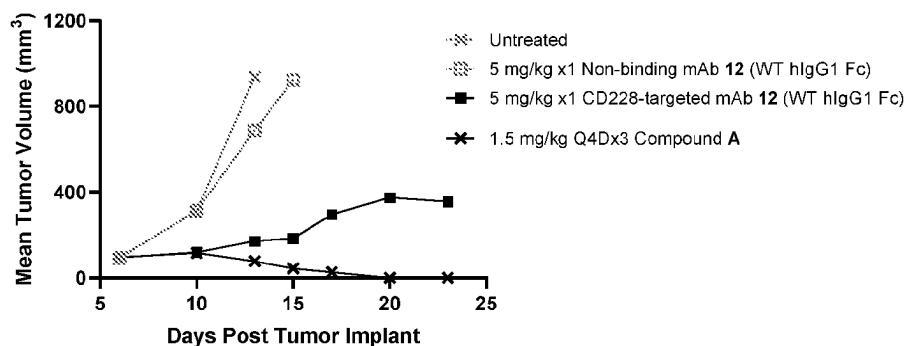


FIG. 25

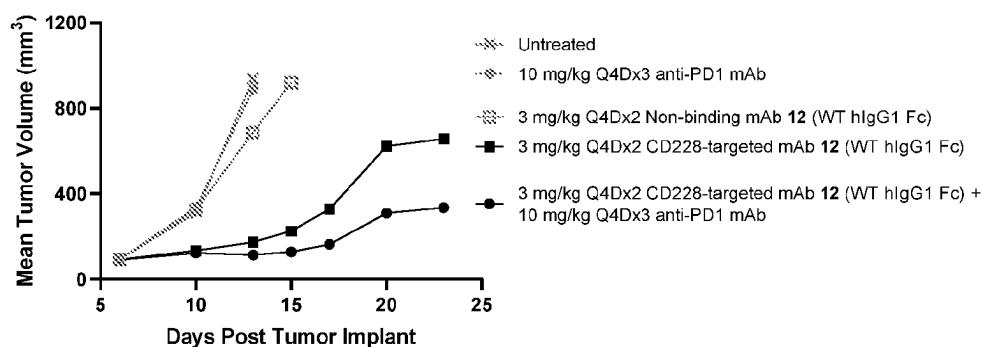


FIG. 26

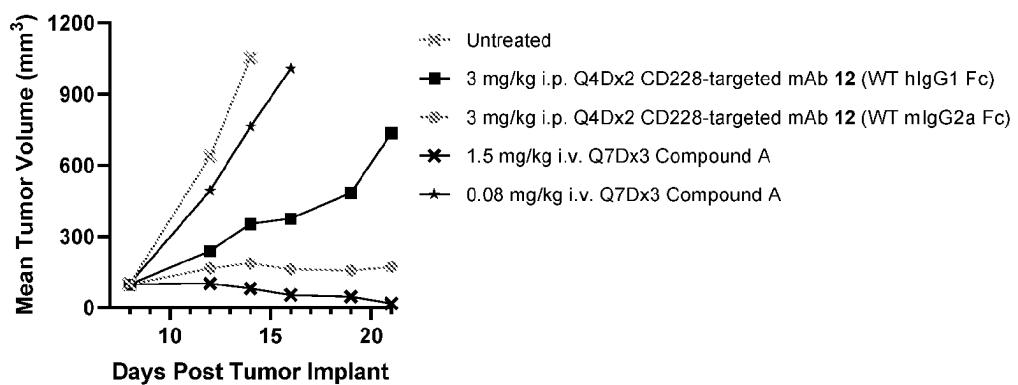


FIG. 27A

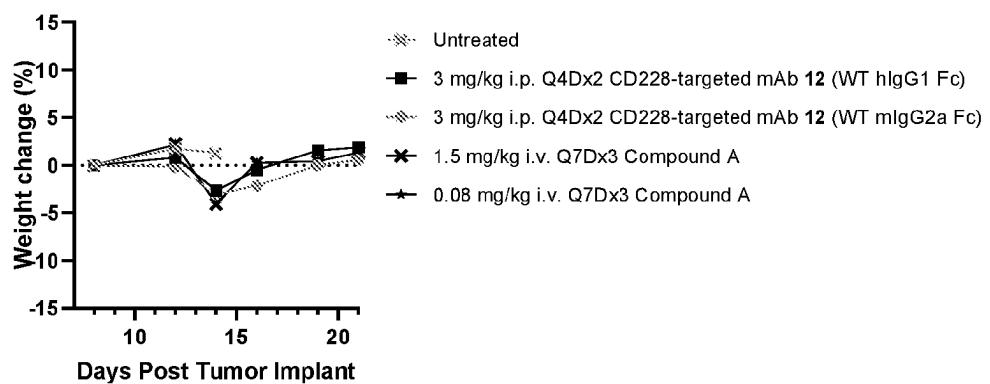


FIG. 27B

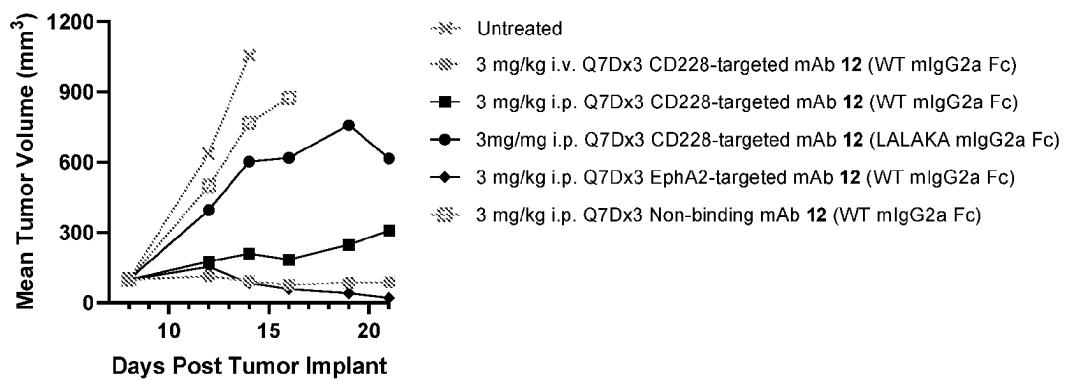


FIG. 28A

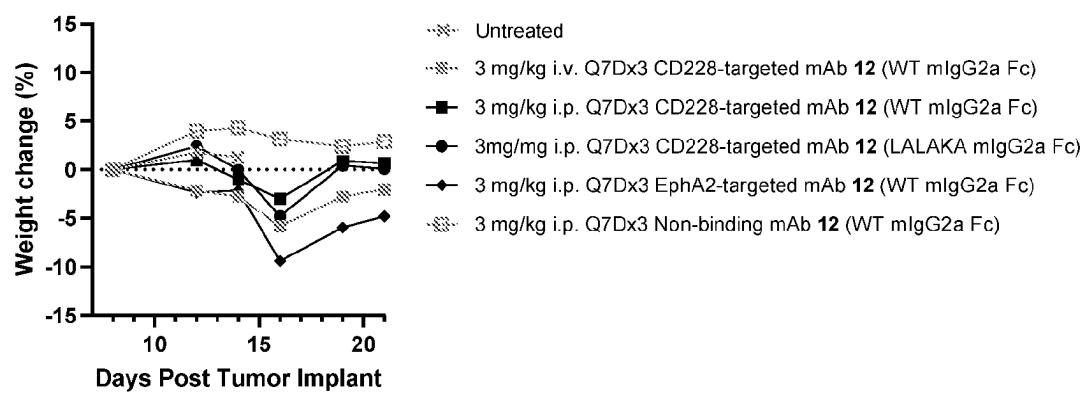


FIG. 28B

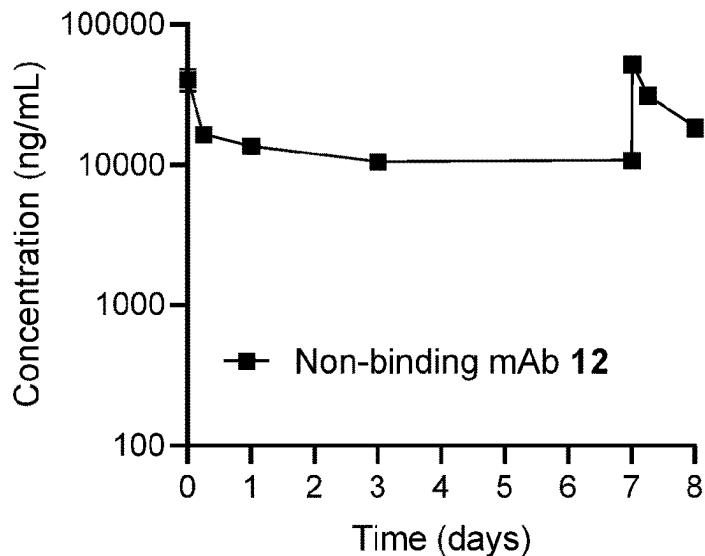


FIG. 29

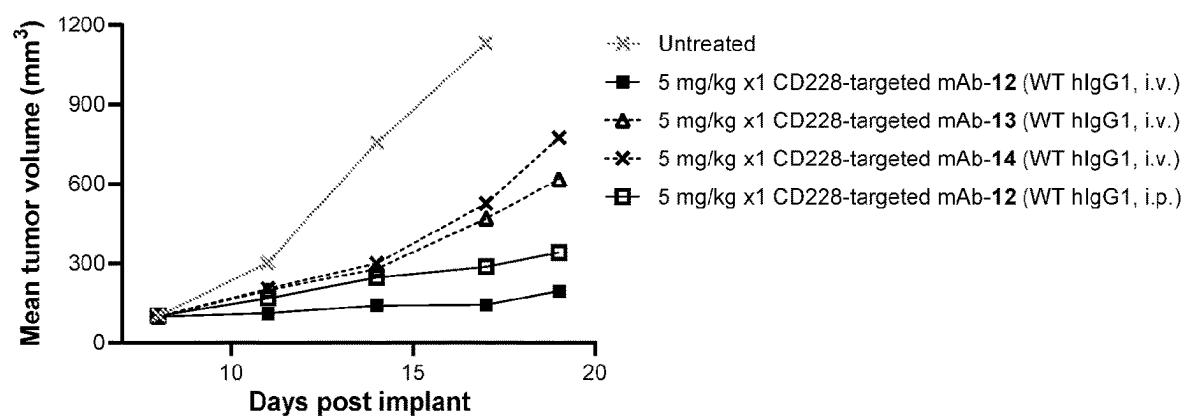


FIG. 30

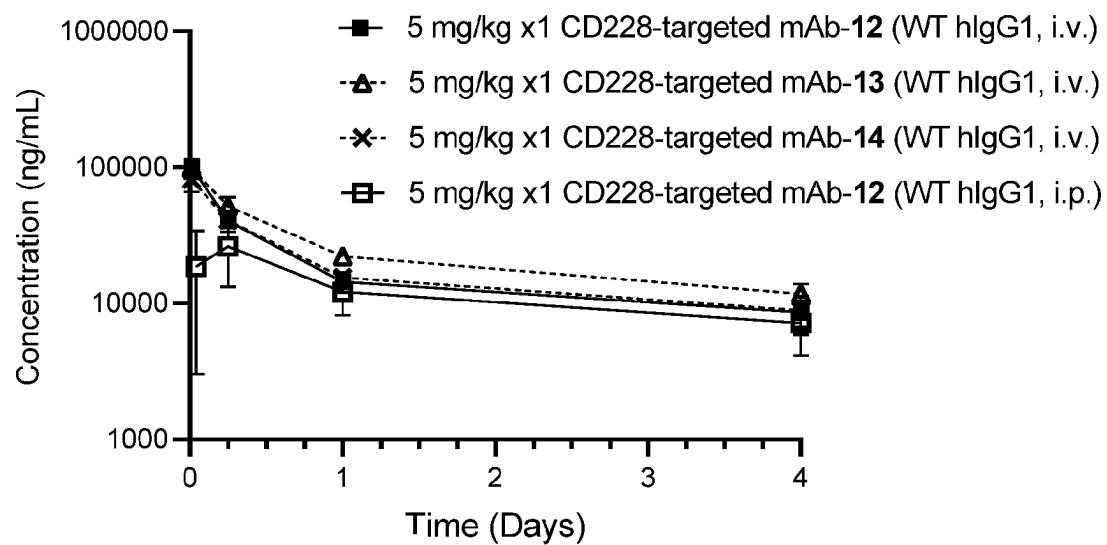


FIG. 31

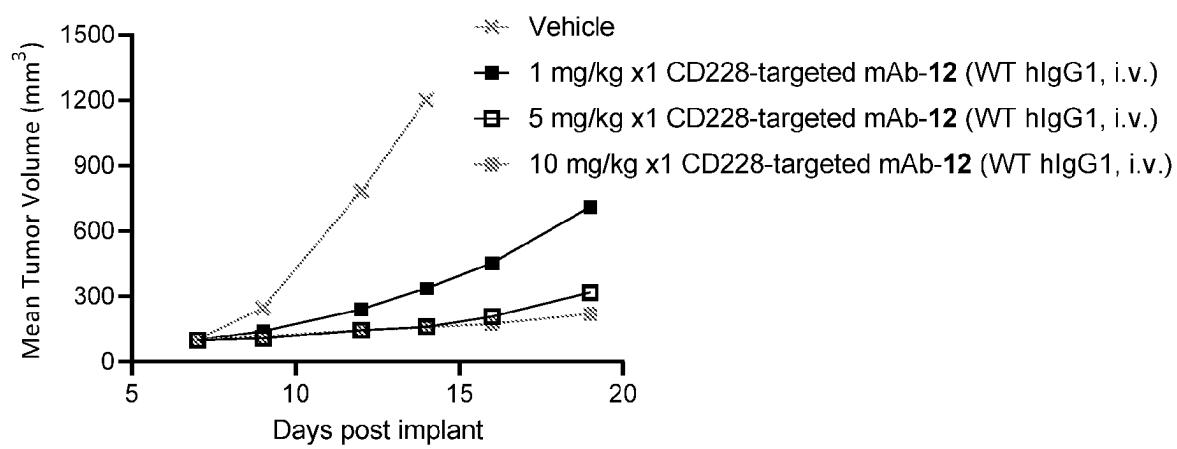


FIG. 32

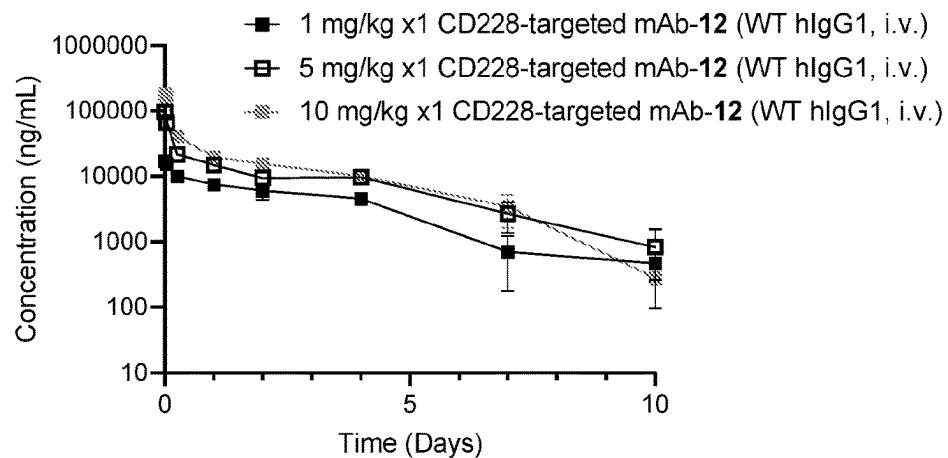


FIG. 33

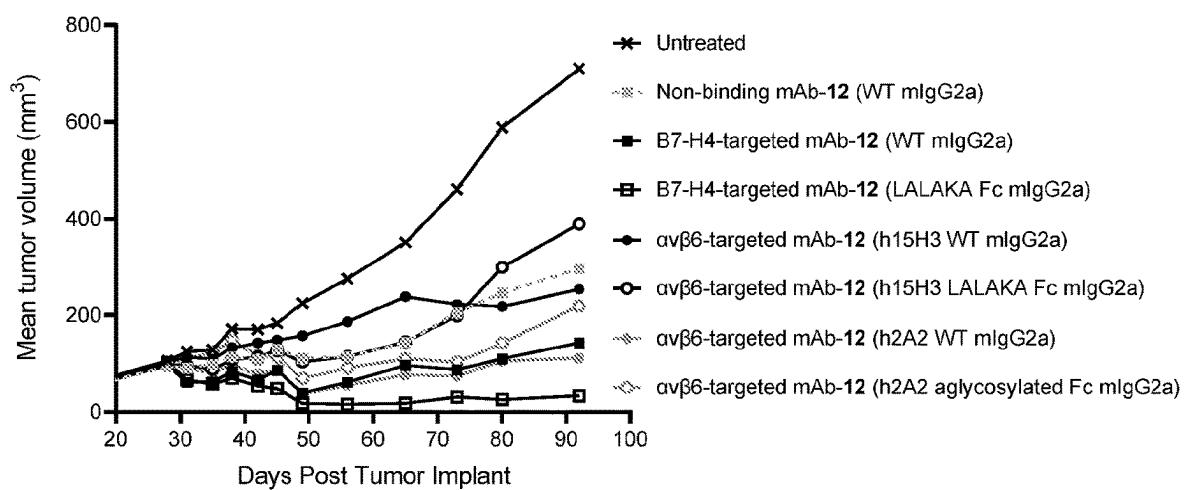


FIG. 34

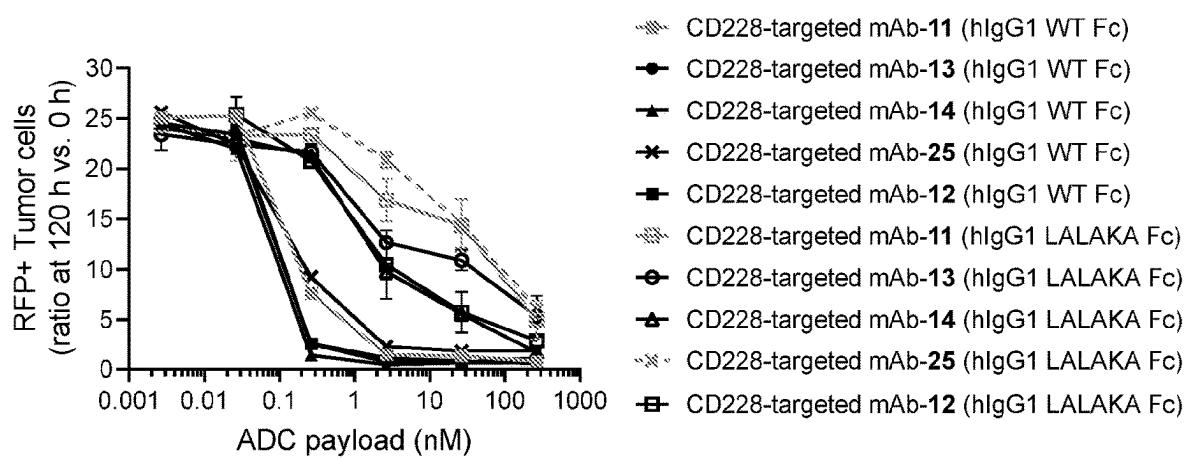


FIG. 35

IMMUNOMODULATORY ANTIBODY-DRUG CONJUGATES

REFERENCE TO THE SEQUENCE LISTING

[0001] The present application is being filed along with a Sequence Listing in electronic format. The Sequence Listing is provided as a file entitled SGENE.010WO.xml created on Apr. 26, 2023, which is 954,186 bytes in size. The information in the electronic format of the Sequence Listing is incorporated herein by reference in its entirety.

BACKGROUND

Field

[0002] The present invention relates to the fields of chemistry and medicine. More particularly, the present invention relates to antibody-drug conjugates, compositions, their preparation, and their use as therapeutic agents.

Description of the Related Art

[0003] The cGAS-STING pathway is an innate immune pathway that recognizes intracellular DNA and triggers a type I interferon and inflammatory cytokine response that is important for both anti-viral and anti-tumor immunity. Upon DNA binding, cGMP-AMP synthase (cGAS) produces cGAMP, which is the endogenous ligand of STING. See, e.g., Villanueva, *Nat. Rev. Drug Disc.* 2019; 18; 15. At the molecular level, upon activation by cGAMP, the transmembrane STING dimer translocates from the endoplasmic reticulum to the Golgi apparatus, ultimately recruiting TANK-binding kinase 1 (TBK1) and the transcription factor interferon regulatory factor 3 (IRF3), leading to induction of type I interferons (IFNs) and an inflammatory response. See Konno, et al., *Cell* 2013; 155; 688-698. This innate immune pathway must be tightly regulated as excessive cGAS-STING activity has been linked to various autoimmune and inflammatory disorders. See Barber, *Nat. Rev. Immunol.* 2015; 15; 760-770; see also, Liu, et al., *N. Engl. J. Med.* 2014; 371; 507-518.

[0004] Exogenous STING agonists can help to overcome the immunosuppressive tumor microenvironment by activating an immune response against a tumor, resulting in tumor regression. See Sun, et al., *Science* 2013; 6121; 786-791; see also, Corrales and Gajewski, *Clinic. Cancer Res.* 2015; 21; 4774-4779. Examples include nucleotide-based STING agonists, which are, like the endogenous ligands, cyclic di-nucleotides. These compounds are typically charged and hydrophilic, susceptible to enzymatic degradation, and have poor bioavailability and pharmacokinetics. Thus, there remains a need for STING agonists with improved pharmacological properties that avoid systemic cytokine induction.

SUMMARY

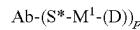
[0005] Some embodiments described herein relate to antibody-drug conjugates (ADCs) that can elicit a localized immune response to target cells, and hence, exhibit reduced off-target toxicity, such as that observed with systemically administered immunostimulatory compounds.

[0006] Some embodiments provide an antibody-drug conjugate (ADC) comprising:

- [0007]** an antigen-binding protein or antigen-binding fragment thereof (e.g., an antibody); and
- [0008]** a compound of Formula (I) as described herein;
- [0009]** wherein the compound of Formula (I) is conjugated to the antigen-binding protein or antigen-binding fragment thereof via a succinimide or hydrolyzed suc-

cinimide covalently linked to a sulfur atom of a cysteine residue of the antigen-binding protein or antigen-binding fragment thereof.

[0010] Some embodiments provide an antibody-drug conjugate (ADC) having the formula:



wherein:

[0011] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);

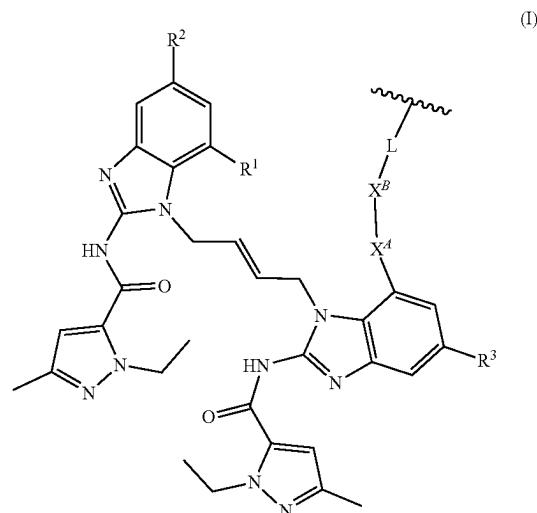
[0012] each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;

[0013] M¹ is a succinimide or a hydrolyzed succinimide;

[0014] subscript p is an integer from 2 to 8; and

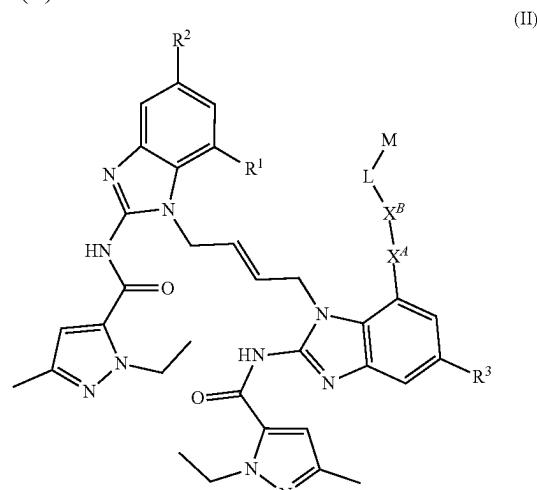
[0015] each (D) is a Drug-Linker Unit of Formula (I), as described herein.

[0016] In some embodiments, Formula (I) has the structure:



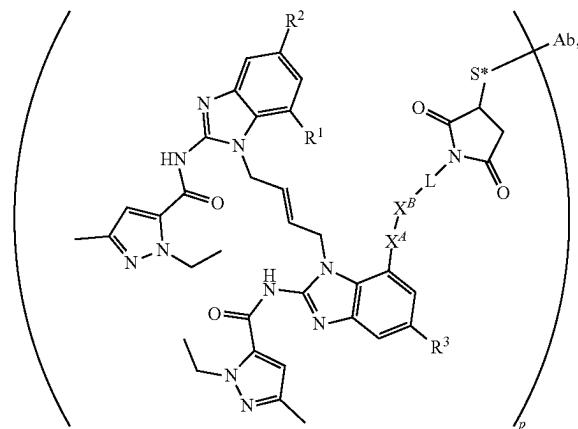
wherein variable groups R¹, R², R³, X^A, and X^B are as defined herein.

[0017] Some embodiments provide a compound of Formula (II):



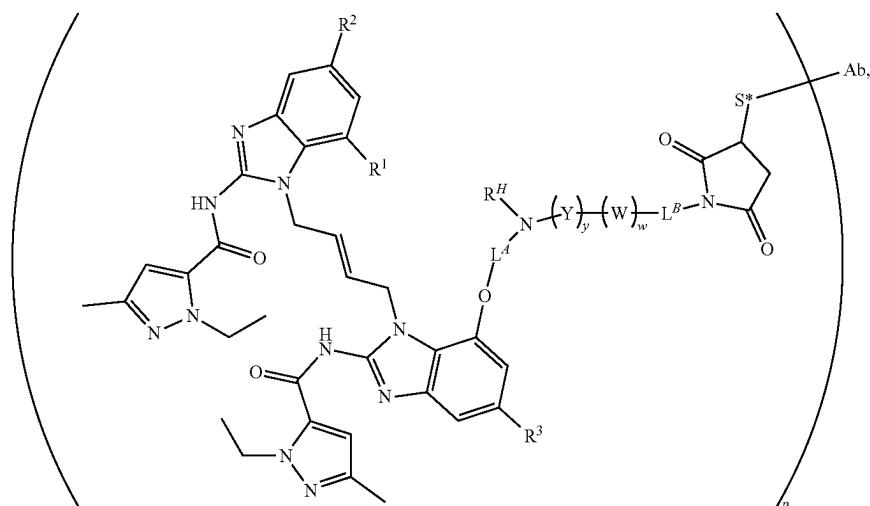
wherein M, L, R¹, R², R³, X^A, and X^B are as defined herein.

[0018] Some embodiments provide an antibody-drug conjugate having the structure:



[0019] wherein Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody), S^* is the sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof, subscript p is an integer from 2 to 8, and the remaining variable groups are as defined herein. In some embodiments, Ab binds CD228. In some embodiments, Ab binds $\alpha\beta 6$. In some embodiments, Ab binds B7-H4.

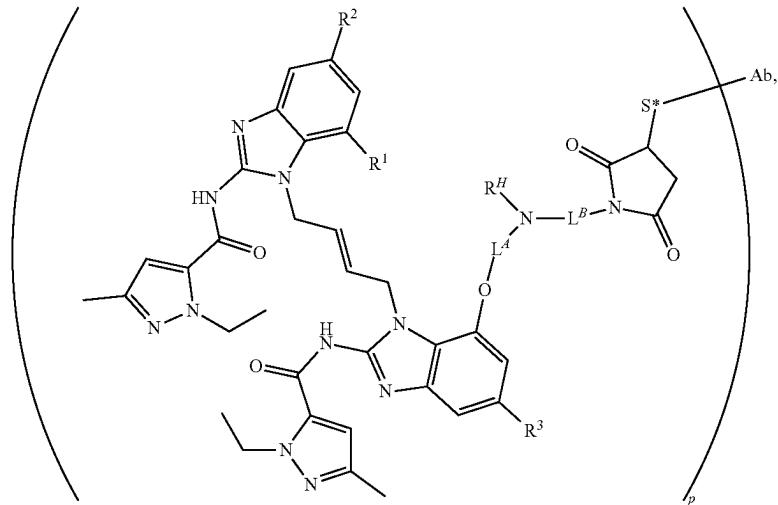
[0020] Some embodiments provide an antibody-drug conjugate having the structure



[0021] wherein Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody), S^* is the sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof, subscript p is an integer from 2 to 8, and the

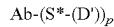
remaining variable groups are as defined herein. In some embodiments, Ab binds CD228. In some embodiments, Ab binds $\alpha\beta 6$. In some embodiments, Ab binds B7-H4.

[0022] Some embodiments provide an antibody-drug conjugate having the structure:



[0023] wherein Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody), S^* is the sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof, subscript p is an integer from 2 to 8, and the remaining variable groups are as defined herein. In some embodiments, Ab binds CD228. In some embodiments, Ab binds av β 6. In some embodiments, Ab binds B7-H4.

[0024] Some embodiments provide an antibody-drug conjugate (ADC) having the formula:



wherein:

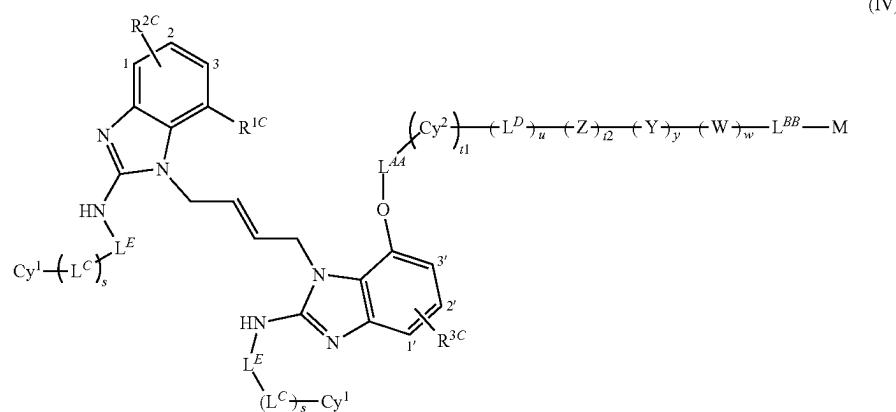
[0025] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);

[0026] each S^* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;

[0027] D' is a Drug-Linker unit that is a radical of the compound of Formula (IV), as described herein; and

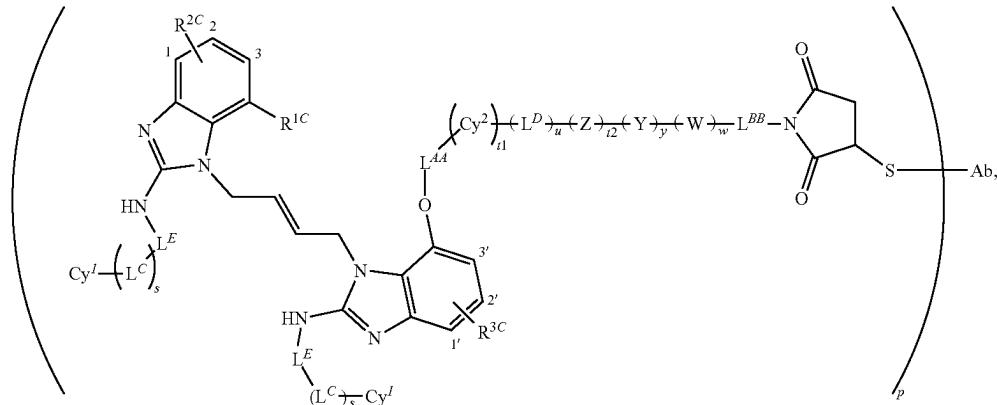
[0028] subscript p is an integer from 2 to 8.

[0029] In some embodiments, Formula (IV) has the structure:



wherein the variables are as defined herein.

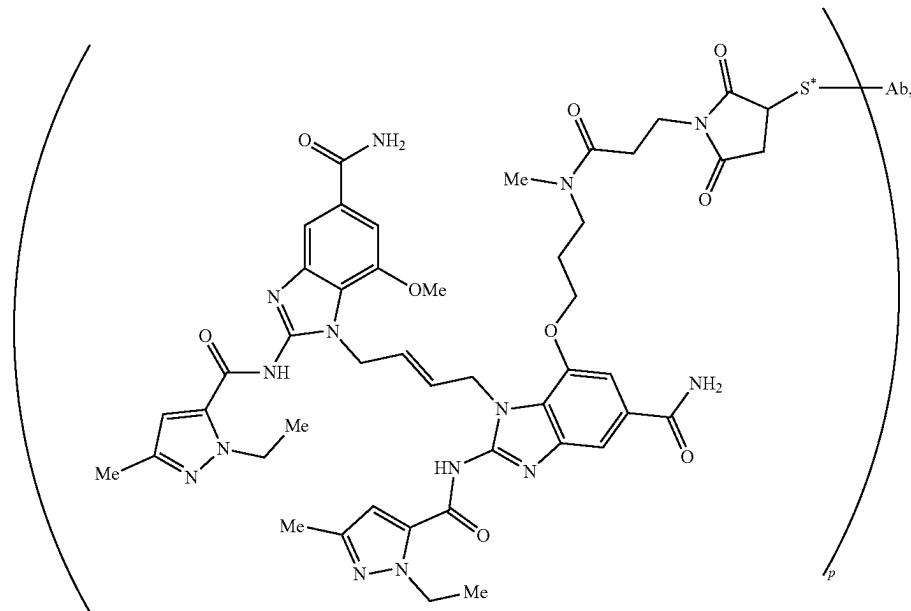
[0030] Some embodiments provide an antibody-drug conjugate having the structure:



wherein Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody), S* is the sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof, subscript p is an integer from 2 to 8, and the remaining variable groups are as

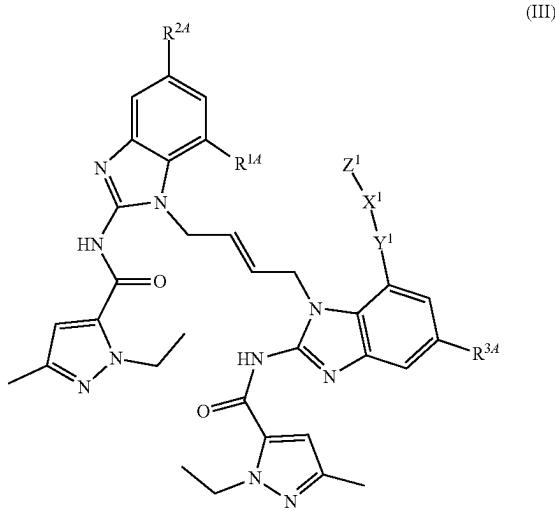
defined herein. In some embodiments, Ab binds CD228. In some embodiments, Ab binds $\alpha\beta\delta 6$. In some embodiments, Ab binds B7-H4.

[0031] Some embodiments provide an antibody-drug conjugate having the structure:



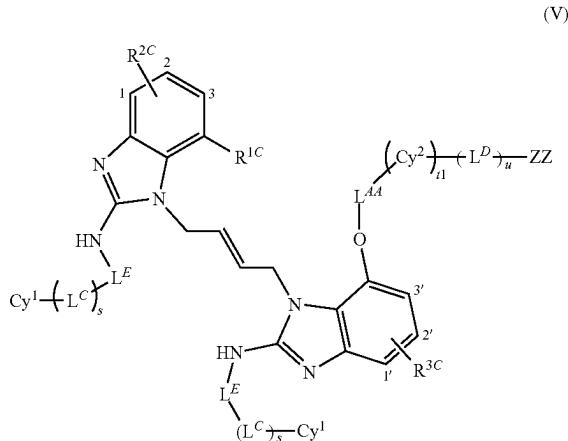
[0032] wherein Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody), S* is the sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof, subscript p is an integer from 2 to 8, and the remaining variable groups are as defined herein. In some embodiments, Ab binds CD228. In some embodiments, Ab binds $\alpha\beta\delta 6$. In some embodiments, Ab binds B7-H4.

[0033] Some embodiments provide a compound of Formula (III):



wherein the variables are as defined herein.

[0034] Some embodiments provide a compound having the structure of Formula (V):



wherein the variables are as defined herein.

[0035] Some embodiments provide a composition comprising a distribution of ADCs as described herein.

[0036] Some embodiments provide a method of treating cancer in a subject in need thereof, comprising administering a therapeutically effective amount of an ADC composition, as described herein, to the subject.

[0037] Some embodiments provide a method of treating cancer in a subject in need thereof, comprising administering a therapeutically effective amount of an ADC, as described herein, to the subject.

[0038] Some embodiments provide a method of inducing an anti-tumor immune response in a subject in need thereof, comprising administering a therapeutically effective amount of an ADC composition, as described herein, to the subject.

[0039] Some embodiments provide a method of inducing an anti-tumor immune response in a subject in need thereof, comprising administering a therapeutically effective amount of an ADC, as described herein, to the subject.

BRIEF DESCRIPTION OF THE DRAWINGS

[0040] FIG. 1 illustrates the response of THP1-Dual™ cells (also referred to as THP1 dual reporter cells) to various small molecule STING agonists.

[0041] FIG. 2 illustrates the response of wild type (WT) and STING-deficient murine bone marrow-derived macrophages to various small molecule STING agonists.

[0042] FIG. 3 illustrates the response of THP1 dual reporter cells to ADCs comprising a non-binding or targeted antibody conjugated to either compound 11 (cleavable linker with compound 1), compound 12 (non-cleavable linker with compound 12a), or compounds 13 or 14 (cleavable linkers with compound 12a).

[0043] FIG. 4 illustrates the response of THP1 dual reporter cells to compound 12 (non-cleavable linker with compound 12a) and compound 16 (cysteine adduct of compound 12 and free drug released from ADCs containing compound 12).

[0044] FIG. 5 illustrates the response of THP1 dual reporter cells to compounds 12a and 15b as a free drug or conjugated to a non-binding or targeted antibody (ADC of compounds 12 and 15) following incubation for 48 hours.

[0045] FIGS. 6A and 6B illustrate the response of SU-DHL-1 lymphoma cells to ADCs comprising a non-binding, antigen C-targeted or PD-L1-targeted antibody conjugated to compound 11 (cleavable linker with compound 1). Both cytokine production (MIP-1 α) (FIG. 6A) and viability (FIG. 6B) are plotted.

[0046] FIG. 7 illustrates the response of THP1 dual reporter cells cultured alone or co-cultured with HEK 293T cells engineered to express target antigen C to ADCs comprising an antigen C-targeted mAb with a IgG1 LALAPG backbone conjugated to compounds 12, 13, or 14.

[0047] FIG. 8 illustrates the bystander activity of ADCs comprising either an EphA2-targeted mAb or a non-binding mAb with a mIgG2a WT or LALAPG backbone conjugated to compound 12 using Renca cancer cells and THP1 dual reporter cells.

[0048] FIGS. 9A-9C illustrate RFP+ MDA-MB-468 tumor cell killing (FIG. 9A) and immune activation (CD8 T cell counts, FIG. 9B; IP-10 production, FIG. 9C) in response to treatment of tumor cell and peripheral blood mononuclear cell (PBMC) co-cultures with compound 16 or conjugates consisting of a non-binding mAb or B7-H4-targeted mAb with a WT or LALAKA Fc backbone conjugated to compound 12. FIG. 9A: RFP+ tumor cell confluence (96 hours); FIG. 9B: CD8+ T cell counts (48 hours); FIG. 9C: IP-10 secretion (48 hours).

[0049] FIG. 10 illustrates RFP+ MDA-MB-468 tumor cell killing in response to treatment of tumor cell and peripheral blood mononuclear cell (PBMC) co-cultures with compound 16 or conjugates consisting of a α v β 6 or B7-H4-targeted mAb with a WT or LALAKA Fc backbone conjugated to compound 12. RFP+ tumor cell confluence at 96 hours is plotted.

[0050] FIG. 11 illustrates RFP+ HCT15 tumor cell killing in response to treatment of tumor cell and peripheral blood mononuclear cell (PBMC) co-cultures with compound 16 or

conjugates of $\alpha\alpha\beta\beta$ -targeted mAb with a WT Fc backbone conjugated to compound 12. RFP+ tumor cell confluence at 72 hours is plotted.

[0051] FIG. 12 illustrates RFP+ HT1080 tumor cell killing in response to treatment of tumor cell and peripheral blood mononuclear cell (PBMC) co-cultures with compound 16 or conjugates consisting of a non-binding mAb or CD228-targeted mAb with a WT Fc backbone conjugated to compound 12. RFP+ tumor cell confluence at 96 hours is plotted.

[0052] FIG. 13 illustrates RFP+ HT1080 tumor cell killing in response to treatment of tumor cell and peripheral blood mononuclear cell (PBMC) co-cultures with compound 16 or conjugates consisting of a non-binding mAb or CD228-targeted mAb with a WT or LALAKA Fc backbone conjugated to compound 12. RFP+ tumor cell confluence at 96 hours is plotted.

[0053] FIGS. 14A and 14B illustrate the response to q7dx3 ADC dosing (3 weekly doses) in a Renca tumor mouse model to evaluate various ADCs comprising a non-binding or EphA2-targeted mAb with a mIgG2a LALAPG backbone conjugated to compound 11 (dosed intraperitoneally), or compound 1 or (E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-(3-morpholinopropoxy)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxamide tris(2,2,2-trifluoroacetate) (Compound A, a reference compound, dosed intravenously). FIG. 14A: tumor growth; FIG. 14B: % weight change.

[0054] FIGS. 15A and 15B illustrate the response to q7dx3 ADC dosing (3 weekly doses) in a Renca tumor mouse model to evaluate various ADCs comprising a non-binding or EphA2-targeted mAb with a mIgG2a LALAPG backbone conjugated to compounds 11 or 12 (dosed intraperitoneally). FIG. 15A: tumor growth; FIG. 15B: % weight change.

[0055] FIGS. 16A and 16B illustrate the response to q7dx3 ADC dosing (3 weekly doses) in a Renca tumor mouse model, which is engineered to express a human protein, to evaluate various ADCs comprising a non-binding or EphA2-targeted mAb with either a mIgG2a wild type (WT) or a mIgG2a LALAPG backbone conjugated to compounds 12 or 15. FIG. 16A: tumor growth; FIG. 16B: % weight change.

[0056] FIG. 17 illustrates the response to q7dx3 dosing (3 weekly doses, intraperitoneally) in a Renca tumor mouse model to evaluate the ADC comprising an EphA2-targeted mAb with a mIgG2a LALAPG backbone conjugated to compound 12 or unconjugated compound 12a.

[0057] FIG. 18 illustrates the response to q7dx3 dosing (3 weekly doses) of various compounds in a Renca tumor model to evaluate a PD-L1-targeted mAb, and various ADCs comprising a non-binding, PD-L1-targeted or antigen C-targeted mAb conjugated to compound 11.

[0058] FIG. 19 illustrates the response to q7dx3 dosing (3 weekly doses) of various compounds in a CT26 tumor model to evaluate unconjugated compound 1, a PD-L1-targeted mAb, and various ADCs comprising a non-binding, antigen C, PD-L1, or EphA2-targeted mAb conjugated to compound 11.

[0059] FIGS. 20A-D illustrate the response to q7dx3 (3 weekly doses) or a single dose of ADC, as indicated, in a MC38 tumor model to evaluate various ADCs comprising a non-binding or EphA2-targeted mAb with a mIgG2a LALAPG backbone conjugated to compound 12. Mice that achieved complete tumor regression in response to ADC treatment were rechallenged with MC38 tumor cells and

tumor growth was monitored. FIG. 20A: tumor growth (wild type (WT) mice); FIG. 20B: % weight change (WT mice); FIG. 20C: tumor growth (STING-deficient Tmem173^{gt} mice); FIG. 20D: tumor growth following MC38 tumor rechallenge.

[0060] FIGS. 21A and 21B illustrate the response to q7dx3 mAb or ADC dosing (3 weekly doses indicated by the arrow heads) in a 4T1 tumor model to evaluate various ADCs comprising a non-binding or EphA2-targeted mAb with a mIgG2a LALAPG backbone conjugated to compound 12. FIG. 21A: tumor growth; FIG. 21B: % weight change.

[0061] FIGS. 22A and 22B illustrates the response to q7dx3 ADC dosing (3 weekly doses) in a Renca tumor mouse model, in which Renca tumor cells are engineered to express murine B7-H4, to evaluate various ADCs comprising a non-binding or B7-H4-targeted mAb with either a mIgG2a wild type (WT) or a mIgG2a LALAKA or LALAPG backbone conjugated to compound 12. FIG. 22A: tumor growth; FIG. 22B: % weight change.

[0062] FIGS. 23A and 23B illustrate the response to q7dx3 ADC dosing (3 weekly doses) or a single dose, as indicated, in an EMT6 tumor mouse model, in which EMT6 tumor cells are engineered to express murine B7-H4, to evaluate various ADCs comprising a non-binding or B7-H4-targeted mAb with either a mIgG2a wild type (WT) or a mIgG2a LALAKA backbone conjugated to compound 12. FIG. 23A: tumor growth; FIG. 23B: % weight change.

[0063] FIG. 24 illustrates the response to q7dx3 ADC dosing (3 weekly doses) or a single dose, as indicated, in an CT26 tumor mouse model, in which CT26 tumor cells are engineered to express murine $\alpha\alpha\beta\beta$, to evaluate various ADCs comprising a non-binding or $\alpha\alpha\beta\beta$ -targeted mAb with either a mIgG2a wild type (WT) or a mIgG2a LALAKA backbone conjugated to compound 12.

[0064] FIG. 25 illustrates the response to a single ADC dose (intraperitoneally) or q4dx3 compound A (3 doses 4 days apart, intravenously) in an LL2 tumor mouse model, in which LL2 tumor cells are engineered to express human CD228, to evaluate various ADCs comprising a non-binding or CD228-targeted mAb with hIgG1 wild type (WT) backbone conjugated to compound 12.

[0065] FIG. 26 illustrates the response to a q4dx2 ADC dosing (2 doses 4 days apart, intraperitoneally) and/or q4dx3 anti-PD1 mAb dosing (3 doses 4 days apart, intraperitoneally) in an LL2 tumor mouse model, in which LL2 tumor cells are engineered to express human CD228, to evaluate various ADCs comprising a non-binding or CD228-targeted mAb with hIgG1 wild type (WT) backbone conjugated to compound 12 as a monotherapy or in combination with a PD-1-targeted mAb.

[0066] FIGS. 27A and 27B illustrate the response to a q4dx2 ADC dosing (2 doses 4 days apart, intraperitoneally) and/or q7dx3 Compound A dosing (3 doses 7 days apart, intravenously) in an LL2 tumor mouse model, in which LL2 tumor cells are engineered to express human CD228. ADCs comprised a CD228-targeted mAb with hIgG1 or mIgG2a wild type (WT) Fc backbone conjugated to compound 12. FIG. 27A: tumor growth; FIG. 27B: % weight change.

[0067] FIGS. 28A and 28B illustrate the response to a q7dx3 ADC dosing (3 doses 7 days apart, intravenously or intraperitoneally as indicated) in an LL2 tumor mouse model, in which LL2 tumor cells are engineered to express human CD228. ADCs comprised a non-binding mAb, EphA2-targeted mAb, or CD228-targeted mAb with a

mIgG2a wild type (WT) or LALAKA backbone conjugated to compound 12. FIG. 28A: tumor growth; FIG. 28B: % weight change.

[0068] FIG. 29 illustrates the pharmacokinetic profile of an ADC comprising a [deglycosylated]non-binding mAb conjugated to compound 12 following administration to male C57BL/6 mice.

[0069] FIG. 30 illustrates the antitumor activity in response to a single dose (intravenous (i.v.) or intraperitoneal (i.p.), as indicated) of ADCs comprising a CD228-targeted mAb with a hIgG1 wild type (WT) Fc backbone conjugated to compound 12, 13, or 14 in an LL2 tumor mouse model in which LL2 tumor cells are engineered to express human CD228.

[0070] FIG. 31 illustrates the pharmacokinetic profile of a single dose (intravenous or intraperitoneal, as indicated) of ADCs comprising a CD228-targeted mAb with a hIgG1 wild type (WT) Fc backbone conjugated to compound 12, 13, or 14 in an LL2 tumor mouse model in which LL2 tumor cells are engineered to express human CD228.

[0071] FIG. 32 illustrates the antitumor activity in response to a single 1, 5, or 10 mg/kg dose (intravenous) of ADCs comprising a CD228-targeted mAb with a hIgG1 wild type (WT) Fc backbone conjugated to compound 12 in an LL2 tumor mouse model in which LL2 tumor cells are engineered to express human CD228.

[0072] FIG. 33 illustrates the pharmacokinetic profile of a single dose (intravenous) of ADCs comprising a CD228-targeted mAb with a hIgG1 wild type (WT) Fc backbone conjugated to compound 12 in an LL2 tumor mouse model in which LL2 tumor cells are engineered to express human CD228.

[0073] FIG. 34 illustrates the antitumor activity in response to a single 3 mg/kg dose (intraperitoneal) of various ADCs comprising a B7-H4 or α v β 6-targeted mAb conjugated to compound 12 in the MDAMB468 xenograft mouse model of breast cancer.

[0074] FIG. 35 illustrates RFP+ HT1080 tumor cell killing in response to treatment of tumor cell and peripheral blood mononuclear cell (PBMC) co-cultures with conjugates consisting of a CD228-targeted mAb with a WT or LALAKA Fc backbone conjugated to compound 11, 12, 13, 14, or 25. The ratio of RFP+ tumor cells at 120 hours relative to 0 hours is plotted.

DETAILED DESCRIPTION

[0075] Provided herein are antibody-drug conjugates (ADCs) that can elicit a localized immune response to target cells, and hence, reduced off-target toxicity, for example, as compared to the toxicity often observed with systemic administration of immunostimulatory compounds, such as STING agonists. The in vivo toxicity of such compounds is often linked to systemic immune activation, resulting in both on- and off-target immune responses. The ADCs described herein include STING agonists as the drug payload to provide localized, selective induction of immune activation. See, e.g., Milling, et al., *Adv. Drug Deliv. Rev.* 2017: 114; 79-101; see also, Hu, et al., *EBioMedicine* 2019: 41; 497-508. This approach can deliver specific STING activation, as well as localized immune cell recruitment, while reducing systemic immune activation and its concomitant adverse effects.

Definitions

[0076] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Methods and materials are described herein for use in the present application; other, suitable methods and materials known in the art in some aspects of this disclosure are also used. The materials, methods, and examples are illustrative only and not intended to be limiting. All publications, patent applications, patents, sequences, database entries, and other references mentioned herein are incorporated by reference in their entireties. In case of conflict, the present specification, including definitions, will control. 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.

[0077] The terms "a," "an," or "the" as used herein not only include aspects with one member, but also include aspects with more than one member. For instance, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a linker" includes reference to one or more such linkers, and reference to "the cell" includes reference to a plurality of such cells.

[0078] The term "about" when referring to a number or a numerical range means that the number or numerical range referred to is an approximation, for example, within experimental variability and/or statistical experimental error, and thus the number or numerical range may vary up to $\pm 10\%$ of the stated number or numerical range. In reference to an ADC composition comprising a distribution of ADCs as described herein, the average number of conjugated STING agonist compounds to an antibody in the composition can be an integer or a non-integer, particularly when the antibody is to be partially loaded. Thus, the term "about" recited prior to an average drug loading value is intended to capture the expected variations in drug loading within an ADC composition. The term "antigen-binding protein or an antigen-binding fragment thereof" as used herein refers to a peptide, polypeptide, protein, or fragment of a protein that has the ability to bind to a desired target antigen. Antigen-binding protein or an antigen-binding fragment thereof include antibodies, intact antibodies, and antibody fragments. In some aspects, the desired target antigen is CD228 or a fragment of CD228. In some aspects, the specified target antigen is α v β 6 or a fragment of α v β 6. In some aspects, the specified target antigen is B7-H4 or a fragment of B7-H4.

[0079] The term "antibody" as used herein covers intact monoclonal antibodies, polyclonal antibodies, monospecific antibodies, multispecific antibodies (e.g., bispecific antibodies), including intact antibodies and antigen binding antibody fragments, and reduced forms thereof in which one or more of the interchain disulfide bonds are disrupted, that exhibit the desired biological activity and provided that the antigen binding antibody fragments have the requisite number of attachment sites for the desired number of attached groups, such as a linker (L), as described herein. In some aspects, the linkers are attached via a succinimide or hydrolyzed succinimide to the sulfur atoms of cysteine residues of reduced interchain disulfide bonds and/or cysteine residues introduced by genetic engineering. The native form of an antibody is a tetramer and characterized by 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 domains (VL and VH) are together primarily responsible for binding to an antigen. The light chain and heavy chain variable domains contains a framework region interrupted by three hypervariable regions, also called “complementarity determining regions” or “CDRs.” In some embodiments, the light chain and heavy chains also contain constant regions that are recognized by and interact with the immune system. (see, e.g., Janeway et al., 2001, *Immuno. Biology*, 5th Ed., Garland Publishing, New York). An antibody includes any isotype (e.g., IgG, IgE, IgM, IgD, and IgA) or subclass (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) thereof. The antibody is derivable from any suitable species. In some aspects, the antibody is of human or murine origin, and in some aspects the antibody is a human, humanized or chimeric antibody. In some aspects, antibodies are fucosylated to varying extents or afucosylated.

[0080] An “intact antibody” is one which comprises an antigen-binding variable region as well as light chain constant domains (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 are either native sequence constant domains (e.g., human native sequence constant domains) or amino acid sequence variants thereof.

[0081] An “antibody fragment” comprises a portion of an intact antibody, comprising the antigen-binding or variable region thereof. Antibody fragments of the present disclosure include at least one cysteine residue (natural or engineered) that provides a site for attachment of a linker and/or linker-drug compound. In some aspects, an antibody fragment includes Fab, Fab', or F(ab')₂.

[0082] As used herein the term “engineered cysteine residue” or “eCys residue” refers to a cysteine amino acid or a derivative thereof that is incorporated into an antibody. In some aspects, one or more eCys residues are incorporated into an antibody, and typically, the eCys residues are incorporated into either the heavy chain or the light chain of an antibody. Generally, incorporation of an eCys residue into an antibody is performed by mutagenizing a nucleic acid sequence of a parent antibody to encode for one or more amino acid residues with a cysteine or a derivative thereof. Suitable mutations include replacement of a desired residue in the light or heavy chain of an antibody with a cysteine or a derivative thereof, incorporation of an additional cysteine or a derivative thereof at a desired location in the light or heavy chain of an antibody, as well as adding an additional cysteine or a derivative thereof to the N- and/or C-terminus of a desired heavy or light chain of an amino acid. Further information can be found in U.S. Pat. No. 9,000,130, the contents of which are incorporated herein in its entirety. Derivatives of cysteine (Cys) include but are not limited to beta-2-Cys, beta-3-Cys, homocysteine, and N-methyl cysteine.

[0083] In some aspects, the antibodies of the present disclosure include those having one or more engineered cysteine (eCys) residues. In some aspects, derivatives of cysteine (Cys) include, but are not limited to beta-2-Cys, beta-3-Cys, homocysteine, and N-methyl cysteine.

[0084] An “antigen” is an entity to which an antibody specifically binds.

[0085] The terms “CD228,” “melanotransferrin,” “MELTF,” “p97” and “MF12” are used interchangeably herein, and, unless otherwise specified, include any naturally occurring variants (e.g., splice variants, allelic variants),

isoforms, and vertebrate species homologs of human CD228. The term encompasses “full length,” unprocessed CD228 as well as any form of CD228 that results from processing within a cell. The amino acid sequence of an exemplary human CD228 is provided in Uniprot #P08582. CD228 is a glycosylphosphatidylinositol-anchored glycoprotein and was first identified as a 97-kDa cell-surface marker for malignant melanoma cells. CD228 is overexpressed on a majority of clinical melanoma isolates and is also observed on many human carcinomas. CD228 has been shown to be expressed in a variety of cancers.

[0086] The terms “ $\alpha v\beta 6$,” “ $\alpha v\beta 6$,” “ $\alpha v\beta 6$,” “ $\alpha v\alpha 6$,” “alpha-v beta-6,” or “P6” are used interchangeably herein, and, unless otherwise specified, include any naturally occurring variants (e.g., splice variants, allelic variants), isoforms, and vertebrate species homologs of human $\alpha v\beta 6$. The term encompasses “full length,” unprocessed $\alpha v\beta 6$ as well as any form of $\alpha v\beta 6$ that results from processing within a cell. An exemplary P6 human sequence is assigned GenBank accession number AAA36122. An exemplary αv human sequence is assigned NCBI NP_002201.1. $\alpha v\beta 6$ is a cell adhesion receptor that binds extracellular matrix proteins such as fibronectin. $\alpha v\beta 6$ is composed of an alpha v subunit and a beta 6 subunit, and is upregulated in multiple cancers, including non-small cell lung cancer (NSCLC). NSCLC is the most common type of lung cancer. In the past year, over 200,000 people were diagnosed with lung cancer, which is the leading cause of cancer death.

[0087] The terms “B7-H4,” “B7X,” “B7H4,” “B7S1,” “B7h.5,” “VCTN1,” or “PRO1291” are used interchangeably herein, and, unless otherwise specified, include any naturally occurring variant (e.g. splice variants, allelic variants), isoforms, and vertebrate species homologs of human B7-H4. The term encompasses “full length,” unprocessed B7-H4 as well as any form of B7-14 that results from processing within a cell. The amino acid sequence of an exemplary human B7-14 is provided in Uniprot #Q7ZD3. B7-H4 is an immune regulatory molecule that shares homology with other B7 family members, including PD-L1. Human B7-H4 is encoded by VTCN1. It is a type I transmembrane protein comprised of both IgV and IgC ectodomains. While B7-H4 expression in healthy tissues is relatively limited at the protein level, B7-H4 is expressed in several solid tumors such as gynecological carcinomas of the breast, ovary, and endometrium. Expression of B7-H4 in tumors tends to correlate with poor prognosis. The receptor for B7-H4 is unknown, but it is believed to be expressed on T cells. B7-H4 is believed to directly inhibit T cell activity.

[0088] The terms “specific binding” and “specifically binds” mean that the antibody or antibody fragment thereof will bind, in a selective manner, with its corresponding target antigen and not with a multitude of other antigens. Typically, the antibody or antibody fragment binds with an affinity of at least about 1×10^{-7} M, for example, 10^{-8} M to 10^{-9} M, 10^{-10} M, 10^{-4} 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.

[0089] The term “amino acid” as used herein, refers to natural and non-natural, and proteogenic amino acids. Exemplary amino acids include, but are not limited to alanine, arginine, aspartic acid, asparagine, histidine, glycine, glutamic acid, glutamine, phenylalanine, lysine, leu-

cine, serine, tyrosine, threonine, isoleucine, proline, tryptophan, valine, cysteine, methionine, ornithine, β -alanine, citrulline, serine methyl ether, aspartate methyl ester, glutamate methyl ester, homoserine methyl ether, and N,N-dimethyl lysine.

[0090] A “sugar moiety” as used herein, refers to a monovalent radical of monosaccharide, for example, a pyranose or a furanose. A sugar moiety may comprise a hemiacetal or a carboxylic acid (from oxidation of the pendant $-\text{CH}_2\text{OH}$ group). In some aspects, the sugar moiety is in the β -D conformation. In some aspects, the sugar moiety is a glucose, glucuronic acid, or mannose group.

[0091] The term “inhibit” or “inhibition of” means to reduce by a measurable amount, or to prevent entirely (e.g., 100% inhibition).

[0092] The term “therapeutically effective amount” refers to an amount of an ADC as described herein that is effective to treat a disease or disorder in a mammal. In the case of cancer, the therapeutically effective amount of the ADC provides one or more of the following biological effects: reduction of the number of cancer cells; reduction of tumor size; inhibition of cancer cell infiltration into peripheral organs; inhibition of tumor metastasis; inhibition, to some extent, of tumor growth; and/or relief, to some extent, of one or more of the symptoms associated with the cancer. For cancer therapy, efficacy, in some aspects, is measured by assessing the time to disease progression (TTP) and/or determining the response rate (RR).

[0093] Unless otherwise indicated or implied by context, the term “substantial” or “substantially” refers to a majority, i.e. >50% of a population, of a mixture, or a sample, typically more than 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%.

[0094] The terms “intracellularly cleaved” and “intracellular cleavage” refer to a metabolic process or reaction occurring inside a cell, in which the cellular machinery acts on the ADC or a fragment thereof, to intracellularly release free drug from the ADC, or other degradant products thereof. The moieties resulting from that metabolic process or reaction are thus intracellular metabolites.

[0095] 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 multiple cancerous cells.

[0096] “Subject” as used herein refers to an individual to which an ADC is administered. Examples of a “subject” include, but are not limited to, a mammal such as a human, rat, mouse, guinea pig, non-human primate, pig, goat, cow, horse, dog, cat, bird and fowl. Typically, a subject is a rat, mouse, dog, non-human primate, or human. In some aspects, the subject is a human.

[0097] The terms “treat” or “treatment,” unless otherwise indicated or implied by context, refer to therapeutic treatment and prophylactic measures to prevent relapse, wherein the object is to inhibit an undesired physiological change or disorder, such as, for example, the development or spread of cancer. For purposes of the present disclosure, 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” in some

aspects also means prolonging survival as compared to expected survival if not receiving treatment.

[0098] In the context of cancer, the term “treating” includes any or all of: inhibiting growth of cancer cells or of a tumor; inhibiting replication of cancer cells, lessening of overall tumor burden or decreasing the number of cancer cells, and ameliorating one or more symptoms associated with the disease.

[0099] The term “salt,” as used herein, refers to organic or inorganic salts of a compound, such as a Drug Unit (D), a linker such as those described herein, or an ADC. In some aspects, the compound contains at least one amino group, and accordingly acid addition salts can be formed with the amino group. 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. A salt may involve the inclusion of another molecule such as an acetate ion, a succinate ion, or other counterion. In some aspects, the counterion is any organic or inorganic moiety that stabilizes the charge on the parent compound. Furthermore, a salt has one or more than one charged atom in its structure. In instances where there are multiple charged atoms as part of the salt, multiple counter ions can be present. Hence, a salt can have one or more charged atoms and/or one or more counterions. A “pharmaceutically acceptable salt” is one that is suitable for administration to a subject as described herein and in some aspects includes salts as described by P. H. Stahl and C. G. Wermuth, editors, *Handbook of Pharmaceutical Salts: Properties, Selection and Use*, Weinheim/Zurich: Wiley-VCH/VHCA, 2002, the list for which is specifically incorporated by reference in its entirety.

[0100] The term “tautomer,” as used herein refers to compounds whose structures differ markedly in arrangement of atoms, but which exist in easy and rapid equilibrium, and it is to be understood that, in some cases, compounds provided herein are depicted as different tautomers, and when compounds have tautomeric forms, all tautomeric forms are intended to be within the scope of the disclosure, and the naming of the compounds does not exclude any tautomer.

[0101] The term “halo” or “halogen” refers to fluoro, chloro, bromo, or iodo (e.g., in some aspects, fluoro or chloro).

[0102] The term “alkyl” refers to an unsubstituted methyl or straight chain or branched, saturated hydrocarbon having the indicated number of carbon atoms (e.g., “ $\text{C}_1\text{-}\text{C}_4$ alkyl,” “ $\text{C}_1\text{-}\text{C}_6$ alkyl,” “ $\text{C}_1\text{-}\text{C}_8$ alkyl,” or “ $\text{C}_1\text{-}\text{C}_{10}$ ” alkyl have from 1 to 4, to 6, 1 to 8, or 1 to 10 carbon atoms, respectively) and is derived by the removal of one hydrogen atom from the parent alkane. Representative “ $\text{C}_1\text{-}\text{C}_8$ 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 $\text{C}_1\text{-}\text{C}_8$ alkyls include, but are not limited to, isopropyl, sec-butyl, isobutyl, tert-butyl, isopentyl, and 2-methylbutyl.

[0103] The term “alkylene” refers to methylene or a bivalent unsubstituted saturated branched or straight chain hydrocarbon of the stated number of carbon atoms (e.g., a

$C_1\text{-}C_6$ alkylene has from 1 to 6 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 the parent alkane. In some aspects, alkylene groups are substituted with 1-6 fluoro groups, for example, on the carbon backbone (as $-\text{CHF}-$ or $-\text{CF}_2-$) or on terminal carbons of straight chain or branched alkynes (such as $-\text{CHF}_2$ or $-\text{CF}_3$). Alkylene radicals include but are not limited to: methylene ($-\text{CH}_2-$), ethylene ($-\text{CH}_2\text{CH}_2-$), n-propylene ($-\text{CH}_2\text{CH}_2\text{CH}_2-$), n-butylene ($-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$), difluoromethylene ($-\text{CF}_2-$), tetrafluoroethylene ($-\text{CF}_2\text{CF}_2-$), and the like.

[0104] The term “alkenyl” refers to an unsubstituted straight chain or branched, hydrocarbon having at least one carbon-carbon double bond and the indicated number of carbon atoms (e.g., “ $\text{C}_2\text{-}\text{C}_8$ alkenyl” or “ $\text{C}_2\text{-}\text{C}_{10}$ ” alkenyl have from 2 to 8 or 2 to 10 carbon atoms, respectively). When the number of carbon atoms is not indicated, the alkenyl group has from 2 to 6 carbon atoms.

[0105] The term “alkynyl” refers to an unsubstituted straight chain or branched, hydrocarbon having at least one carbon-carbon triple bond and the indicated number of carbon atoms (e.g., “ $\text{C}_2\text{-}\text{C}_8$ alkynyl” or “ $\text{C}_2\text{-}\text{C}_{10}$ ” alkynyl have from 2 to 8 or 2 to 10 carbon atoms, respectively). When the number of carbon atoms is not indicated, the alkynyl group has from 2 to 6 carbon atoms.

[0106] The term “heteroalkyl” refers to a stable straight or branched chain saturated hydrocarbon having the stated number of total atoms and at least one (e.g., 1 to 15) heteroatom selected from the group consisting of O, N, Si and S. In some aspects, the carbon and heteroatoms of the heteroalkyl group are oxidized (e.g., to form ketones, N-oxides, sulfones, and the like) and in some aspects, the nitrogen atoms are quaternized. The heteroatom(s) are placed at any interior position of the heteroalkyl group and/or at the position at which the heteroalkyl group is attached to the remainder of the molecule. In some aspects, heteroalkyl groups are substituted with 1-6 fluoro groups, for example, on the carbon backbone (as $-\text{CHF}-$ or $-\text{CF}_2-$) or on terminal carbons of straight chain or branched heteroalkyls (such as $-\text{CHF}_2$ or $-\text{CF}_3$). Examples of heteroalkyl groups include, but are not limited to, $-\text{CH}_2\text{-CH}_2\text{-O-CH}_3$, $-\text{CH}_2\text{-CH}_2\text{-NH-CH}_3$, $-\text{CH}_2\text{-CH}_2\text{-N(CH}_3)_2$, $-\text{C(=O)-NH-CH}_2\text{-CH}_2\text{-NH-CH}_3$, $-\text{C(=O)-N(CH}_3)\text{-CH}_2\text{-CH}_2\text{-N(CH}_3)_2$, $-\text{C(=O)-NH-CH}_2\text{-NH-C(=O)-CH}_2\text{-CH}_3$, $-\text{C(=O)-N(CH}_3)\text{-CH}_2\text{-CH}_2\text{-N(CH}_3)\text{-C(=O)-CH}_2\text{-CH}_3$, $-\text{O-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH(CH}_3)$, $-\text{O-CH}_2\text{-CH}_2\text{-CH}_2\text{-N(CH}_3)_2$, $-\text{O-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(=O)-CH}_2\text{-CH}_3$, $-\text{O-CH}_2\text{-CH}_2\text{-CH}_2\text{-N(CH}_3)_2$, $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-NH(CH}_3)$, $-\text{O-CH}_2\text{-CH}_2\text{-CH}_2\text{-N(CH}_3)_2$, $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(=O)-CH}_2\text{-CH}_3$, $-\text{CH}_2\text{-CH}_2\text{-S-CH}_2\text{-CH}_3$, $-\text{CH}_2\text{-CH}_2\text{-S(O)-CH}_3$, $-\text{NH-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(=O)-CH}_2\text{-CH}_3$, $-\text{CH}_2\text{-CH}_2\text{-O-CF}_3$, and $-\text{Si(CH}_3)_3$. In some aspects, up to two heteroatoms are consecutive, such as, for example, $-\text{CH}_2\text{-NH-OCH}_3$ and $-\text{CH}_2\text{-O-Si(CH}_3)_3$. A terminal polyethylene glycol (PEG) moiety is a type of heteroalkyl group.

[0107] The term “heteroalkylene” refers to a bivalent unsubstituted straight or branched group derived from het-

eroalkyl (as defined herein). Examples of heteroalkylene groups include, but are not limited to, $-\text{CH}_2\text{-CH}_2\text{-O-CH}_2-$, $-\text{CH}_2\text{-CH}_2\text{-O-CF}_2-$, $-\text{CH}_2\text{-CH}_2\text{-NH-CH}_2\text{-CH}_2\text{-NH-CH}_2-$, $-\text{C(=O)-N(CH}_3)\text{-CH}_2\text{-CH}_2\text{-N(CH}_3)\text{-CH}_2-$, $-\text{C(=O)-NH-CH}_2\text{-CH}_2\text{-NH-C(=O)-CH}_2\text{-CH}_2-$, $-\text{C(=O)-N(CH}_3)\text{-CH}_2\text{-CH}_2\text{-N(CH}_3)\text{-C(=O)-CH}_2\text{-CH}_2-$, $-\text{O-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-CH}_2\text{-CH}_2\text{-NH-CH}_2-$, $-\text{O-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(=O)-CH}_2\text{-CH}_2\text{-NH-CH}_2-$, $-\text{O-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(=O)-CH}_2\text{-CH}_2\text{-N(CH}_3)\text{-C(=O)-CH}_2\text{-CH}_2-$, $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-CH}_2\text{-N(CH}_3)\text{-CH}_2-$, $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(=O)-CH}_2\text{-CH}_2\text{-N(CH}_3)\text{-CH}_2-$, $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(=O)-CH}_2\text{-CH}_2\text{-N(CH}_3)\text{-C(=O)-CH}_2\text{-CH}_2-$, $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-CH}_2\text{-N(CH}_3)\text{-CH}_2-$, $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(=O)-CH}_2\text{-CH}_2\text{-N(CH}_3)\text{-C(=O)-CH}_2\text{-CH}_2-$, $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-CH}_2\text{-N(CH}_3)\text{-CH}_2-$, $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-NH-C(=O)-CH}_2\text{-CH}_2\text{-N(CH}_3)\text{-C(=O)-CH}_2\text{-CH}_2-$, and $-\text{NH-CH}_2\text{-CH}_2\text{(NHCH}_3)\text{-CH}_2-$. A bivalent polyethylene glycol (PEG) moiety is a type of heteroalkylene group.

[0108] The term “alkoxy” refers to an alkyl group, as defined herein, which is attached to a molecule via an oxygen atom. For example, alkoxy groups include, but are not limited to methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, sec-butoxy, tert-butoxy, n-pentoxy and n-hexaoxy.

[0109] The term “alkylthio” refers to an alkyl group, as defined herein, which is attached to a molecule via a sulfur atom. For example, alkythio groups include, but are not limited to thiomethyl, thioethyl, thio-n-propyl, thio-iso-propyl, and the like.

[0110] The term “haloalkyl” refers to an unsubstituted straight chain or branched, saturated hydrocarbon having the indicated number of carbon atoms (e.g., “ $\text{C}_1\text{-}\text{C}_4$ alkyl,” “ $\text{C}_1\text{-}\text{C}_6$ alkyl,” “ $\text{C}_1\text{-}\text{C}_8$ alkyl,” or “ $\text{C}_1\text{-}\text{C}_{10}$ ” alkyl have from 1 to 4, to 6, 1 to 8, or 1 to 10 carbon atoms, respectively) wherein at least one hydrogen atom of the alkyl group is replaced by a halogen (e.g., fluoro, chloro, bromo, or iodo). When the number of carbon atoms is not indicated, the haloalkyl group has from 1 to 6 carbon atoms. Representative $\text{C}_1\text{-}\text{C}_6$ haloalkyl groups include, but are not limited to, trifluoromethyl, 2,2,2-trifluoroethyl, and 1-chloroisopropyl.

[0111] The term “haloalkoxy” refers to a haloalkyl group, as defined herein, which is attached to a molecule via an oxygen atom. For example, haloalkoxy groups include, but are not limited to trifluoromethoxy, 2,2,2-trifluoroethoxy, and 1,1,1-trifluoro2-methylpropoxy.

[0112] The term “cycloalkyl” refers to a cyclic, saturated or partially unsaturated hydrocarbon having the indicated number of carbon atoms (e.g., “ $\text{C}_{3\text{-}8}$ cycloalkyl” or “ $\text{C}_{3\text{-}6}$ ” cycloalkyl have from 3 to 8 or 3 to 6 carbon atoms, respectively). When the number of carbon atoms is not indicated, the cycloalkyl group has from 3 to 6 carbon atoms. Cycloalkyl groups include bridged, fused, and spiro ring systems, and bridged bicyclic systems where one ring is aromatic and the other is unsaturated. Representative “ $\text{C}_{3\text{-}6}$ cycloalkyl” groups include, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0113] The term “aryl” refers to an unsubstituted monovalent carbocyclic aromatic hydrocarbon radical of 6-10 carbon atoms derived by the removal of one hydrogen atom from a single carbon atom of a parent aromatic ring system. Aryl groups include, but are not limited to, phenyl, naphthyl, anthracenyl, biphenyl, and the like.

[0114] The term “heterocycle” refers to a saturated or partially unsaturated ring or a multiple condensed ring system, including bridged, fused, and spiro ring systems. In some aspects, heterocycles are described by the total number of atoms in the ring system, for example a 3-10 membered heterocycle has 3 to 10 total ring atoms. The term includes single saturated or partially unsaturated rings (e.g., 3, 4, 5, 6 or 7-membered rings) from about 1 to 6 carbon atoms and from about 1 to 3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur in the ring. In some aspects, the ring is substituted with one or more (e.g., 1, 2 or 3) oxo groups and the sulfur and nitrogen atoms may also be present in their oxidized forms. Such rings include but are not limited to azetidinyl, tetrahydrofuryl and piperidinyl. The term “heterocycle” also includes multiple condensed ring systems (e.g., ring systems comprising 2, 3 or 4 rings) wherein a single heterocycle ring (as defined above) is condensed with one or more heterocycles (e.g., decahydronaphthyridinyl), carbocycles (e.g., decahydroquinolyl) or aryls. In some aspects, the rings of a multiple condensed ring system are connected to each other via fused, spiro and bridged bonds when allowed by valency requirements. It is to be understood that the point of attachment of a multiple condensed ring system (as defined above for a heterocycle) can be at any position of the multiple condensed ring system including a heterocycle, aryl and carbocycle portion of the ring. It is also to be understood that the point of attachment for a heterocycle or heterocycle multiple condensed ring system can be at any suitable atom of the heterocycle or heterocycle multiple condensed ring system including a carbon atom and a heteroatom (e.g., a nitrogen). Exemplary heterocycles include, but are not limited to aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, homopiperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, tetrahydrofuryl, dihydrooxazolyl, tetrahydropyranyl, tetrahydrothiopyranyl, 1,2,3,4-tetrahydroquinolyl, benzoxazinyl, dihydrooxazolyl, chromanyl, 1,2-dihydropyridinyl, 2,3-dihydrobenzofuranyl, 1,3-benzodioxolyl, and 1,4-benzodioxanyl.

[0115] The term “heteroaryl” refers to an aromatic hydrocarbon ring system with at least one heteroatom within a single ring or within a fused ring system, selected from the group consisting of O, N and S. The ring or ring system has $4n+2$ electrons in a conjugated π system where all atoms contributing to the conjugated π system are in the same plane. In some aspects, heteroaryl groups have 5-10 total ring atoms and 1, 2, or 3 heteroatoms (referred to as a “5-10 membered heteroaryl”). Heteroaryl groups include, but are not limited to, imidazole, triazole, thiophene, furan, pyrrole, benzimidazole, pyrazole, pyrazine, pyridine, pyrimidine, and indole.

[0116] The term “hydroxyl” refers to an —OH radical.

[0117] The term “cyano” refers to a —CN radical.

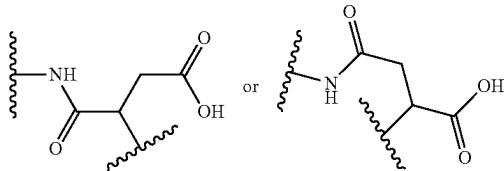
[0118] The term “carboxy” refers to a —C(=O)OH radical.

[0119] The term “oxo” refers to a =O radical.

[0120] The term “succinimide” as used as part of an antibody-drug conjugate (ADC) refers to:

where the wavy lines indicate attachment to a Drug-Linker Unit or antigen-binding protein or an antigen-binding fragment thereof.

[0121] The term “hydrolyzed succinimide” as used as part of an antibody-drug conjugate (ADC) refers to:



where the wavy lines indicate attachment to a Drug-Linker Unit or antigen-binding protein or an antigen-binding fragment thereof.

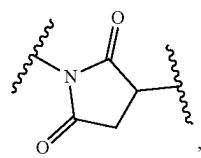
[0122] The term “optionally substituted” indicates that the referenced moiety is unsubstituted or substituted with the indicated groups.

[0123] It will be appreciated by those skilled in the art that compounds of this disclosure having a chiral center may exist in and be isolated in optically active and racemic forms.

[0124] As used herein, the term “free drug” refers to a biologically active species that is not covalently attached to an antibody. Accordingly, free drug refers to any unconjugated compound, including a compound as it exists immediately upon cleavage from the ADC. In some aspects, the release mechanism is via a cleavable linker in the ADC, or via intracellular conversion or metabolism of the ADC. In some aspects, the free drug will be protonated and/or may exist as a charged moiety. The free drug is a pharmacologically active species which is capable of exerting the desired biological effect. In some aspects, the pharmacologically active species is the parent drug alone. In some aspects, the pharmacologically active species is the parent drug bonded to a component or vestige of the ADC (e.g., a component of the linker, succinimide, hydrolyzed succinimide, and/or antibody that has not undergone subsequent intracellular metabolism). In some aspects, free drug refers to a compound of Formula (I), as described herein, for example, wherein one or more of X^P , Y, W, A, and M¹ are absent. In some aspects, free drug refers to a compound of Formula (II), as described herein. In some aspects, free drug refers to a compound of Formula (II-A), as described herein. In some aspects, free drug refers to a compound of Formula (III), as described herein. In some aspects, free drug refers to a compound of Formula (IV), as described herein. In some aspects, free drug refers to a compound of Formula (V), as described herein.

[0125] As used herein, the term “Drug Unit” refers to the free drug that is conjugated to an antigen-binding protein or an antigen-binding fragment thereof in an ADC, as described herein. In some aspects, the Drug Unit includes all or portions of non-cleavable linking components that conjugate the drug to the antigen-binding protein or an antigen-binding fragment thereof.

[0126] As used herein, the term “Drug-Linker Unit” refers to a drug and linking components (whether cleavable or non-cleavable) that conjugate the drug to an antigen-binding protein or an antigen-binding fragment thereof.



[0127] As used herein, the term “antibody-drug conjugate” or simply “ADC” refers to an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody) conjugated to a Drug Unit as described herein. In some aspects, an antibody-drug conjugate typically binds to target antigen (e.g., CD228, α v β 6, or B7-H4) on a cell surface followed by internalization of the antibody-drug conjugate into the cell where the Drug Unit is released.

[0128] As used herein, the term “ADC composition” refers to a composition comprising a distribution of ADCs having different numbers of Drug Units conjugated to an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody).

Antibody-Drug Conjugate (ADC) Compounds

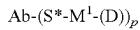
[0129] Some embodiments provide an antibody-drug conjugate (ADC) comprising:

[0130] an antigen-binding protein or antigen-binding fragment thereof; and

[0131] a compound of Formula (I) as described herein;

[0132] wherein the compound of Formula (I) is conjugated to the antigen-binding protein or antigen-binding fragment thereof via a succinimide or hydrolyzed succinimide covalently linked to a sulfur atom of a cysteine residue.

[0133] Some embodiments provide an antibody-drug conjugate (ADC) having the formula:



[0134] wherein:

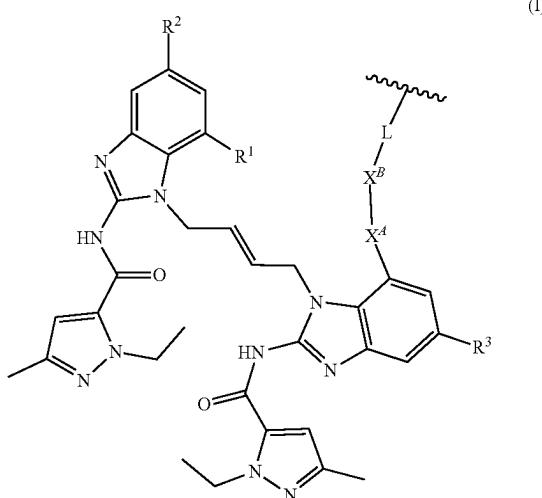
[0135] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);

[0136] each S^* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;

[0137] M^1 is a succinimide or a hydrolyzed succinimide;

[0138] subscript p is an integer from 2 to 8; and

[0139] each (D) is a Drug-Linker Unit of Formula (I):



[0140] wherein:

[0141] $\sim\sim\sim$ represents covalent attachment of L to M^1 ;

[0142] R^1 is hydrogen, hydroxyl, C_{1-6} alkoxy, $-(\text{CH}_2)_n-\text{NR}^A\text{R}^B$, or PEG2 to PEG4;

[0143] each R^2 and R^3 are independently $-\text{CO}_2\text{H}$, $-(\text{C}_2\text{O})_m-\text{NR}^C\text{R}^D$, or $-(\text{CH}_2)_n-\text{NR}^E\text{R}^F$;

[0144] each R^A , R^B , R^C , R^D , R^E , and R^F are independently hydrogen or C_{1-3} alkyl;

[0145] each subscript n is independently an integer from 0 to 6;

[0146] each subscript m is independently 0 or 1;

[0147] each subscript q is an integer from 0 to 6;

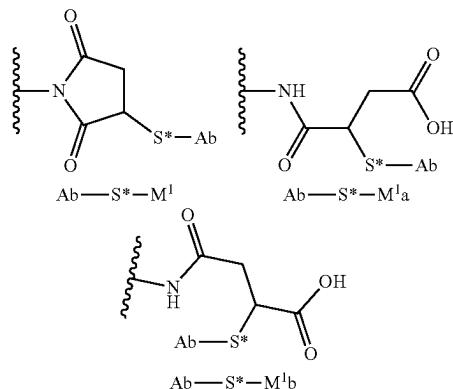
[0148] X^4 is $-\text{CH}_2-$, $-\text{O}-$, $-\text{S}-$, $-\text{NH}-$, or $-\text{N}(\text{CH}_3)-$;

[0149] X^B is absent or a 2-16 membered heteroalkylene;

[0150] X^B , M^1 , and L are each independently optionally substituted with a PEG Unit from PEG2 to PEG72; and

[0151] L is an optional linker as described herein. When present, L is linked via a covalent bond to X^B , or X^A if X^B is absent, as depicted in Formula (I). When L is absent, M^1 is linked via a covalent bond to X^B , or X^A if X^B is absent, as depicted in Formula (I).

[0152] In some embodiments, M^1 is a succinimide. In some embodiments, M^1 is a hydrolyzed succinimide. It will be understood that a hydrolyzed succinimide may exist in two regioisomeric form(s). Those forms are exemplified below for hydrolysis of M^1 bonded to $^*\text{S}-\text{Ab}$, wherein the structures representing the regioisomers from that hydrolysis are formula M^1a and M^1b ; wherein the wavy lines adjacent to the bonds represent the covalent attachment to Formula (I).



[0153] The M or M^1 groups, when present, are capable of covalent attachment to an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody) to an A group, when present (or a W, Y, or X^B group if subscript a and/or subscript w and/or subscript y are 0). In this regard an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody) has a functional group that can form a bond with a functional group of M or M^1 . In some embodiments, useful functional groups present on an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody), either naturally or via chemical manipu-

lation include, but are not limited to, sulfhydryl ($-\text{SH}$), amino, hydroxyl, carboxy, and the anomeric hydroxyl group of a carbohydrate. In one aspect, the antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody) functional groups are sulfhydryl and amino. In some embodiments, sulfhydryl groups are generated by reduction of an intramolecular disulfide bond of an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody). Alternatively, in some embodiments, sulfhydryl groups are generated by reaction of an amino group of a lysine moiety of an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody) using 2-iminothiolane (Traut's reagent) or another sulfhydryl generating reagent. In some embodiments, M or M^1 forms a bond with a sulfur atom of the antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody). In some embodiments, the sulfur atom is derived from a sulfhydryl group of the antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody).

[0154] In some embodiments, L has the formula $-(\text{A})_a-(\text{W})_w-(\text{Y})_y-$, wherein:

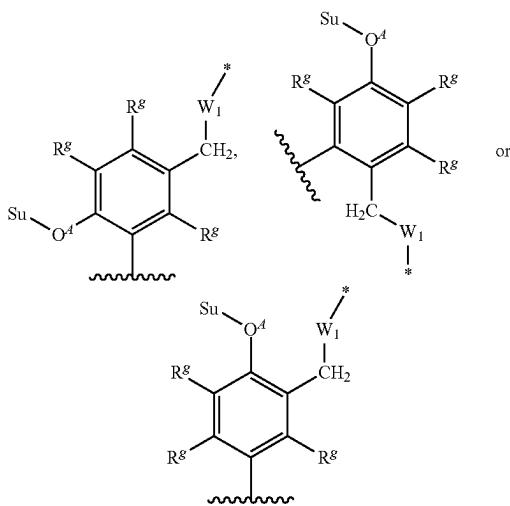
[0155] A is a C_{2-20} alkylene optionally substituted with 1-3 R^{a1} ; or a 2 to 40 membered heteroalkylene optionally substituted with 1-3 R^{b1} ;

[0156] each R^{a1} is independently selected from the group consisting of: C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, $-\text{OH}$, $=\text{O}$, $-\text{NR}^{d1}\text{R}^{e1}$, $-\text{C}(\text{O})\text{NR}^{a1}\text{R}^{e1}$, $-\text{C}(\text{O})(\text{C}_{1-6} \text{ alkyl})$, and $-\text{C}(\text{O})\text{O}(\text{C}_{1-6} \text{ alkyl})$;

[0157] each R^{b1} is independently selected from the group consisting of: C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, $-\text{OH}$, $-\text{NR}^{d1}\text{R}^{e1}$, $-\text{C}(\text{O})\text{NR}^{d1}\text{R}^{e1}$, $-\text{C}(\text{O})(\text{C}_{1-6} \text{ alkyl})$, and $-\text{C}(\text{O})\text{O}(\text{C}_{1-6} \text{ alkyl})$;

[0158] each R^{d1} and R^{e1} are independently hydrogen or C_{1-3} alkyl;

[0159] W is from 1-12 amino acids or has the structure:



[0160] wherein Su is a Sugar moiety;

[0161] $-\text{O}^4-$ represents a glycosidic bond;

[0162] each R^9 is independently hydrogen, halogen, $-\text{CN}$, or $-\text{NO}_2$;

[0163] W_1 is absent or $-\text{O}-\text{C}(=\text{O})-$;

[0164] $\sim\sim\sim$ represents covalent attachment to A or M^1 ;

[0165] * represents covalent attachment to Y, X^A , or X^B in Formula (I);

[0166] Y is a self-immolative moiety, a non-self-immolative releasable moiety, or a non-cleavable moiety;

[0167] subscript a is 0 or 1;

[0168] subscript y is 0 or 1; and

[0169] subscript w is 0 or 1.

[0170] In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is hydroxyl. In some embodiments, R^1 is C_{1-6} alkoxy. In some embodiments, R^1 is methoxy. In some embodiments, R^1 is $-(\text{C}_{1-6} \text{ alkyl})\text{C}_{1-6}$ alkoxy. In some embodiments, R^1 is methoxyethyl. In some embodiments, R^1 is PEG2 to PEG4.

[0171] In some embodiments, R^1 is $-(\text{CH}_2)_n-\text{NR}^A\text{R}^B$. In some embodiments, R^A and R^B are both hydrogen. In some embodiments, R^A and R^B are independently C_{1-3} alkyl. In some embodiments, one of R^A and R^B is hydrogen and the other of R^A and R^B is C_{1-3} alkyl. In some embodiments, the C_{1-3} alkyl is methyl. In some embodiments, each subscript n is 0. In some embodiments, each subscript n is 1. In some embodiments, each subscript n is 2. In some embodiments, each subscript n is 3, 4, 5, or 6.

[0172] In some embodiments, each R^2 and R^3 are independently $-\text{CO}_2\text{H}$, $-(\text{C}=\text{O})_m-\text{NR}^C\text{R}^D$, or $(\text{CH}_2)_q-\text{NR}^E\text{R}^F$; and R^2 and R^3 are the same. In some embodiments, each R^2 and R^3 are independently $-\text{CO}_2\text{H}$, $-(\text{C}=\text{O})_m-\text{NR}^C\text{R}^D$, or $-(\text{CH}_2)_q-\text{NR}^E\text{R}^F$; and R^2 and R^3 are different.

[0173] In some embodiments, R^2 is $-(\text{C}=\text{O})_m-\text{NR}^C\text{R}^D$. In some embodiments, R^3 is $-(\text{C}=\text{O})_m-\text{NR}^C\text{R}^D$. In some embodiments, R^C and R^D are both hydrogen. In some embodiments, R^C and R^D are each independently C_{1-3} alkyl. In some embodiments, the C_{1-3} alkyl is methyl. In some embodiments, one of R^C and R^D is hydrogen and the other of R^C and R^D is C_{1-3} alkyl. In some embodiments, each subscript m is 0. In some embodiments, each subscript m is 1.

[0174] In some embodiments, R^2 is $-(\text{CH}_2)_q-\text{NR}^E\text{R}^F$. In some embodiments, R^3 is $-(\text{CH}_2)_q-\text{NR}^E\text{R}^F$. In some embodiments, R^E and R^F are both hydrogen. In some embodiments, R^E and R^F are each independently C_{1-3} alkyl. In some embodiments, the C_{1-3} alkyl is methyl. In some embodiments, one of R^E and R^F is hydrogen and the other of R^E and R^F is C_{1-3} alkyl. In some embodiments, each subscript q is 0. In some embodiments, each subscript q is an integer from 1 to 6. In some embodiments, each subscript q is 1. In some embodiments, each subscript q is 2. In some embodiments, each subscript q is 3, 4, 5, or 6.

[0175] In some embodiments, R^3 is $-\text{CO}_2\text{H}$. In some embodiments, R^2 is $-\text{CO}_2\text{H}$.

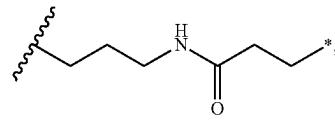
[0176] In some embodiments, X^A is $-\text{CH}_2-$. In some embodiments, X^A is $-\text{O}-$. In some embodiments, X^A is $-\text{S}-$. In some embodiments, X^A is $-\text{NH}-$. In some embodiments, X^A is $-\text{N}(\text{CH}_3)-$.

[0177] In some embodiments, X^B is a 2-16 membered heteroalkylene. In some embodiments, X^B is a 2-12 membered heteroalkylene. In some embodiments, X^B is a 2-10 membered heteroalkylene. In some embodiments, X^B is a 2-8 membered heteroalkylene. In some embodiments, X^B is a 4-8 membered heteroalkylene. In some embodiments, the heteroalkylene is straight chained. In some embodiments, the heteroalkylene is branched. In some embodiments, the heteroalkylene is branched, having 1-4 methyl groups. In

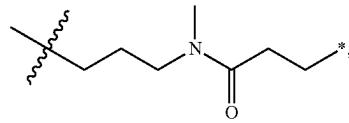
some embodiments, the heteroalkylene is branched, having 1 or 2 methyl groups. In some embodiments, the heteroalkylene is substituted with 1-3 fluoro groups. In some embodiments, X^B comprises one or two nitrogen atoms. In some embodiments, X^B comprises one or two oxo groups. In some embodiments, X^B comprises one nitrogen atom and one oxo group. In some embodiments, X^B comprises two nitrogen atoms and two oxo groups. In some embodiments, X^B comprises a carbamate.

[0178] In some embodiments, the covalent attachment of Y and X^B comprises an amide. In some embodiments, the covalent attachment of Y and X^B comprises a carbamate. In some embodiments, the covalent attachment of Y and X^B comprises an ether.

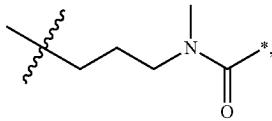
[0179] In some embodiments, X^B is



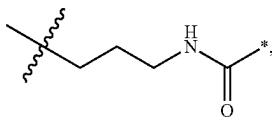
wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L, when present, or M¹. In some embodiments, X^B is



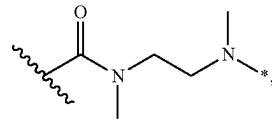
wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L, when present, or M¹. In some embodiments, X^B is



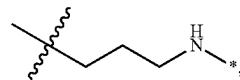
wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L, when present, or M¹. In some embodiments, X^B is



wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L, when present, or M¹. In some embodiments, X^B is

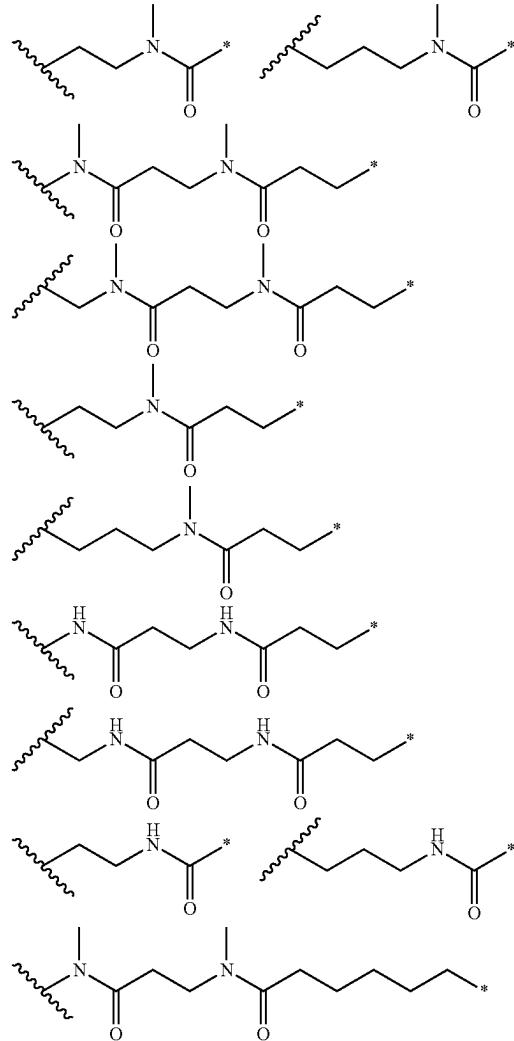


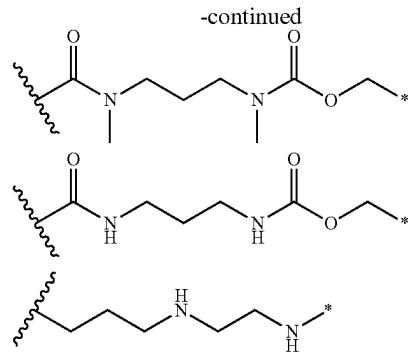
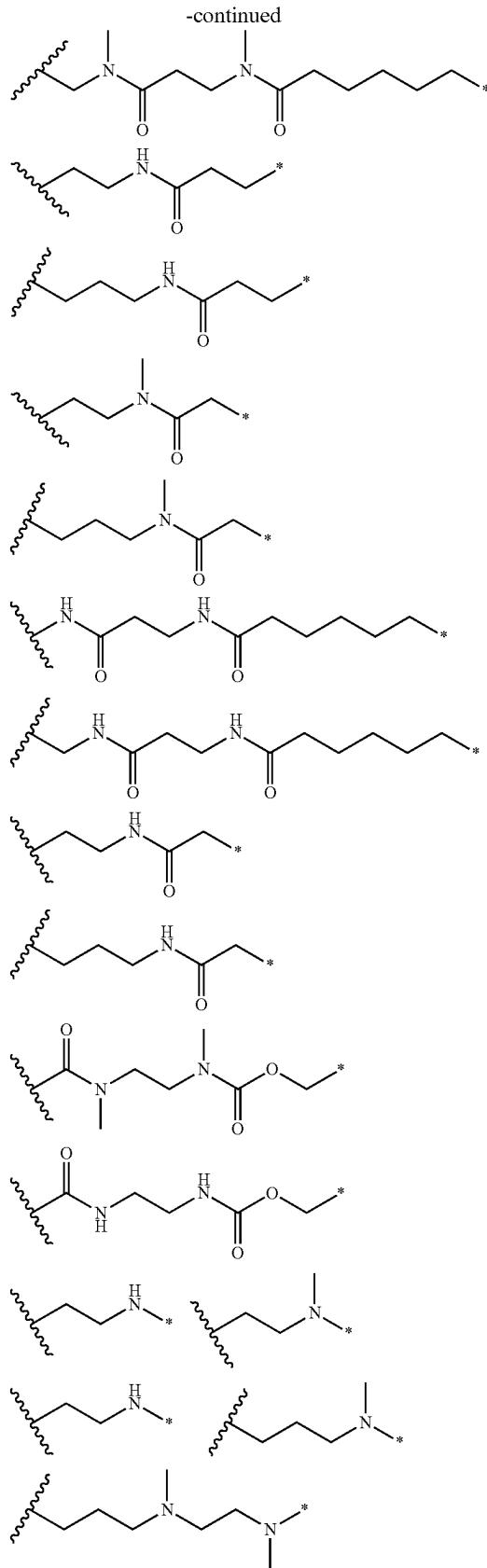
wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L, when present, or M¹. In some embodiments, X^B is



wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L, when present, or M¹.

[0180] In some embodiments, X^B is selected from the group consisting of the structures below, wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L, when present, or M¹.



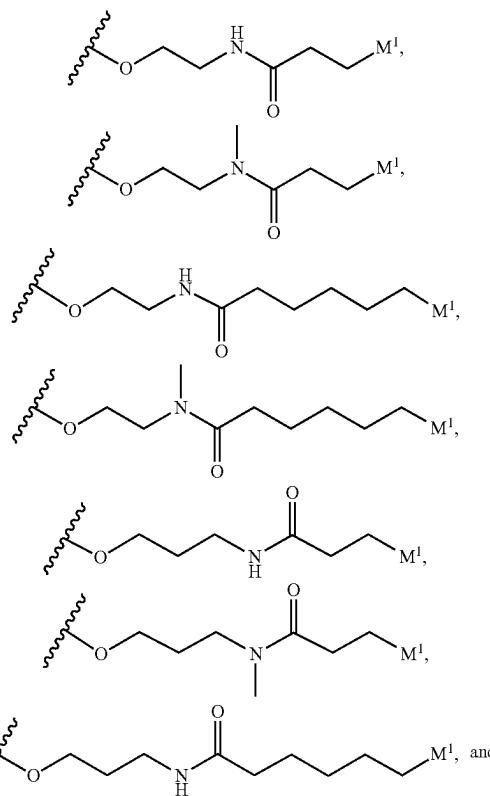


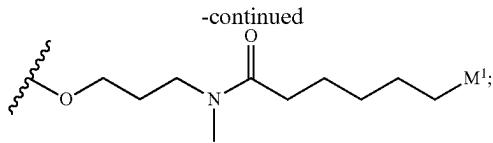
[0181] In some embodiments, one of X^B and L is substituted with a PEG Unit from PEG2 to PEG72, as described herein. In some embodiments, X^B and L are each substituted with an independently selected PEG Unit from PEG2 to PEG72, as described herein. In some embodiments, each PEG Unit from PEG2 to PEG72 can range from PEG8 to PEG12, PEG12 to PEG24, or PEG36 to PEG72. In some embodiments, each PEG Unit from PEG2 to PEG72 is PEG8 to PEG24.

[0182] In some embodiments, X^B and L are unsubstituted.

[0183] In some embodiments, R^1 is methoxy; R^2 and R^3 are both $-\text{C}(=\text{O})\text{NH}_2$; and X^A is $-\text{O}-$.

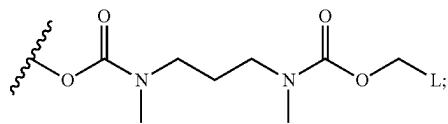
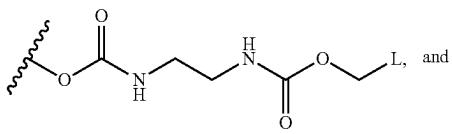
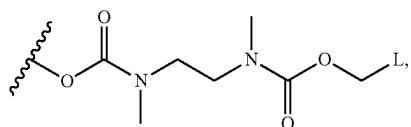
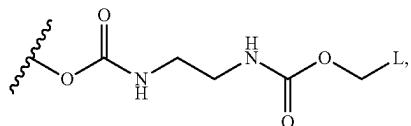
[0184] In some embodiments, L is absent and $X^A-X^B-M^1$ is selected from the group consisting of:





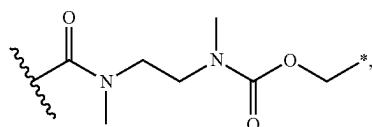
wherein represents covalent attachment to the remainder of Formula (I).

[0185] In some embodiments, $X^A - X^B - L$ is selected from:

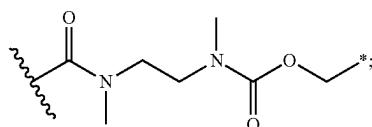


wherein represents covalent attachment to the remainder of Formula (I).

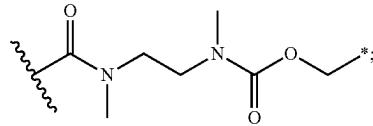
[0186] In some embodiments, R^1 is methoxy and R^2 and R^3 are both $-C(=O)NH_2$. In some embodiments, X^A is $-O-$ and X^B is



wherein represents covalent attachment to X^A and * represents covalent attachment to L , when present, or M^1 . In some embodiments, R^1 is methoxy; R^2 and R^3 are both $-C(=O)NH_2$; X^A is $-O-$; and X^B is



wherein represents covalent attachment to X^A and * represents covalent attachment to L , when present, or M^1 . In some embodiments, R^1 is methoxy; R^2 and R^3 are both $-C(=O)NH_2$; X^A is $-O-$; X^B is



represents covalent attachment to X^A and * represents covalent attachment to L ; and subscript a and subscript y are both 0.

[0187] In some embodiments, X^B is absent.

[0188] In some embodiments, subscript p is an integer from 2 to 8, from 2 to 6, from 2 to 4, from 4 to 8, or from 6 to 8. In some embodiments, subscript p is 2, 4, 6, or 8. In some embodiments, subscript p is 2. In some embodiments, subscript p is 4. In some embodiments, subscript p is 6. In some embodiments, subscript p is 8. In some alternative embodiments, subscript p is an integer from 1 to 16. Accordingly, in any of the structures shown here, subscript p may alternatively be defined to be an integer from 1 to 16.

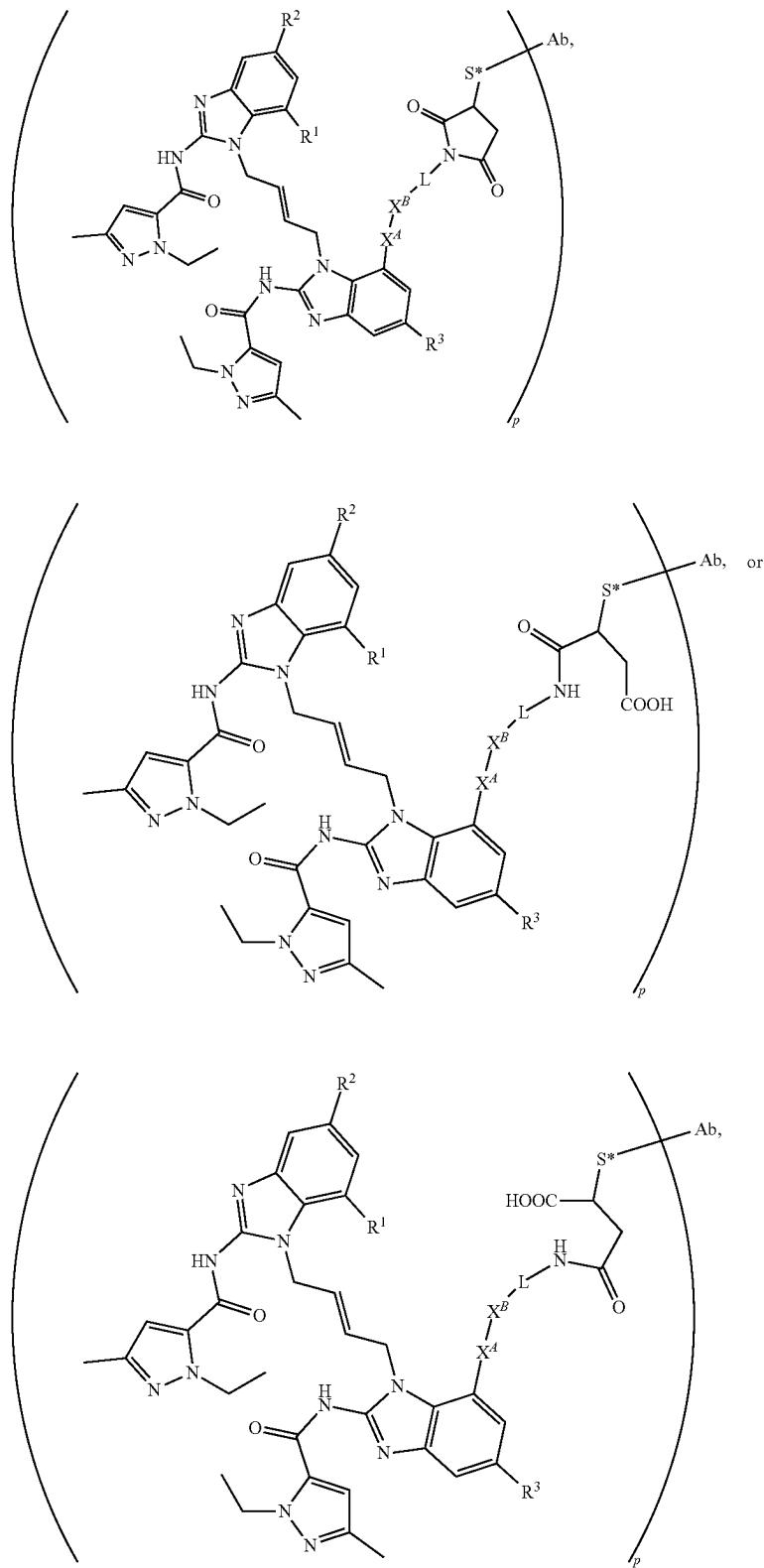
[0189] In some embodiments, X^B is absent and L is covalently attached to X^A . In some embodiments, X^B is absent and Y is covalently attached to X^A . In some embodiments, X^B is absent and Y is absent, and W is covalently attached to X^A . In some embodiments, X^B is absent, Y is absent, W is absent, and A is covalently attached to X^A .

[0190] In some embodiments, X^B is 2-16 membered heteroalkylene and L is covalently attached to X^B . In some embodiments, X^B is 2-16 membered heteroalkylene and Y is covalently attached to X^B . In some embodiments, X^B is 2-16 membered heteroalkylene, Y is absent, and W is covalently attached to X^B . In some embodiments, X^B is 2-16 membered heteroalkylene, Y is absent, W is absent, and A is covalently attached to X^B .

[0191] In some embodiments, W_1 is $-OC(=O)-$ and subscript y is 1. In some embodiments, X^A is $-O-$ and X^B and W_1 are absent. In some embodiments, X^A is NH or $-O-$, X^B is absent, and W_1 is $-OC(=O)$. In some embodiments, X^A is $-N(CH_3)-$, X^B is absent, and W_1 is $-OC(=O)$. In some embodiments, X^A is $-S-$, X^B is absent, and W_1 is $-OC(=O)$. In some embodiments, W_1 is $-OC(=O)-$ and X^B is covalently attached to W via $-O-$ or $-NH-$.

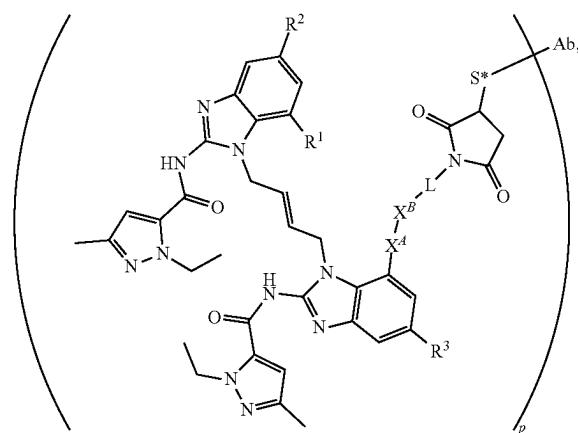
[0192] In some embodiments, A is covalently attached to M^1 . In some embodiments, when subscript a is 0, W is covalently attached to M^1 . In some embodiments, when subscript a is 0 and subscript w is 0, Y is covalently attached to M^1 . In some embodiments, when subscripts a , y , and w , are each 0, X^B is covalently attached to M^1 .

[0193] In some embodiments, the ADC has the formula:

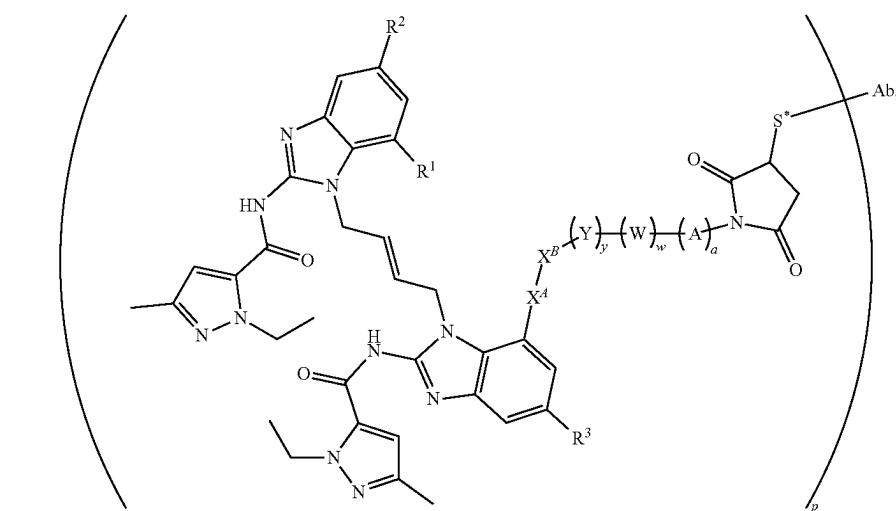


wherein:

- [0194] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);
- [0195] each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;
- [0196] R¹, R², R³, X^A, X^B, and L are as defined above in connection with Formula (I); and each subscript p is independently an integer from 2 to 8.
- [0197] In some aspects, the ADC has the formula:



- [0198] wherein:
- [0199] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);
- [0200] each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;
- [0201] R¹, R², R³, X^A, X^B, and L are as defined above in connection with Formula (I); and each subscript p is independently an integer from 2 to 8.
- [0202] In some aspects, the ADC has the formula:



[0203] wherein:

[0204] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);

[0205] each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;

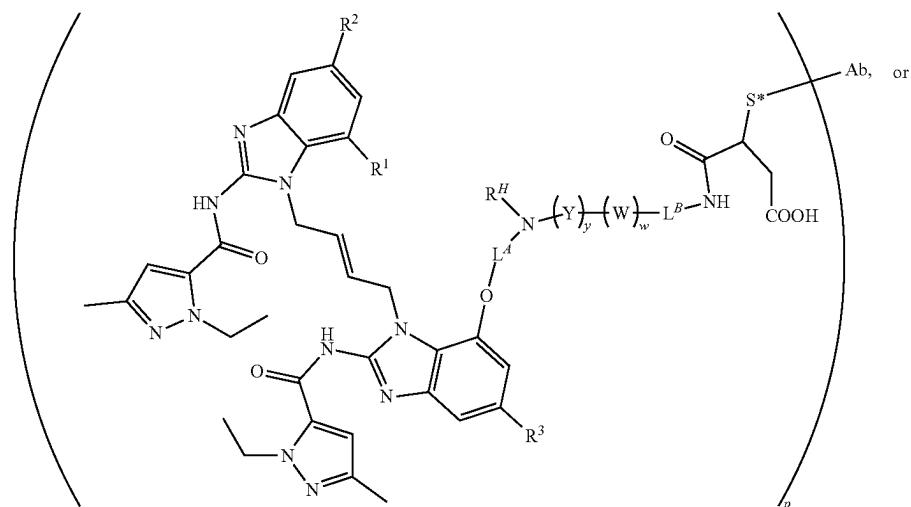
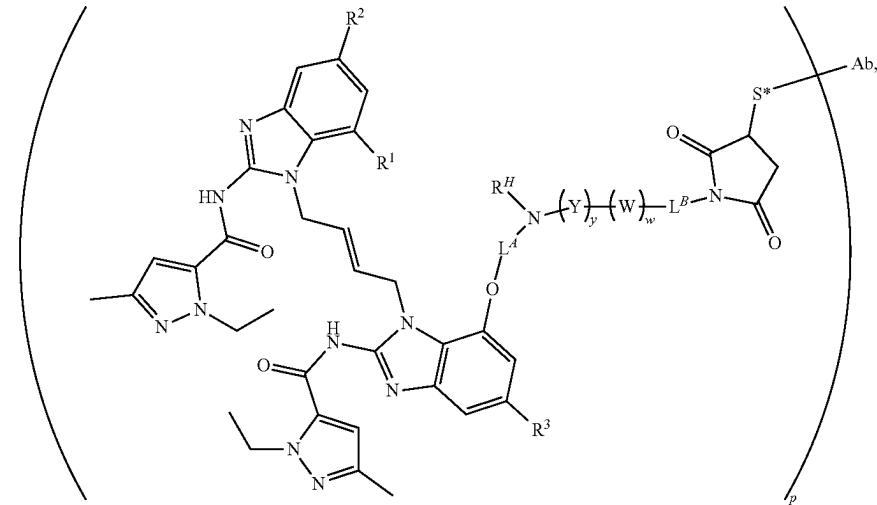
[0206] R¹, R², R³, X^A, X^B, Y, W, and A are as defined above in connection with Formula (I);

[0207] each subscript y is independently 0 or 1;

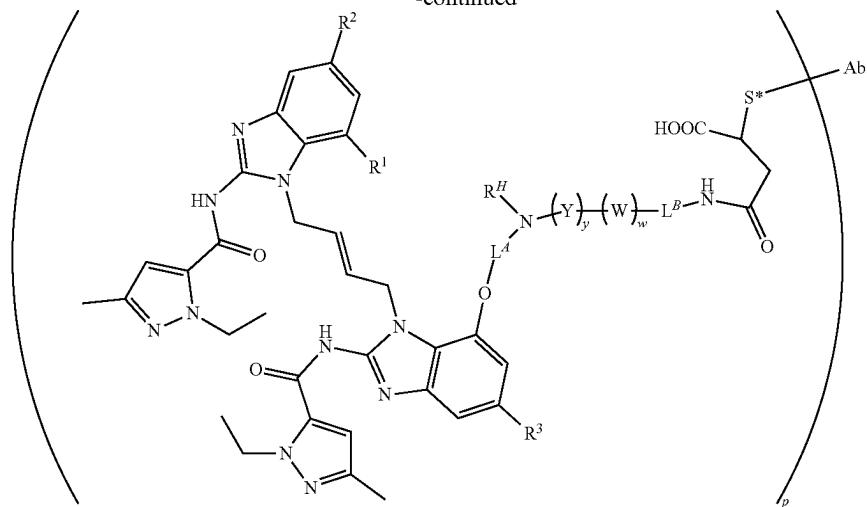
[0208] each subscript w is independently 0 or 1;

[0209] each subscript a is independently 0 or 1; and each subscript p is independently an integer from 2 to 8.

[0210] In some embodiments, the ADC has the formula:



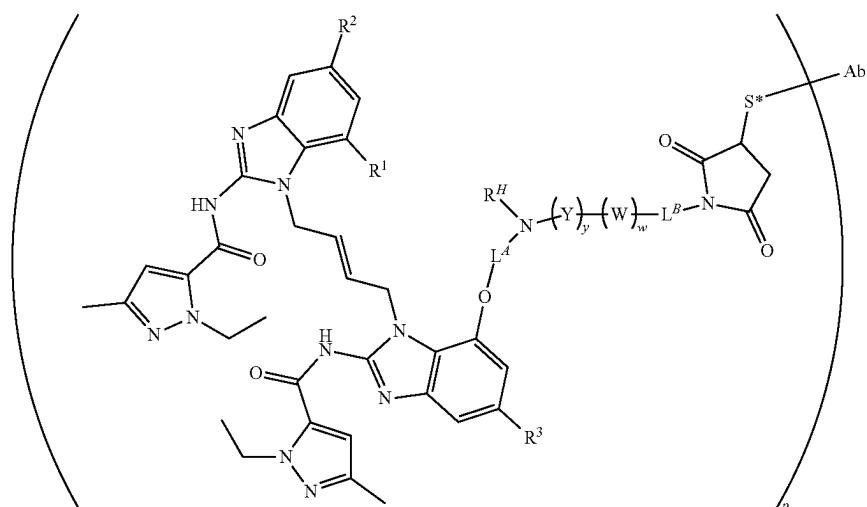
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[0211] wherein:

- [0212] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);
- [0213] each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;
- [0214] R¹, R², R³, L^A, R^H, Y, W, and L^B are as defined below in connection with Formula (II-A);
- [0215] each subscript y is independently 0 or 1;
- [0216] each subscript w is independently 0 or 1; and
- [0217] each subscript p is independently an integer from 2 to 8.

[0218] In some aspects, the ADC has the formula:

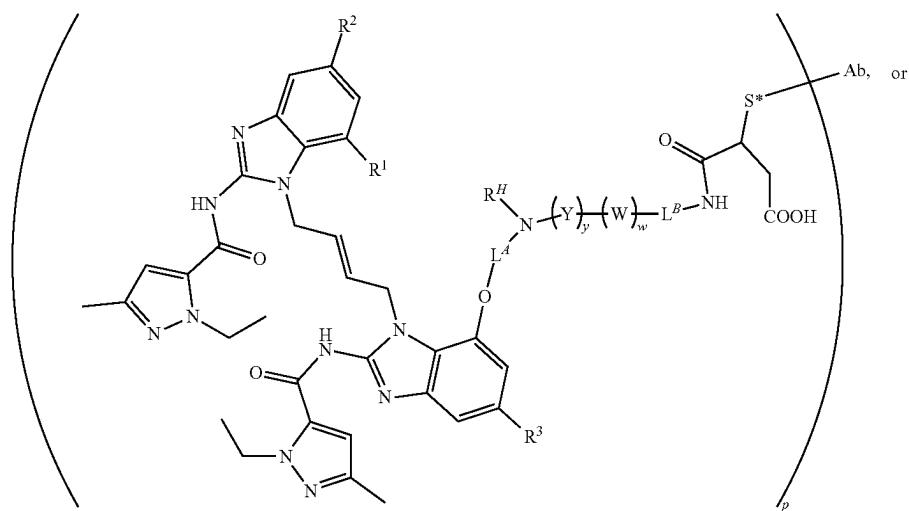
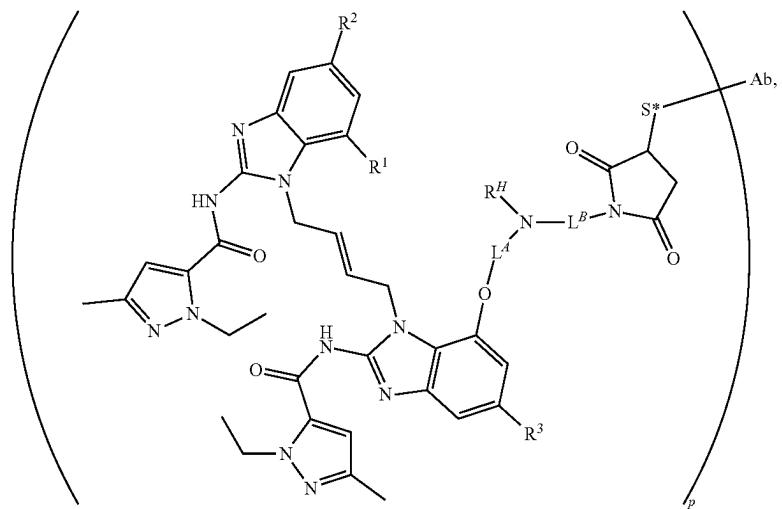


[0219] wherein:

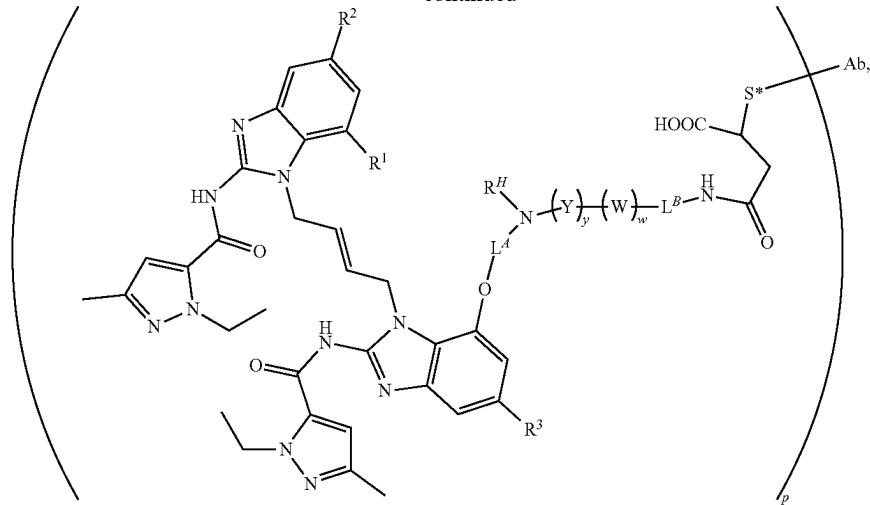
- [0220] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);
- [0221] each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;

- [0222] R¹, R², R³, L^A, R^H, Y, W, and L^B are as defined below in connection with Formula (II-A);
- [0223] each subscript y is independently 0 or 1;
- [0224] each subscript w is independently 0 or 1; and
- [0225] each subscript p is independently an integer from 2 to 8.

[0226] In some embodiments, the ADC has the formula:



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[0227] wherein:

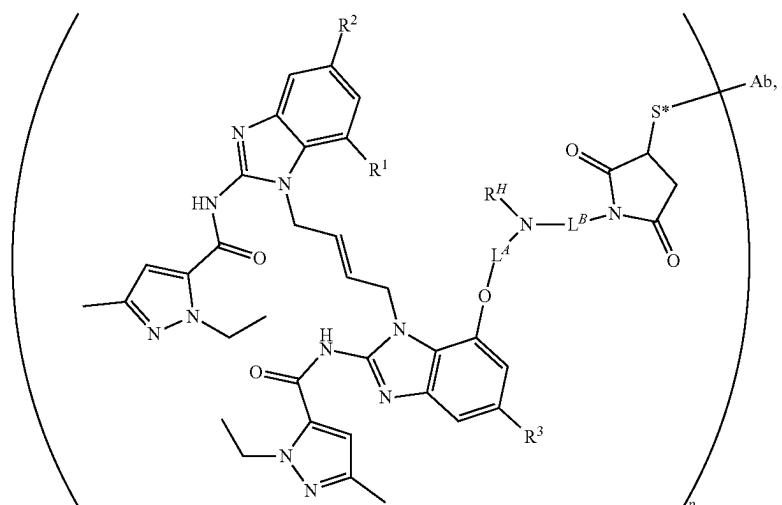
[0228] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);

[0229] each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;

[0230] R¹, R², R³, L^A, R^H, and L^B are as defined below in connection with Formula (II-B); and

[0231] each subscript p is independently an integer from 2 to 8.

[0232] In some aspects, the ADC has the formula:



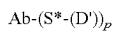
[0233] wherein:

[0234] Ab is an antibody;

[0235] R¹, R², R³, L^A, R^H, and L^B are as defined below in connection with Formula (II-B); and

[0236] each subscript p is independently an integer from 2 to 8.

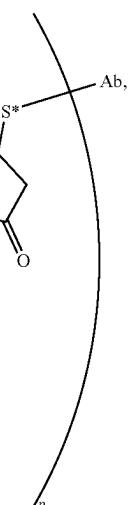
[0237] Some embodiments provide an antibody-drug conjugate (ADC) having the formula:



wherein:

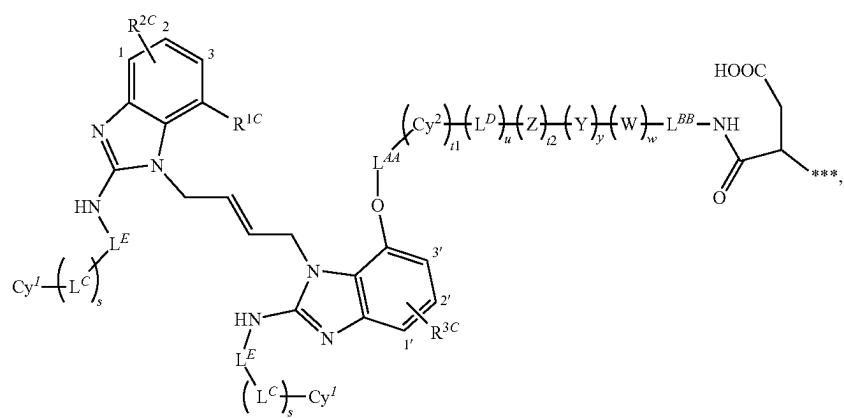
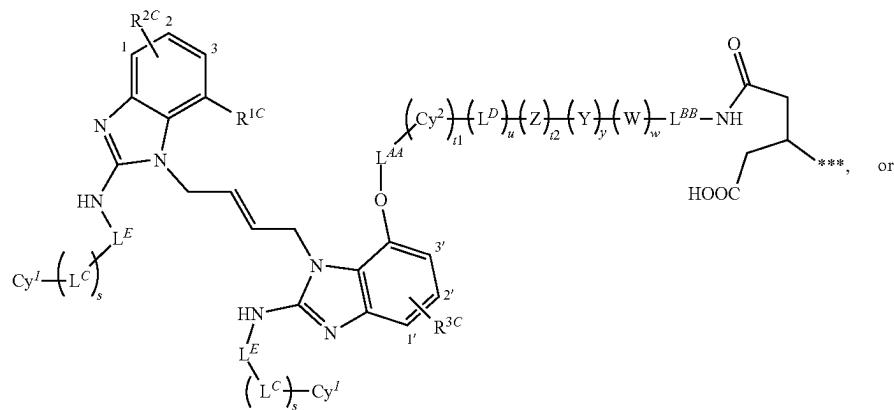
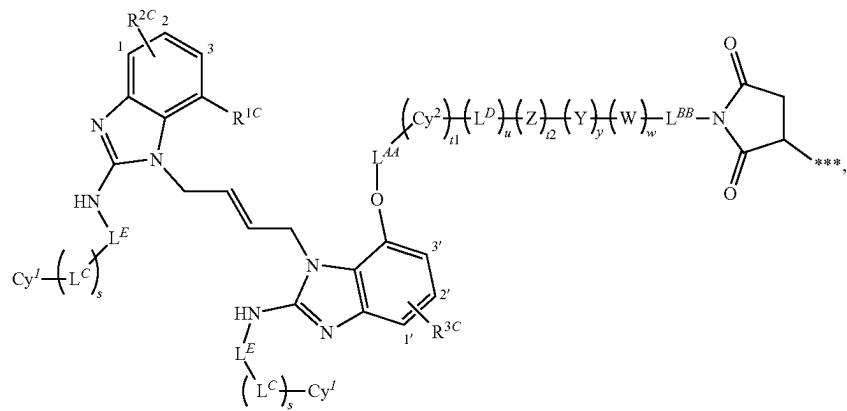
[0238] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);

[0239] each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;



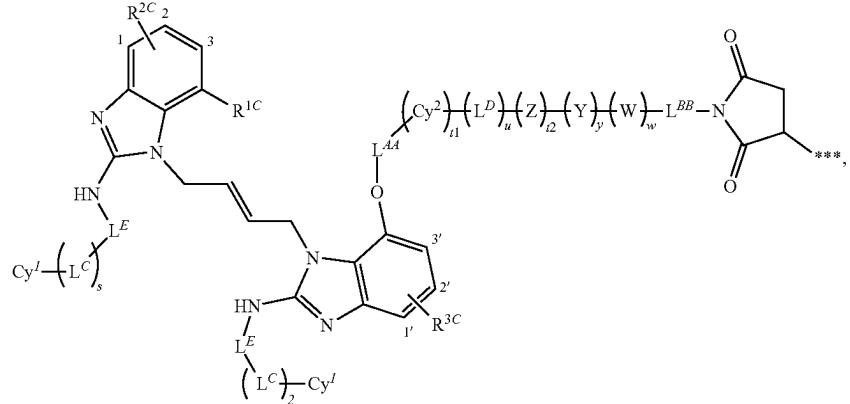
[0240] D' is a Drug-Linker Unit that is a radical of the compound of Formula (IV), as described below; and subscript p is an integer from 2 to 8.

[0241] In some embodiments, the radical of the compound of Formula (IV) comprises a radical in substituent M within Formula (IV). In some embodiments, the Drug-Linker Unit D' has the structure:



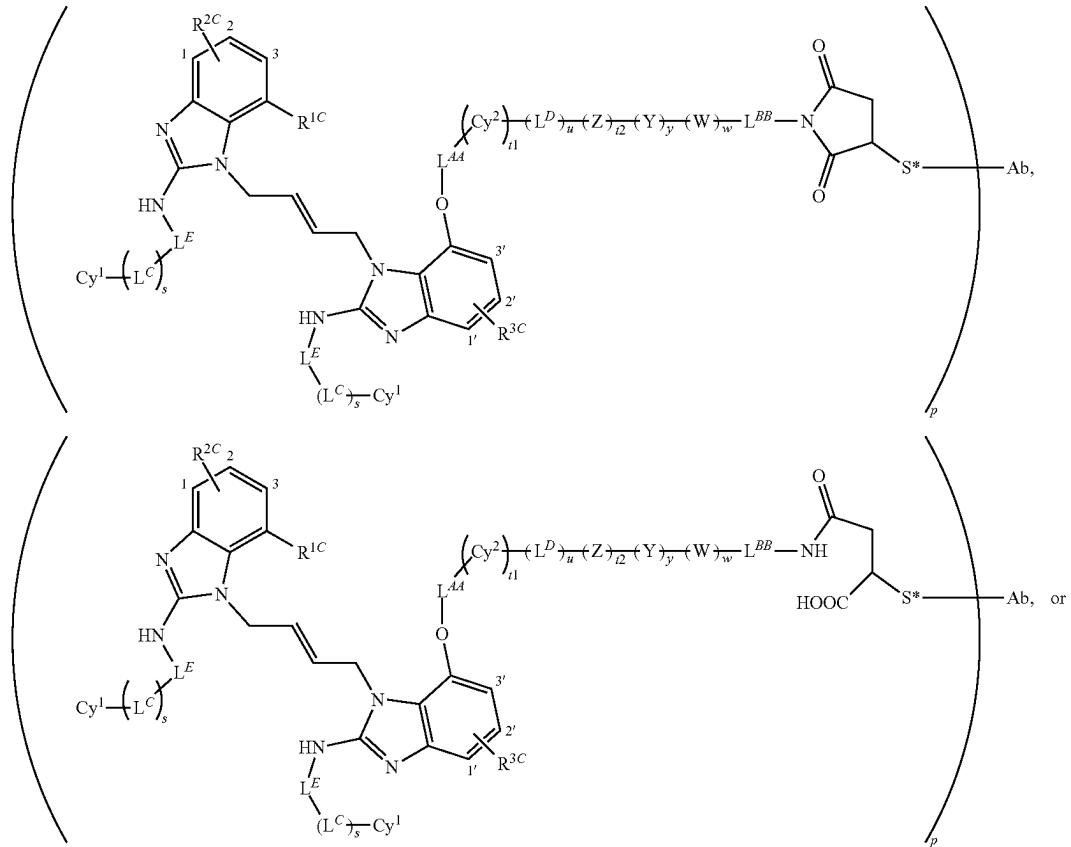
where *** indicates attachment to S* and the remaining variables are as defined below in connection with Formula (IV).

[0242] In some aspects, the Drug-Linker Unit D' has the structure:

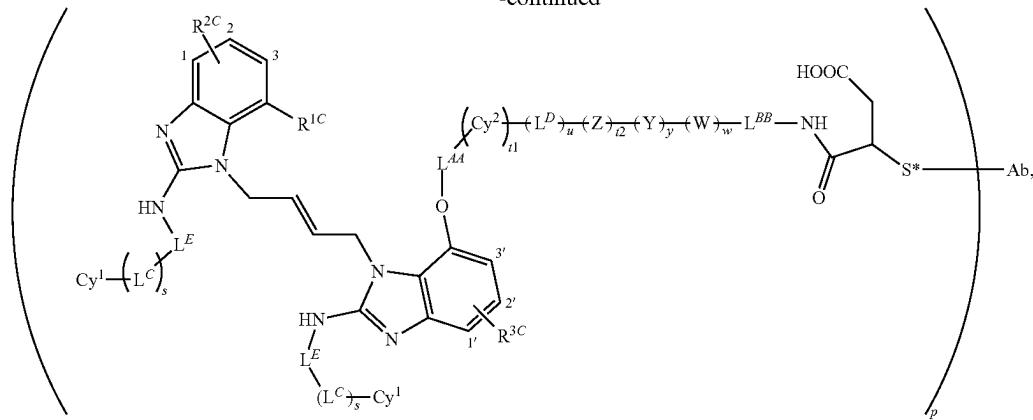


where *** indicates attachment to S* and the remaining variables are as defined below in connection with Formula (IV).

[0243] In some embodiments, the ADC has the formula:



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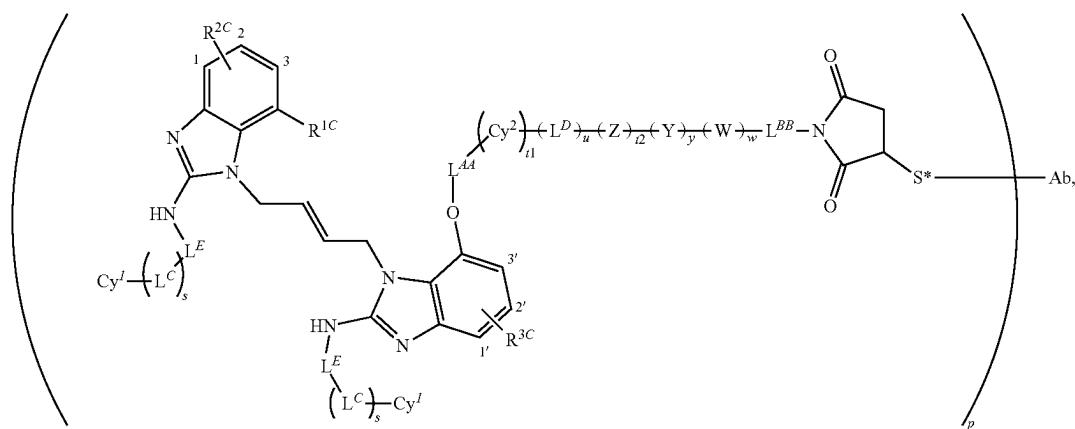
[0244] wherein:

[0245] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);

[0246] each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;

[0247] each subscript p is independently an integer from 2 to 8; and the remaining variables are as defined below in connection with Formula (IV).

[0248] In some aspects, the ADC has the formula:



[0249] wherein:

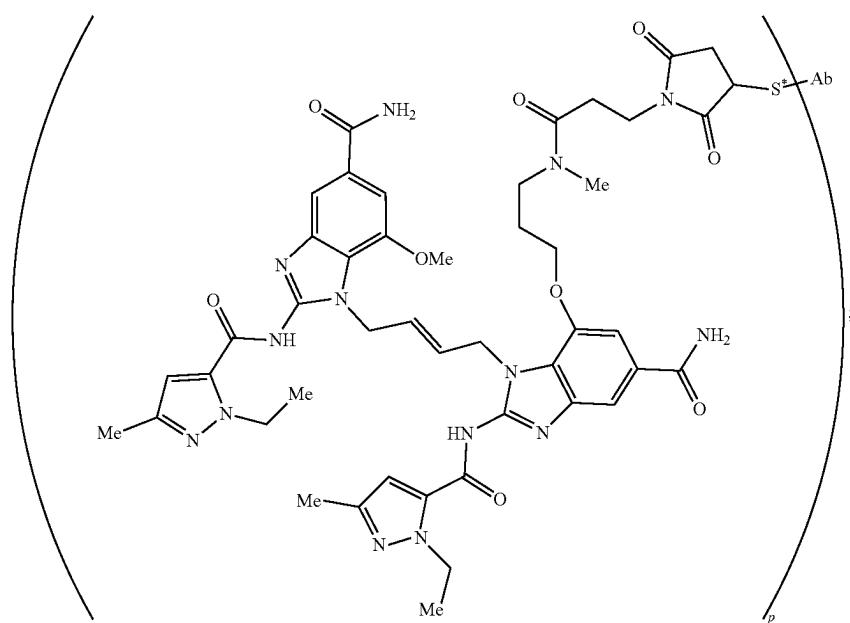
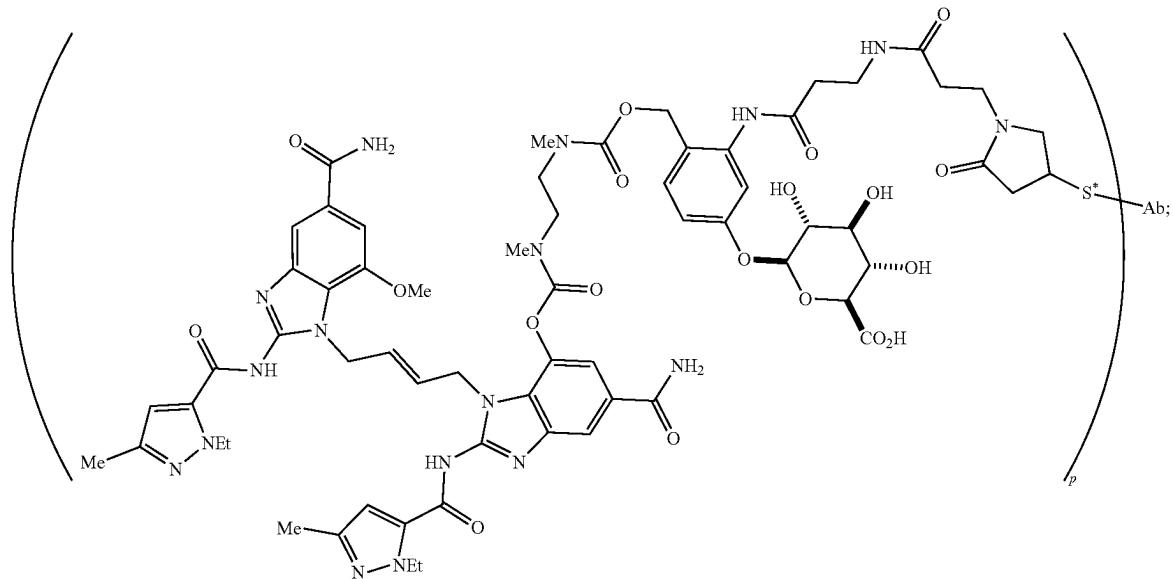
[0250] Ab is an antigen-binding protein or an antigen-binding fragment thereof (e.g., an antibody);

[0251] each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;

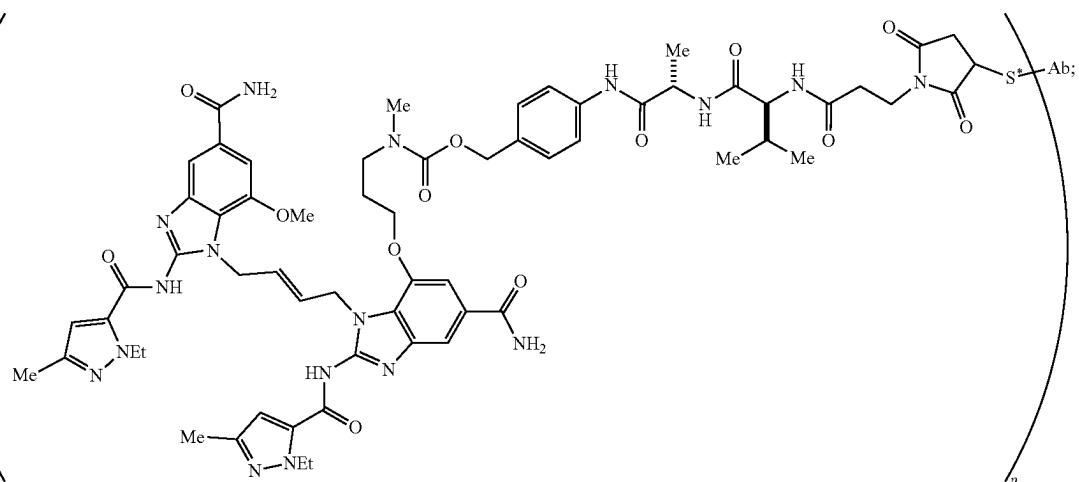
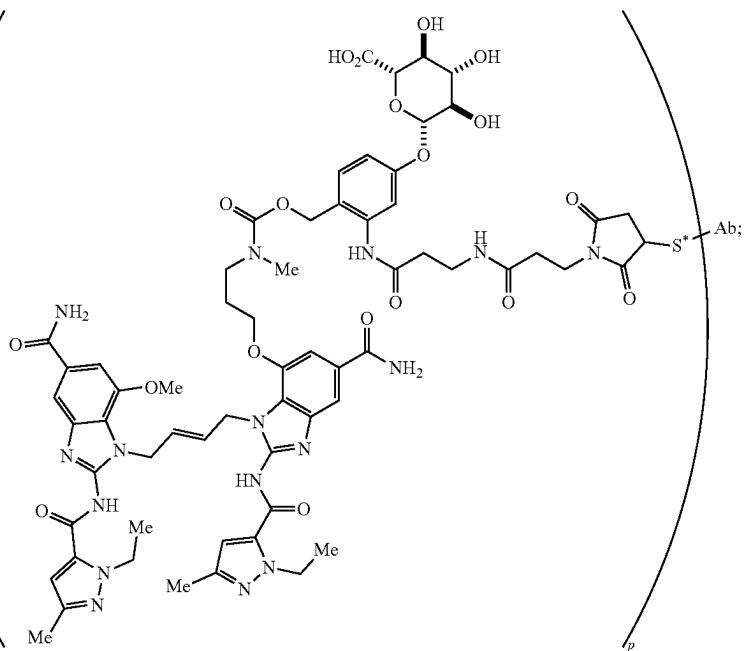
[0252] each subscript p is independently an integer from 2 to 8; and

[0253] the remaining variables are as defined below in connection with Formula (IV).

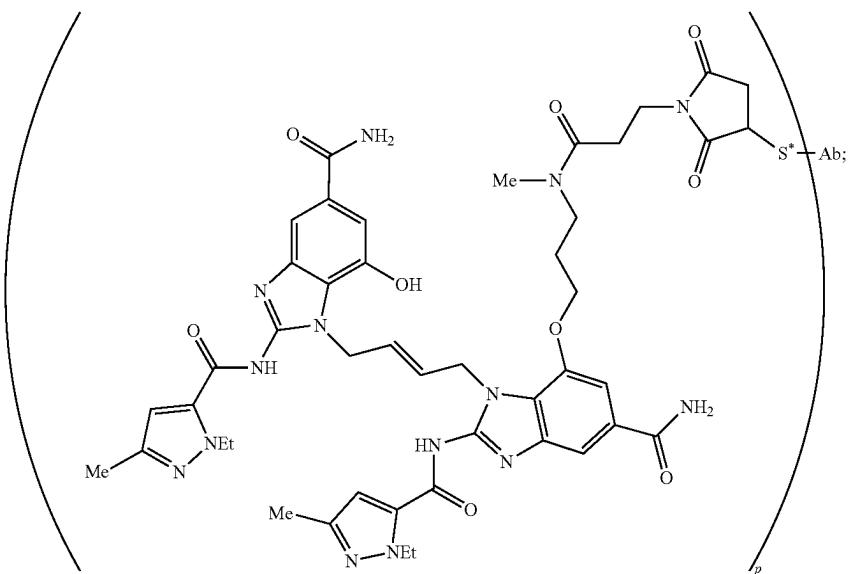
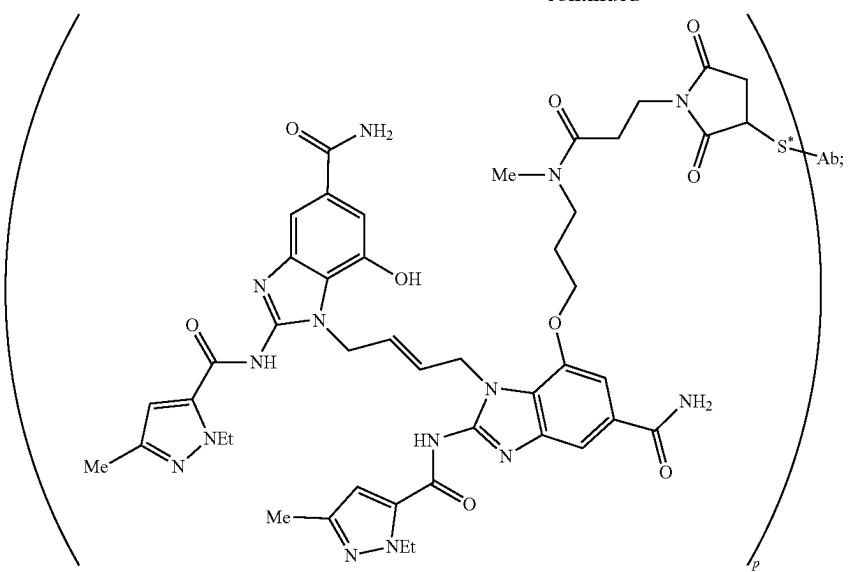
[0254] Some embodiments provide an antibody-drug conjugate (ADC) selected from the group consisting of:



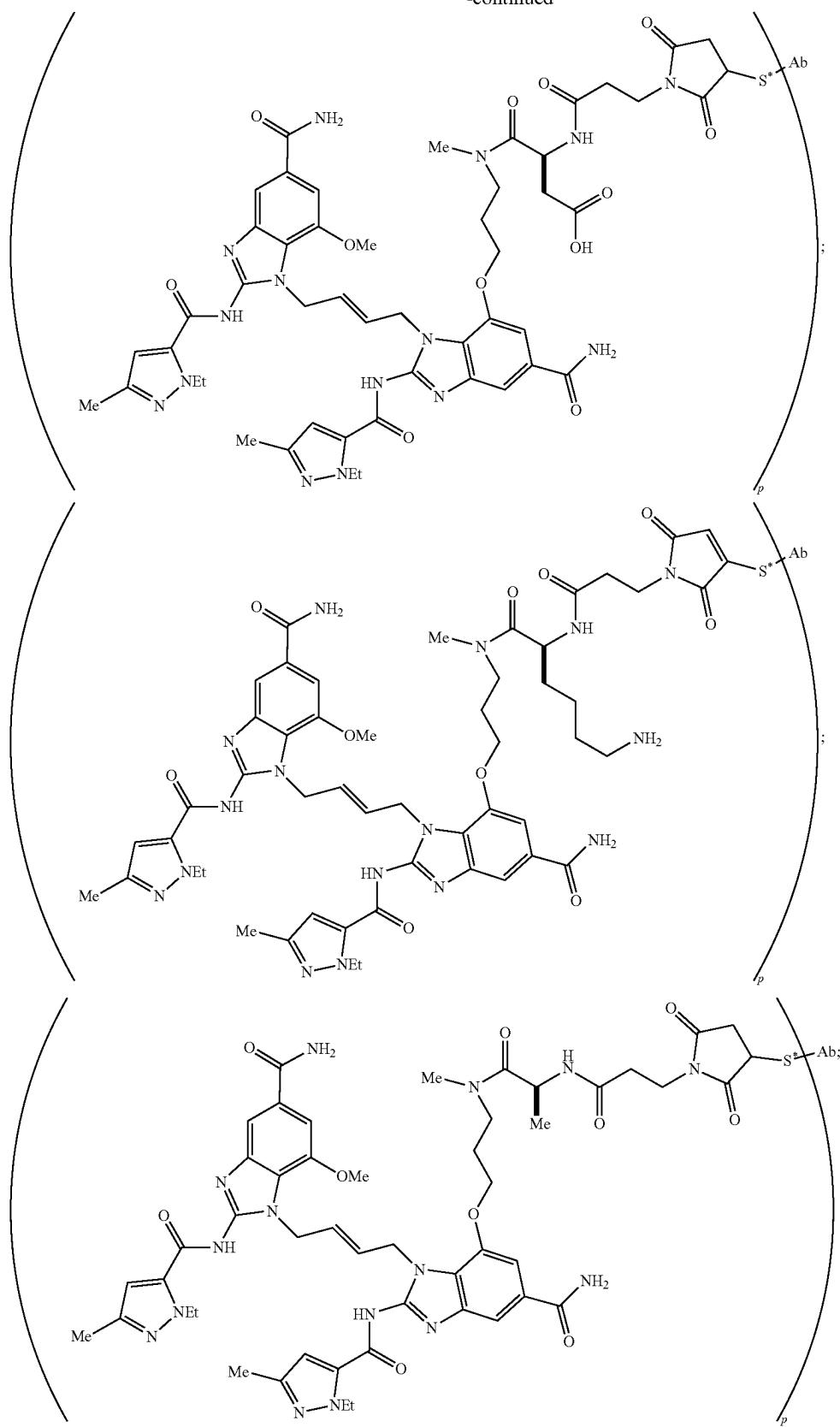
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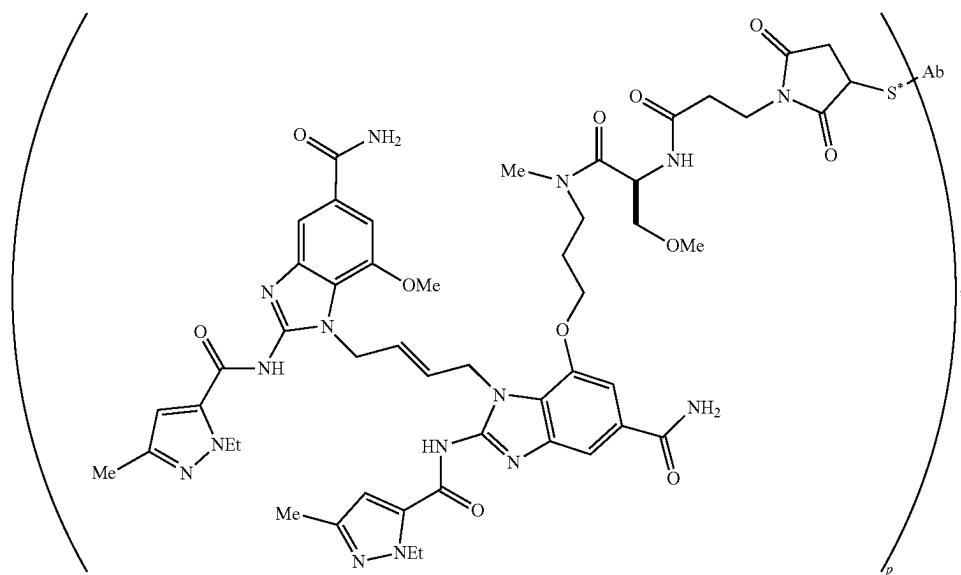
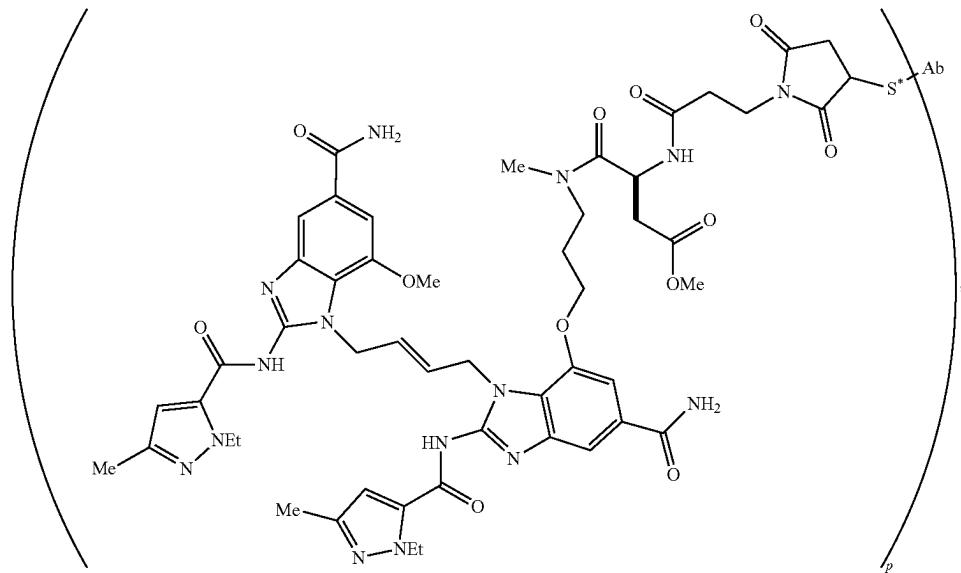
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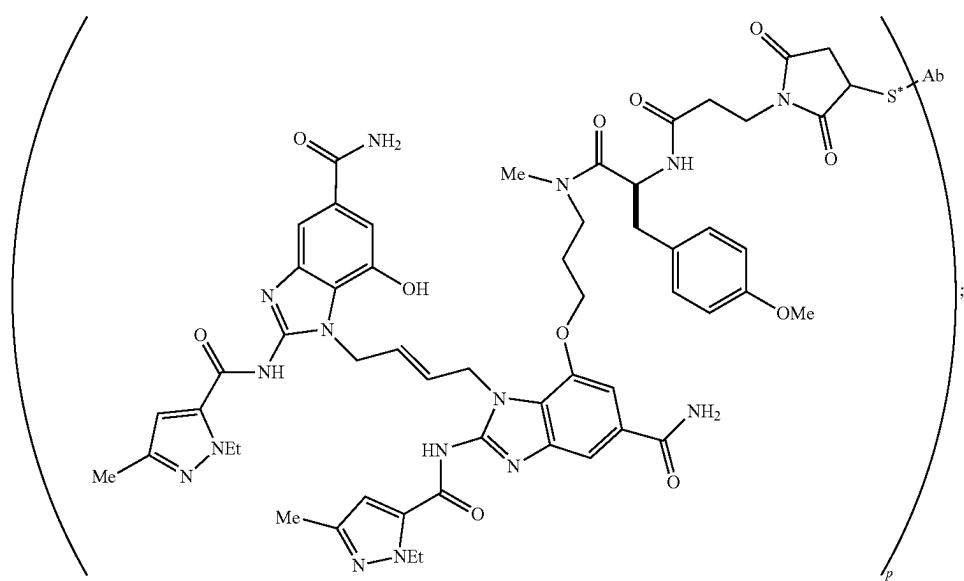
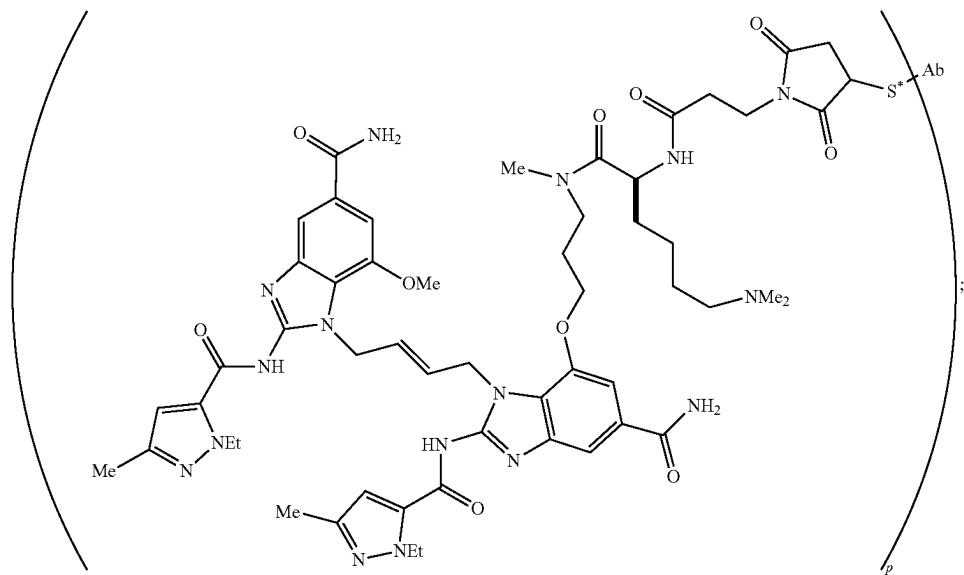
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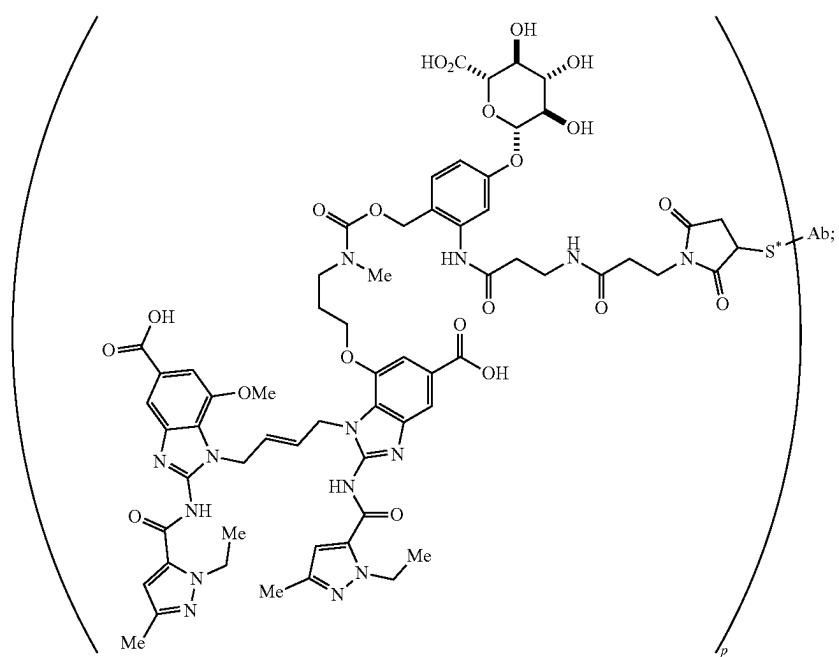
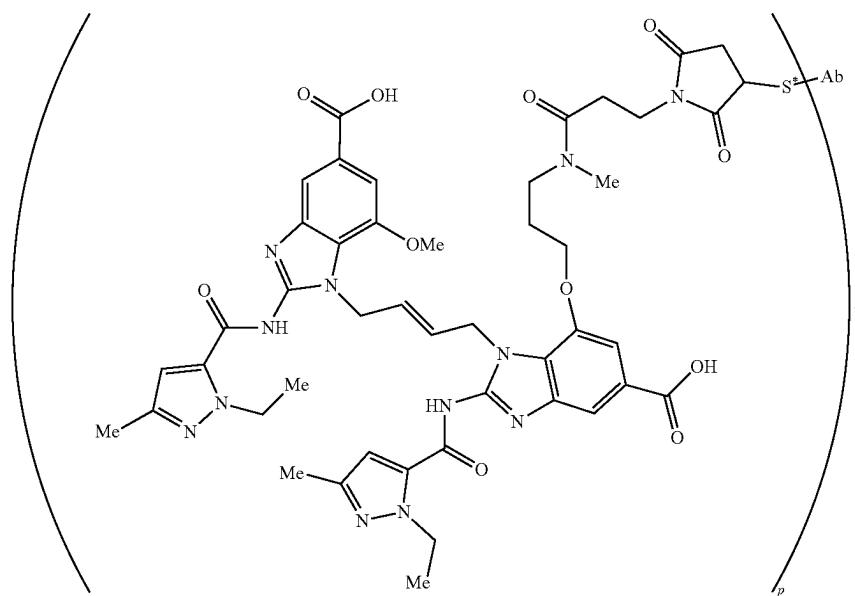
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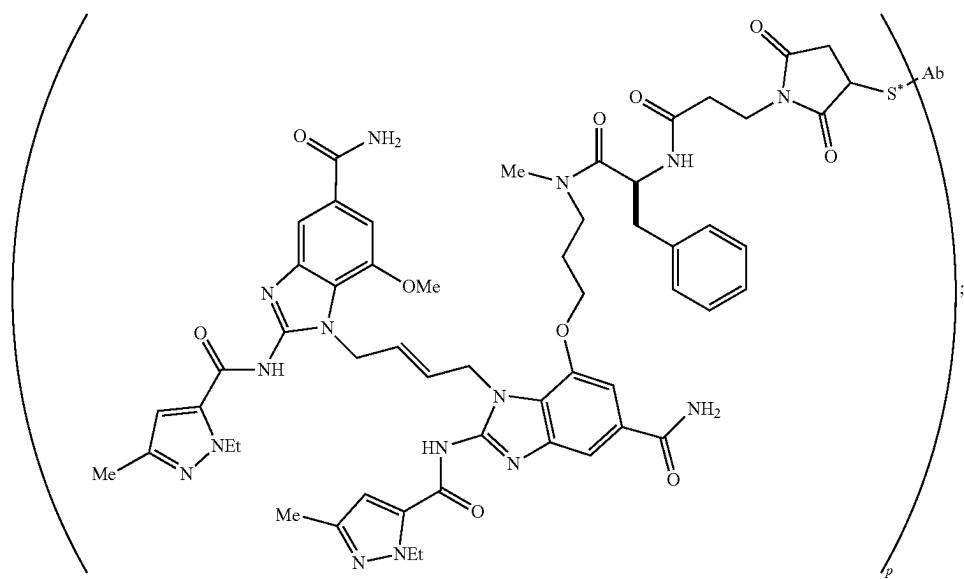
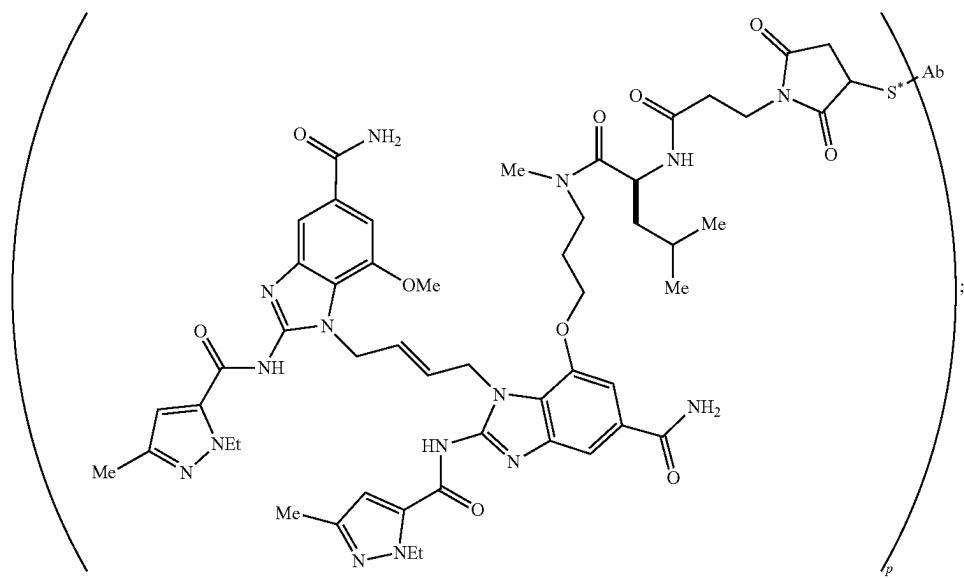
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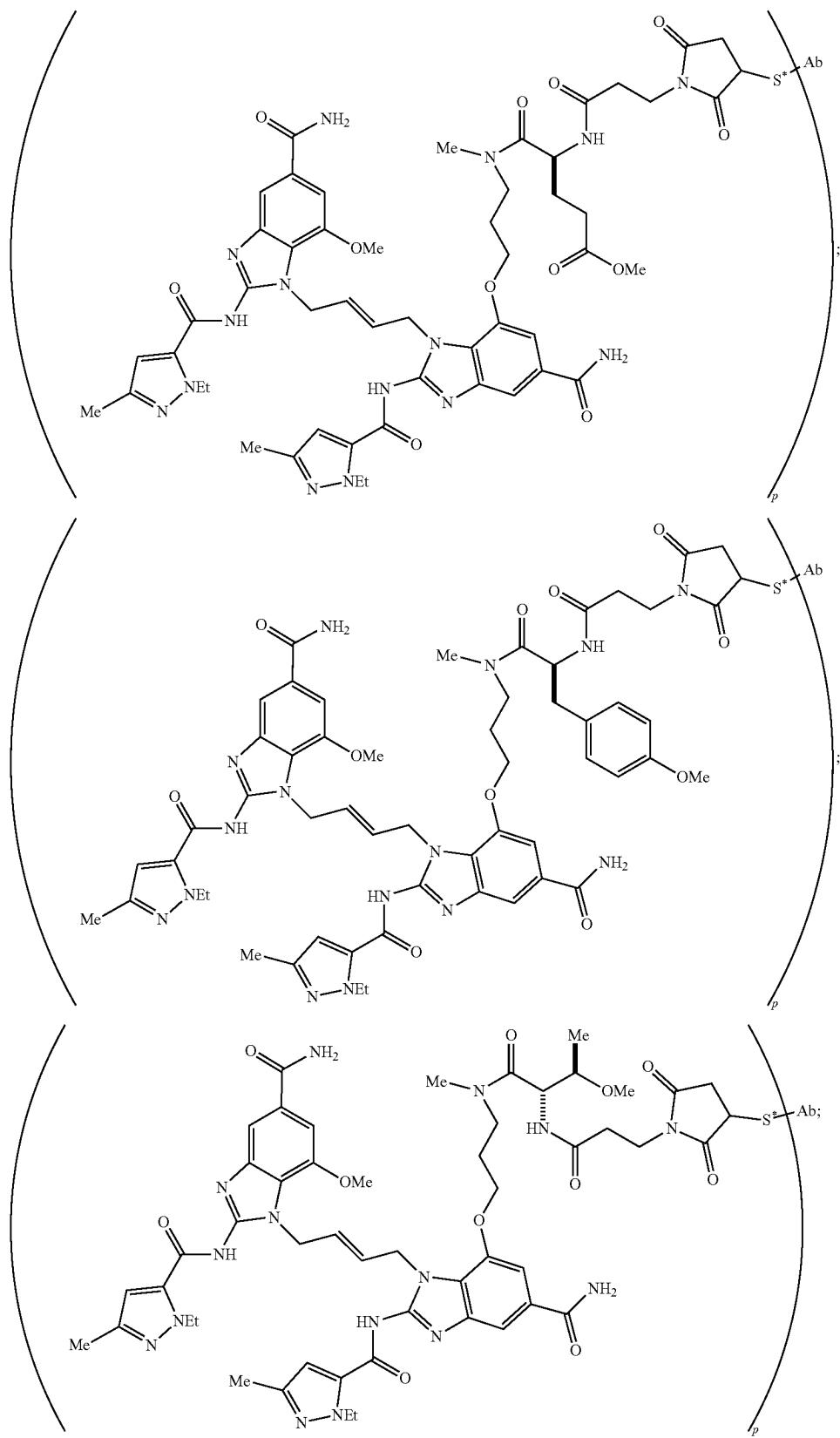
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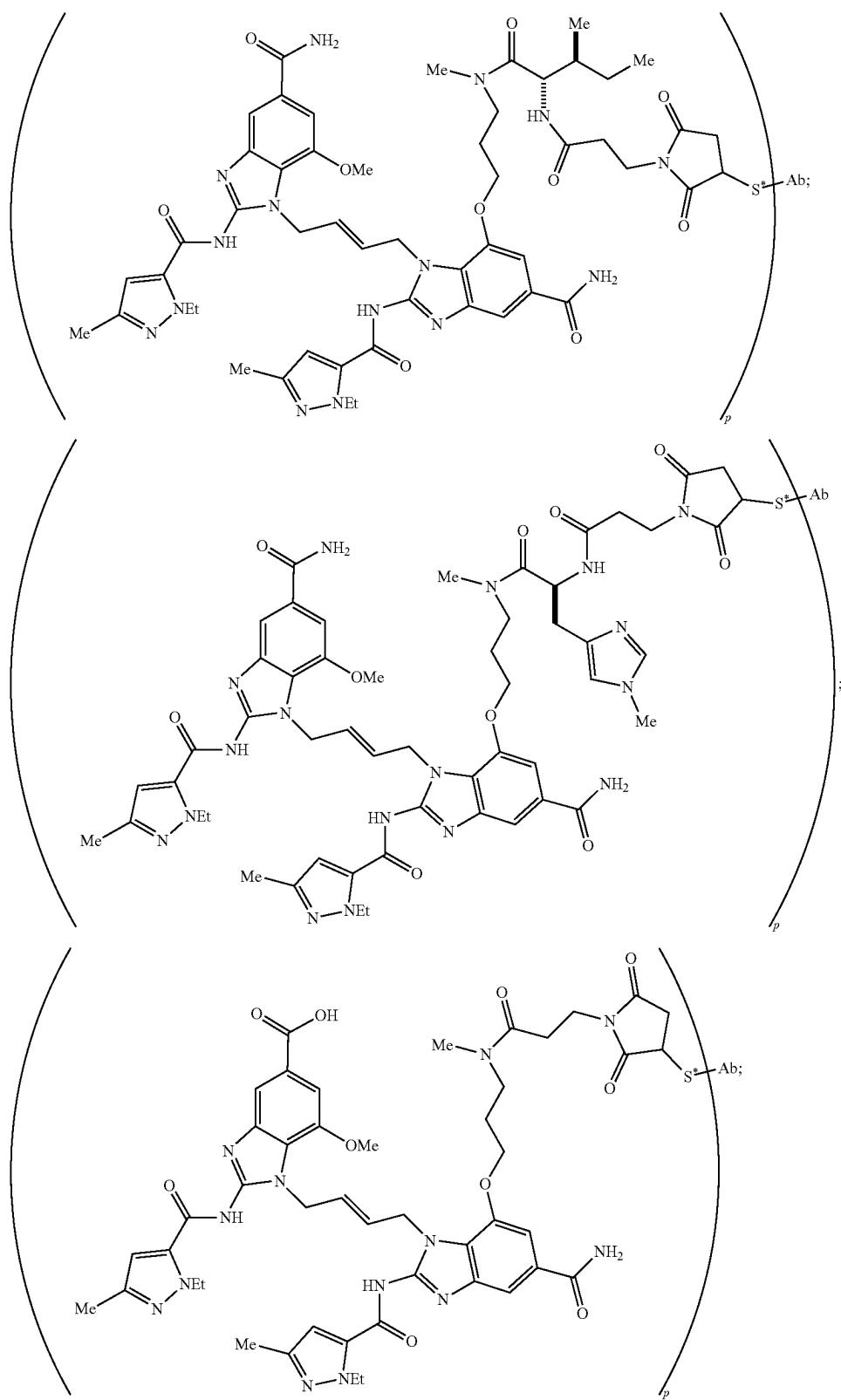
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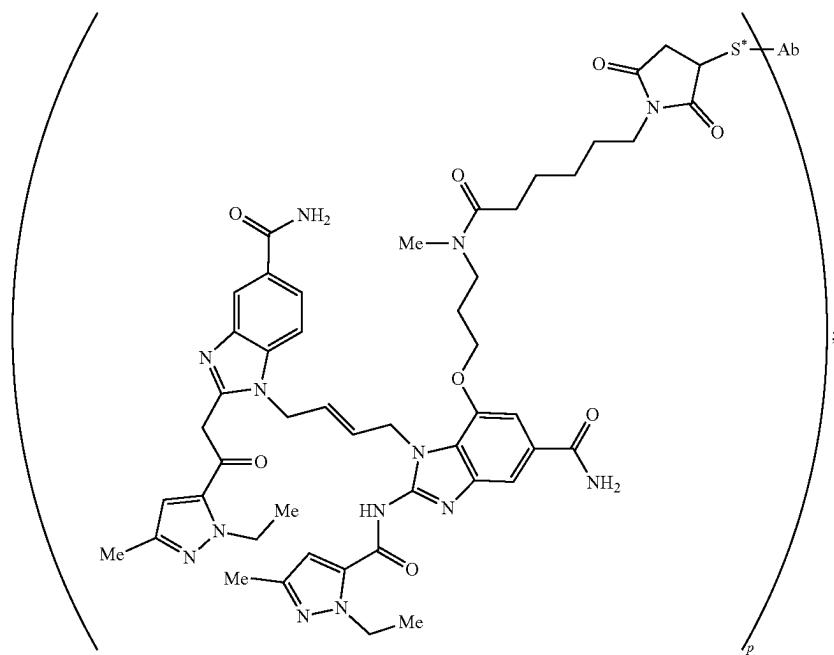
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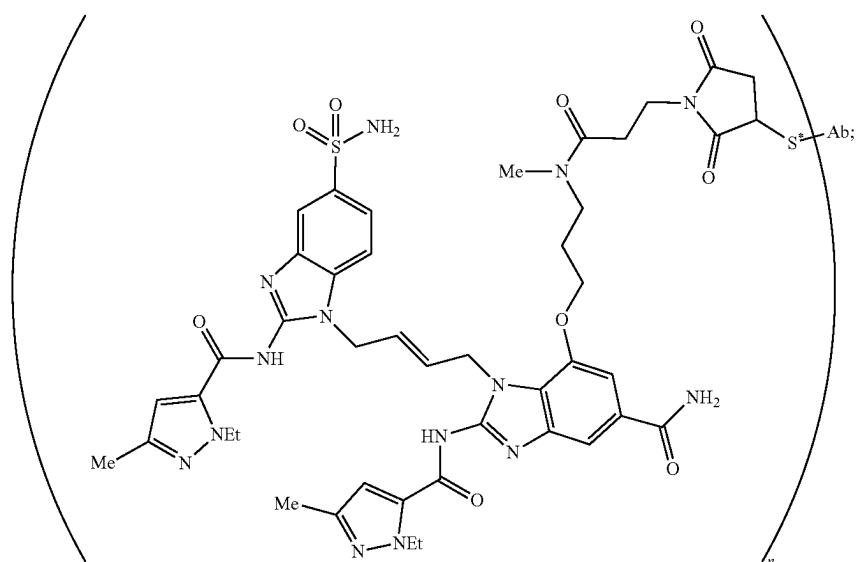
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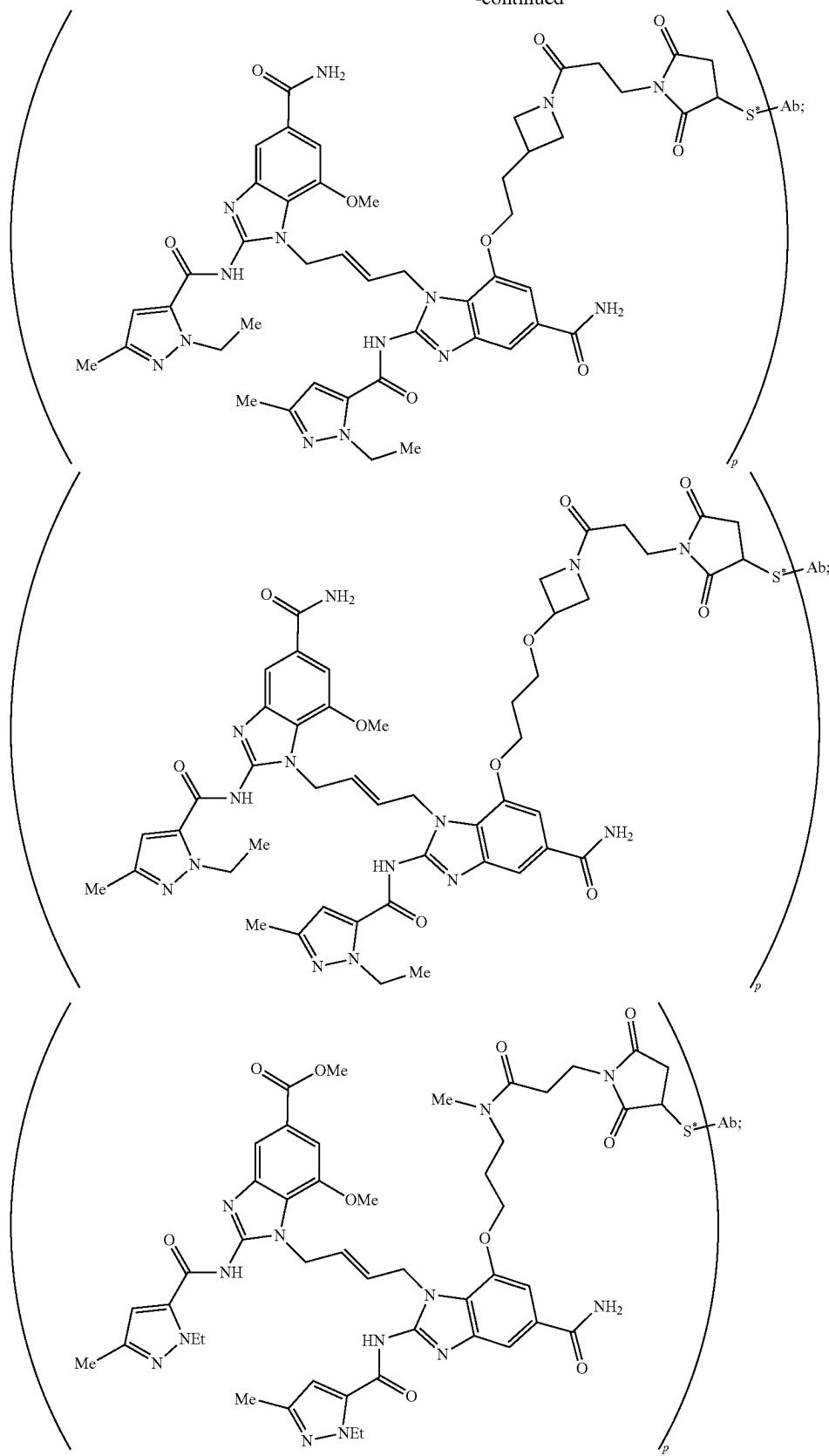
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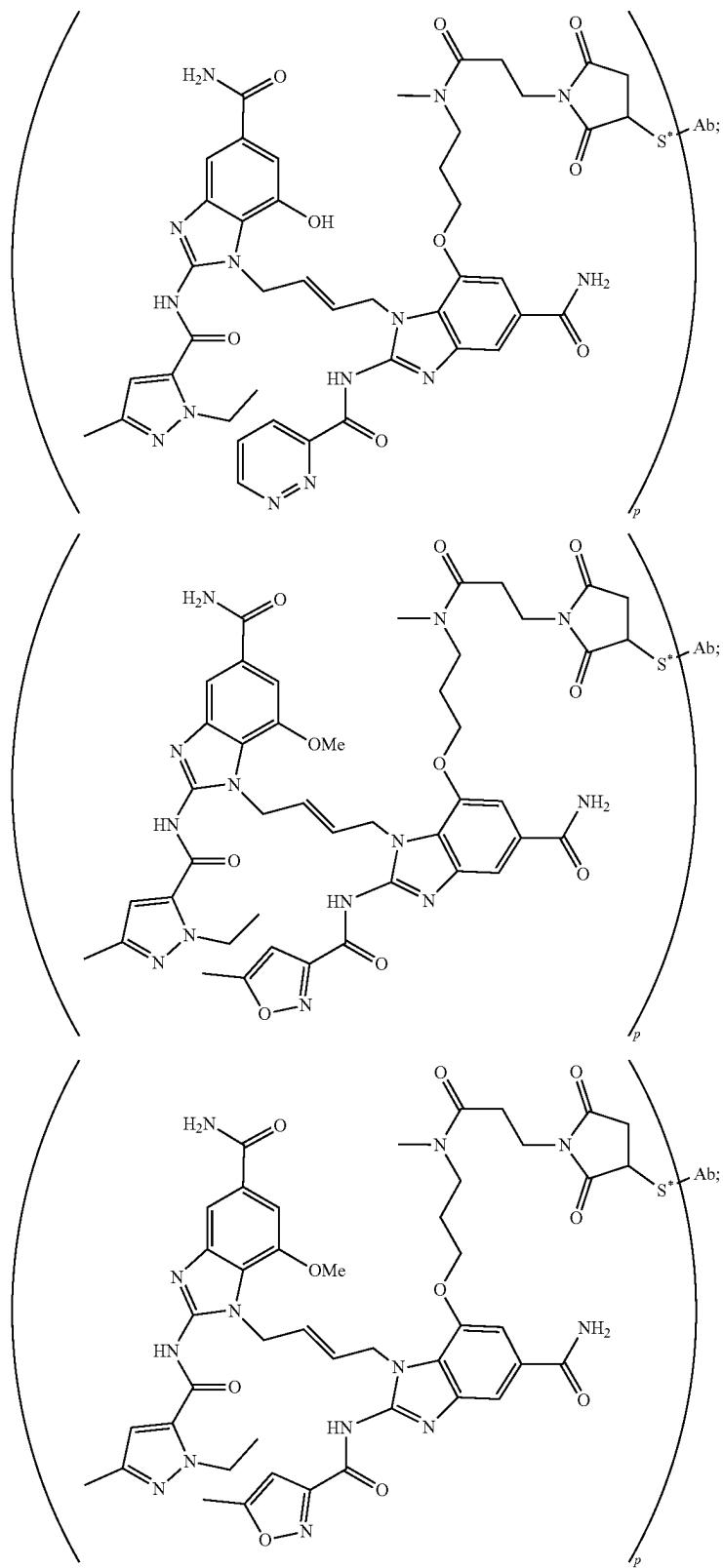
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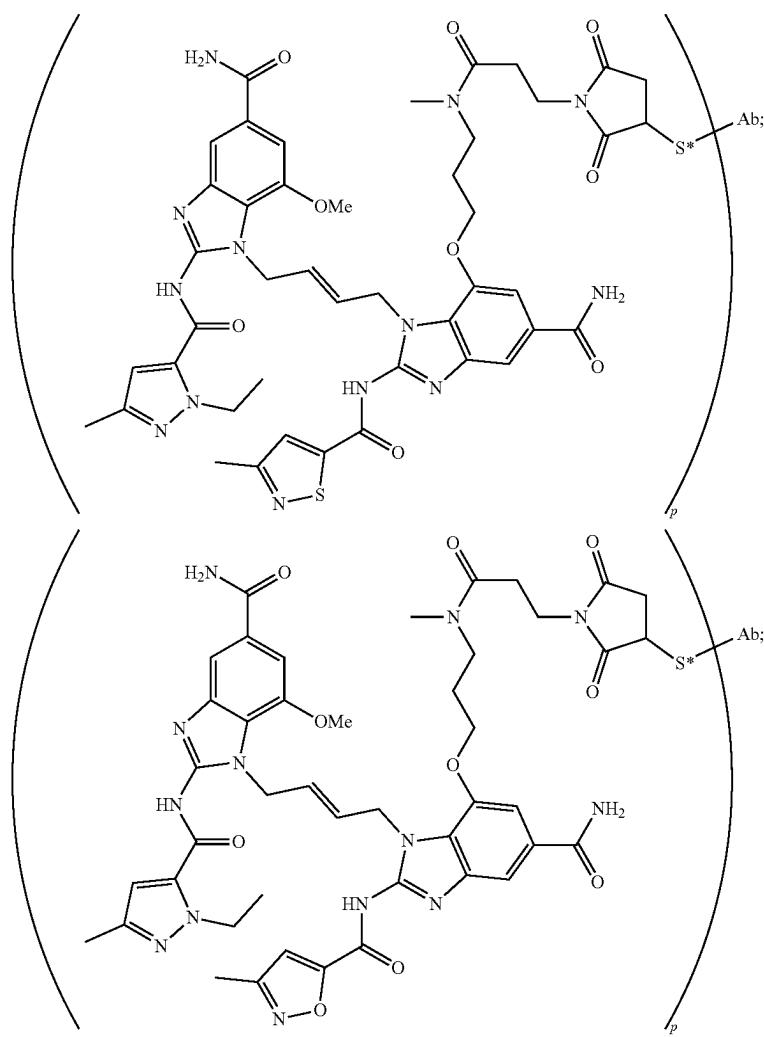
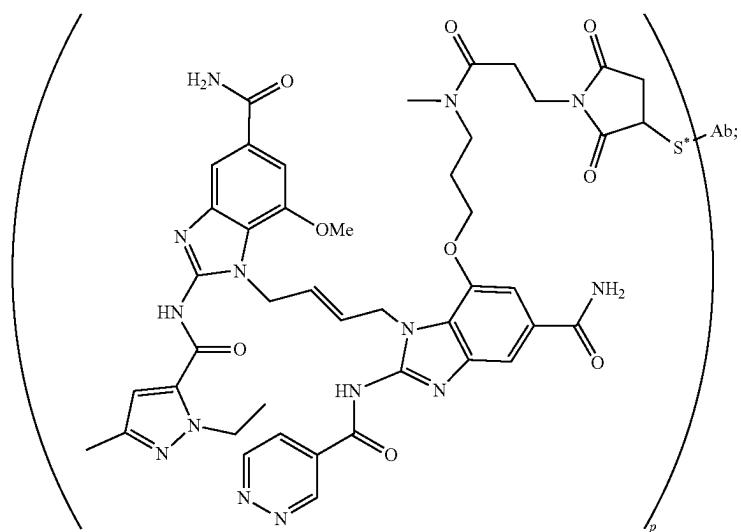
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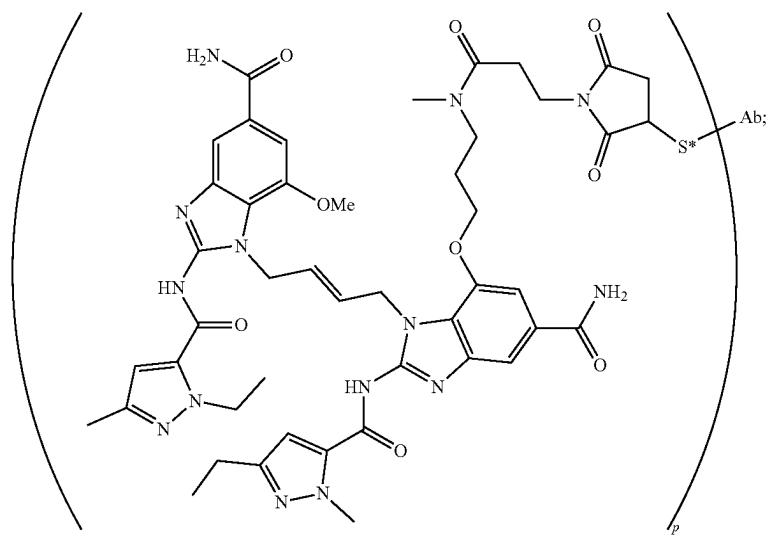
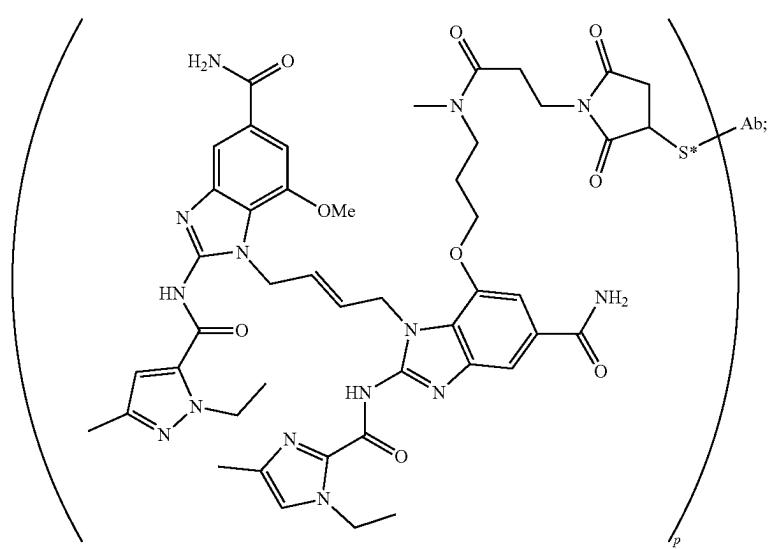
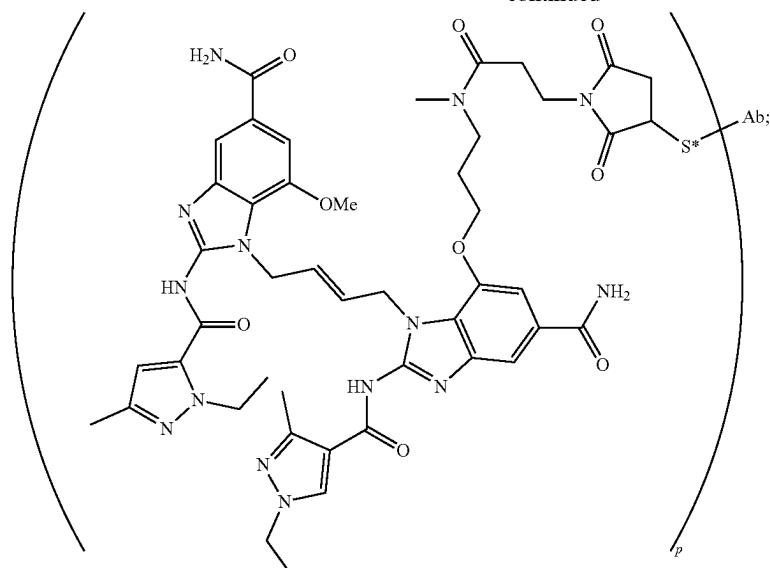
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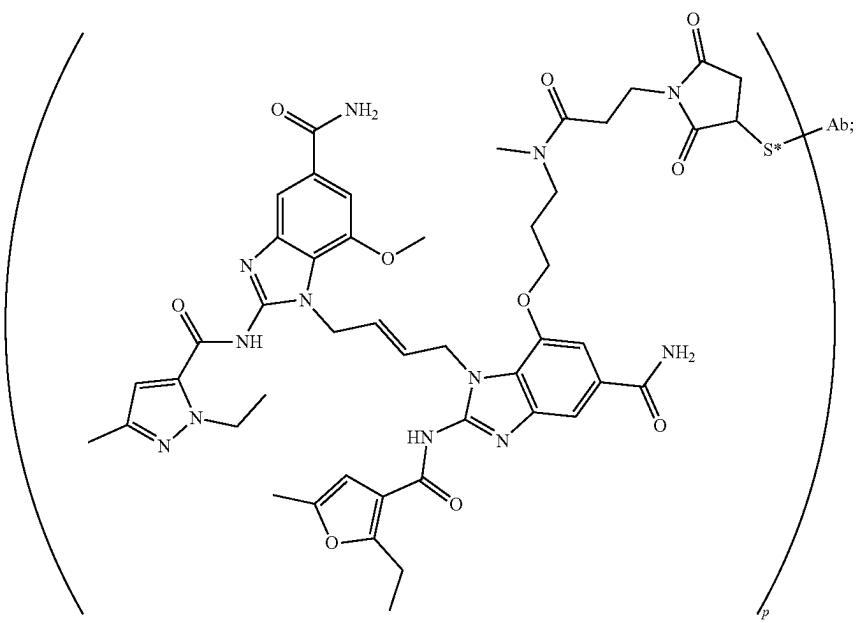
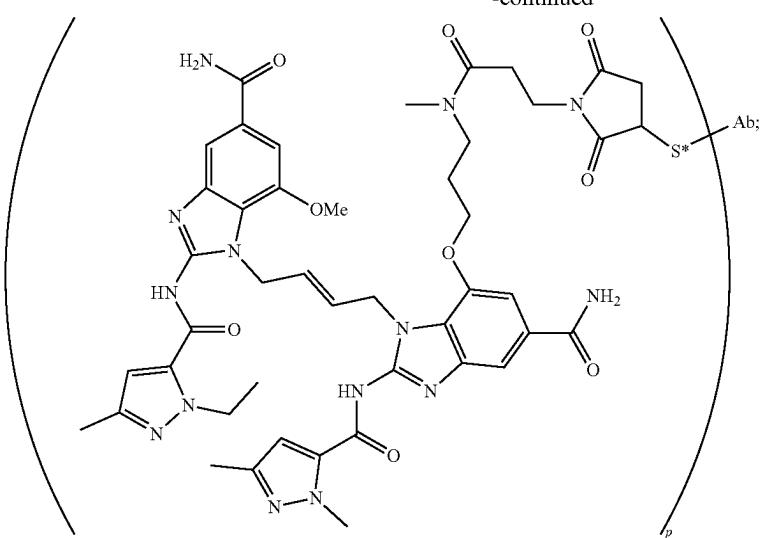
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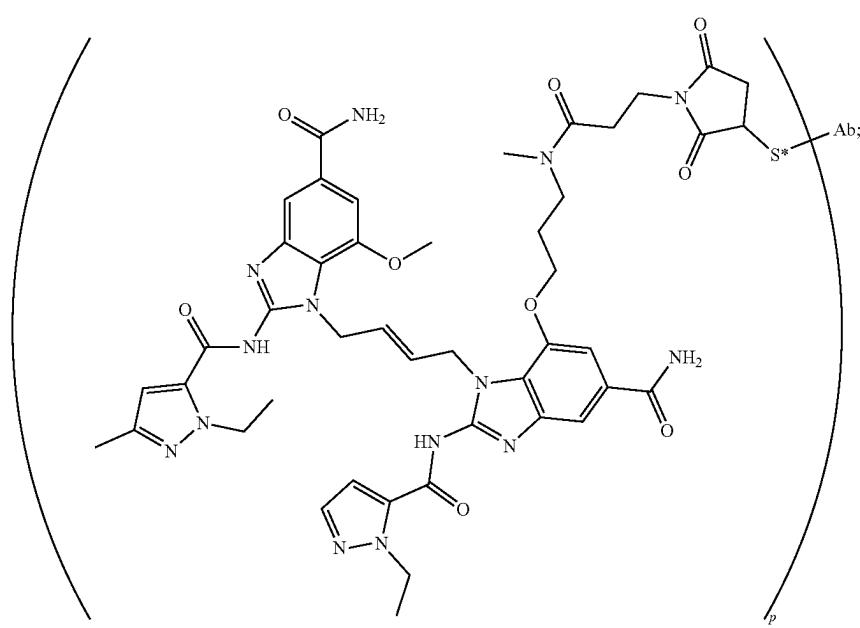
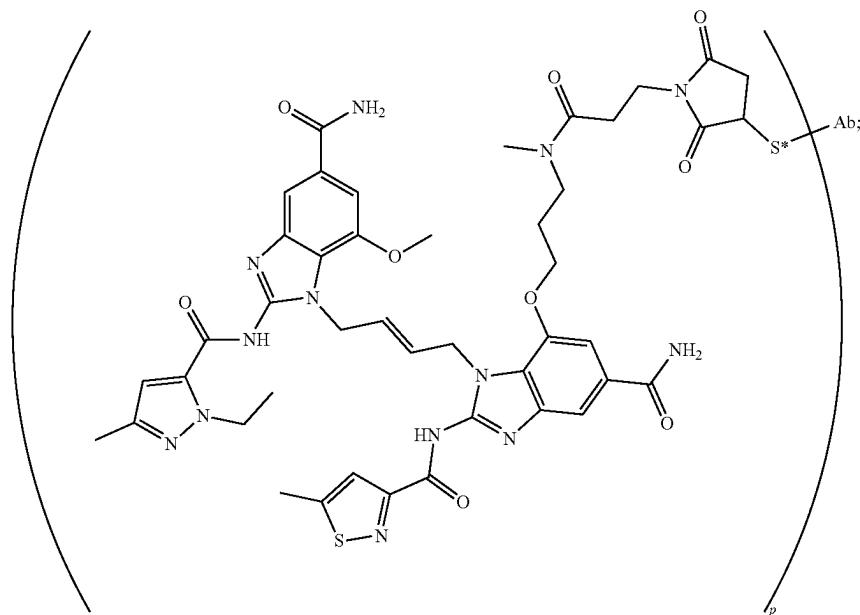
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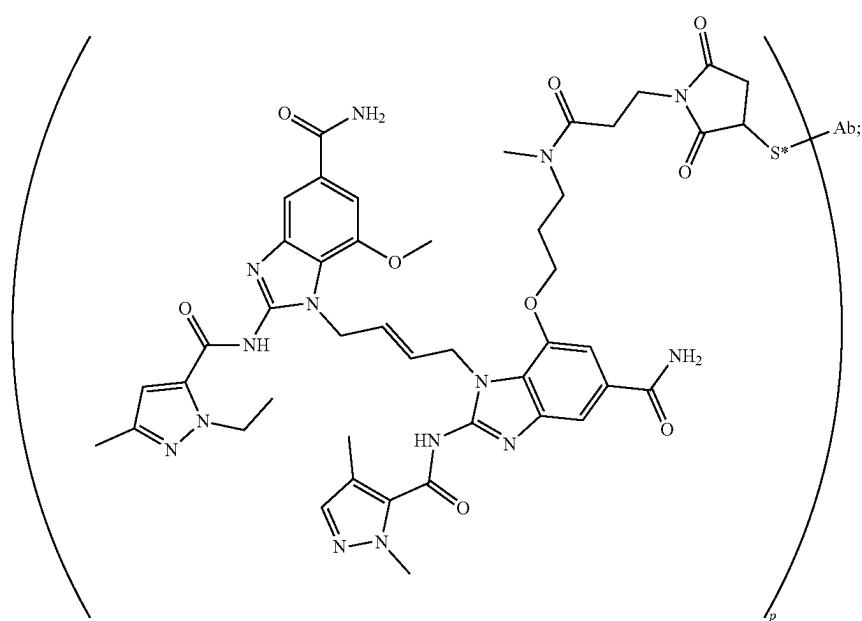
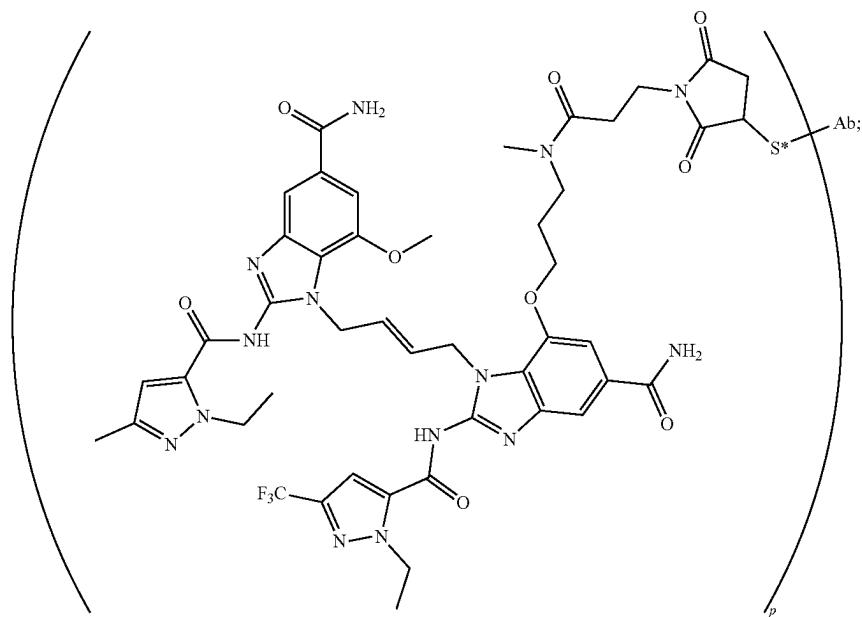
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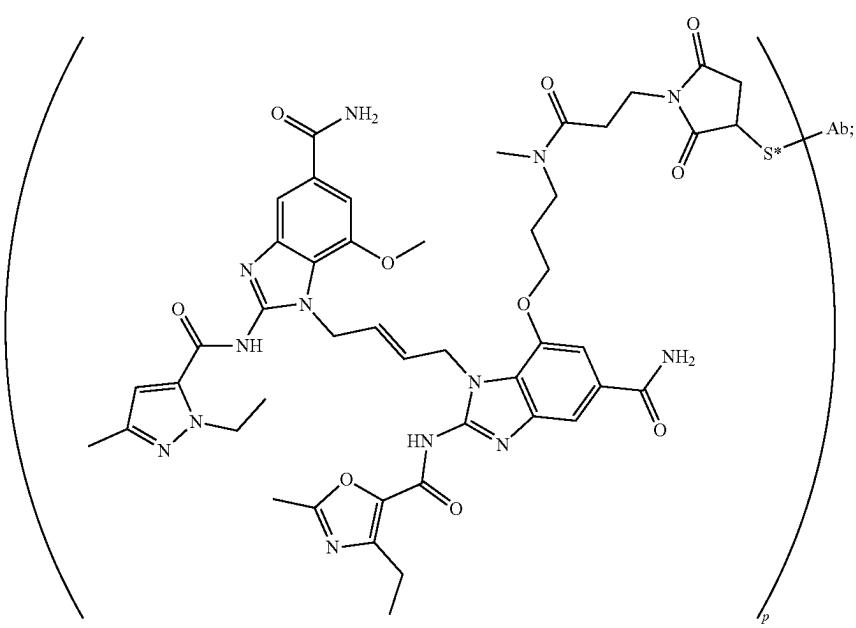
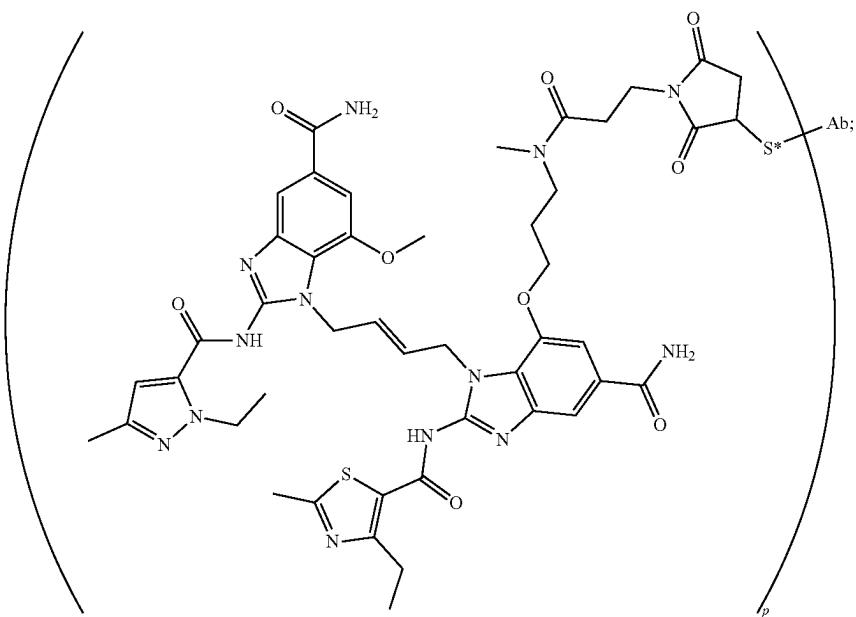
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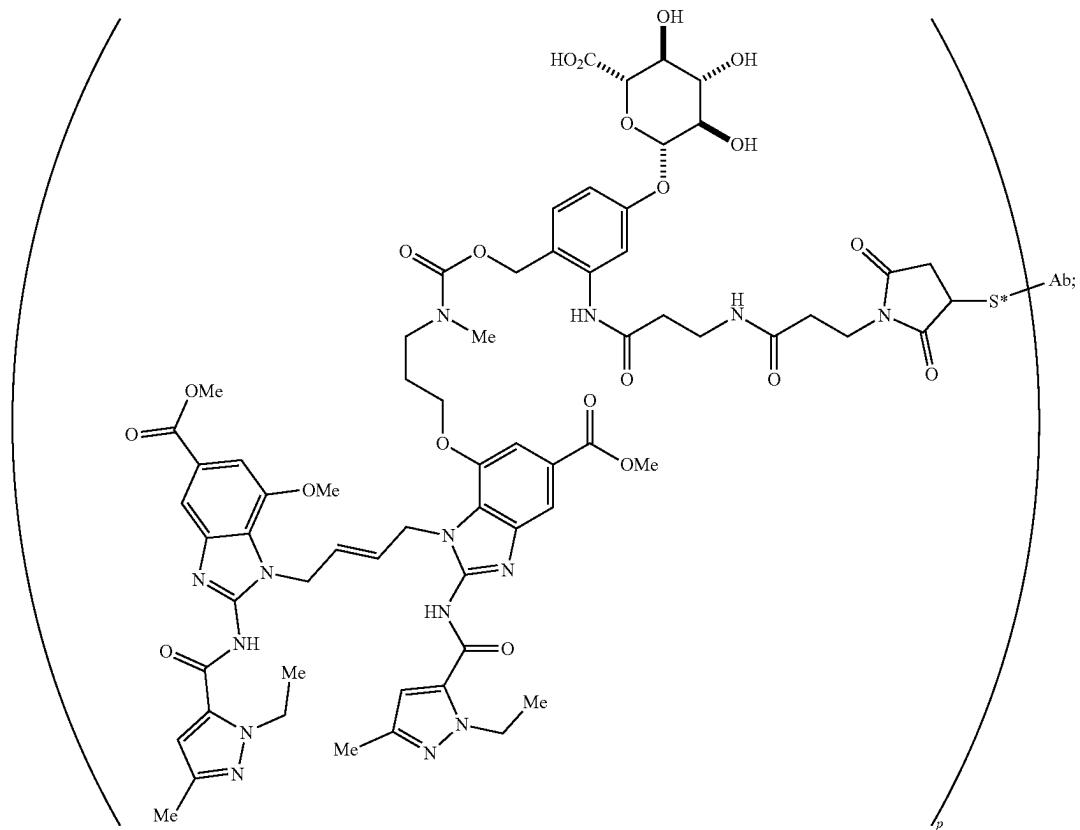
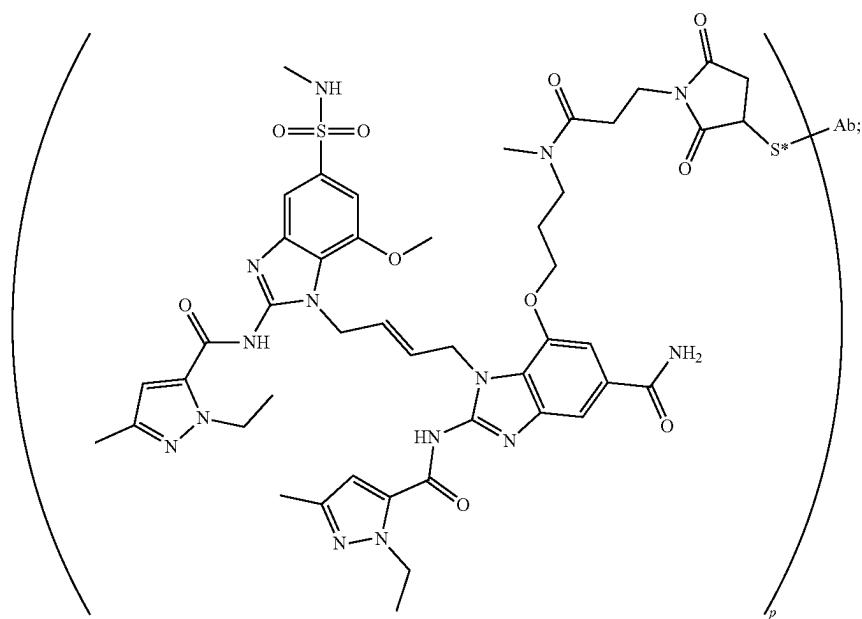
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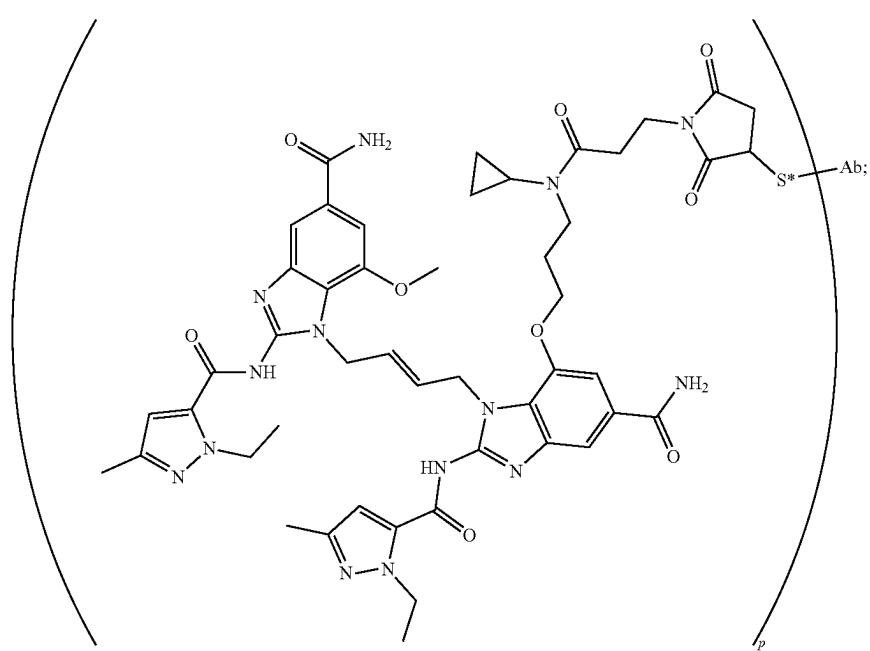
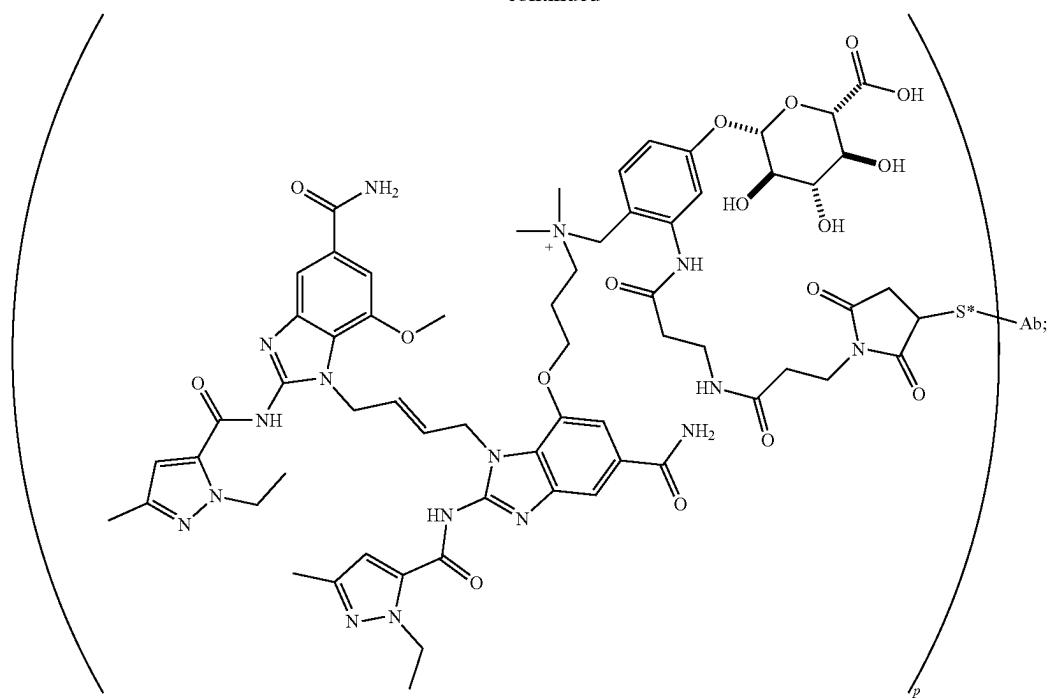
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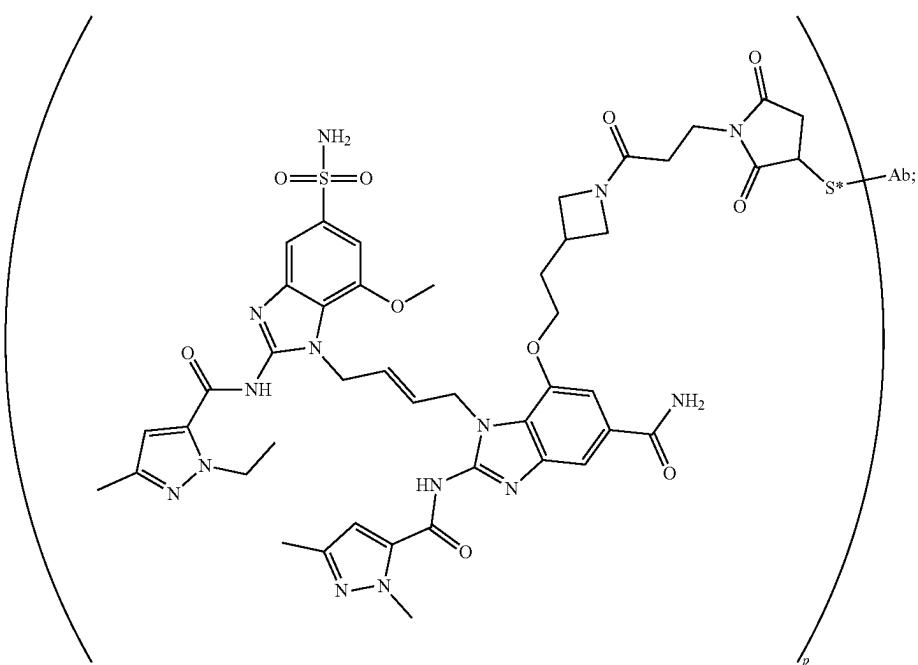
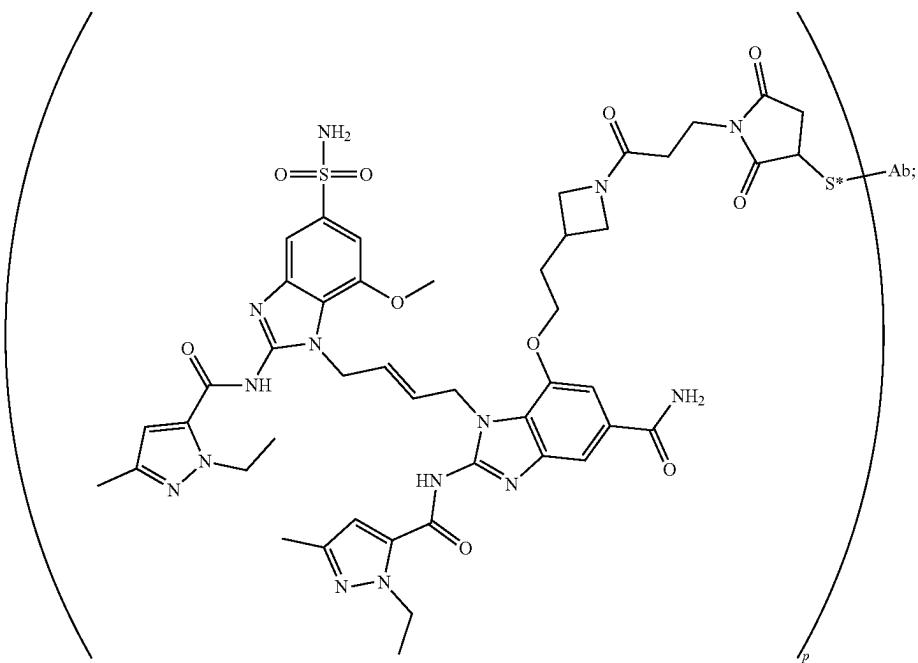
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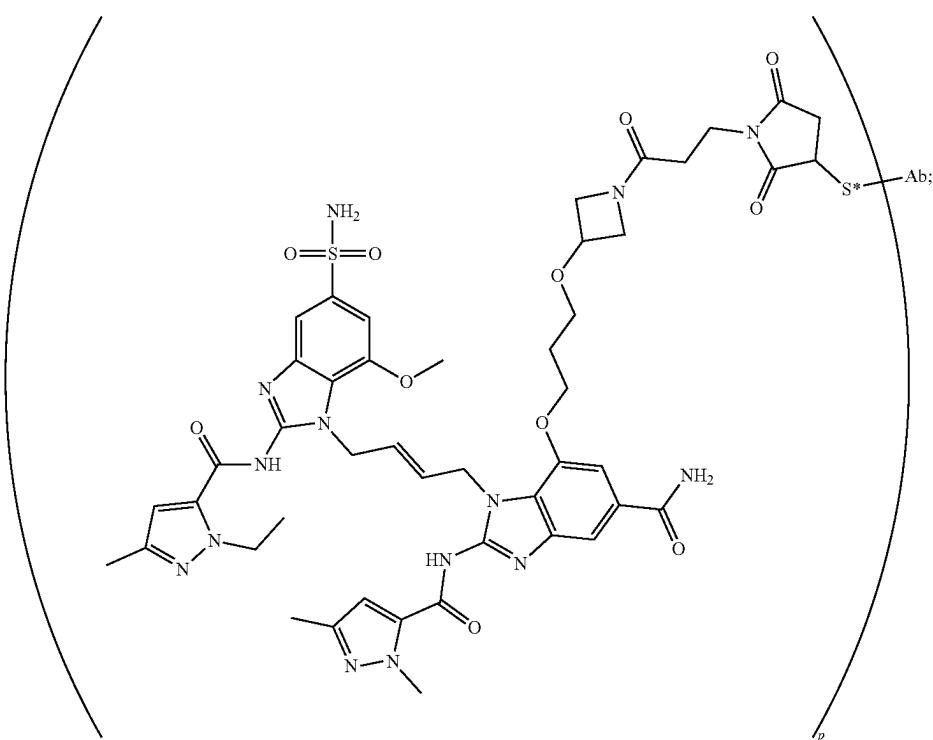
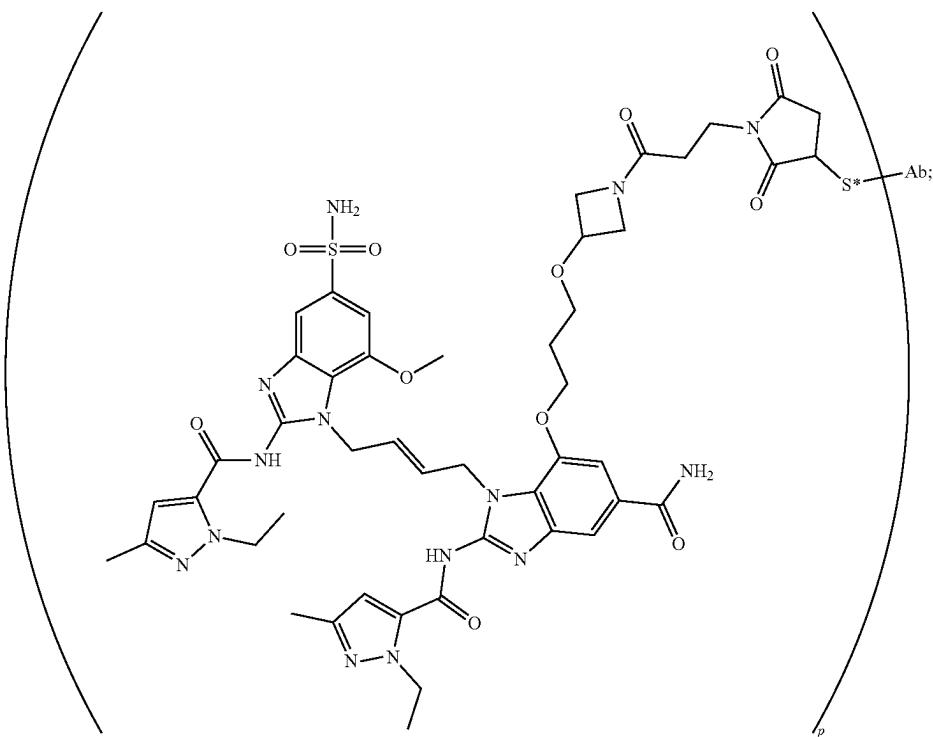
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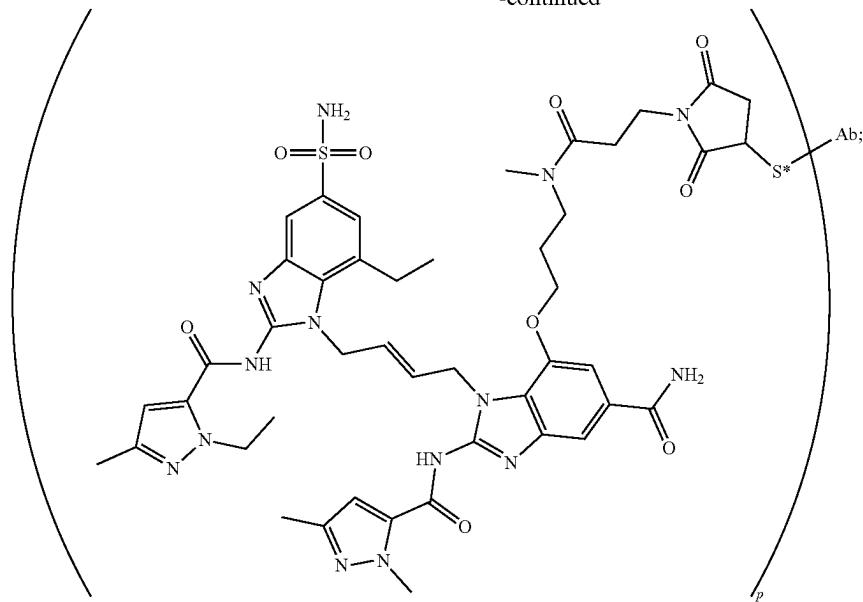
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and pharmaceutically acceptable salts thereof,

[0255] wherein:

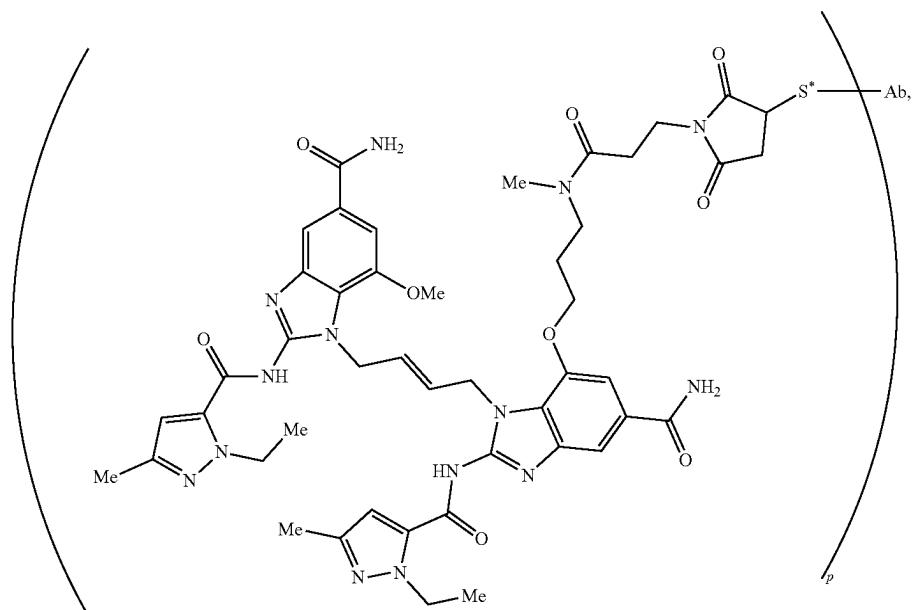
[0256] Ab is an antigen-binding protein or an anti-

gen-binding fragment thereof (e.g., an antibody);

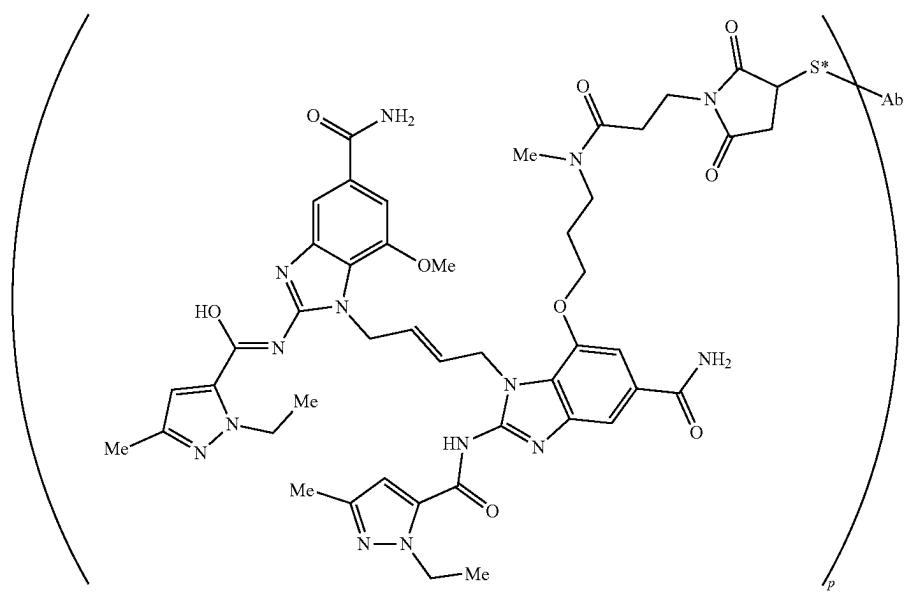
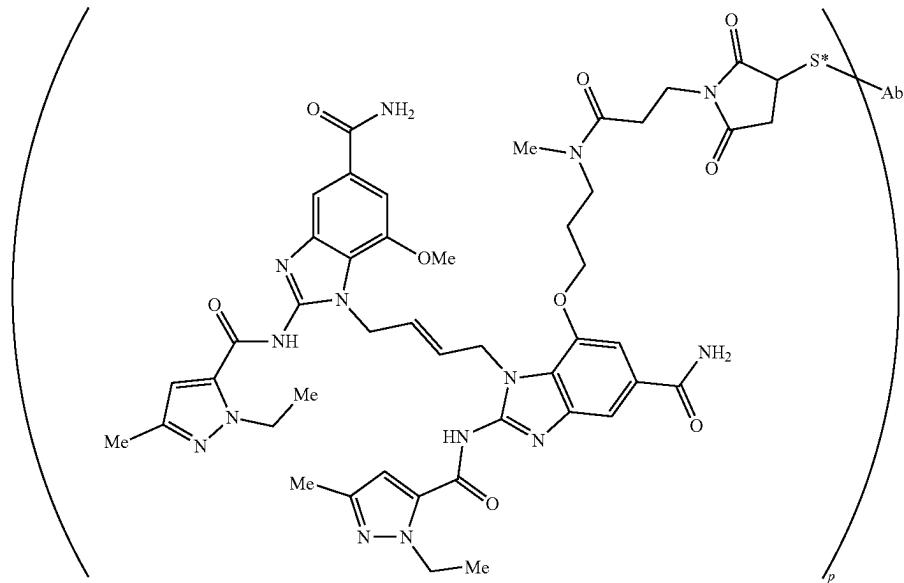
[0257] each S^* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof; and

[0258] each subscript p is independently an integer from 2 to 8.

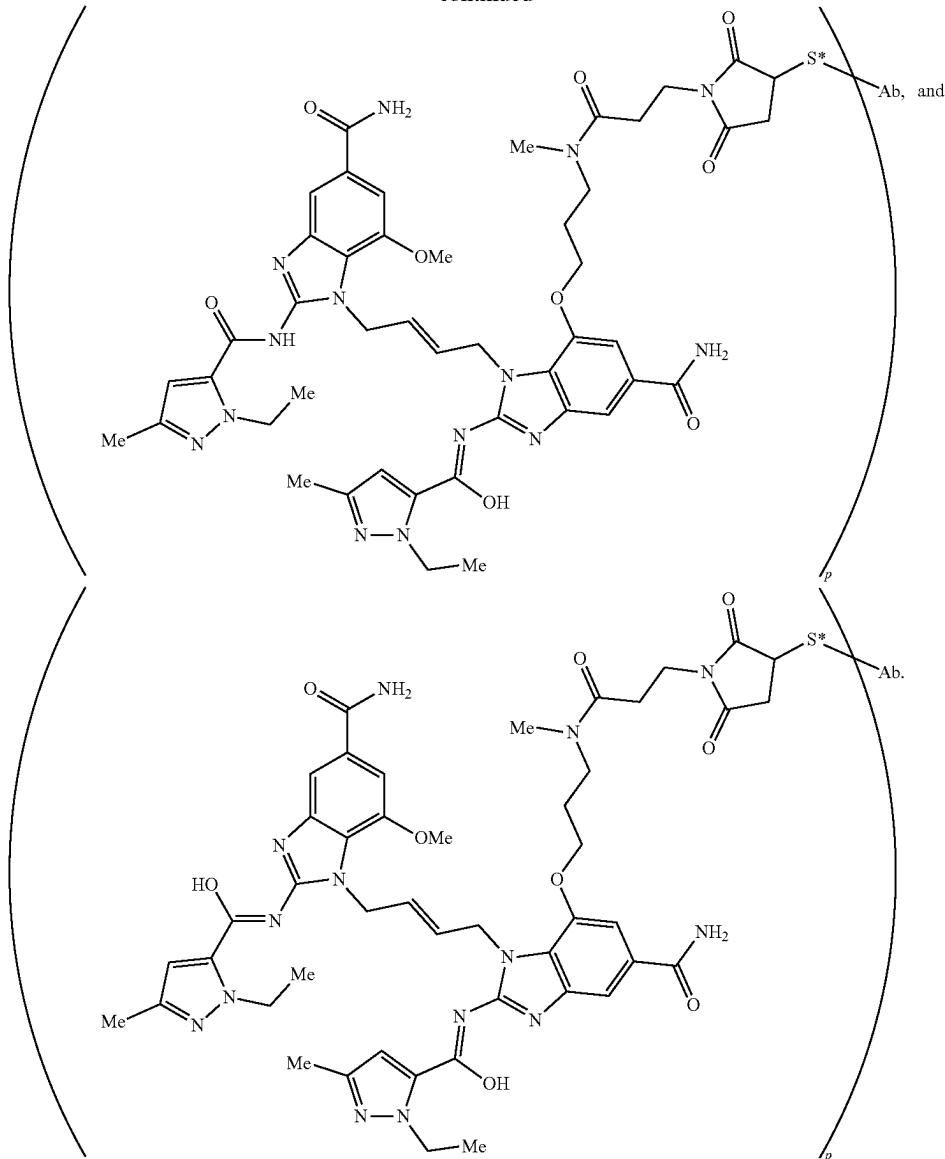
[0259] The structures shown above include all tautomeric forms. Thus, for example, the structure:



is to be understood as encompassing the following tautomeric forms:



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Antigen Binding Proteins and Fragments Thereof (e.g., Antibodies)

[0260] In some embodiments, an antibody is a polyclonal antibody. In some embodiments, an antibody is a monoclonal antibody. In some embodiments, an antibody is chimeric. In some embodiments, an antibody is humanized. In some embodiments, an antibody is fully human. In some embodiments, an antibody is an antigen binding fragment.

[0261] 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.

[0262] 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 protein, a peptide, a carbohydrate, a chemical, nucleic acid, or fragments thereof). In some embodiments, a monoclonal antibody (mAb) to an antigen-of-interest is prepared by using any technique known in the art which provides for the production of antibody molecules by continuous cell lines in culture.

[0263] Useful monoclonal antibodies include, but are not limited to, human monoclonal antibodies, humanized monoclonal antibodies, or chimeric human-mouse (or other spe-

cies) monoclonal antibodies. The antibodies include full-length antibodies and antigen binding fragments thereof. Human monoclonal antibodies may 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).

[0264] In some embodiments, an antibody includes a functionally active fragment, derivative or analog of an antibody that binds specifically to target cells (e.g., cancer cell antigens) or other antibodies bound to cancer cells or matrix. In this regard, “functionally active” means that the fragment, derivative or analog is able to bind specifically to target cells. To determine which CDR sequences bind the antigen, synthetic peptides containing the CDR sequences are typically used in binding assays with the antigen by any 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. Immunol.* 125(3):961-969).

[0265] Additionally, recombinant antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which are typically obtained 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 a constant region derived from a human immunoglobulin. See, e.g., U.S. Pat. Nos. 4,816,567; and 4,816,397, which are incorporated herein by reference in their entirities. Humanized antibodies are antibody molecules from non-human species having one or more CDRs from the non-human species and a framework region from a human immunoglobulin molecule. See, e.g., U.S. Pat. No. 5,585,089, which is incorporated herein by reference in its entirety. In some embodiments, such chimeric and humanized monoclonal antibodies 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. Pat. No. 4,816,567; European Patent Publication No. 012 023; Berter et al., 1988, *Science* 240:1041-1043; Liu et al., 1987, *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu et al., 1987, *J. Immunol.* 139:3521-3526; Sun et al., 1987, *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura et al., 1987, *Cancer. Res.* 47:999-1005; Wood et al., 1985, *Nature* 314:446-449; and Shaw et al., 1988, *J. Natl. Cancer Inst.* 80:1553-1559; Morrison, 1985, *Science* 229:1202-1207; Oi et al., 1986, *BioTechniques* 4:214; U.S. Pat. No. 5,225,539; Jones et al., 1986, *Nature* 321: 522-525; Verhoeven et al., 1988, *Science* 239: 1534; and Beidler et al., 1988, *J. Immunol.* 141:4053-4060; each of which is incorporated herein by reference in its entirety.

[0266] In some embodiments, an antibody is a completely human antibody. In some embodiments, an antibody is produced using transgenic mice that are incapable of expressing endogenous immunoglobulin heavy and light chain genes, but which are capable of expressing human heavy and light chain genes.

[0267] In some embodiments, an antibody is an intact or fully-reduced antibody. The term ‘fully-reduced’ is meant to refer to an antibody in which all four inter-chain disulfide linkages have been reduced to provide eight thiols that can be attached to a linker (L).

[0268] In some embodiments, attachment to an antibody is via thioether, amine, or amide linkages from native and/or engineered cysteine, lysine, or methionine residues, or from an amino acid residue engineered to participate in a cycloaddition reaction (such as a click reaction) with the corresponding linker intermediate. See, e.g., Macrlc, et al., *PLOS One* 2019: 14(1); e0209860. In some embodiments, an antibody is an intact or fully-reduced antibody, or is an antibody bearing an engineered cysteine, lysine, or methionine group that is modified with a functional group that can participate in, for example, click chemistry or other cycloaddition reactions for attachment of other components of the ADC as described herein (e.g., Diels-Alder reactions or other [3+2] or [4+2]cycloadditions).

[0269] Antibodies that bind specifically to a cancer cell antigen are available commercially or produced by any method known to one of skill in the art such as, e.g., chemical synthesis or recombinant expression techniques. The nucleotide sequences encoding antibodies that bind specifically to a cancer cell antigen are obtainable, e.g., from the GenBank database or similar database, literature publications, or by routine cloning and sequencing.

[0270] In some embodiments, the antibody is used for the treatment of a cancer (e.g., an antibody approved by the FDA and/or EMA). Antibodies that bind specifically to a cancer cell antigen are available commercially or produced by any method known to one of skill in the art such as, e.g., recombinant expression techniques. The nucleotide sequences encoding antibodies that bind specifically to a cancer cell antigen are obtainable, e.g., from the GenBank database or similar database, literature publications, or by routine cloning and sequencing.

[0271] In some embodiments, an antibody can bind specifically to a receptor or a receptor complex expressed on lymphocytes. The receptor or receptor complex can comprise 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.

[0272] In some embodiments, an antibody can bind specifically to a cancer cell antigen. It will be understood that the antibody component in an ADC is an antibody in residue form such that “Ab” in the ADC structures described herein incorporates the structure of the antibody.

[0273] Non-limiting examples of antibodies that can be used for treatment of cancer and antibodies that bind specifically to tumor associated antigens are disclosed in Franke, A. E., Sievers, E. L., and Scheinberg, D. A., “Cell surface receptor-targeted therapy of acute myeloid leukemia: a review” *Cancer Biother Radiopharm.* 2000, 15, 459-76; Murray, J. L., “Monoclonal antibody treatment of solid tumors: a coming of age” *Semin Oncol.* 2000, 27, 64-70; Breitling, F., and Dubel, S., *Recombinant Antibodies*, John Wiley, and Sons, New York, 1998, each of which is hereby incorporated by reference in its entirety.

[0274] Embodiments of antibodies that bind to one or more of cancer cell antigens and immune cell antigens are provided below.

[0275] Non-limiting examples of target antigens and associated antibodies useful for the treatment of cancer and antibodies that bind specifically to cancer cell antigens (also called tumor antigens), include B7-DC (e.g., Catalog #PA5-20344); BCMA; B7-H3 (e.g., enoblituzumab, omburtamab, MGD009, MGC018, DS-7300); B7-H4 (e.g., Catalog #14-5949-82); B7-H6 (e.g., Catalog #12-6526-42); B7-H7; C₅ complement (e.g., BCD-148; CAN106); CA-125; CA9 (e.g., girentuximab); CCR8 (e.g., JTX-1811); CLEC12A (e.g., tepoditamab); CSPG4 (e.g., U.S. Pat. No. 10,822,427); CCNB1; DDR1; de2-7 EGFR (e.g., MAb 806); DPEP1; DR4 (e.g., mapatumumab); endosialin (e.g., ontuzumab); ENPP1; EPCAM (e.g., adecatumumab); EPHA2; ERBB2 (e.g., trastuzumab); ERBB3; ERV MER34_1; FAP (e.g., sibrotuzumab); FasL; FGFR2 (e.g., aprutumab); FGFR4 (e.g., MM-161); FLT3 (e.g., 4G8SDIEM); FBP; FucGM1 (e.g., BMS-986012); FZD8; G250; GAGE; GD2 (e.g., dinutuximab); gpNMB (e.g., glembatumumab); GPR87; GUCY2C (e.g., indusatumab); HAVCR2; IDO1; ITGB6; ITGB8; LICAM (e.g., JCAR023); MRC1 (e.g., ThermoFisher Catalog #12-2061-82); ML-IAP (e.g., 88C570, ThermoFisher Catalog #40958); NT5E (e.g., 7G2, ThermoFisher Catalog #41-0200); OY-TES1; p53; p53mutant; PAX5; PDPN (e.g., ThermoFisher Catalog #14-5381-82); VSIR (e.g., ThermoFisher Catalog #PA5-52493); Dectin2 (e.g., ThermoFisher Catalog #MA5-16250); PAX3 (e.g., GT1210, ThermoFisher Catalog #MA5-31583); Sialyl-Thomsen-nouveau-antigen (e.g., Eavarone et al. PLoS One, 2018; 13(7): e0201314); PDGFR-B (e.g., rinucumab); ADAM12 (e.g., Catalog #14139-1-AP); ADAM9 (e.g., IMGC936); AFP (e.g., ThermoFisher Catalog #PA5-25959); AGR2 (e.g., ThermoFisher Catalog #PA5-34517); AKAP-4 (e.g., Catalog #PA5-52230); androgen receptor (e.g., ThermoFisher Catalog #MA5-13426); ALPP (e.g., Catalog #MA5-15652); CD44 (e.g., RG7356); AMHR2 (e.g., ThermoFisher Catalog #PA5-13902); ANTXR1 (e.g., Catalog #MA1-91702); ARTN (e.g., ThermoFisher Catalog #PA5-47063); av06; CA19-9 (e.g., AbGn-7; MVT-5873); carcinoembryonic antigen (e.g., arcitumomab; cergutuzumab; amunaleukin; labetuzumab); CD115 (e.g., axatilimab; cabralizumab; emactuzumab); CD137 (e.g., ADG106; CTX-471); CD147 (e.g., gavilimomab; metuzumab); CD155 (e.g., U.S. Publication No. 2018/0251548); CD274 (e.g., adebrelimab; atezolizumab; gavrilimumab); CDCP1 (e.g., RG7287); CDH3 (e.g., PCA062); CDH6 (e.g., HKT288); CEACAM1; CEACAM6; CLDN18.1 (e.g., zolbetuximab); CLDN18.2 (e.g., zolbetuximab); CLPTM1L; CS-1 (e.g., tigatuzumab); GD3 (e.g., mitumomab); HLA-G (e.g., TTX-080); IL1RAP (e.g., nidanilimab); LAG-3 (e.g., encelimab); LY6G6D (e.g., PA5-23303); LYPD1 (e.g., ThermoFisher Catalog #PA5-26749); MAD-CT-2; MAGEA3 (e.g., ThermoFisher Catalog #60054-1-IG); MAGEA4 (e.g., Catalog #MA5-26117); MAGEC2 (e.g., ThermoFisher Catalog #PA5-64010); MLANA (e.g., Catalog #MA5-15237); MELTF (e.g., ThermoFisher Catalog #H00004241-M04A); MSLN (e.g., 5B2, Catalog #MA5-11918); MUC1 (e.g., MH1 (CT2), ThermoFisher Catalog #MA5-11202); MUC5AC (e.g., 45M1, Catalog #MA5-12178); MYCN (e.g., NCM-II 100, ThermoFisher Catalog #MA1-170); NCAM1 (e.g., ThermoFisher Catalog #MA5-11563); Nectin-4 (e.g., enfurtagomab); NY-BR-1 (e.g., NY-BR-1 No. 2, Catalog #MA5-12645); PSMA (e.g., BAY 2315497); PSA (e.g., ThermoFisher Catalog #PA1-38514; Daniels-Wells et al. BMC Cancer, 2013; 13:195); PSCA (e.g., AGS-1C4D4);

PTK7 (e.g., cofetuzumab); PVRIG; Ras mutant (e.g., Shin et al. Sci Adv. 2020; 6(3):eaay2174); RET (e.g., WO2020210551); RGS5 (e.g., TF-TA503075); RhoC (e.g., ThermoFisher Catalog PA5-77866); ROR2 (e.g., BA3021); ROS1 (e.g., WO2019107671); SART3 (e.g., TF 18025-1-AP); SLC12A2 (e.g., ThermoFisher Catalog #13884-1-AP); SLC38A1 (e.g., ThermoFisher Catalog #12039-1-AP); SLC39A6 (e.g., ladiratuzumab); SLC44A4 (e.g., ASG-5ME); SLC7A11 (e.g., ThermoFisher Catalog #PA1-16893); SLITRK6 (e.g., sirtratumab); SSX2 (e.g., ThermoFisher Catalog #MA5-24971); survivin (e.g., PA1-16836); TACSTD2 (e.g., PA5-47074); TAG-72 (e.g., MA1-25956); TIGIT (e.g., etigilimab); TM4SF5 (e.g., 18239-1-AP); TMPRSS11D (e.g., PA5-30927); TNFRSF12 (e.g., BAY-356); TRAIL (e.g., Catalog #12-9927-42); Trem2 (e.g., PY314); TRP-2 (e.g., PA5-52736); uPAR (e.g., ATN-658); UPK1B (e.g., ThermoFisher Catalog #PA5-56863); UPK2 (e.g., ThermoFisher Catalog #PA5-60318); UPK3B (e.g., ThermoFisher Catalog #PA5-52696); VEGF (e.g., GNR-011); VEGFR2 (e.g., gentuximab); CD44 (e.g., RG7356); WT1 (e.g., ThermoFisher Catalog #MA5-32215); XAGE1 (e.g., ThermoFisher Catalog #PA5-46413); CTLA4 (e.g., ipilimumab); Sperm protein 17 (e.g., BS-5754R); TLR2/4/1 (e.g., tomoralinab); B7-1 (e.g., galiximab); ANXA1 (e.g., Catalog #71-3400); BCR-ABL; CAMPATH-1 (e.g., alemtuzumab; ALLO-647; ANT1034); CD123 (e.g., BAY-943; CSL360); CD19 (e.g., ALLO-501); CD20 (e.g., divozilimab; ibritumomab); CD30 (e.g., iratuzumab); CD33 (e.g., lintuzumab; BI 836858; AMG 673); CD352 (e.g., SGN-CD352A); CD37 (e.g., ililotomab; GEN3009); CD40 (e.g., dacetuzumab; lucatumumab); CD45 (e.g., apamistamab); CD48 (e.g., SGN-CD48A); CXCR4 (e.g., ulotropilumab); ETV6-AML (e.g., Catalog #PA5-81865); ROR1 (e.g., cirmituzumab); CD74 (e.g., milatuzumab); SIT1 (e.g., PA5-53825); SLAMF7 (e.g., Elotuzumab); Axl (e.g., BA3011; tilvestamab); Siglecs 1-16 (see, e.g., Angata et al. Trends Pharmacol Sci. 2015; 36(10): 645-660); SIRPa (e.g., Catalog #17-1729-42); SIRPg (e.g., PA5-104381); OX40 (e.g., ABM193); PROM1 (e.g., Catalog #14-1331-82); TMEM132A (e.g., Catalog #PA5-62524); TMEM40 (e.g., PA5-60636); PD-1 (e.g., balstilimab; budigalimab; geptanolimab); ALK (e.g., DLX521); CCR4 (e.g., AT008; mogamulizumab-kpck); CD27 (e.g., varlilumab); CD278 (e.g., feladilimab; vopratelimab); CD32 (e.g., mAb 2B6); CD47 (e.g., letaplimab; magrolimab); and CD70 (e.g., cusatuzumab).

[0276] In some embodiments, an antibody can bind specifically to a cancer cell antigen associated with a solid tumor and/or a hematological cancer. Non-limiting examples of target antigens and associated antibodies that bind specifically to cancer cell antigens associated with a solid tumor and/or a hematological cancer target antigen include Axl (e.g., BA3011; tilvestamab); B7-H3 (e.g., enoblituzumab, omburtamab, MGD009, MGC018, DS-7300); B7-H4 (e.g., Catalog #14-5949-82); B7-H6 (e.g., Catalog #12-6526-42); B7-H7; Siglecs 1-16 (see, e.g., Angata et al. Trends Pharmacol Sci. 2015; 36(10): 645-660); SIRPa (e.g., Catalog #17-1729-42); SIRPg (e.g., PA5-104381); OX40 (e.g., ABM193); PROM1 (e.g., Catalog #14-1331-82); TMEM132A (e.g., Catalog #PA5-62524); TMEM40 (e.g., PA5-60636); PD-1 (e.g., balstilimab; budigalimab; geptanolimab); ALK (e.g., DLX521); CCR4 (e.g., AT008; mogamulizumab-kpck); CD27 (e.g., varlilumab);

CD278 (e.g., feladilimab; vopratelimab); CD32 (e.g., mAb 2B6); CD47 (e.g., letaplimab; magrolimab); and CD70 (e.g., cusatuzumab).

[0277] In some embodiments, an antibody can bind specifically to a cancer cell antigen associated with a solid tumor. Non-limiting examples of target antigens and associated antibodies that bind specifically to solid-tumor-associated target antigens include PAX3 (e.g., GT1210, ThermoFisher Catalog #MA5-31583); Sialyl-Thomsen-nouveau-antigen (e.g., Eavarone et al. *PLoS One.* 2018; 13(7): e0201314); PDGFR-B (e.g., rinucumab); ADAM12 (e.g., Catalog #14139-1-AP); ADAM9 (e.g., IMGC936); AFP (e.g., ThermoFisher Catalog #PA5-25959); AGR2 (e.g., ThermoFisher Catalog #PA5-34517); AKAP-4 (e.g., Catalog #PA5-52230); androgen receptor (e.g., ThermoFisher Catalog #MA5-13426); ALPP (e.g., Catalog #MA5-15652); CD44 (e.g., RG7356); AMHR2 (e.g., ThermoFisher Catalog #PA5-13902); ANTXR1 (e.g., Catalog #MA1-91702); ARTN (e.g., ThermoFisher Catalog #PA5-47063); cv β 6; CA19-9 (e.g., AbGn-7; MVT-5873); carcinoembryonic antigen (e.g., arcitumomab; cergutuzumab; amunaleukin; labetuzumab); CD115 (e.g., axatilimab; cabiralizumab; emactuzumab); CD137 (e.g., ADG106; CTX-471); CD147 (e.g., gavilimomab; Metuzumab); CD155 (e.g., U.S. Publication No. 2018/0251548); CD274 (e.g., adebrelimab; atezolizumab; garivulimab); CDCP1 (e.g., RG7287); CDH3 (e.g., PCA062); CDH6 (e.g., HKT288); CEACAM1; CEACAM6); CLDN18.1 (e.g., zolbetuximab); CLDN18.2 (e.g., zolbetuximab); CLPTM1L; CS-1 (e.g., tigatuzumab); GD3 (e.g., mitumomab); HLA-G (e.g., TTX-080); IL1RAP (e.g., nidanilimab); LAG-3 (e.g., encelimab); LY6G6D (e.g., PA5-23303); LYPD1 (e.g., ThermoFisher Catalog #PA5-26749); MAD-CT-2; MAGEA3 (e.g., ThermoFisher Catalog #60054-1-IG); MAGEA4 (e.g., Catalog #MA5-26117); MAGEC2 (e.g., ThermoFisher Catalog #PA5-64010); MLANA (e.g., Catalog #MA5-15237); MELTF (e.g., ThermoFisher Catalog #H00004241-M04A); MSLN (e.g., 5B2, Catalog #MA5-11918); MUC1 (e.g., MH1 (CT2), ThermoFisher Catalog #MA5-11202); MUC5AC (e.g., 45M1, Catalog #MA5-12178); MYCN (e.g., NCM-II 100, ThermoFisher Catalog #MA1-170); NCAM1 (e.g., ThermoFisher Catalog #MA5-11563); Nectin-4 (e.g., enfortumab); NY—BR-1 (e.g., NY—BR-1 No. 2, Catalog #MA5-12645); PSMA (e.g., BAY 2315497); PSA (e.g., ThermoFisher Catalog #PA1-38514; Daniels-Wells et al. *BMC Cancer* 2013; 13:195); PSCA (e.g., AGS-1C₄D4); PTK7 (e.g., cofetuzumab); PVRIG; Ras mutant (e.g., Shin et al. *Sci Adv.* 2020; 6(3):eaay2174); RET (e.g., WO2020210551); RGS5 (e.g., TF-TA503075); RhoC (e.g., ThermoFisher Catalog PA5-77866); ROR2 (e.g., BA3021); ROS1 (e.g., WO2019107671); SART3 (e.g., TF 18025-1-AP); SLC12A2 (e.g., ThermoFisher Catalog #13884-1-AP); SLC38A1 (e.g., ThermoFisher Catalog #12039-1-AP); SLC39A6 (e.g., ladiratuzumab); SLC44A4 (e.g., ASG-5ME); SLC7A11 (e.g., ThermoFisher Catalog #PA1-16893); SLTRK6 (e.g., sirtratumab); SSX2 (e.g., ThermoFisher Catalog #MA5-24971); survivin (e.g., PA1-16836); TACSTD2 (e.g., PA5-47074); TAG-72 (e.g., MA1-25956); TIGIT (e.g., etigilimab); TM4SF5 (e.g., 18239-1-AP); TMPRSS11D (e.g., PA5-30927); TNFRSF12 (e.g., BAY-356); TRAIL (e.g., Catalog #12-9927-42); Trem2 (e.g., PY314); TRP-2 (e.g., PA5-52736); uPAR (e.g., ATN-658); UPK1B (e.g., ThermoFisher Catalog #PA5-56863); UPK2 (e.g., ThermoFisher Catalog #PA5-60318); UPK3B (e.g.,

ThermoFisher Catalog #PA5-52696); VEGF (e.g., GNR-011); VEGFR2 (e.g., gentuximab); CD44 (e.g., RG7356); WT1 (e.g., ThermoFisher Catalog #MA5-32215); XAGE1 (e.g., ThermoFisher Catalog #PA5-46413); and CTLA4 (e.g., ipilimumab).

[0278] In some embodiments, an antibody can bind specifically to a cancer cell antigen associated with a hematological cancer. Non-limiting examples of target antigens and associated antibodies that bind specifically to hematological cancer cell target antigens include Sperm protein 17 (e.g., BS-5754R); TLR2/4/1 (e.g., Tomaralimab); B7-1 (e.g., galiximab); ANXA1 (e.g., Catalog #71-3400); BCR-ABL; CAMPATH-1 (e.g., alemtuzumab; ALLO-647; ANT1034); CD123 (e.g., BAY-943; CSL360); CD19 (e.g., ALLO-501); CD20 (e.g., divozilimab; ibritumomab); CD30 (e.g., iratumumab); CD33 (e.g., lintuzumab; BI 836858; AMG 673); CD352 (e.g., SGN-CD352A); CD37 (e.g., liilotomab; GEN3009); CD40 (e.g., dacetuzumab; lucatumumab); CD45 (e.g., apamistamab); CD48 (e.g., SGN-CD48A); CXCR4 (e.g., ulocuplumab); ETV6-AML (e.g., Catalog #PA5-81865); ROR1 (e.g., cirmtuzumab); CD74 (e.g., milatuzumab); SIT1 (e.g., PA5-53825); and SLAMF7 (e.g., elotuzumab).

[0279] In some embodiments, an antibody is used that binds specifically to a target antigen (e.g., an antigen associated with a disease or disorder). Antibodies that bind specifically to a target antigen (e.g., an antigen associated with a disease or disorder) are available commercially or are produced by any method known to one of skill in the art such as, e.g., recombinant expression techniques. The nucleotide sequences encoding antibodies that bind specifically to a target antigen (e.g., an antigen associated with a disease or disorder) are obtainable, e.g., from the GenBank database or similar database, literature publications, or by routine cloning and sequencing.

[0280] Non-limiting examples of target antigens and associated antibodies that bind specifically to target antigens (e.g., an antigen associated with a disease or disorder, or an antigen associated with an immune cell) include CD163 (e.g., TBI 304H); TIGIT (e.g., etigilimab); DCSIGN (see, e.g., International Publication No. WO2018134389); IFNAR1 (e.g., faralimomab); ASCT2 (e.g., idactamab); ULBP1/2/3/4/5/6 (e.g., PA5-82302); CLDN1 (e.g., INSERM anti-Claudin-1); CLDN2 (see, e.g., International Publication No. WO2018123949); IL-21R (e.g., PF-05230900); DCIR; DCLK1 (see, e.g., International Publication No. WO2018222675); Dectin1 (see, e.g., U.S. Pat. No. 9,045,542); GITR (e.g., ragifilimab); ITGAV (e.g., abituzumab); LY9 (e.g., PA5-95601); MICA (e.g., 1E2C8, Catalog #66384-1-IG); MICB (e.g., Catalog #MA5-29422); NOX1 (e.g., Catalog #PA5-103220); CD2 (e.g., BTI-322; siplizumab); CD247 (e.g., AFM15); CD25 (e.g., basiliximab); CD28 (e.g., REGN5668); CD3 (e.g., otelixizumab; visilizumab); CD38 (e.g., felzartamab; AMG 424); CD3E (e.g., foralumab; teplizumab); CD5 (e.g., MAT 304; zolimomab aritox); ALPPL2 (e.g., Catalog #PA5-22336); B7-2 (e.g., Catalog #12-0862-82); B7-H3 (e.g., enoblituzumab, omburtamab, MGD009, MGC018, DS-7300); B7-H4 (e.g., Catalog #14-5949-82); B7-H6 (e.g., Catalog #12-6526-42); B7-H7; BAFF-R (e.g., Catalog #14-9117-82); BMPR2; BORIS; CD112 (see, e.g., U.S. Publication No. 20100008928); CD24 (see, e.g., U.S. Pat. No. 8,614,301); CD244 (e.g., R&D AF1039); CD30L (see, e.g., U.S. Pat. No. 9,926,373); CD3D; CD3G; CD79A (see, e.g., Interna-

tional Publication No. WO 2020252110); CD83 (e.g., CBT004); CD97; CDH17 (see, e.g., International Publication No. WO 2018115231); CLDN16; CLDN19; CYP1B1; DPEP3; DPP4; DSG2 (see, e.g., U.S. Pat. No. 10,836,823); EPHA receptors; epidermal growth factor; FAS; FGFR1 (e.g., RG7992); FGFR3 (e.g., vofatamab); FN1; FOLR1 (e.g., farletuzumab); FSHR; FZD5; GM2 (e.g., BIW-8962); GM3 (e.g., racotumomab); GPA33 (e.g., KRN330); GPC3 (e.g., codrituzumab); HAS3; HLA-E; HLA-F; HLA-DR; ICAM1; IFNAR2; IL13Ra2; IL-5R (e.g., benralizumab); KISS1R; LAMPI; LAYN; LCK; legumain; LILRB2; LILRB4; LMP2; MAD-CT-1; MAGEA1 (e.g., Catalog #MA5-11338); MerTk (e.g., DS5MMER, Catalog #12-5751-82); MFSD13A; hTERT; gp100; Fas-related antigen 1; a metalloproteinase; Mincle (e.g., OTI2A8, Catalog #TA505101); NA17; NY-ESO-1 (e.g., E978m, Catalog #35-6200); polysialic acid (see, e.g., Watzlawik et al. *J Nat Sci.* 2015; 1(8):e141); PR1; Sarcoma translocation breakpoints; SLC10A2 (e.g., ThermoFisher Catalog #PA5-18990); SLC17A2 (e.g., ThermoFisher Catalog #PA5-106752); SLC39A5 (e.g., ThermoFisher Catalog #MA5-27260); SLC6A15 (e.g., ThermoFisher Catalog #PA5-52586); SLC6A6 (e.g., ThermoFisher Catalog #PA5-53431); SLC7A5; and CALCR (see, e.g., International Publication No. WO 2015077826).

[0281] In some embodiments, an antibody can bind specifically to an antigen associated with anemia. A non-limiting example of an antibody that binds specifically to an antigen associated with anemia includes CD163 (e.g., TBI-304H).

[0282] In some embodiments, an antibody can bind specifically to an antigen associated with a viral infection. Non-limiting examples of target antigens and associated antibodies that binds specifically to an antigen associated with a viral infection include DCSIGN (see, e.g., International Publication No. WO2018134389); IFNAR1 (e.g., faralimomab); ASCT2 (e.g., idactamab); ULBP1/2/3/4/5/6 (e.g., PA5-82302); and CLDN1 (e.g., INSERM anti-Claudin-1).

[0283] In some embodiments, an antibody can bind specifically to an antigen associated with an autoimmune disease. Non-limiting examples of target antigens and associated antibodies that bind specifically to an antigen associated with an autoimmune disease include CLDN2 (see, e.g., International Publication No. WO 2018123949); IL-21R (e.g., PF-05230900); DCIR; DCLK1 (see, e.g., WO2018222675); Dectin1 (see, e.g., U.S. Pat. No. 9,045,542); GITR (e.g., ragifilimab); ITGAV (e.g., abituzumab); LY9 (e.g., PA5-95601); MICA (e.g., 1E2C8, Catalog #66384-1-IG); MICB (e.g., Catalog #MA5-29422); NOX1 (e.g., Catalog #PA5-103220); CD2 (e.g., BTI-322; siplizumab); CD247 (e.g., AFM15); CD25 (e.g., basiliximab); CD28 (e.g., REGN5668); CD3 (e.g., oteziximab; visilizumab); CD38 (e.g., felzartamab; AMG 424); CD3E (e.g., foralumab; teplizumab); and CD5 (e.g., MAT 304; zolimumab artox).

[0284] In some embodiments, the antibody is a non-targeted antibody, for example, a non-binding or control antibody. 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 80%, at least 85%, at least 90%, 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: 7 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 96%, at least 97%, at least 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.

[0285] 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 of SEQ ID NOS: 12, 13, 14, 15, 16, and 17, respectively. 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 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 18 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 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 19. In some embodiments, the anti-EphA2 antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 20 or SEQ ID NO: 21 and a light chain comprising the amino acid sequence of SEQ ID NO: 22. In some embodiments, the anti-EphA2 antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 23 or SEQ ID NO: 24 and a light chain comprising the amino acid sequence of SEQ ID NO: 25. In some embodiments, the anti-EphA2 antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 26 or SEQ ID NO: 27 and a light chain comprising the amino acid sequence of SEQ ID NO: 28. In some embodiments, the antibody is h1C1 or 1C1.

[0286] In some embodiments, the target antigen of an ADC disclosed herein is CD228. In some embodiments, the antigen-binding protein or an antigen-binding fragment thereof is hL49 HALC hlgG1. In some embodiments, the antigen-binding protein or an antigen-binding fragment thereof comprises the following 6 CDRs:

[0287] an CDR-11 comprising the amino acid sequence of SEQ ID NO: 29;

[0288] an CDR-H2 comprising the amino acid sequence of SEQ ID NO: 30;

[0289] an CDR-H3 comprising the amino acid sequence of SEQ ID NO: 31;

[0290] an CDR-L1 comprising the amino acid sequence of SEQ ID NO: 32;

[0291] an CDR-L2 comprising the amino acid sequence of SEQ ID NO: 33; and

[0292] an CDR-L3 comprising the amino acid sequence of SEQ ID NO: 34.

[0293] In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 35 and the VL has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 36. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 35 and the VL comprises the amino acid sequence of SEQ ID NO: 36. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 37 or SEQ ID NO: 38 and an LC comprising the amino acid sequence of SEQ ID NO: 39. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 40 or SEQ ID NO: 41 and an LC comprising the amino acid sequence of SEQ ID NO: 42.

[0294] In some embodiments, the target antigen of an ADC disclosed herein is $\alpha v \beta 6$. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof is h2A2 HCLG hIgG1. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises the following 6 CDRs:

[0295] an CDR-H1 comprising the amino acid sequence of SEQ ID NO: 43;

[0296] an CDR-H2 comprising the amino acid sequence of SEQ ID NO: 44;

[0297] an CDR-H3 comprising the amino acid sequence of SEQ ID NO: 45;

[0298] an CDR-L1 comprising the amino acid sequence of SEQ ID NO: 46;

[0299] an CDR-L2 comprising the amino acid sequence of SEQ ID NO: 47; and

[0300] an CDR-L3 comprising the amino acid sequence of SEQ ID NO: 48.

[0301] In some embodiments, the antigen binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 49 and the VL has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 50. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 49 and the VL comprises the amino acid sequence of SEQ ID NO: 50. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 51 or SEQ ID NO: 52 and an LC comprising the amino acid sequence of SEQ ID NO: 53. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 54 or SEQ ID NO: 55 and an LC comprising the amino acid sequence of SEQ ID NO: 56.

[0302] In some embodiments, the target antigen of an ADC disclosed herein is B7-H4. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof is B7H41001 hIgG1. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises the following 6 CDRs:

[0303] an CDR-H1 comprising the amino acid sequence of SEQ ID NO: 57;

[0304] an CDR-H2 comprising the amino acid sequence of SEQ ID NO: 58;

[0305] an CDR-H3 comprising the amino acid sequence of SEQ ID NO: 59;

[0306] an CDR-L1 comprising the amino acid sequence of SEQ ID NO: 60;

[0307] an CDR-L2 comprising the amino acid sequence of SEQ ID NO: 61; and

[0308] an CDR-L3 comprising the amino acid sequence of SEQ ID NO: 62.

[0309] In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 63 and the VL has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 64. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 63 and the VL comprises the amino acid sequence of SEQ ID NO: 64. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 65 or SEQ ID NO: 66 and an LC comprising the amino acid sequence of SEQ ID NO: 67. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 68 or SEQ ID NO: 69 and an LC comprising the amino acid sequence of SEQ ID NO: 70.

[0310] In some embodiments, the antigen-binding protein or antigen-binding fragment thereof is selected from the group consisting of B7H4-15461, B7H4-20500, B7H4-20501, B7H4-20502.1, B7H4-22208, B7H4-15462, B7H4-22213, B7H4-15465, B7H4-20506, B7H4-15483, B7H4-20513, B7H4-22216, B7H4-15489, B7H4-20516, B7H4-15472, B7H4-15503, B7H4-15495, B7H4-15478, B7H4-15441, and B7H4-20496. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises VH CDR1, VH CDR2, VH CDR3 and VL CDR1, VL CDR2, and VL CDR3 sequences selected from the group consisting of:

[0311] (a) SEQ ID NOS: 71-76, respectively;

[0312] (b) SEQ ID NOS: 79-84, respectively;

[0313] (c) SEQ ID NOS: 87-92, respectively;

[0314] (d) SEQ ID NOS: 95-100, respectively;

[0315] (e) SEQ ID NOS: 103-108, respectively;

[0316] (f) SEQ ID NOS: 111-116, respectively;

[0317] (g) SEQ ID NOS: 119-124, respectively;

[0318] (h) SEQ ID NOS: 127-132, respectively;

[0319] (i) SEQ ID NOS: 135-140, respectively;

[0320] (j) SEQ ID NOS: 143-148, respectively;

[0321] (k) SEQ ID NOS: 151-156, respectively;

[0322] (l) SEQ ID NOS: 159-164, respectively;

[0323] (m) SEQ ID NOS: 167-172, respectively;

[0324] (n) SEQ ID NOS: 175-180, respectively;

- [0325] (o) SEQ ID NOs: 183-188, respectively;
- [0326] (p) SEQ ID NOs: 191-196, respectively;
- [0327] (q) SEQ ID NOs: 199-204, respectively;
- [0328] (r) SEQ ID NOs: 207-212, respectively;
- [0329] (s) SEQ ID NOs: 215-220, respectively; and
- [0330] (t) SEQ ID NOs: 223-228, respectively.

[0331] In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 77, 85, 93, 101, 109, 117, 125, 133, 141, 149, 157, 165, 173, 181, 189, 197, 205, 213, 221, and 229 and the VL has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 78, 86, 94, 102, 110, 118, 126, 134, 142, 150, 158, 166, 174, 182, 190, 198, 206, 214, 222, and 230, respectively. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH has an amino acid sequence selected from the group consisting of SEQ ID NOs: 77, 85, 93, 101, 109, 117, 125, 133, 141, 149, 157, 165, 173, 181, 189, 197, 205, 213, 221, and 229 and the VL has an amino acid sequence selected from the group consisting of SEQ ID NOs: 78, 86, 94, 102, 110, 118, 126, 134, 142, 150, 158, 166, 174, 182, 190, 198, 206, 214, 222, and 230, respectively. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, and 269 and an LC comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, and 270, respectively.

[0332] In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises CDR, VH, VL, HC, and LC sequences having at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity

to the amino acid sequence of SEQ ID NOs 271-1032. In some embodiments, the antigen-binding protein or antigen-binding fragment thereof comprises CDR, VH, VL, HC, and LC amino acid sequences according to SEQ ID NOs 271-1032.

[0333] In some embodiments, antigen binding proteins (ABPs), including antigen binding fragments thereof, (e.g., antibodies and antigen binding fragments thereof) that bind CD228, $\alpha\text{v}\beta 6$, B7-H4, EphA2, or CD30 are provided herein. The antigen binding proteins and fragments contain an antigen binding domain that specifically binds to CD228, $\alpha\text{v}\beta 6$, B7-H4, EphA2, or CD30, including to human CD228, $\alpha\text{v}\beta 6$, B7-H4, EphA2, or CD30. In some embodiments, anti-CD228, anti- $\alpha\text{v}\beta 6$, anti-B7-H4, anti-EphA2, or anti-CD30 antibody-drug conjugates (ADCs) comprise an anti-CD228, anti- $\alpha\text{v}\beta 6$, anti-B7-H4, anti-EphA2, or anti-CD30 ABP as described above conjugated to a drug-linker described herein. In some embodiments, these anti-CD228 ADCs are used to treat CD228-expressing cancers such as melanoma, pancreatic cancer, mesothelioma, colorectal cancer, lung cancer, thyroid cancer, breast cancer, cholangiocarcinoma, esophageal cancer and head and neck cancer. In some embodiments, these anti-B7-H4 ADCs are used to treat B7-H4-expressing cancers such as breast cancer, ovarian cancer, lung cancer, endometrial cancer, cholangiocarcinoma, or gallbladder cancer. In some embodiments, these anti- $\alpha\text{v}\beta 6$ ADCs are used to treat $\alpha\text{v}\beta 6$ -expressing cancers such as non-small cell lung cancer (NSCLC), head and neck cancer, esophageal cancer, breast cancer, ovarian cancer, bladder cancer, skin cancer (SCC), ovarian cancer, cervical cancer, gastric cancer, and pancreatic cancer. In some embodiments, these anti-CD30 ADCs are used to treat CD30-expressing diseases such as cancer, autoimmune diseases, and other infectious diseases. In further embodiments, these anti-CD30 ADCs are used to treat solid and liquid tumors, and autoimmune diseases such as HIV and AIDS. In some embodiments, these anti-EphA2 ADCs are used to treat EphA2-expressing cancers such as esophageal cancer, bladder cancer, renal cell carcinoma, colon cancer, ovarian cancer, endometrial cancer, cervical cancer, or melanoma.

TABLE OF SEQUENCES

SEQ ID NO	Description	Sequence
1	cAC10 CDR- H1	DYYIT
2	cAC10 CDR- H2	WIYPGSGNTKYNEKFKG
3	cAC10 CDR- H3	YGNYWFAY
4	cAC10 CDR- L1	KASQSVDFDGDSYMN
5	cAC10 CDR- L2	AASNLES
6	cAC10 CDR- L3	QQSNEDPWT
7	cAC10 VH	QIQLQQSGPEVVKPGASVKISCKASGYTFTDYYITWVKQKPGQGLEWIGWIYPGSGNTKYNEKFKGKATLTVDTSSTAFMQLSSLTSEDTAVYFCANYGNWFAYWGQGTQVTVSA

TABLE OF SEQUENCES - continued

SEQ ID NO	Description	Sequence
8	cAC10 VL	DIVLTQSPASLAISLGQRATISCKASQSVDGDSYMNWYQQKPGQPPKVLIYAASNLESGIPA RFSGSGSGTDFTLNIHPVEEEDAATYYCQGSNEDPWTFGGGTKEIK
9	cAC10 HC	QIQLQQSGPEVVKPGASVKISCKASGYTFTDYYITWVKQKPGQGLEWIGWIYPGSGNTKYNEK FKGKATLTVDTSSSTAFMQLSSLSEDATAVYFCANYGNYWFAYWGQGTQVTVAAST KGPSVFPPLAPSSKTSGGTAALGCLVKDYPFPEPVTSWNNSGALTSGVHTFPAVLQSS GLYSLSVVTVPSSSLGTQTYICNVNHHPSNTKVDKKVEPKSCDKTHTCPPCPAPEELLGG PSVFLFPPPKDTLMIISRTPEVTCVVVDVSHEDPEVKFNWYWDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSSLSPGK
10	cAC10 HC v2	QIQLQQSGPEVVKPGASVKISCKASGYTFTDYYITWVKQKPGQGLEWIGWIYPGSGNTKYNEK FKGKATLTVDTSSSTAFMQLSSLSEDATAVYFCANYGNYWFAYWGQGTQVTVAAST KGPSVFPPLAPSSKTSGGTAALGCLVKDYPFPEPVTSWNNSGALTSGVHTFPAVLQSS GLYSLSVVTVPSSSLGTQTYICNVNHHPSNTKVDKKVEPKSCDKTHTCPPCPAPEELLGG PSVFLFPPPKDTLMIISRTPEVTCVVVDVSHEDPEVKFNWYWDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSSLSPGK
11	cAC10 LC	DIVLTQSPASLAISLGQRATISCKASQSVDGDSYMNWYQQKPGQPPKVLIYAASNLES GIPARFSGSGSGTDFTLNIHPVEEEDAATYYCQGSNEDPWTFGGGTKEIKR TVAAPSIFIPPSDEQLKSGTASVVCLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS KDSTYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFRNRGEC
12	h1C1 CDR-H1	HYMMA
13	h1C1 CDR-H2	RIGPSGGPTHYADSVKG
14	h1C1 CDR-H3	YDSGYDYVAVAGPAEYFQH
15	h1C1 CDR-L1	RASQSISTWLA
16	h1C1 CDR-L2	KASNLHT
17	h1C1 CDR-L3	QQYNSYSRT
18	h1C1 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGKGLEWVSRIGPSGGPTHYAD SVKGRTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDGSYDGYDYVAVAGPAEYFQHWGQGTL VTVSS
19	h1C1 VL	DIQMTQSPSSLSASVGDRVITTCRASQSIWTWLAQYQQKPGKAPKLLIYKASNLHTGVPSRFSG SGSGCTFSLTIISGLQPDDFATYYCQYNSRTFGQGTKVEIK
20	h1C1 HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGKGLEWVSRIGPSGGPTHYAD SVKGRTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDGSYDGYDYVAVAGPAEYFQHWGQGTL VTVSSASTKGPSVFLAPSSKTSGGTAALGCLVKDYPFPEPVTSWNNSGALTSGVHTFPAVLQSS SGLYSLSSVVTPSSSLGTQTYICNVNHHPSNTKVDKKVEPKSCDKTHTCPPCPAPEELLGGPSVF LFPKPKDTLMIISRTPEVTCVVVDVSHEDPEVKFNWYWDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMIIIEALIINIIYTQKSLSSLSPGK
21	h1C1 HC v2	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGKGLEWVSRIGPSGGPTHYAD SVKGRTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDGSYDGYDYVAVAGPAEYFQHWGQGTL VTVSSASTKGPSVFLAPSSKTSGGTAALGCLVKDYPFPEPVTSWNNSGALTSGVHTFPAVLQSS SGLYSLSSVVTPSSSLGTQTYICNVNHHPSNTKVDKKVEPKSCDKTHTCPPCPAPEELLGGPSVF LFPKPKDTLMIISRTPEVTCVVVDVSIIEDPEVKFNWYWDGVEVIIINAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSSLSPGK

TABLE OF SEQUENCES - continued

SEQ ID NO	Description	Sequence
22	h1C1 LC	DIQMTQSPSSLSASVGDRVTITCRASQSISTWLAWYQQKPGKAPKLLIYKASNLHTGVPSRFSG SGSGTEFSLTISGLQPDDFATYYCQQYNSYSRTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGT ASVVCFLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDS KDSTYSLSSLTLSKADYEKHKVYACEVTHQGLSPVTKSFNRGEC
23	h1C1 mIgG2a HC	EVQLLESGGGVLQPGGSLRLSCAASGFTFSHYMMMAWVRQAPGKGLEWVSRIGPSSGGPTHYAD SVKGRTFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDGYDGYVAVAGPAEYFQHWGQGTL VTVSSAKTTAPSVPYPLAPVCGDTGSSVTLGCLVKGYFPEPVTLWNNSGLSSGVHTFPBVQI DLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIF PPKIKDVLMLISLSPIVTCVVVDSEDDPDVQIISWFVNNEVHTAQQTQTHREDYNSTLRVVSALP IQHQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVT DFMPEDIYVEWTNNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNNVERNSYCSVVHEGL HNHHTKSFNSRTPGK
24	h1C1 mIgG2a HC v2	EVQLLESGGGVLQPGGSLRLSCAASGFTFSHYMMMAWVRQAPGKGLEWVSRIGPSSGGPTHYAD SVKGRTFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDGYDGYVAVAGPAEYFQHWGQGTL VTVSSAKTTAPSVPYPLAPVCGDTGSSVTLGCLVKGYFPEPVTLWNNSGLSSGVHTFPBVQI DLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIF PPKIKDVLMLISLSPIVTCVVVDSEDDPDVQIISWFVNNEVHTAQQTQTHREDYNSTLRVVSALP IQHQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVT DFMPEDIYVEWTNNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNNVERNSYCSVVHEGL HNHHTKSFNSRTPGK
25	h1C1 mK LC	DIQMTQSPSSLSASVGDRVTITCRASQSISTWLAWYQQKPGKAPKLLIYKASNLHTGVPSRFSG SGSGTEFSLTISGLQPDDFATYYCQQYNSYSRTFGQGTKVEIKRADAAPTVSIFPPSSEQLTSGG ASVVCFLNNNFYPKDINVWKWIDGSRQNGVLNSWTDQSKDSTSMSSTLTKDEYERIINS YTCEATHKTSTSPIVKSFNRNEC
26	h1C1 mIgG2a LALAPG HC	EVQLLESGGGVLQPGGSLRLSCAASGFTFSHYMMMAWVRQAPGKGLEWVSRIGPSSGGPTHYAD SVKGRTFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDGYDGYVAVAGPAEYFQHWGQGTL VTVSSAKTTAPSVPYPLAPVCGDTGSSVTLGCLVKGYFPEPVTLWNNSGLSSGVHTFPBVQI DLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKCPAPNAAGGSPVF PPKIKDVLMLISLSPIVTCVVVDSEDDPDVQIISWFVNNEVHTAQQTQTHREDYNSTLRVVSALP PIQHQDWMSGKEFKCKVNNKDLGAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVT TDFMPEDIYVEWTNNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNNVERNSYCSVVHEGL HNHHTKSFNSRTPGK
27	h1C1 mIgG2a LALAPG HC v2	EVQLLESGGGVLQPGGSLRLSCAASGFTFSHYMMMAWVRQAPGKGLEWVSRIGPSSGGPTHYAD SVKGRTFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDGYDGYVAVAGPAEYFQHWGQGTL VTVSSAKTTAPSVPYPLAPVCGDTGSSVTLGCLVKGYFPEPVTLWNNSGLSSGVHTFPBVQI DLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKCPAPNAAGGSPVF PPKIKDVLMLISLSPIVTCVVVDSEDDPDVQIISWFVNNEVHTAQQTQTHREDYNSTLRVVSALP PIQHQDWMSGKEFKCKVNNKDLGAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQVTLTCMVT TDFMPEDIYVEWINNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNNVERNSYCSVVHEGL HNHHTKSFNSRTPGK
28	h1C1 LALAPG mK LC	DIQMTQSPSSLSASVGDRVTITCRASQSISTWLAWYQQKPGKAPKLLIYKASNLHTGVPSRFSG SGSGTEFSLTISGLQPDDFATYYCQQYNSYSRTFGQGTKVEIKRADAAPTVSIFPPSSEQLTSGG ASVVCFLNNNFYPKDINVWKWIDGSRQNGVLNSWTDQSKDSTSMSSTLTKDEYERHNS YTCEATHKTSTSPIVKSFNRNEC
29	hL49 HA CDR-H1	SGYWN
30	hL49 HA CDR-H2	YISDSGITYYYNPSLKS
31	hL49 HA CDR-H3	RTLATYYAMDY
32	hL49 LC CDR-L1	RASQLVIISDGNTYLII
33	hL49 LC CDR-L2	RVSINRFS
34	hL49 LC CDR-L3	SQSTHVPPT
35	hL49 HA VH	QVQLQESGPGLVKPSETSLTCTVSGDSITSGYWNWIRQPPGKGLEYIGYISDSGITYYY PSLKSRTVISRTDKNQYSLKLSSVTAADTAVYYCARRTLATYYAMDYWGQGTIVTSS

TABLE OF SEQUENCES - continued

SEQ ID NO	Description	Sequence
36	hL49 LC VL	DFVMTQSPLSLPVTLGQPASISCRASQSLVHSDGNTYLNHWYQQRPGQSPRLLIYRVSNRFSGV DRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPPTFGQGTKEIK
37	hL49 HA HC	QVQLQESGPGLVKPSETSLTCTVSGDSITSGYWNNWIRQPPGKLEYIGYISDSGITYYNPSLKS RVTISRDTSKNQYSLKLSVTAAADTAVYYCARRTLATYYAMDYWGQGLTVTVSSASTKGPSV FPLAPSSKSTSGGTAAALGCLVKDVFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSVVTVP SSSLGTQTYICNVNHKPSNTKVDDKKVEPKSCDKTHTCPCCPAPELLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNNAKTKPREEQYNSTYRVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQOPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL SLSPGK
38	hL49 HA HC v2	QVQLQESGPGLVKPSETSLTCTVSGDSITSGYWNNWIRQPPGKLEYIGYISDSGITYYNPSLKS RVTISRDTSKNQYSLKLSVTAAADTAVYYCARRTLATYYAMDYWGQGLTVTVSSASTKGPSV FPLAPSSKSTSGGTAAALGCLVKDVFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSVVTVP SSSLGTQTYICNVNHKPSNTKVDDKKVEPKSCDKTHTCPCCPAPELLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNNAKTKPREEQYNSTYRVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQOPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL SLSPG
39	hL49 LC LC	DFVMTQSPLSLPVTLGQPASISCRASQSLVHSDGNTYLNHWYQQRPGQSPRLLIYRVSNRFSGV DRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPPTFGQGTKEIKRTVAAPSVFIPPPSDEQ LKSGTASVVCLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTSYLSSTLTLSKADYE KHKVYACEVTHQGLSPVTKSFNRGEC
40	hL49 HA LALAKA HC	QVQLQESGPGLVKPSETSLTCTVSGDSITSGYWNNWIRQPPGKLEYIGYISDSGITYYNPSLKS RVTISRDTSKNQYSLKLSVTAAADTAVYYCARRTLATYYAMDYWGQGLTVTVSSASTKGPSV FPLAPSSKSTSGGTAAALGCLVKDVFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSVVTVP SSSLGTQTYICNVNHKPSNTKVDDKKVEPKSCDKTHTCPCCPAPEAAGGSPVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNNAKTKPREEQYNSTYRVSVLTVLHQDWLN GKEYCAVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQOPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL SLSPGK
41	hL49 HA LALAKA HC v2	QVQLQESGPGLVKPSETSLTCTVSGDSITSGYWNNWIRQPPGKLEYIGYISDSGITYYNPSLKS RVTISRDTSKNQYSLKLSVTAAADTAVYYCARRTLATYYAMDYWGQGLTVTVSSASTKGPSV FPLAPSSKSTSGGTAAALGCLVKDVFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSVVTVP SSSLGTQTYICNVNHKPSNTKVDDKKVEPKSCDKTHTCPCCPAPEAAGGSPVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNNAKTKPREEQYNSTYRVSVLTVLHQDWLN GKEYCAVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQOPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL SLSPG
42	hL49 LC LALAKA LC	DFVMTQSPLSLPVTLGQPASISCRASQSLVHSDGNTYLNHWYQQRPGQSPRLLIYRVSNRFSGV DRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPPTFGQGTKEIKRTVAAPSVFIPPPSDEO LKSGTASVVCLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTSYLSSTLTLSKADYE KHKVYACEVTHQGLSPVTKSFNRGEC
43	H2A2 HC CDR-H1	DYNVN
44	H2A2 HC CDR-H2	VINPKYGTTRYNQKFKG
45	H2A2 HC CDR-H3	GLNAWDY
46	H2A2 LG CDR-L1	GASENIY GALN
47	H2A2 LG CDR-L2	GATNLED
48	H2A2 LG CDR-L3	QNLVTTPYT
49	h2A2 HC VH	QFQLVQSGAEVKPGASVKSCKASGYSPTDYNVNWVRQAPGQGLEWIGVINPKYGTTRYN QKFGRATLTVDKSTSTAYMELSSLRSEDAVYYCTRGLNAWDYWGQGLTVTVSS
50	h2A2 LG VL	DIQMTQSPLSLASAVGDRVITCGASENIY GALN WYQQKPGKAPKLLIY GATNLEDGVPSRFG SGSGRDYTFITSSLQPEDIA TYCQNVLTTPYTFGQGTKEIK

TABLE OF SEQUENCES - continued

SEQ ID NO	Description	Sequence
51	h2A2 HC HC	QFQLVQSGAEVKPGASVKVSCKASGYSF TDYNVNWVRQAPGQGLEWIGVINPKYGTTRYN QKFGRATLTVDKSTSTAYMELSSLRSED TAVYYCTRGLNAWDYWGQGTLVTVSSASTKGPS VFPLAPSSKSTSGGTAALGCLVKD YFPEPPTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTV PSSSLGTQTYICNVNHPKSNTKVDKKVEPKSCDKTHTCPPCPAPEELLGGPSVLFPPKPKDTLM SRTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWL NGKEYKCKVSNKALPAPIKTISKA KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYP PSDIA VEWESENQGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQGNVFSCVMHEALHNHYTQKS LSLSPGK
52	h2A2 HC HC v2	QFQLVQSGAEVKPGASVKVSCKASGYSF TDYNVNWVRQAPGQGLEWIGVINPKYGTTRYN QKFGRATLTVDKSTSTAYMELSSLRSED TAVYYCTRGLNAWDYWGQGTLVTVSSASTKGPS VFPLAPSSKSTSGGTAALGCLVKD YFPEPPTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTV PSSSLGTQTYICNVNHPKSNTKVDKKVEPKSCDKTHTCPPCPAPEELLGGPSVLFPPKPKDTLM SRTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWL NGKEYKCKVSNKALPAPIKTISKA KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYP PSDIA VEWESENQGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQGNVFSCVMHEALHNHYTQKS LSLSPG
53	h2A2 LG LC	DIQMTQSPSSLSASVGDRVTITCGASENIYGALNWYQQKPGKAPKLLIYGATNLEDGVPSRFSG SGSGRDYTFITSSLQPEDIA YYCQN VETTPYTFQGQTKLEIKRTVAAPS VFIFPPSDEQLKSGTA SVVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSTTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
54	h2A2 HC LALAKA HC	QFQLVQSGAEVKPGASVKVSCKASGYSF TDYNVNWVRQAPGQGLEWIGVINPKYGTTRYN QKFGRATLTVDKSTSTAYMELSSLRSED TAVYYCTRGLNAWDYWGQGTLVTVSSASTKGPS VFPLAPSSKSTSGGTAALGCLVKD YFPEPPTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTV PSSSLGTQTYICNVNHPKSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVLFPPKPKDTLM SRTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWL NGKEYKCAVSNKALPAPIKTISKA KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYP PSDIA VEWESENQGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQGNVFSCVMHEALHNHYTQKS LSLSPGK
55	h2A2 HC LALAKA HC v2	QFQLVQSGAEVKPGASVKVSCKASGYSF TDYNVNWVRQAPGQGLEWIGVINPKYGTTRYN QKFGRATLTVDKSTSTAYMELSSLRSED TAVYYCTRGLNAWDYWGQGTLVTVSSASTKGPS VFPLAPSSKSTSGGTAALGCLVKD YFPEPPTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTV PSSSLGTQTYICNVNHPKSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVLFPPKPKDTLM SRTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWL NGKEYKCAVSNKALPAPIKTISKA KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYP PSDIA VEWESENQGPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQGNVFSCVMHEALHNHYTQKS LSLSPG
56	h2A2 LG LALAKA LC	DIQMTQSPSSLSASVGDRVTITCGASENIYGALNWYQQKPGKAPKLLIYGATNLEDGVPSRFSG SGSGRDYTFITSSLQPEDIA YYCQN VLTPYTFQGQTKLEIKRTVAAPS VFIFPPSDEQLKSGTA SVVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSTTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
57	B7H41001 CDR-H1	SGSYYWG
58	B7H41001 CDR-H2	NIYYSGSTYYNPSLRS
59	B7H41001 CDR-H3	EGSYPNQFDP
60	B7H41001 CDR-L1	RASQSVSSNLA
61	B7H41001 CDR-L2	GASTRAT
62	B7H41001 CDR-L3	QQYHSFPFT
63	B7H41001 VH	QLQLQESGPGLVKPSETSLTCTVSGGSIKSGSYYWGWIRQPPGKGLEWIGNIYSGSTYYNPS LRSRVTISVDTSKNQFSKLSSVTAADTAVYYCAREGSYSPNQFDPWGQGTLVTVSS
64	B7H41001 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS GSGTEFTLTISLQSEDFAVYYCQQYIISFPFTFGGGTKVEIK
65	B7H41001 HC	QLQLQESGPGLVKPSETSLTCTVSGGSIKSGSYYWGWIRQPPGKGLEWIGNIYSGSTYYNPS LRSRVTISVDTSKNQFSKLSSVTAADTAVYYCAREGSYSPNQFDPWGQGTLVTVSSASTKGPS VFPLAPSSKSTSGGTAALGCLVKD YFPEPPTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTV

TABLE OF SEQUENCES - continued

SEQ ID NO	Description	Sequence
		PSSSLGTQTYICNVNHHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLM SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDELTKNQVSLTCLVKGFYPSDIA VEWESENQGPENNYKTPPVLDSGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPKG
66	B7H41001 HC v2	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGGWIROPPGKLEWIGNIYYSGSTYYNPS LRSRVTISVDTSKNQFSKLSSVTAADTAVYYCAREGSYPNQFPDWGQGTLTVVSSASTKGPS VFPLAPSSKSTSGTAALGCLVKDVFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT PSSSLGTQTYICNVNHHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLM SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDELTKNQVSLTCLVKGFYPSDIA VEWESENQGPENNYKTPPVLDSGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPKG
67	B7H41001 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS GSGTEFTLTISLQSEDFAVYYCQYHSFPFTFGGGTKVEIKRTVAAPSIFPPSDQQLKSGTAS VVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSTTLSKADYEKHKVYA CEVTHQGLSSPVTKSFNRGEC
68	B7H41001 LALAKA HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGGWIROPPGKLEWIGNIYYSGSTYYNPS LRSRVTISVDTSKNQFSKLSSVTAADTAVYYCAREGSYPNQFPDWGQGTLTVVSSASTKGPS VFPLAPSSKSTSGTAALGCLVKDVFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT PSSSLGTQTYICNVNHHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLM SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCAVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDELTKNQVSLTCLVKGFYPSDIA VEWESENQGPENNYKTPPVLDSGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPKG
69	B7H41001 LALAKA HC v2	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGGWIROPPGKLEWIGNIYYSGSTYYNPS LRSRVTISVDTSKNQFSKLSSVTAADTAVYYCAREGSYPNQFPDWGQGTLTVVSSASTKGPS VFPLAPSSKSTSGTAALGCLVKDVFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT PSSSLGTQTYICNVNHHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLM SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCAVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDELTKNQVSLTCLVKGFYPSDIA VEWESENQGPENNYKTPPVLDSGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPKG
70	B7H41001 LALAKA LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS GSGTEFTLTISLQSEDFAVYYCQYHSFPFTFGGGTKVEIKRTVAAPSIFPPSDQQLKSGTAS VVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSTTLSKADYEKHKVYA CEVTHQGLSSPVTKSFNRGEC
71	B7H4-15461 CDR-H1	GSISSSSYYWG
72	B7H4-15461 CDR-H2	NIYYSGSTYYNPSLKS
73	B7H4-15461 CDR-H3	AREGSYPNWFPDP
74	B7H4-15461 CDR-L1	RASQSVSSNL
75	B7H4-15461 CDR-L2	GASTRAT
76	B7H4-15461 CDR-L3	QQYHSFPFT
77	B7H4-15461 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSYYWGGWIROPPGKLEWIGNIYYSGSTYYNPSL KSRVTISVDTSKNQFSKLSSVTAADTAVYYCAREGSYPNWFDPDWGQGTLTVSS
78	B7H4-15461 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS GSGTEFTLTISLQSEDFAVYYCQYHSFPFTFGGGTKVEIK
79	B7H4-20500 CDR-H1	GSIKSGSHYWG
80	B7H4-20500 CDR-H2	NIYYSGSTYYNPSLRS

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SEQ ID NO	Description	Sequence
81 B7H4-20500	AREGSYPNWFDP CDR-H3	
82 B7H4-20500	RASQSVSSNLA CDR-L1	
83 B7H4-20500	GASTRAT CDR-L2	
84 B7H4-20500	QQYHSFPFT CDR-L3	
85 B7H4-20500	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIROPPGKGLEWIGNIYYSGSTYYNPS VH LRSRVTISVDTSKNQFSKLSSVTAADTAVYYCAREGSYPNWFDPWGQGTLTVSS	
86 B7H4-20500	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS VL GSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIK	
87 B7H4-20501	GSIKSGSHYWG CDR-H1	
88 B7H4-20501	NIYYSGSTYYNPSLKS CDR-H2	
89 B7H4-20501	AREGSYPNWLDP CDR-H3	
90 B7H4-20501	RASQSVSSNLA CDR-L1	
91 B7H4-20501	GASTRAT CDR-L2	
92 B7H4-20501	QQYHSFPFT CDR-L3	
93 B7H4-20501	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIROPPGKGLEWIGNIYYSGSTYYNPS VH LKSRTVISVDTSKNQFSKLSSVTAADTAVYYCAREGSYPNWLDPWGQGTLTVSS	
94 B7H4-20501	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS VL GSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIK	
95 B7H4- 20502.1	GSIKSGSYWG CDR-H1	
96 B7H4- 20502.1	NIYYSGSTYYNPSLKS CDR-H2	
97 B7H4- 20502.1	AREGSYPNQFDP CDR-H3	
98 B7II4- 20502.1	RASQSVSSNLA CDR-L1	
99 B7H4- 20502.1	GASTRAT CDR-L2	
100 B7H4- 20502.1	QQYHSFPFT CDR-L3	
101 B7H4- 20502.1 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGWIROPPGKGLEWIGNIYYSGSTYYNPS LKSRTVISVDTSKNQFSKLSSVTAADTAVYYCAREGSYPNQFDPWGQGILTVSS	
102 B7H4- 20502.1 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS GSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIK	

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SEQ ID NO	Description	Sequence
103	B7H4-22208 CDR-H1	GSIKSGSHYWG
104	B7H4-22208 CDR-H2	NIYYSGSTYYNPSLKS
105	B7H4-22208 CDR-H3	AREGSYPNWFDP
106	B7H4-22208 CDR-L1	RASQSVSTNLAA
107	B7H4-22208 CDR-L2	DASARVT
108	B7II4-22208 CDR-L3	QQYHSFPFT
109	B7H4-22208 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIROPPGKGLEWIGNIYYSGSTYYNPS LKSRTMSVDTSKNQFSKLSSVTAADTAVYYCAREGSYPNWFPWGQGTIVTVSS
110	B7H4-22208 VL	EIVLTQSPATLSVSPGERATLSCRASQSVSTNLAWYQQKPGQAPRLLIYDASARVTGIPARFSG SGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIK
111	B7H4-15462 CDR-H1	GSISSSSYYWG
112	B7H4-15462 CDR-H2	NIYYSGSTYYNPSLKS
113	B7H4-15462 CDR-H3	AREGSYTTVLDV
114	B7H4-15462 CDR-L1	RASQSVSSSYLA
115	B7H4-15462 CDR-L2	GASSRAT
116	B7H4-15462 CDR-L3	QQAASYPLT
117	B7H4-15462 VII	QLQLQESGPGLVKPSETLSLTCTVSGGISSSSSYYWGWIROPPGKGLEWIGNIYYSGSTYYNPSL KSRVTISVDTSKNQFSKLSSVTAADTAVYYCAREGSYTTVLNWGQGTMVTVSS
118	B7H4-15462 VL	EIVLTQSPGTLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGS GSGTDFLTISRLEPEDFAVYYCQQAASYPLTFGGGTKEIK
119	B7H4-22213 CDR-H1	GSIGRGSYYWG
120	B7H4-22213 CDR-H2	NIYYSGSTYYNPSLKS
121	B7H4-22213 CDR-H3	AREGSYTTVLDV
122	B7H4-22213 CDR-L1	RASQSVASSHLA
123	B7H4-22213 CDR-L2	DAVSRAT
124	B7H4-22213 CDR-L3	QQAASYPLT
125	B7H4-22213 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIGRGSYYWGWIROPPGKGLEWIGNIYYSGSTYYNPS LKSRTISVDTSKNQFSKLSSVTAADTAVYYCAREGSYTTVLNWGQGTMVTVSS
126	B7H4-22213 VL	EIVLTQSPGTLSSLSPGERATLSCRASQSVASSHLAWYQQKPGQAPRLLIYDAVSRATGIPDRFSG GSGTDFLTISRLEPEDFAVYYCQQAASYPLTFGGGTKEIK

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SEQ ID NO	Description	Sequence
127 B7H4-15465	GSISGGYYYWS CDR-H1	
128 B7H4-15465	NIYYSGSTYYNPSLKS CDR-H2	
129 B7H4-15465	ARESSTISADFDL CDR-H3	
130 B7H4-15465	RASQGISRWLA CDR-L1	
131 B7H4-15465	AASSLQS CDR-L2	
132 B7H4-15465	QQAHTFPYT CDR-L3	
133 B7H4-15465 VH	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSSGGYYYWSWIRQHPGKGLEWIGNIYYSGSTYYNPS LKSRTVTISVDTSKNQFSKLSSVTAADTAVYYCARESSTISADFDLWGRGTLVTVSS	
134 B7H4-15465 VL	DIQMTQSPSSVSASVGDRVITICRASQGISRWLAQYQQKPGKAPKLLIYAASSLQSGVPSRFSG SGSGTDFTLTISLQPEDFATYYCQQAHTFPYTFGGTTKVEIK	
135 B7H4-20506	GSISHGGYYYWS CDR-H1	
136 B7H4-20506	NIYYSGSTYYNPSLKS CDR-H2	
137 B7H4-20506	ARESSTISADFDL CDR-H3	
138 B7H4-20506	RASQGISRWLA CDR-L1	
139 B7H4-20506	AASSLQS CDR-L2	
140 B7H4-20506	QQAHTFPYT CDR-L3	
141 B7H4-20506 VH	QVQLQESGPGLVKPSQTLSLTCTASGGISIHGGYYYWSWIRQHPGKGLEWIGNIYYSGSTYYNPS LKSRTVTMSVDTSKNQFSKLSSVTAADTAVYYCARESSTISADFDLWGRGTLVTVSS	
142 B7H4-20506 VL	DIQMTQSPSSVSASVGDRVITICRASQGISRWLAQYQQKPGKAPKLLIYAASSLQSGVPSRFSG SGSGTDFTLTISLQPEDFATYYCQQAHTFPYTFGGTTKVEIK	
143 B7H4-15483	GSISGGYYYWS CDR-H1	
144 B7H4-15483	NIYYSGSTYYNPSLKS CDR-H2	
145 B7H4-15483	ARGLSTIDEAFDP CDR-H3	
146 B7H4-15483	RASQSISSWLA CDR-L1	
147 B7H4-15483	KASSLES CDR-L2	
148 B7H4-15483	QQDNSYPYT CDR-L3	
149 B7H4-15483 VH	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSSGGYYYWSWIRQHPGKGLEWIGNIYYSGSTYYNPS LKSRTVTISVDTSKNQFSKLSSVTAADTAVYYCAGLSTIDEAFDPWGQGTLVTVSS	
150 B7H4-15483 VL	DIQMTQSPSTLSASVGDRVITICRASQSISSWLAQYQQKPGKAPKLLIYKASSLESQGVPSRFSGS GSGTEFTLTISLQPDDFATYYCQODNSYPYTFGGTTKVEIK	

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SEQ ID NO	Description	Sequence
151	B7H4-20513 CDR-H1	GSISDGSYWS
152	B7H4-20513 CDR-H2	NIYYSGSTYYNPSLRS
153	B7H4-20513 CDR-H3	ARGLSTIDEAFDP
154	B7H4-20513 CDR-L1	RASQSISSWLA
155	B7H4-20513 CDR-L2	KASSLES
156	B7H4-20513 CDR-L3	QQDNSYPYT
157	B7H4-20513 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISDGYYWSWIRQHPGKGLEWIGNIYYSGSTYYNPS LRSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCARGLSTIDEAFDPWGQGTLTVSS
158	B7H4-20513 VL	DIQMTQSPSTLSASVGDRVITCRASQSISSWLAZYQQKPGKAPKLLIYKASSLESGVPSRFSGS GSGTEFTLTISLQPDDFATYYCQQDNSYPYTFGGGTKVEIK
159	B7H4-22216 CDR-H1	GSISDGSYWS
160	B7H4-22216 CDR-H2	NIYYSGSTYYNPSLRS
161	B7H4-22216 CDR-H3	ARGLSTIDEAFDP
162	B7H4-22216 CDR-L1	RASKSISSWLA
163	B7H4-22216 CDR-L2	EASSLHS
164	B7H4-22216 CDR-L3	QQDNSYPYT
165	B7H4-22216 VH	QVQLQESGPGLVKPQSQTLSLTCTVSGGSISDGYYWSWIRQHPGKGLEWIGNIYYSGSTYYNPS LRSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCARGLSTIDEAFDPWGQGTLTVSS
166	B7H4-22216 VL	DIQMTQSPSTLSASVGDRVITCRASKSISSSWLAZYQQKPGKAPKLLIYEASSLHSGVPSRFSGS GSGTEFTLTISLQPDDFATYYCQQDNSYPYTFGGGTKVEIK
167	B7H4-15489 CDR-H1	GSISSYYWS
168	B7H4-15489 CDR-H2	YIYSSGSTNYNPSLKS
169	B7H4-15489 CDR-H3	ARGSGQYAAPDYGMD
170	B7H4-15489 CDR-L1	RASQSISSWLA
171	B7H4-15489 CDR-L2	KASSLES
172	B7H4-15489 CDR-L3	QQDNSFPFT
173	B7H4-15489 VH	QVQLQESGPGLVKPSETLSLTCTVSGGSISSSYYWSWIRQPPGKGLEWIGYIYSSGSTNYNPSLKS RTVTSVDTSKNQFSLKLSSVTAADTAVYYCARGSGQYAAPDYGMDVWQGTTTVSS
174	B7H4-15489 VL	DIQMTQSPSTLSASVGDRVITCRASQSISSWLAZYQQKPGKAPKLLIYKASSLESGVPSRFSGS GSGTEFTLTISLQPDDFATYYCQQDNSFPFTFGGGTKVEIK

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SEQ ID NO	Description	Sequence
175	B7H4-20516 CDR-H1	GSIISYYWG
176	B7H4-20516 CDR-H2	YIYSSGSTSYPNPSLKS
177	B7H4-20516 CDR-H3	ARGSGLYAAPDYGLDV
178	B7H4-20516 CDR-L1	RASQSISSWLA
179	B7H4-20516 CDR-L2	KASSLES
180	B7H4-20516 CDR-L3	QQDNSFPFT
181	B7H4-20516 VH	QVQLQESGPGLVKPSETLSLTCTVSGGSIIISYYWGWIROQPPGKGLEWIGYIYSSGSTSYPNPSLKS RTVTISVDTSKNQFSLKLSSVTAADTAVYYCARGSGLYAAPDYGLDVWQGTTTVSS
182	B7H4-20516 VL	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESQGVPSRFSGS GSGTEFTLTISSLQPDFFATYYCQDNSFPFTFGGGTKVEIK
183	B7H4-15472 CDR-H1	FTFSSYAMS
184	B7H4-15472 CDR-H2	TISGGGSTYYADSVKG
185	B7H4-15472 CDR-H3	ARGAGHYDLVGRY
186	B7H4-15472 CDR-L1	RASQSISSYLN
187	B7H4-15472 CDR-L2	AASSLQS
188	B7H4-15472 CDR-L3	QQLYSLPPT
189	B7H4-15472 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSTISGGGSTYYADS VKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGAGHYDLVGRYWGQGTLVTVSS
190	B7H4-15472 VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCQQLYSLPPTFGGGTKVEIK
191	B7H4-15503 CDR-H1	FTFSSYAMS
192	B7H4-15503 CDR-H2	AISGGGSTYYADSVKG
193	B7H4-15503 CDR-H3	ARVGPRALNY
194	B7H4-15503 CDR-L1	RASQDISSWLA
195	B7H4-15503 CDR-L2	AASSLQS
196	B7H4-15503 CDR-L3	QQATSYPPWT
197	B7H4-15503 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGGGSTYYADS VKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVGFRALNYWGQGTTTVSS
198	B7H4-15503 VL	DIQLTQSPSSVSASVGDRVTITCRASQDISSWLAWYQQKPGKAPKLLIYAASSLQSGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCQQATSYPPWTFGGGTKVEIK

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SEQ ID NO	Description	Sequence
199	B7H4-15495 CDR-H1	GTFSSYAIS
200	B7H4-15495 CDR-H2	GIIPIFGTASYAQKFQG
201	B7H4-15495 CDR-H3	ARQQYDGRRYFGL
202	B7H4-15495 CDR-L1	RASQSVSSNLA
203	B7H4-15495 CDR-L2	SASTRAT
204	B7H4-15495 CDR-L3	QQVNWPPT
205	B7H4-15495 VH	QVQLVQSGAEVKPGSSVKVSCKASGGTFSSYAI SWVRQAPGQGLEWMGGI IPIFGTASYAQK FQGRVTITADESTSTAYMELSSLRSEDTAVYYCARQQYDGRRYFGLWGRGTLTVSS
206	B7H4-15495 VL	EIVMTQSPATLSVPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYSASTRATGIPARFSGS GSGTEFTLTISLQSEDFAVYYCQQVNWPPTFGGGTKVEIK
207	B7H4-15478 CDR-H1	GTFSSYAIS
208	B7H4-15478 CDR-H2	GIIPIFGTANYAQKFQG
209	B7H4-15478 CDR-H3	ARGGPWFDP
210	B7H4-15478 CDR-L1	RASQSISSWLA
211	B7H4-15478 CDR-L2	KASSLES
212	B7H4-15478 CDR-L3	QQYNNSYPFPFT
213	B7H4-15478 VH	QVQLVQSGAEVKPGSSVKVSCKASGGTFSSYAI SWVRQAPGQGLEWMGGI IPIFGTANYAQK FQGRVTITADESTSTAYMELSSLRSEDTAVYYCARGGPWFDPWGQGTLTVSS
214	B7H4-15478 VL	DIQMTQSPSTLSASVGDRVITCRASQSISSWLA WYQQKPGKAPKLLIYKASSLES GSGTEFTLTISLQPDDFATYYCQQYN NSYPFPFTFGGGTKVEIK
215	B7H4-15441 CDR-H1	FTFSSYAMS
216	B7H4-15441 CDR-H2	AISGSGGSTSYADSVKG
217	B7H4-15441 CDR-H3	AKPSLATMLAFDI
218	B7H4-15441 CDR-L1	RASQSISSWLA
219	B7H4-15441 CDR-L2	DASSLES
220	B7H4-15441 CDR-L3	QQSKSYPR
221	B7H4-15441 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAM SWVRQAPGKGLEWVAISGSGGSTSYADS VKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCA KPSLATMLAFDIWGQGTMVTVSS
222	B7H4-15441 VL	DIQMTQSPSTLSASVGDRVITCRASQSISSWLA WYQQKPGKAPKLLIYDASSLES GSGTEFTLTISLQPDDFATYYCQQSKSYPR TFGGGTKEIK

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SEQ ID NO	Description	Sequence
223 B7H4-20496	GSTSSVYVWS CDR-H1	
224 B7H4-20496	SILVSGSTYYNPSLKS CDR-H2	
225 B7H4-20496	ARAVSFLDV CDR-H3	
226 B7H4-20496	RASQSISSYLN CDR-L1	
227 B7H4-20496	GASSLQS CDR-L2	
228 B7H4-20496	QQSYDPPWT CDR-L3	
229 B7H4-20496 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSVYWSWIROQPPGKGLEWIGSILVSGSTYYNPSL KSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARAVSPLDVWGQGTVMIVSS	
230 B7H4-20496 VL	DIQMTQSPSSLASAVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYGASSLQSGVPSRFGS GSGTDPFTLISSLQPEDFATYYCQSYDPPWTGGGTKEIK	
231 B7H4-15461 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYWGWIRQPPGKGLEWIGNIYYSGSTYYNPSL KSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNWFDPWGQGTLVTVSSASTKGPSV FPLAPSSKSTSGGTAAALGCLVKDVFPEPVTVSWNSGALTSGVHTFPAPLQSSGLYSLSSVVTVP SSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL GKEYKCKVSNKALPAPIEKTIKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKSL LSLSPGK	
232 B7H4-15461 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS GSGTEFTLTISSLQSEDFAVYYCQYHSFPFTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTAS VVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLKADYEKHKVYA CEVTHQGLSSPVTKSFNRGEC	
233 B7H4-20500 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIROQPPGKGLEWIGNIYYSGSTYYNPS LRSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNWFDPWGQGTLVTVSSASTKGPS FPLAPSSKSTSGGTAAALGCLVKDVFPEPVTVSWNSGALTSGVHTFPAPLQSSGLYSLSSVVTVP PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLM SRTPEVTCVVVDVSHEDPEVKFNWYDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL GKEYKCKVSNKALPAPIEKTIKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIA EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKSL LSLSPGK	
234 B7H4-20500 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS GSGTEFTLTISSLQSEDFAVYYCQYHSFPFTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTAS VVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLKADYEKHKVYA CEVTHQGLSSPVTKSFNRGEC	
235 B7H4-20501 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIROQPPGKGLEWIGNIYYSGSTYYNPS LKSRTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNWLDPWGQGTLVTVSSASTKGPS FPLAPSSKSTSGGTAAALGCLVKDVFPEPVTVSWNSGALTSGVHTFPAPLQSSGLYSLSSVVTVP PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLM SRTPEVTCVVVDVSHEDPEVKFNWYDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL GKEYKCKVSNKALPAPIEKTIKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIA EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKSL LSLSPGK	
236 B7H4-20501 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS GSGTEFTLTISSLQSEDFAVYYCQYHSFPFTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTAS VVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLKADYEKHKVYA CEVTHQGLSSPVTKSFNRGEC	
237 B7H4- 20502 .1 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYWGWIRQPPGKGLEWIGNIYYSGSTYYNPS LKSRTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNQFPWGQGILTVTVSSASTKGPSV FPLAPSSKSTSGGTAAALGCLVKDVFPEPVTVSWNSGALTSGVHTFPAPLQSSGLYSLSSVVTVP SSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL	

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SEQ ID NO	Description	Sequence
		GKEYKCKVSNKALPAPIEKTISKAKGQPQREPQVYTLPPSRDELTKNQVSLLTCLVKGFYPDSIAV EWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKSLSLSPGK
238 B7H4- 20502 .1 LC	EIVMTQSPATLSVSPGERATLSCRASQS VSSNLA WYQQKPGQAPRLLI YGASTRATGIPARFSGS GSGTEFTLTISSLQSEDFAVYYCQYHSFPFTFGGGTKVEIKRTVAAPS VFIFPPSDEQLKSGTAS VVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	
239 B7H4-22208 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIROQPPKGLEWIGNIYYSGSTYYNPS LKSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCAREGSYTTVNLNVGQGMVTVSSASTKGPSV FPLAPSSKSTSGGAALGCLVKD YFPEPVTVWSNGALTSGVHTFP AVLQSSGLYSLSSVVTVP SSSLGTQTYICCNVNHKPSNTKVDKKVEPKSCDKTHTCPCPAPEL LGGPSVFLFPPKPKDLMIS RTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLN GKEYKCKVSNKALPAPIEKTISKAKGQPQREPQVYTLPPSRDELTKNQVSLLTCLVKGFYPDSIA IAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKSLSLSPGK	
240 B7H4-22208 LC	EIVMTQSPATLSVSPGERATLSCRASQS VSTNLA WYQQKPGQAPRLLI YDASARVTGIPARFSG SGSGTEFTLTISSLQSEDFAVYYCQYHSFPFTFGGGTKVEIKRTVAAPS VFIFPPSDEQLKSGTAS VVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	
241 B7H4-15462 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSSYYWGWIROQPPKGLEWIGNIYYSGSTYYNPSL LKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYTTVNLNVGQGMVTVSSASTKGPSV FPLAPSSKSTSGGAALGCLVKD YFPEPVTVWSNGALTSGVHTFP AVLQSSGLYSLSSVVTVP SSSLGTQTYICCNVNHKPSNTKVDKKVEPKSCDKTHTCPCPAPEL LGGPSVFLFPPKPKDLMIS RTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL GKEYKCKVSNKALPAPIEKTISKAKGQPQREPQVYTLPPSRDELTKNQVSLLTCLVKGFYPDSIA EWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKSLSLSPGK	
242 B7H4-15462 LC	EIVLTQSPGTLSLSPGERATLSCRASQS VSSSYLAWYQQKPGQAPRLLI YGASSRATGIPDRFSGS GSGTDFTLTI SRLPEDFAVYYCQQAASYPLTFGGGT KVEIKRTVAAPS VFIFPPSDEQLKSGTAS VVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	
243 B7H4-22213 HC	QLQLQESGPGLVKPSETLSLTCTVSGGISIGRGSSYYWGWIROQPPKGLEWIGNIYYSGSTYYNPS LKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYTTVNLNVGQGMVTVSSASTKGPSV FPLAPSSKSTSGGAALGCLVKD YFPEPVTVWSNGALTSGVHTFP AVLQSSGLYSLSSVVTVP PSSSLGTQTYICCNVNHKPSNTKVDKKVEPKSCDKTHTCPCPAPEL LGGPSVFLFPPKPKDLMIS RTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPQREPQVYTLPPSRDELTKNQVSLLTCLVKGFYPDSIA VEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKSLSLSPGK	
244 B7H4-22213 LC	EIVLTQSPGTLSLSPGERATLSCRASQS VASSHLAWYQQKPGQAPRLLI YDAVS RATGIPDRFSG SGSGTDFTLTI SRLPEDFAVYYCQQAASYPLTFGGGT KVEIKRTVAAPS VFIFPPSDEQLKSGTAS ASVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	
245 B7H4-15465 HC	QVQLQESGPGLVKPQS QTL SLTCTVSGGISISSGGYYWSWIRQHPKGLEWIGNIYYSGSTYYNPS LKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARESSTISADF DLWGRGTLTVVSSASTKGPSV FPLAPSSKSTSGGAALGCLVKD YFPEPVTVWSNGALTSGVHTFP AVLQSSGLYSLSSVVTVP PSSSLGTQTYICCNVNHKPSNTKVDKKVEPKSCDKTHTCPCPAPEL LGGPSVFLFPPKPKDLMIS RTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPQREPQVYTLPPSRDELTKNQVSLLTCLVKGFYPDSIA VEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKSLSLSPGK	
246 B7H4-15465 LC	DIQMTQSPSSVASVGDRVTITCRASQGISRWLAWYQQKPGKAPKLLI YAASSLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQAHTFPYTFGGGT KVEIKRTVAAPS VFIFPPSDEQLKSGTAS VVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	
247 B7H4-20506 HC	QLQLQESGPGLVKPSETLSLTCTA SGGSISHGGYWSWIRQHPKGLEWIGNIYYSGSTYYNPS LKSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCARESSTISADF DLWGRGTLTVVSSASTKGPSV FPLAPSSKSTSGGAALGCLVKD YFPEPVTVWSNGALTSGVHTFP AVLQSSGLYSLSSVVTVP PSSSLGTQTYICCNVIKPSNTKVDKKVEPKSCDKTHTCPCPAPEL LGGPSVFLFPPKPKDLMIS RTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPQREPQVYTLPPSRDELTKNQVSLLTCLVKGFYPDSIA VEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQKSLSLSPGK	

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SEQ ID NO	Description	Sequence
248 B7H4-20506 LC		DIQMTQSPSSVSAVGDRVTITCRASQGISRWLAWYQQKPGKAPKLLIYAASSLQSGVPSRFSG SGSGTDFTLTISLQPEDFATYYCQQAHTFPYTFGGGTKEIKRTVAAPSVIDFPPSDEQLKSGTA SVVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
249 B7H4-15483 HC		QVQLQESGPGLVKPQSOTSLTCTVSGGSISSGGGYWWSWIROHPGKLEWIGNIYYSGSTYYNPS LRSRVTISVDTSKNQFSKLSSVTAADTAVYYCARGLSTIDEAFDPWGQGTLTVSSASTKGPS VFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSVVT PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPCCPAPEELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTIKAKGQPREPVYTLPPSRDELTKNQVSLTCLVKGFYPSDIA VEWESENQOPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQ KSLSLSPKG
250 B7H4-15483 LC		DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESQVPSRFSGS GSGTEFTLTISLQPDDFATYYCQCDNSYPYTFGGGTKEIKRTVAAPSVIDFPPSDEQLKSGTA SVVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
251 B7H4-20513 HC		QQLQESGPGLVKPSETSLTCTVSGGISDGSYWWSWIROHPGKLEWIGNIYYSGSTYYNPS LRSRVTMSVDTSKNQFSKLSSVTAADTAVYYCARGLSTIDEAFDPWGQGTLTVSSASTKG VFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSVVT PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPCCPAPEELLGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL WLNKEYKCKVSNKALPAPIEKTIKAKGQPREPVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESENQOPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQ KSLSLSPKG
252 B7H4-20513 LC		DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESQVPSRFSGS GSGTEFTLTISLQPDDFATYYCQCDNSYPYTFGGGTKEIKRTVAAPSVIDFPPSDEQLKSGTA SVVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
253 B7H4-22216 HC		QVQLQESGPGLVKPQSOTSLTCTVSGGISDGSYWWSWIROHPGKLEWIGNIYYSGSTYYNPS LRSRVTMSVDTSKNQFSKLSSVTAADTAVYYCARGLSTIDEAFDPWGQGTLTVSSASTKG VFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSVVT PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTIICTCCPAPAPEELLGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL WLNKEYKCKVSNKALPAPIEKTIKAKGQPREPVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESENQOPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQ KSLSLSPKG
254 B7H4-22216 LC		DIQMTQSPSTLSASVGDRVTITCRASKSISSWLAWYQQKPGKAPKLLIYEASSLIISGVPSRFSGS GSGTEFTLTISLQPDDFATYYCQCDNSYPYTFGGGTKEIKRTVAAPSVIDFPPSDEQLKSGTA SVVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
255 B7H4-15489 HC		QVQLQESGPGLVKPSETSLTCTVSGGISSSYYWWSIROPPGKLEWIGIYIYSGSTYNPSLKS RVTISVDTSKNQFSKLSSVTAADTAVYYCARSGQYAAPDYGMDVWQGTTTVSSASTKG PSVFLAPSSKSTSGGTAALGCLVKDYFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSV TPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPCCPAPEELLGGPSVFLFPPKPKD MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL WLNKEYKCKVSNKALPAPIEKTIKAKGQPREPVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESENQOPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQ KSLSLSPKG
256 B7H4-15489 LC		DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESQVPSRFSGS GSGTEFTLTISLQPDDFATYYCQCDNSYPFTFGGGTKEIKRTVAAPSVIDFPPSDEQLKSGTAS VVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTSKADYEKHKVYA CEVTHQGLSSPVTKSFNRGEC
257 B7H4-20516 HC		QVQLQESGPGLVKPSETSLTCTVSGGISISYYWGWROPPGKLEWIGIYIYSGSTSYNPSLKS RVTISVDTSKNQFSKLSSVTAADTAVYYCARSGQYAAPDYGMDVWQGTTTVSSASTKG PSVFLAPSSKSTSGGTAALGCLVKDYFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSV TPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPCCPAPEELLGGPSVFLFPPKPKD MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL WLNKEYKCKVSNKALPAPIEKTIKAKGQPREPVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESENQOPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQ KSLSLSPKG

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258 B7H4-20516 LC		DIQMTQSPSTLSASVGDRVITTCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPSRSGS GSGTETFTLTISLQLQDDFATYYCQODNSPPFTFGGGTKVEIKRTVAAPSVDIIFPPSDBQLKSGTAS VVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYA CEVTHQGLSSPVTKSFRNRGEC
259 B7H4-15472 HC		EVQILLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSTISGSGGSTYYADS VKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARGAGHYDLVGRYWGQGT LTVSSASTK GPSVPLAPSSKSTSGGTAALGCLVKDYFPEPVTVWSN SGA L TSVHFTPAVLQSSGLYSLSSV VTVPSSSLGTQTYICNVN H KPNSNTKVDKKVEPKSCDKTHTCPCPAPELLGGPSVFLFPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYV DGEVHN AKTPREEQYN STYRVVSVLTVLHQD WLNGKEYKCKVS N KALPAPIEKTISAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAV EWSNGQ PENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQ KSLSLSPGK
260 B7H4-15472 LC		DIQMTQSPSLSASVGDRVITTCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRSGS GSGTDFLTISLQLQPEDFATYYCQOLYSLPPTFGGGTKVEIKRTVAAPSVDIIFPPSDBQLKSGTAS VVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYA CEVTHQGLSSPVTKSFRNRGEC
261 B7H4-15503 HC		EVQILLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADS VKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARGVFRALNYWGQGT LTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVWSN SGA L TSVHFTPAVLQSSGLYSLSSV SSSLGTQTYICNVN H KPNSNTKVDKKVEPKSCDKTHTCPCPAPELLGGPSVFLFPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYV DGEVHN AKTPREEQYN STYRVVSVLTVLHQDWL GKEYKCKVS N KALPAPIEKTISAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQ PENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQKSL SLSPGK
262 B7H4-15503 LC		DIQLTQSPSSVSASVGDRVITTCRASQDISSWLAWYQQKPGKAPKLLIYAASSLQSGVPSRSGS GSGTDFLTISLQLQPEDFATYYCQCATSYPPWTGGGT KVEIKRTVAAPSVDIIFPPSDEQLKSGT ASVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTL SKADYEKHKV YACEVTHQGLSSPVTKSFRNRGEC
263 B7H4-15495 HC		QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAI SWVRQAPGQGLEWMGGIIPIFGTASYAQK FQGRVTITADESTSTAYMELSSLRSED TAVYYCARQYDGR YFGLWGRGTLTVSSASTKG SVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVWSN SGA L TSVHFTPAVLQSSGLYSLSSV VPSSSLGTQTYICNVN H KPNSNTKVDKKVEPKSCDKTHTCPCPAPELLGGPSVFLFPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYV DGEVHN AKTPREEQYN STYRVVSVLTVLIIQD WLNGKEYKCKVS N KALPAPIEKTISAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAV EWSNGQ PENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQKSL KSLSLSPGK
264 B7H4-15495 LC		EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYASSTRATGIPARFSGS GSGTETFTLTISLQLQEDFAYYYCQVNWVPPFTFGGGTKVEIKRTVAAPSVDIIFPPSDBQLKSGT SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTL SKADYEKHKV ACEVTHQGLSSPVTKSFRNRGEC
265 B7H4-15478 HC		QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAI SWVRQAPGQGLEWMGGIIPIFGTANYAQK FQGRVTITADESTSTAYMELSSLRSED TAVYYCARGGPWFD PWQGT LTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVWSN SGA L TSVHFTPAVLQSSGLYSLSSV SLGTQTYICNVN H KPNSNTKVDKKVEPKSCDKTHTCPCPAPELLGGPSVFLFPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYV DGEVHN AKTPREEQYN STYRVVSVLTVLHQDWLNGK EYKCKVS N KALPAPIEKTISAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV ESNGQ PENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQKSL PGK
266 B7H4-15478 LC		DIQMTQSPSTLSASVGDRVITTCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPSRSGS GSGTETFTLTISLQLQDDFATYYCQQYNSYPPFTFGGGTKVEIKRTVAAPSVDIIFPPSDBQLKSGT SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTL SKADYEKHKV ACEVTHQGLSSPVTKSFRNRGEC
267 B7H4-15441 HC		EVQILLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADS VKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAGPSLATMLAFDIWGQGT MVTVSSASTKG PSVFLAPSSKSTSGGTAALGCLVKDYFPEPVTVWSN SGA L TSVHFTPAVLQSSGLYSLSSV TVPSSSLGTQTYICNVN H KPNSNTKVDKKVEPKSCDKTHTCPCPAPELLGGPSVFLFPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYV DGEVHN AKTPREEQYN STYRVVSVLTVLHQD WLNGKEYKCKVS N KALPAPIEKTISAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAV EWSNGQ PENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQ KSLSLSPGK

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268 B7H4-15441 LC		DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYDASSLESGVPSRSGS GSGTETFTLTISLQPDFFATYYCQOSKSYPRTFGGGTKVEIKRTVAAPSVFIPPPSDQLKSGTAS VVCLLNNFYFREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTTLSKADYEKHKVYA CEVTHQGLSSPVTKSFNRGEC
269 B7H4-20496 HC		OLQLQESGPGLVKPSETLSLTCTVSGGSISSSVYYWSWIROPPGKGLEWIGSILVSGSTYYNPSL KSRVTISVDTSKNQFSLKLSVTAAADTAVYYCARAVSFLDVWGQGTMVIVSSASTKGPSVFPL APSSKSTSGTTAALGCLVKDYFPPEPVTVSWNSGALTSGVHTFPAVLQSSGLYLSLSSVTPSS LGTQTYICNVNHKPNSNTKVDKKVEPKSCDKTHTCPPCPAPEELLGGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE YKCKVSNKALPAPIEKTISAKGQPREPQVYTLPPSDELTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQKSLSLSP GK
270 B7H4-20496 LC		DIQMTQSPSSLASASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYGASSLQSGVPSRSGS GSGTETFTLTISLQPDFFATYYCQSYDPWTFGGGTKVEIKRTVAAPSVFIPPPSDQLKSGTAS SVVCLLNNFYFREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTTLSKADYEKHKVYA ACEVTHQGLSSPVTKSFNRGEC
271 SG-559- 01/PD-L1 CDR-H1	TAAIS	
272 SG-559- 01/PD-L1 CDR-H2	GIIPIFGKAHYAQKPGQ	
273 SG-559- 01/PD-L1 CDR-H3	KFHFGSGSPFGMDV	
274 SG-559- 01/PD-L1 CDR-L1	RASQSVSSYLA	
275 SG-559- 01/PD-L1 CDR-L2	DASN RAT	
276 SG-559- 01/PD-L1 CDR-L3	QQR SNWPT	
277 SG-559- 01/PD-L1 VH	QVQLVQSGAEVKKPGSSVKVSCKTGDTFSTAISWVRQAPGQGLEWMGGIIPIFGKAHYAQK FQGRVTITADESTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGT TVVSS	
278 SG-559- 01/PD-L1 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPA RFSGSGSGTDFTLTISLLEPEDFAVYYCQQRSNWPTFGQGTKVEIK	
279 h1F6 CDR- H1	NYGMN	
280 h1F6 CDR- H2	WINTYTGEPTYADAFKG	
281 h1F6 CDR- H3	DYGDYGM DY	
282 h1F6 CDR- L1	RASKSVSTSGYSFMH	
283 h1F6 CDR- L2	LASNLES	
284 h1F6 CDR- L3	QHSREVPW T	
285 h1F6 VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYGMNWVRQAPGQGLKWMGWINTYTGEPTY ADAFKGRVTMTRDT SISTAYMELSSLRSDDTAVYYCARDYGDYGM DWQGTTV VSS	
286 h1F6 VL	DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSFMIIWYQQKPGQPPKLLIYLASNLES GVPDRFSGSGSGTDFTLTISSLQAEDEVAVYYCQHSREVPWTFGQGTKVEIK	

TABLE OF SEQUENCES - continued

SEQ ID NO	Description	Sequence
287	h1F6 HC	QVQLVQSGAEVKPGASVKVSCKASGYTFTNYGMNWRQAPGQGLKWMGWINTYTGEPTY ADAFKGRVTMTRDTSI STAYMELSLRLSDDTAVYYCARDYGDYGMMDYWGQGTTVSSAS TKGSPVFPLAPSSKSTSGGAALGCLVKDYFPEPFTVWSNSGALTSGVHTFPAAVLQSSGL YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVVDKVEPKSCDKTHTCPCPAPELLGGPS VFLFPKPKDTLMSRTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNAKTKPREEQYNST YRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPSRDELT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMEALHNHYTQKSLSLSPKG
288	h1F6 LC	DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSFMHWYQQKPGQPPKLLIYLASNLES GVPDFRGSGSGTDFTLTISLQAEDVAVYYCQHSREVPTFGQGTKVEIKRTVAAPSVF IFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSL STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
289	TROP2 CDR-H1	NYGMN
290	TROP2 CDR-H2	WINTYTGEPTYTDDFKG
291	TROP2 CDR-H3	GGFGSSYWYFDV
292	TROP2 CDR-L1	KASQDVSIAVA
293	TROP2 CDR-L2	SASYRYT
294	TROP2 CDR-L3	QQHYITPLT
295	TROP2 VH	QVQLQSGSEKKPGASVKVSCKASGYTFTNYGMNWRQAPGQGLKWMGWINTYTGEPT YTDDFKGRFAFSLDTSVSTAYLQISSLKADDTAVYFCARGGFSSYWYFDVWGQGSLSVTVSS
296	TROP2 VL	DIQLTQSPSSLASAVGDRVSITCKASQDVSIAVA WYQQKPGKAPKLLIYSASYRTGVP DRFSGSGSGTDFTLTISLQPEDFAVYYCQHYITPLTFGAGTKVEIK
297	TROP2 CDR-H1	TAGMQ
298	TROP2 CDR-H2	WINTHSGVPKYAEDFKG
299	TROP2 CDR-H3	SGFGSSYWYFDV
300	TROP2 CDR-L1	KASQDVSTAVA
301	TROP2 CDR-L2	SASYRYT
302	TROP2 CDR-L3	QQHYITPLT
303	TROP2 VH	QVQLVQSGAEVKPGASVKVSCKASGYTFTTAGMQWVRQAPGQGLEWMGWINTHSGVPKY AEDFKGRVTISADTSTSTAYLQSSLKSED TAVYYCARSGFGSSYWYFDVWGQGTLVTVSS
304	TROP2 VL	DIQLTQSPSSLASAVGDRVTITCKASQDVSTAVAWYQQKPGKAPKLLIYSASYRTGVP SRFSG SGSGTDFTLTISLQPEDFAVYYCQHYITPLTFGQGTKLEIK
305	MICA CDR-H1	SQNIY
306	MICA CDR-H2	YIEPYNVVPMYNPFKKG
307	MICA CDR-H3	SGSSNF DY

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
308	MICA CDR-L1	SASSISSSHYLH
309	MICA CDR-L2	RTSNLAS
310	MICA CDR-L3	QQGSSLPLT
311	MICA VH	EIQLVQSGAEVKPGASVKVSCKASGYAFTSQNIYWVRQAPGQGLEWIGYIEPYNVVPMYNPKFKGRATLTVDKSTSTAYLELSSLRSEDTAVYYCARSGSSNFDYWGQGTLVTVSS
312	MICA VL	DIQLTQSPSSLSASVGDRVITITCSASSISSSHYLHWYQQKPGKSPKLLIYRTSNLASGVPSRFSGSGSTDYTLTISSLQPEDFATYYCQQGSSLPLTFGQGTKVEIK
313	MICA CDR-H1	NYAMH
314	MICA CDR-H2	LIWYDGSNKFYGDSVKG
315	MICA CDR-H3	EGSGHY
316	MICA CDR-L1	RASQGISSALA
317	MICA CDR-L2	DASSLES
318	MICA CDR-L3	QQFNSYPIT
319	MICA VH	QVQLVESGGVVQPGRSRLSCAASGFTFSNYAMHWVRQAPGEGLEWVALIWDGSNKFYGDSVKGRFTISRDNSKNTLYLQMNSLAAEDTAVYYCAREGSGHYWGQGTLVTVSS
320	MICA VL	AIQLTQSPSSLSASVGDRVITITCRASQGISSALAWYQQKPGKVPKSLIYDASSLESGVPSRFSGSGSTDFTLTISLQPEDFATYYCQQFNSYPITFGQGTRLEIK
321	MICA CDR-H1	NYAMS
322	MICA CDR-H2	YISPGGDYIYYADSVKG
323	MICA CDR-H3	DRRHYGSYAMDY
324	MICA CDR-L1	RSSKSLLLHSNLNTLY
325	MICA CDR-L2	RMSNLAS
326	MICA CDR-L3	MQHLEYPFT
327	MICA VH	QVQLVESGGGLVKPGGSLRLSCAASGFTFSNYAMSWIRQAPGKGLEWVSYIISPGGDYIYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCTDRRHYGSYAMDYWGQGTLVTVSS
328	MICA VL	DIVMTQSPSLPVTPGEPAISCRSSKSLLHSNLNTLYWFHQPGQSPQILIYRMSNLASGVPPDRFGSGSGTAGTLKISRVEAEDGVYYCMQHLEYPFTPGPGTKLEIK
329	MICA CDR-H1	TYAFH
330	MICA CDR-H2	GIVPIFGTLKYAQKFQD
331	MICA CDR-H3	AIQLEGGRPFDH

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
332	MICA CDR-L1	RASQGITSYLA
333	MICA CDR-L2	AASALQS
334	MICA CDR-L3	QQVNRGAAIT
335	MICA VH	QVQLVQSGAEVKPGSSVRVSCRASGGSSTTYAFHWVRQAPGQGLEWMGGIVPIFGTLKYAQ KFQDRVTLTADKSTGTAYMELNSRLDDTAVYYCARAIQLEGRPFDHWGQGTQTVSA
336	MICA VL	DIQLTQSPSFLSASVGDRVТИCRASQGITSYLA YQQKPGKAPKLLIYAASALQSGVPSRFSGR GSGTEFTLTISLQPEDFATYYCQQVNNGAAITFGHGTRLDIK
337	ITGav/CD51 CDR-H1	RYTMH
338	ITGav/CD51 CDR-H2	VISFDGSNKYYVDSDKG
339	ITGav/CD51 CDR-H3	EARGSYAFDI
340	ITGav/CD51 CDR-L1	RASQSVSSYLA
341	ITGav/CD51 CDR-L2	DASNRAT
342	ITGav/CD51 CDR-L3	QQRSNWPPFT
343	ITGav/CD51 VH	QVQLVESGGVVQPGRSRRLSCAASGFTFSRYTMHWRQAPGKGLEWVAVISFDGSNKYY DSVKGRFTISRDNSENTLYLQVNILRAEDTAVYYCAREARGSYAFDIWGQGTMVTVSS
344	ITGav/CD51 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLA YQQKPGQAPRLLIYDASNRATGIPARFSGS GSGTDFLTISLQPEDFAVYYCQQRSNWPPFTFGPGTKVDIK
345	ITGav CDR-H1	SFWMH
346	ITGav CDR-H2	YINPRSGYTEYNEIFRD
347	ITGav CDR-H3	FLGRGAMDY
348	ITGav CDR-L1	RASQDISNYLA
349	ITGav CDR-L2	YTSKIHS
350	ITGav CDR-L3	QQGNTFPYT
351	ITGav VH	QVQLQQSGGELAKPGASVKVSCKASGYTFSSFWMHWRQAPGQGLEWIGYINPRSGYTEYNE IIFRDKATMTDTSTSTAYMELSSLRSED TAVYYCASFLGRGAMDYWGQGTTVSS
352	ITGav VL	DIQMTQSPSSLSASVGDRVТИCRASQDISNYLA YQQKPGKAPKLLIYYTSKIHSGVPSRFSGR GSGTDYTFITISLQPEDIATYYCQQGNTFPYTFGQGTVKEIK
353	gpA33 CDR-H1	TSSYYWG
354	gpA33 CDR-H2	TIYYNGSTYYSPSLKS
355	gpA33 CDR-H3	QGYDIKINIDV

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
356	gpA33 CDR- L1	RASQSVSSYLA
357	gpA33 CDR- L2	VASN RAT
358	gpA33 CDR- L3	QQR SNWPLT
359	gpA33 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISTSSYYWGWI RQPPGKGLEWIGTIYYNGSTYYSPSL KSRVSISVDT SKNQFS LKLSSVTAA DTSVYYCARQGYDIKINIDVWGQGTTVTVSS
360	gpA33 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLA WYQQKPGQAPRLLIYVASNRATGIPARFSGS GSGTDF TLTISSLEPEDFAVYYCQQR SNWPLTFGGGT KVEIK
361	IL1Rap CDR- H1	SSWMN
362	IL1Rap CDR- H2	RIYPGDGNTHYAQKFQG
363	IL1Rap CDR- H3	GYLDPM DY
364	IL1Rap CDR- L1	QASQGINNYLN
365	IL1Rap CDR- L2	YTSGLHA
366	IL1Rap CDR- L3	QQYSILPWT
367	IL1Rap VH	QVQLVQSGA EVKKPGSSV KVSKAS GYAF TSSWMN WVRQAPGQGLEWMGRI YPGDGNTHY AQKFQGRV LTADK STAYMEL SLSR SEDTA VYYC GE GYLD PMDY WCG QGTL TVSS
368	IL1Rap VL	DIQMTQSPSSLSASVGDRV TITC QASQGINNYLN WYQQKPGKAPK LLIHYT SGLHAGVPSRF SG SGSGTDYTLTISSLEPEDV ATYYCQ QYSILPWT FCG GTKVEIK
369	EpCAM CDR-H1	SYGMH
370	EpCAM CDR-H2	VISYDG SNKYYAD SVKG
371	EpCAM CDR-H3	DMGWGSGWRPYYYYGMDV
372	EpCAM CDR-L1	RTSQSISSYLN
373	EpCAM CDR-L2	WASTRES
374	EpCAM CDR-L3	QQSYDIPYT
375	EpCAM VH	EVQLLESGGVVQPGRS LRLSCAAS GFTFSSYGMHW VRQAPGKGLEWVA V I SYDGSN KYYAD SVKG RFTI S RDNS KNTLYLQM NSLRAE DTAVYYCA KDMG WGS GWRP YYYYGMDV WGQ GTT VTVSS
376	EpCAM VL	ELQMTQSPSSLSASVGDRV TITC RTSQSIS SSYLN WYQQKPGQPPK LLIYWA STRESGV PDR FSGS GSGTDF TLTISSLQ PEDSAT YYCQ QSYDIPYT FGQ GTKLEIK
377	EpCAM CDR-H1	NYWMS
378	EpCAM CDR-H2	NIKQDGSEKFYAD SVKG
379	EpCAM CDR-H3	VGPSWEQDY

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
380	EpCAM CDR-L1	TGSSSNIGSYYGVH
381	EpCAM CDR-L2	SDTNRPS
382	EpCAM CDR-L3	QSYDKGFGHRV
383	EpCAM VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYWMSWVRQAPGKGLEWVANI KQDGSEKFYA DSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARVGPSWEQDYWGQGTLVTVSA
384	EpCAM VL	QSVLTQPPSVSGAPGQRVTISCTGSSNIGSYYGVHWYQQLPGTAPKLLIYSDTNRPSGVPDFRS GSKSGTSASLAITGLQAEDAYYCQSYDKFGIIRVFGGGTKLTVL
385	EpCAM CDR-H1	SYAIS
386	EpCAM CDR-H2	GIIPIFGTANYAQKFQG
387	EpCAM CDR-H3	GLLNYY
388	EpCAM CDR-L1	RASQSVSSNLA
389	EpCAM CDR-L2	GASTTAS
390	EpCAM CDR-L3	QQYNNWPPAYT
391	EpCAM VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAI SWVRQAPGQGLEWMGGI IPIFGTANYAQK FQGRVTITADESTAYMELSSLRSED TAVYYCARGLLWNYWGQGTLVTVSS
392	EpCAM VL	EIVMTQSPATLSVSPGERATLSCRASQS VSSNLAWYQQKPGQAPRLLI YGASTTASGIPARFSAS GSGTDFTLTISSLQSEDFAVYYCQQYNNWPPAYTFGQGTKEIK
393	EpCAM CDR-H1	NYGMN
394	EpCAM CDR-H2	WINTYTGEPTYGEDFKG
395	EpCAM CDR-H3	FGNYVDY
396	EpCAM CDR-L1	RSSKNLLHSNGITYLY
397	EpCAM CDR-L2	QMSNLAS
398	EpCAM CDR-L3	AQNLEIPRT
399	EpCAM VH	QVQLVQSGPEVKPGASVKVSCKASGYTFTNYGMNWVRQAPGQGLEWMGWINTYTGEPTY GEDFKGRFAFSLDTSASTAYMELSSLRSED TAVYYFCARFGNYVDYWGQGSLVTVSS
400	EpCAM VL	DIVMTQSPPLSPVTPGEPA SISCRSSKNLLHSNGITYLYWYLQKPGQSPQLLIYQMSNLASGVPD RFSSSGSGTDFTLKISRVEADVGVYYCAQNLEI PRTFGQGTKEIK
401	EpCAM CDR-H1	KYGMN
402	EpCAM CDR-H2	WINTYTEEPTYGDDFKG
403	EpCAM CDR-H3	FGSAVDY

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
404	EpCAM CDR-L1	RSSKSLLHSNGITYLY
405	EpCAM CDR-L2	QMSNRAS
406	EpCAM CDR-L3	AQNLELPRT
407	EpCAM VH	QIQLVQSGPEVKKPGEVKISCKASGYTFTKYGMNWVKQAPGQGLKWMGWINTYTEEPTYG DDFKGRFTFLDTSTAYLEISSLRSEDATYFCARFGSAVDYWGQGTLVTVSS
408	EpCAM VL	DIVMTQSALSNPVTLGESGSISCRSSKSLLHSNGITYLYWYLQPGQSPQLLIYQMSNRASGVPD RFSSSGSGTDFTLKISRVEAEDVGVYYCAQNLELPRTFGQGKLEMKR
409	EpCAM CDR-H1	DYSMH
410	EpCAM CDR-H2	WINTETGEPTYADDFKG
411	EpCAM CDR-H3	TAVY
412	EpCAM CDR-L1	RASQEISVSL
413	EpCAM CDR-L2	ATSTLDS
414	EpCAM CDR-L3	LQYASYPWT
415	EpCAM VH	QVKLQESGPTELKKGETVKISCKASGYTFTDYSMHWVKQAPGKGLKWMGWINTETGEPTYA DDFKGRFAFSLETSASTAYLQINNLKNEDATYFCARTAVYWGQGTTVSS
416	EpCAM VL	DIQMTQSPSLSASLGERVSLTCRASQEISVSLSWLQQEPDGTIKRLIYATSTLDGVPKRFSGR SGSDYSLTISSEDFDVYCLQYASYPWTFGGGTKLEIKR
417	CD352 CDR-H1	NYGMN
418	CD352 CDR-H2	WINTYSGEPRYADDFKG
419	CD352 CDR-H3	DYGRWYFDV
420	CD352 CDR-L1	RASSSVSHMH
421	CD352 CDR-L2	ATSNLAS
422	CD352 CDR-L3	QQWSSTPRT
423	CD352 VH	QIQLVQSGSELKKPGAVSVCKASGYTFTNYGMNWVRQAPGQDLKWMGWINTYSGEPRYA DDFKGRFVFSLDKSVNTAYLQISSLKAEDTAVYYCARDYGRWYFDVWQGTTVSS
424	CD352 VL	QIVLQSQSPATLSSLPGERATMSCRASSSVSHMHYQQKPGQAPRPWIYATSNLASGVPARFSGS GSGTDYTLTISSLEPEDFAVYYCQWSSTPRTFGGGTKVEIKR
425	CS1 CDR-H1	RYWMS
426	CS1 CDR-H2	EINPDSSTINYAPSLKD
427	CS1 CDR-H3	PDGNYWYFDV
428	CS1 CDR-L1	KASQDVGIAVA
429	CS1 CDR-L2	WASTRHT

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
430	CS1 CDR-L3	QQYSSYPYT
431	CS1 VH	EVQLVESGGGLVQPGGSLRLSCAASGFDFSRWMSWVRQAPGKGLEWIGEINPDSSTINYAPS LKDKEIISRDNAKNNSLYLQMNSLRAEDTAVYYCARPDGNYWYFDVWGQGTLVTVSS
432	CS1 VL	DIQMTQSPSLSASVGDRVTITCKASQDVIAVAVYQQKPGKVPKLLIYWASTRHTGVPRDRFS GSGSGTDFTLTISLQPEDVATYCCQQYSYPYTFGQGTKVEIKR
433	CD38 CDR-H1	SFAMS
434	CD38 CDR-H2	AISGSGGGTYYADSVKG
435	CD38 CDR-H3	DKILWFGEPVFDY
436	CD38 CDR-L1	RASQSVSSYLA
437	CD38 CDR-L2	DASN RAT
438	CD38 CDR-L3	QQRSNWPPT
439	CD38 VH	EVQLLESGGGLVQPGGSLRLSCAVSGFTFNSFAMS WVRQAPGKGLEWVSAISGSGGGTYYAD SVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYFCAKD KILWFGE PVFDYWGQGTLVTVSS
440	CD38 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLA WYQQKPGQAPRLLIYDASNRATGIPARFSGS GSGTDF TLTISSLEPEDFAVYYCQQR SNWPPTFGQGTKVEIKR
441	CD25 CDR-H1	SYRMH
442	CD25 CDR-H2	YINPSTGYTEYNQKFKD
443	CD25 CDR-H3	GGGVFDY
444	CD25 CDR-L1	SASSSI SYMH
445	CD25 CDR-L2	TTSNLAS
446	CD25 CDR-L3	HQRSTYPLT
447	CD25 VH	QVQLVQSGAEVKKP GSSVKVSCKASGYTFTSYRMHWVRQAPGQGLEWIGYINPSTGYTEYNQ KFKDKATITADESTNTAYMELSSLRSEDTAVYYCARGGGVFDYWGQGTLVTVSS
448	CD25 VL	DIQMTQSPSTLSASVGDRVTITCSASSSI SYMH YQQKPGKAPKLLIYTTSNLASGVPARFSGSG SGTEFTLTISLQPDDFATYYCHQRSTYPLTFGQGTKVEVK
449	ADAM9 CDR-H1	SYWMH
450	ADAM9 CDR-H2	EIIIPINGHTNYNEKFKS
451	ADAM9 CDR-H3	GGYYYYGSRDYFDY
452	ADAM9 CDR-L1	KASQSVDYDGDSYMN
453	ADAM9 CDR-L2	AASDLES
454	ADAM9 CDR-L3	QQSHEDPFT

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
455	ADAM9 VH	QVQLQQPGAEVLVKPGASVQLSCKASGYTFTSYWMHWVKQRPGQGLEWIGEIIPINGHTNYNE KFKSKATLTLDKSSSTAYMQLSSLASEDASAVYYCARGGYYYYGSRDYFDYWQGTTLVSS
456	ADAM9 VL	DIVLTQSPASLAVALGQRATISCKASQSVYDGDGSYMNWYQQIPGQPPKLLIYAASDLESGIPA RFGSGSGTDFTLNIHPVEEEDAATYYCQQSHEDPFTFGGGTKLEIK
457	ADAM9 CDR-H1	SYWMH
458	ADAM9 CDR-H2	EIIPIFGHTNYNEKPKS
459	ADAM9 CDR-H3	GGYYYYPRQGFLDY
460	ADAM9 CDR-L1	KASQSVVDYSGDSYMN
461	ADAM9 CDR-L2	AASDLES
462	ADAM9 CDR-L3	QQSHEDPFT
463	ADAM9 VH	EVQLVESGGGLVKGGSRLSCAASGFTFSSYWMHWVRQAPGKGLEWVGEEIIPIFGHTNYNEK FKSRFTISLDNSKNTLYLQMGLRAEDTAVYYCARGGYYYYPRQGFLDYWGQGTTVTVSS
464	ADAM9 VL	DIVLTQSPDSLAVSLGERATISCKASQSVDYSQDSYMNWYQQKPGQPPKLLIYAASDLESGIPA RFGSGSGTDFTLTISSLEPEDFATYYCQQSHEDPFTFGGGTKLEIK
465	CD59 CDR-H1	SYGMN
466	CD59 CDR-H2	YISSSSSTIYYADSVKG
467	CD59 CDR-H3	GPGMDV
468	CD59 CDR-L1	KSSQSVLYSSNNKNYLA
469	CD59 CDR-L2	WASTRES
470	CD59 CDR-L3	QQYYSTPQLT
471	CD59 VH	QVQLQQSGGGVVQPGRSGLSCKASGFTFSSYGMNWVRQAPGKGLEWVSYISSSSSTIYYADS VKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGPGMDVWGQGTTVTVS
472	CD59 VL	DIVLTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYLAWYQQKPGQPPKLLIYWASTRESGV PDRFGSGSGTDFTPAISSLQAEDVAVYYCQQYYSTPQLTFGGGTVVDIK
473	CD19 (hBU12) CDR-H1	TSGMGVG
474	CD19 (hBU12) CDR-H2	HIWWDKKRYNPALKS
475	CD19 (hBU12) CDR-H3	MELWSYYFDY
476	CD19 (hBU12) CDR-L1	SASSSVSYMH

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
477	CD19 (hBU12) CDR-L2	DTSKLAS
478	CD19 (hBU12) CDR-L3	FQGSVYPFT
479	CD19 (hBU12) VH	QVQLQESGPGLVKPSQTLSTCTVSGGSISTSGMGVGWIRQHPGKGLEIGHIWWDDDKRYNP ALKSRVTISVDTSKNQFSLKLSVTAAADTAVYYCARMELWSYYFDYWGQGTLVTVSS
480	CD19 (hBU12) VL	EIVLTQSPATLSSLPGERATLSCSASSSVSYMHWYQQKPGQAPRLLIYDTSKLASGIPARFSGSG SGTDPFTLTISLEPEDVAVYYCFQGSVYPFTFGQGTLKLEIKR
481	CD19 (hBU12) HC	QVQLQESGPGLVKPSQTLSTCTVSGGSISTSGMGVGWIRQHPGKGLEIGHIWWDDDKR YNPALKSRTVISVDTSKNQFSLKLSVTAAADTAVYYCARMELWSYYFDYWGQGTLVTVSS ASTKGPSVPFLAPSSKSTSGTAALGCLVKDYFPEPVTVWSNSGALTSGVHTFPAILQSS GLYSLSVVTPVPSLGTQTYICNVNHKPSNTVKDKVEPKSCDKTHTCPGCPAPELGG PSVLFPPPKDKTLMIISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESENQGPENNYTTPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCVMHEALHNHYTQKSLSLSPKG
482	CD19 (hBU12) LC	EIVLTQSPATLSSLPGERATLSCSASSSVSYMHWYQQKPGQAPRLLIYDTSKLASGIPAR FSGSGSGTDFTLTISLEPEDVAVYYCFQGSVYPFTFGQGTLKLEIKRTVAAPSFIGPPS DEQLKSGTASVVCILNNFVPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
483	CD138 CDR-H1	NYWIE
484	CD138 CDR-H2	EILPGTGRTIYNEKFKG
485	CD138 CDR-H3	RDYYGNFYAMDY
486	CD138 CDR-L1	SASQGINNYLN
487	CD138 CDR-L2	YTSTLQS
488	CD138 CDR-L3	QQYSKLPRT
489	CD138 VH	QVQLQQSGSELMMPGASVKISCKATGYTFSNYWEWVKQRPGHGLEIGEILPGTGR NEFKKGKATFTADISSNTVQMQLSSLTSEDASAVYYCARRDYYGNFYAMDYWGQGTSVT VSS
490	CD138 VL	DIQMTQSTSSLSASLGDRVТИCSASQGINNYLNWYQQKPDGTVELLIYYTSTLQSGVP SRFSGSGSGTDYSLTISNLEPEDIGTYYCQQYSKLPRTFGGGTKLEIK
491	CD166 CDR-H1	TYGMGVG
492	CD166 CDR-H2	NIWWSEDKHYSPSLKS
493	CD166 CDR-H3	IDYGNDYAFTY
494	CD166 CDR-L1	RSSKSLLHSNGITYLY
495	CD166 CDR-L2	QMSNLAS
496	CD166 CDR-L3	AQNLELPYT
497	CD166 VH	QITLKESGPTLVKPTQTLTCTSGFSLSTYGMGVGWIROPPGKALEWLANIWWSEDKHYSP LKSRLTITKDTSKNQVVLITNVDPVTATYYCVQIDYGNDYAFTYWGQGTLVTVSS

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SEQ ID NO	Description	Sequence
498	CD166 VL	DIVMTQSPLSLPVTPGEPAISCRSSKSLLHSNGITYLYWYLQKPGQSPQLIYQMSNLASGVPD RFSGSGSGTDFTLKISRVEAEDVGVYYCAQNLELPYTFQGQGTKLEIK
499	CD56 CDR-H1	SFGMH
500	CD56 CDR-H2	YISSGSFTIYYADSVKG
501	CD56 CDR-H3	MRKGYAMDY
502	CD56 CDR-L1	RSSQIITHSDGNTYLE
503	CD56 CDR-L2	KVSNRFS
504	CD56 CDR-L3	FQGSHVPHT
505	CD56 VH	QVQLVESGGVVQPGRSRLSCAASGFTFSSFGMHWVRQAPGKGLEWVAYISSLGFTIYYADS VKGRPTISRDNSKNTLYLQMNSLRAEDTAVYYCARMRKGYAMDYWGQGTLVTVSS
506	CD56 VL	DVVMTOQSPLSLPVTLGQPASISCRSSQIIHSDGNTYLEWFQQRPGQSPRLLIYKVSNRFSGVPPDR RFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVPHTFGQGQGTKVEIK
507	CD74 CDR-H1	NYGVN
508	CD74 CDR-H2	WINPNTGEPTFDDDFKG
509	CD74 CDR-H3	SRGKNEAWFAY
510	CD74 CDR-L1	RSSQSLVHRNGNTYLN
511	CD74 CDR-L2	TVSNRFS
512	CD74 CDR-L3	SQSSHVPPT
513	CD74 VH	QVQLQQSGSEKKPGASVKVSCKASGYTFTNYGVNWIKQAPGQGLQWMGWINPNTGEPTFD DDFKGRFAFLDTSVSTAYLQISSLKADDTAVYFCRSRGKNEAWFAYWGQGTLVTVSS
514	CD74 VL	DIQLTQSPLSLPVTLGQPASISCRSSQSLVHRNGNTYLHWFFQQRPGQSPRLLIYTWSNRFSGVPPD RFSGSGSGTDFTLKISRVEAEDVGVYFCQSHPPTFGAGTRLEIK
515	CEACAM5 CDR-H1	TYWMS
516	CEACAM5 CDR-H2	EIHPSSTINYAPS LKD
517	CEACAM5 CDR-H3	LYFGFPWFAY
518	CEACAM5 CDR-L1	KASQDVGT SVA
519	CEACAM5 CDR-L2	WTSTRHT
520	CEACAM5 CDR-L3	QQYSLYRS
521	CEACAM5 VH	EVQLVESGGVVQPGRSRLSCSAGFDFTTYWMSWVRQAPGKGLEWIGEIHPSSTINYAPS LKDRFTISRDNAKNTLFLQMDSLRPEDTGVYFCASLYFGFPWFAYWGQGTPVTVSS

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SEQ ID NO	Description	Sequence
522	CEACAM5 VL	DIQLTQSPSSLSASVGDRVTITCKASQDVGTSAWYQQKPGKAPKLLIYWTRHTGVPSRFSG SGSGTDFTFTISSLQPEDIATYYCQQYSLYRSPFGQGTKVEIK
523	CanAg CDR- H1	YYGMN
524	CanAg CDR- H2	WIDTTTGEPTYAQKFQG
525	CanAg CDR- H3	RGPYNWYFDV
526	CanAg CDR- L1	RSSKSLLHSNGNTLY
527	CanAg CDR- L2	RMSNLVS
528	CanAg CDR- L3	LQHLEYPFT
529	CanAg VH	QVQLVQSGAEVKKPGETVKISCKASDYTFYYGMNWVKQAPGQGLKWMGWIDTTGEPTYA QKFQGRIAFSLETSASTAYLQIKSLKSEDTATYFCARRGPYNWYFDVWGQGTTVTVSS
530	CanAg VL	DIVMTQSPLSVPVTPGEPVSISCRSSKSLLHSNGNTLYWFLQRPGQSPQLLIYRMSNLVSGVPD RFSGSGSGTAFTLIRISRVEAEDVGYYYCLQIILEYPFTFGPGTKLELK
531	DLL-3 CDR- H1	NYGMN
532	DLL-3 CDR- H2	WINTYTGEPTYADDFKG
533	DLL-3 CDR- H3	IGDSSPSDY
534	DLL-3 CDR- L1	KASQSVSNDDVV
535	DLL-3 CDR- L2	YASNRYT
536	DLL-3 CDR- L3	QQDYTSPWT
537	DLL-3 VH	QVQLVQSGAEVKKP GASVKVSKASGYTFTNYGMNWVRQAPGQGLEWMGWINTYTGEPTY ADDFKGRVTMTDTSTSTAYMELRSLSRSDDTAVYYCARIGDSSPSDYWGQGTLVTVSS
538	DLL-3 VL	EIVMTQSPATLSVSPGERATLSCKASQSVSNDDVVYQQKPGQAPRLIIYYASNRYTGIPA RFSGSGSGTEFTLTISLQSEDFAVYYCQQDYTSPWTFGQGTLKLEIK
539	DPEP-3 CDR-H1	SYWIE
540	DPEP-3 CDR-H2	EILPGSGNTYYNERFKD
541	DPEP-3 CDR-H3	RAAAAYS NPEWFAY
542	DPEP-3 CDR-L1	TASSSVNSFY LH
543	DPEP-3 CDR-L2	STS NLAS
544	DPEP-3 CDR-L3	HQYHRSPYT
545	DPEP-3 VH	QVQLVQSGAEVKKP GS SVK VSK ASGGT FSSY WI EW VR QAP GQGLE W M GE IL PG SG NT YY NE RFKDRVTITA DEST STAY MEL S L R S E D T AV YY CARR A A Y Y S N P E W F A Y W G Q G T L V T V S S

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
546	DPEP-3 VL	EIVLTQSPATLSLSPGERATLSCTASSSVNSFYLHWYQQKPGGLAPRLLIYSTSNLASGIPDRFSGS GSGTDFTLTISRLPEDFAVYYCHQYHRSPTYTFQGTKEIK
547	EGFR CDR-H1	SYWMQ
548	EGFR CDR-H2	TIYPGDGDTTYTQKFQG
549	EGFR CDR-H3	YDAPGYAMDY
550	EGFR CDR-L1	RASQDINNYLA
551	EGFR CDR-L2	YTSTLHP
552	EGFR CDR-L3	LQYDNLLYT
553	EGFR VH	QVQLVQSGAEVAKPGASVKLSCKASGYTFTSYWMQWVKQRPGQGLECIGTIYPGDGDTTYTQ KFQGKATLTADKSSSTAYMQLSSLRSEDSAVYYCARYDAPGYAMDYWGQGTIVTVSS
554	EGFR VL	DIQMTQSPSSLSASVGDRVITCRASQDINNYLAWYQHKPGKGPKLIHYTSTLHPGIPSRSFGS GSGRDYSFSISSLQPEDIATYYCLQYDNLLYTFQGTKEIK
555	EGFR CDR-H1	RDFAWN
556	EGFR CDR-H2	YISYNGNTRYQPSLKS
557	EGFR CDR-H3	ASRGPPY
558	EGFR CDR-L1	HSSQDINSNIG
559	EGFR CDR-L2	HGTNLDD
560	EGFR CDR-L3	VQYAQFPWT
561	EGFR VH	EVQLQESGPGLVKPSQTLSLTCTVSGYSISRDFAWNWIQPPGKGLEWMGYIISYNGNTRYQPS LKSRTISRDTSKNQFFKLKNSTAAADTATYYCVTASRGFPYWQGTIVTVSS
562	EGFR VL	DIQMTQSPSSMSVGDRVITCHSSQDINSNIGWLQQKPGKSFKGLIYHGTNLDDGVPSRSFGS GSGTDYTLTISSLQPEDFATYYCVQYAQPPWTFGGGTKEIK
563	EGFR CDR-H1	NYGVH
564	EGFR CDR-H2	VIWSGGNTDYNTPFTS
565	EGFR CDR-H3	ALTYYYDYEFAV
566	EGFR CDR-L1	RASQSIGTNIH
567	EGFR CDR-L2	YASESIS
568	EGFR CDR-L3	QQNNNWPTT
569	EGFR VH	QVQLQSGPGLVQPSQSLSITCTVSGFSLTNYGVHVVRQSPGKGLEWLGVIVSGGNTDYNTPF TSRSLINKDNSKSQVFFKMNSLQSNDTAIYYCARALTYYYDYEFAVWGQGTIVTVSA

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SEQ ID NO	Description	Sequence
570	EGFR VL	DILLTQSPVILSVSPGERVSFSCRASQSIGTNIHWYQQRTNGSPRLLIKYASESISGIPSRFSGSGSG TDFTLSINSVESEDIADYYCQQNNWPTTFGAGTKLELK
571	FRa CDR-H1	GYFMN
572	FRa CDR-H2	RIHPYDGDTFYNQKFQG
573	FRa CDR-H3	YDGSRAMDY
574	FRa CDR-L1	KASQSVSFAGTSLMH
575	FRa CDR-L2	RASNLEA
576	FRa CDR-L3	QQSREYPYT
577	FRa VH	QVQLVQSGAEVVVKPGASVKISCKASGYTFTGYFMNWVKQSPGQSLEWIGRIHPYDGDTFY NQKFGQKATLTVDKSSNTAHMELLSLTSEDFAVYCYTRYDGSRAMDYWGQGTTVTVSS
578	FRa VL	DIVLTQSPSLAVSLGQPAIIISCKASQSVSFAGTSLMHWYHQKPGQQPRLLIYRASNLEAGVPD RFSGSGSKTDFTLTISPVEAEDAATYYCQQSREYPYTFFGGTKLEIK
579	FRa CDR-H1	GYGLS
580	FRa CDR-H2	MISSGGSYTYYADSVKG
581	FRa CDR-H3	HGDPPAWFAY
582	FRa CDR-L1	SVSSSISSNNLH
583	FRa CDR-L2	GTSNLAS
584	FRa CDR-L3	QQWSSYPYMYT
585	FRa VH	EVQLVESGGVVQPGRSRLSCSASGFTFSGYGLSWVRQAPGKGLEWVAMISSGGSYTYY ADSVKGRFAISRDNAKNTLFLQMDSLRPEDTGVYFCARHGDDPAWFAYWGQGTPVTVSS
586	FRa VL	DIQLTQSPSSLASAVGDRVITICVSSSISSNNLHWYQQKPGKAPKPWIYGTSNLASGVPSRFSG SGSGTDYTFITSSLQPEDIATYYCQQWSSYPYMYTFFGQGTTKVEIK
587	MUC-1 CDR-H1	NYWMN
588	MUC-1 CDR-H2	EIRLKSNNYTTHYAESVKG
589	MUC-1 CDR-H3	HYYFDY
590	MUC-1 CDR-L1	RSSKLLLHSNGITYFF
591	MUC-1 CDR-L2	QMSNLAS
592	MUC-1 CDR-L3	AQNLELPPT
593	MUC-1 VH	EVQLVESGGGLVQPGGSMRLSCVASGFPPSNYWMNWVRQAPGKGLEWVGIRLKSNNYTH YAESVKGRTFISRDDSNSLYLQMSNLKTEDTAVYYCTRHYYFDYWGQGTLVTVSS
594	MUC-1 VL	DIVMTQSPSLSNPVTGPGEPASISCRSSKSLLHSNGITYFFWYLQKPGQSPQLLIYQMSNLASGVPD RFSGSGSGTDFTLRISRVEAEDGVVYCAQNLELPPTFGQGTTKVEIK
595	Mesothelin CDR-H1	SYWIG
596	Mesothelin CDR-H2	IIDPGDSRTRYSPSFQG

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
597	Mesothelin CDR-H3	GQLYGGTYMDG
598	Mesothelin CDR-L1	TGTSSDIGGYNSVS
599	Mesothelin CDR-L2	GVNNRPS
600	Mesothelin CDR-L3	SSYDIESATPV
601	Mesothelin VH	QVELVQSGAEVKKGESLKISCKGGYSPTSYWIGWVRQAPGKGLEWNGIIDPGDSRTRYSPSF QGQTISADKSISTAYLQWSSLKASDTAMYYCARGQLYGGTYMDGWGQGTLTVSS
602	Mesothelin VL	DIALTQPASVGSPGQSITISCTGTSSDIGGYNSVSQYQQHPGKAPKLMIVGVNNRPSGV SNRFSGSKSGNTASLTISGLQAEDeadYYCSSYDIESATPVFGGKLTVL
603	ROR-1 CDR-H1	AYNIH
604	ROR-1 CDR-H2	SFDPYDGGSSYNQKFKD
605	ROR-1 CDR-H3	GWYYFDY
606	ROR-1 CDR-L1	RASKSISKYLA
607	ROR-1 CDR-L2	SGSTLQS
608	ROR-1 CDR-L3	QQHDESPYT
609	ROR-1 VH	QVQLQESGPLVKPSQTLSLTCTVSGYAFTAYNIHWVRQAPGQGLEWMGSFDPYDGSSYNQ KFKDLRTISKDTSKNQVVLTMTNMDPVDATYYCARGWYYFDYWGHTLTVSS
610	ROR-1 VL	DIVMTQTPLSLPVTPGEPAISCRASKSISKYLAWYQQKPGQAPRLLIYSGSTLQSGIPPRFSGSG YGTDFTLTINNIESEDAAYFCQQHDESPYTGFEGTKVEIK
611	B7-H3 CDR-H1	SFGMH
612	B7-H3 CDR-H2	YISSDSSAIYYADTVKG
613	B7-H3 CDR-H3	GRENIYYGSRLDY
614	B7-H3 CDR-L1	KASQNVDTNVA
615	B7-H3 CDR-L2	SASYRYS
616	B7-H3 CDR-L3	QQYNNYPFT
617	B7-H3 VH	DVQLVESGGGLVQPGGSRKLSCAASGFTFSSFGMHWVRQAPEKGGLEWVAYISSDSSAIYY ADTVKGRFTISRDNPKNTLFLQMITSRSEDTAMYYCGRGRENIYYGSRLDYWGQGTTLVSS
618	B7-H3 VL	DIAMTQSQKFMSTSVDGDRVSVTCKASQNVDTNVAWYQQKPGQSPKALIYSASYRYSVPD RFTGSGSGTDFTLTINNVQSEDLAEYFCQQYNNYPFTFGSGTKLEIK
619	B7-H3 CDR-H1	SYGMS
620	B7-H3 CDR-H2	TINSGGSNTYYPDSDLKG

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
621	B7-H3 CDR- H3	HDGGAMDY
622	B7-H3 CDR- L1	RASESIYSYLA
623	B7-H3 CDR- L2	NTKTLPE
624	B7-H3 CDR- L3	QHHYGTTPWTT
625	B7-H3 VH	EVQLVESGGGLVKGSSLRLSCAASGFTPSSYGMWSVRQAPGKGLEWVATINSIGGSNTYY PDSLKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHDGGAMDYWGQGTTVSS
626	B7-H3 VL	DIQMTQSPSLSASVGDRVITCRASESIYSYLAQYQQKPGKAPKLLVYNTKTLPEGVPSRFS GSGTDFTLTISSLQPEDFATYYCQIIIIYGTTPWTFGQGTRLEIK
627	B7-H3 CDR- H1	SFGMH
628	B7-H3 CDR- H2	YISSSGSGTIYYADTVKG
629	B7-H3 CDR- H3	HGYRYEGFDY
630	B7-H3 CDR- L1	KASQNVDTNVA
631	B7-H3 CDR- L2	SASYRYS
632	B7-H3 CDR- L3	QQYNNYPFT
633	B7-H3 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTPSSFGMHWVRQAPGKGLEWVAYISSLGGTIVY YADTVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHGYRYEGFDYWGQGTTVSS
634	B7-H3 VL	DIQMTQSPSFLSASVGDRVITCKASQNVDTNVAWYQQKPGKAPKALIYSASYRYSGVPSRFS GSGSGTDFTLTISSLQPEDFAEYFCQQYNNYPFTFGQGTRLEIK
635	B7-H3 CDR- H1	NYVMH
636	B7-H3 CDR- H2	YINPYNDDVKYNEKFKG
637	B7-H3 CDR- H3	WGYYGSPLYYFDY
638	B7-H3 CDR- L1	RASSRLIYMH
639	B7-H3 CDR- L2	ATSNLAS
640	B7-H3 CDR- L3	QQWNSNPPT
641	B7-H3 VH	EVQLQSGPELVKGASVKMSCKASGYTFTNYVMHWVKQKPGQGLEWIGYINPYNDDVKYN EKFKGKATQTSDFKSSSTAYMELSSLTSEDAVYYCARWGGYGSPLYYFDYWGQGTTVSS
642	B7-H3 VL	QIVLQSPTILSASPGEKVMTCRASSRLIYMHWYQQKPGSSPKPWYATSNLASGVPAR FSGSGSGTYSLSLTISRVEAEDAATYYCQQWNSNPPTFGTGTKEIK
643	B7-H3 CDR- H1	NYVMH
644	B7-H3 CDR- H2	YINPYNDDVKYNEKFKG

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SEQ ID NO	Description	Sequence
645	B7-H3 CDR- H3	WGYYGSPLYYFDY
646	B7-H3 CDR- L1	RASSRLIYMH
647	B7-H3 CDR- L2	ATSNLAS
648	B7-H3 CDR- L3	QQWNSNPPT
649	B7-H3 VH	QVQLVQSGAEVKKPSSVKVSCKASGYTFTNYVMHWVRQAPGQGLEWMGYINPYNDDVKY NE KFKGRVTITADESTSTAYMELSSLRSEDTAVYYCARWGGYGSPLYYFDYWGQGTLVTVSS
650	B7-H3 VL	EIVLTQSPATLSLSPGERATLSCRASSRLIYMHWYQQKPGQAPRPLIYATSNLASGIPARFSGSGS GTDFTLTISSLPEPEDFAVYYCQQWNSNPPTFGQGTLKVEIK
651	B7-H3 CDR- H1	SYTIH
652	B7-H3 CDR- H2	YINPNSRNTDYAQKFQG
653	B7-H3 CDR- H3	YSGSTPYWYFDV
654	B7-H3 CDR- L1	RASSSVSYMN
655	B7-H3 CDR- L2	ATSNLAS
656	B7-H3 CDR- L3	QQWSSNPLT
657	B7-H3 VH	EVQLVQSGAEVKKPSSVKVSCKASGYSFTSYTIHWVRQAPGQGLEWMGYINPNSRNTDYAQ KFQGRVTLTADKSTSTAYMELSSLRSEDTAVYYCARYSGSTPYWYFDVWCQGTTTVSS
658	B7-H3 VL	DIQLTQSPSFLSASVGDRVITCRASSSVSYMNWYQQKPGKSPKPWIYATSNLASGVPSRFSVS VSGTEHTLTLISSLQPEDFATYYCQQWSNNPLTFGQGTLKLEIK
659	B7-H3 CDR- H1	SYWMH
660	B7-H3 CDR- H2	LIHPDSGSTNYNEMFKN
661	B7-H3 CDR- H3	GGRLYFDY
662	B7-H3 CDR- L1	RSSQSLVHSNGDTYLR
663	B7-H3 CDR- L2	KVSNRFS
664	B7-H3 CDR- L3	SQSTHVPYT
665	B7-H3 VH	EVQLVQSGAEVKKPSSVKVSCKASGYTFTSSYWMHWVRQAPGQGLEWIGLIHPDSGSTNYNE MFKNRATLTVDRTSTSTAYVELSSLRSEDTAVYFCAGGGRLYFDYWGQGTTTVSS
666	B7-H3 VL	DVVMQTQSPSLPVTPGEPAISCRRSSQSLVHSNGDTYLRWYLQKPGQSPQLLIYKVSNRFSGV DRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPYTFGGGTKVEIK
667	B7-H3 CDR- H1	SYWMH
668	B7-H3 CDR- H2	LIHPESGSTNYNEMFKN

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SEQ ID NO	Description	Sequence
669	B7-H3 CDR-H3	GGRLYFDY
670	B7-H3 CDR-L1	RSSQSLVHSNQDTYL
671	B7-H3 CDR-L2	KVSNRFS
672	B7-H3 CDR-L3	SQSTHVPYT
673	B7-H3 VH	EVQLVSGAENVKPGSSVKVSCKASGYTFSSYWMHWVRQAPGQGLEWIGLIHPESGSTNY NEMFKNRATLTVDRSTSTAYMELSSLRSEDTAVYYCAGGGRLYFDYWQGTTVTVSS
674	B7-H3 VL	DIVMTQSPSLPVTGPGEPAASICRSSQSQLVHSNQDTYLRWYLQKPGQSPQLLIYKVSNRFSGVPD RFSGSGSGTDFTLKISRVEADVGVYYCSQSTHVPYTFGGGTKVEIK
675	B7-H3 CDR-H1	SGYSH
676	B7-H3 CDR-H2	YIHSSGSTNYNPSLKS
677	B7-H3 CDR-H3	YDDYFEY
678	B7-H3 CDR-L1	KASQNVGFNVAW
679	B7-H3 CDR-L2	SASYRYS
680	B7-H3 CDR-L3	QQYNWYPFT
681	B7-H3 VH	EVQLQESGPLVKPSETLSLCAVTGYSITSGYSWHWIQFPNGLEWMGYIHSSGSTNY NPSLKSRSISRDTSKNQFFLKLSSVTAADTAVYYCAGYDDYFEYWGQGTTVTVSS
682	B7-H3 VL	DIQMTQSPSSLSASVGDRVITITCKASQNVGFNVAWYQQKPGKSPKALIYSASYRYSGV PSRSGSGSGTDFTLTISLQPEDFAEYFCQQYNWYPFTFGQGTKLEIK
683	B7-H3 CDR-H1	NYDIN
684	B7-H3 CDR-H2	WIFPGDDSTQYNEKFKG
685	B7-H3 CDR-H3	QTTGTWFAY
686	B7-H3 CDR-L1	RASQSISDYLY
687	B7-H3 CDR-L2	YASQSI
688	B7-H3 CDR-L3	QNGHSFPLT
689	B7-H3 VH	QVQLVSGAENVKPGASVKLSCKTSGYTFPTNYDINWVRQRPGQGLEWIGWIFPGDDSTQY NEFKFKGKATLTTDTSTSTAYMELSSLRSEDTAVYFCARQTTGTWFAYWGQGTLVTVSS
690	B7-H3 VL	EIVMTQSPATLSVSPGERVTLSCRASQSIISDYLYWYQQKSHESPRLLIKYASQSIISGIPA RFSGSGSGSEFTLTINSVEPEDVGVYYCQNGHSFPLTFQGQGTKLEIK
691	B7-H3 VH	QVQLQQSGAENVKPGSSVKVSCKASGGTFSSYAIISWVRQAPGQGLEWMGGIIIPILGIAN YAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARGGSGSYHMDVWGKGTTVTVSS
692	B7-H3 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWSQQKPGQAPRLLIYDASNRTGIP ARFSGSGSGTDFTLTISLQPEDFAVYYCQQRSNWPPRITFGQGTRLEIK

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SEQ ID NO	Description	Sequence
693	B7-H3 CDR-H1	IYNVH
694	B7-H3 CDR-H2	TIFPGNGDTSYNQKFKD
695	B7-H3 CDR-H3	WDDGNVGVFAH
696	B7-H3 CDR-L1	RASENIINNYLT
697	B7-H3 CDR-L2	HAKTLAE
698	B7-H3 CDR-L3	QHHYGTPPT
699	B7-H3 VH	QVQLQQPGAEVKPGASVKMSCKASGYTFTIYNVHWIKQTPGQGLEWMGTIFPGNGDTSQNQFKDKATLTTDKSSKTAYMQLMSLTSEDSAVYYCARWDDGNVGVFAHWGQGTLTVSA
700	B7-H3 VL	DIQMTQSPASLSASVGGETVTITCRASENIINNYLTWFQQKQGKSPQLLVYHAKTLAEGVPSRFSGSGSGTQFSLKINSLQPEDFGSYYCQHYGTPPTFGGGTKLEIK
701	B7-H3 VH	EVQLVQSGAEVKKPGASVKVSCKASGYTFTIYNVHWVRQAPGQGLEWMGTIFPGNGDTSYNQFKDKVTMTTDTSTSTAYMELSSLRSEDATAVYYCARWDDGNVGVFAHWGQGTLTVSS
702	B7-H3 VL	DIQMTQSPSSLASAVGDRVTITCRASENIINNYLTWFQQKQGKSPQLLIYHAKTLAEGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQHHYGTPPTFGGGTKVEIK
703	B7-H3 VH	EVQLVQSGAEVKKPGASVKVSCKASGYTFTIYNVHWIRQAPGQGLEWMGTIFPGNGDTSYNQFKDRATLTTDKSTKTAYMELRSRSDDTAVYYCARWDDGNVGVFAHWGQGTLTVSS
704	B7-H3 VL	DIQMTQSPSSLASAVGDRVTITCRASENIINNYLTWFQQKPGKAPKLLVYHAKTLAEGVPSRFSGSGSGTQFTLTISLQPEDFATYYCQHHYGTPPTFGQGTTKLEIK
705	HER3 H	QVQLQQWGAGLLKPSETLSLTCAVYGGSGYWWIRQAPGKLEWIGEINHSGSTNYNPSLKSRTVITSVETSNQFLSKLSSVTAADTAVYYCARDKWTWYFDLWRGRTLTVTSSASTKGPSVPLAPSSKSTSGTAALGCLVKDYFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSVVTVFVSSSLIGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPCCPAPELLGGPSVFLFPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYKCKVSVNKGKLPAPIEKTISKTKQPREPQVYTLPPSREEMTKNQVPSDIATEWESENQOPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQKSLSLSPKG
706	HER3 L	DIEMTQSPDSLAVSLGERATINCRRSSQSVLYSSSNRNYLAWYQONPGQOPPKLLIYWASTRESGVPDFRGSGSGTDFLTLTISLQAEDVAVYYCQYYSTPRTFGQGTTKVEIKRTVAAPSVIDFPPSDEQLKSGTASVCLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
707	HER3 H	EVQLLESGGGLVQPGGSLRLSCAASGFTFHYVMAWVRQAPGKLEWVSSISSSGWTLYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCTRGLKMATIFDVWQGQTLTVSSA STKGPSVPLAPCRSRTSEESTAALGCLVKDYFPEPVTVWSNSGALTSGVIIITFPAVLQSSGLYSLSVVTVFVSSSLIGTQTYICNVNHKPSNTKVDKTVERKCCVECPCCPAPPVAGPSVFLFPPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSVNKGKLPAPIEKTISKTKQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIATEWESENQOPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQKSLSLSPKG
708	HER3 L	QSAITQPAVGSGPGQSITISCTGTSVDGSYNNVSVWYQQHPGKAPKLIYEVSRQPSGVSNRFSGSKSGNTASLTISLQTEDEADYYCCSYAGSSIFVIFGGGTKVTVLGQPKAAPS VTLFPSSSEELQANKATLVCVLSDFYGPAGTVANKADGSPVKVGVE TTKPSKQSNKNYAASSYLSLTPEQWKS
709	HER3 H	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMS WVRQAPGKLEWVSAINSQGKSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARWGDGE GFPD I WGQGTLTVSSA STKGPSVPLAPSSKSTSGTAALGCLVKDYFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSVVTVFVSSSLIGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPCCPAPELLGGPSVFLFPPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYKCKVSVNKGKLPAPIEKTISKTKQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIATEWESENQOPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCVMHEALHNHYTQKSLSLSPKG

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SEQ ID NO	Description	Sequence
710	HER3 L	DIQMTQSPSSLSASVGDRVTITCRASQGINSWLAWYQQKPGKAPKLLIYGASSLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQYSSFPTTFQGQTKVEIKRTVAAPSVFIFPPSDEQLKSGTA SVVCLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
711	HER3 H	QVQLVQSGAEVKPGASVKVSCKASGYTFRRSSYISWVRQAPGQGLEWMGWYAGTGSPSYN QKLQRVRTMTTDTSSTAYMELRSRSDTAVYYCARHRDYYNSLTYWGQGTIVTVSSAST KGPSVFPLAEEKLTSGGTAALGCLVKDYFPEPVTSWNNSGALTSGVHTFPAPLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHPKPSNTKVDKVVEPKSCDKTHTCPPCAPELLGGPSVLFPPPKP DTLMISRTPEVTCVVVDVSIIEDPEVKFNWYVDGVEVIINAKTPREEQYNSTYRVVSVLTVLII QDWLNKEYCKVSNKALPAPIEKTISKAKGQPREFQVYTLPPSRDELTKNQVSLTCLVKGFY PSDIAVEWESENQPEENNYKTTPPVLDSDGSFFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPG
712	HER3 L	DIVMTQSPDSLAVSLGERATINCKSSQSVLNSGNQKNYLWTWYQQKPGQPPKLLIYWASTRESG VPDRFSGSGSGTDFTLTISSLQADEDVAVYYCQSDYSYPYTFQGQTKLEIKRTVAAPSVFIFPPSD EQLKSGTASVVCVLLNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTTLSKAD YEKHKVYACEVTHQGLSSPVTKSFNRGEC
713	PTK7 CDR-H1	TSNMGVG
714	PTK7 CDR-H2	IIIWWDDDKYYSPLSKS
715	PTK7 CDR-H3	SNYGYAWFAY
716	PTK7 CDR-L1	KASQDIYPYLN
717	PTK7 CDR-L2	RTNRLLD
718	PTK7 CDR-L3	LQYDEFPLT
719	PTK7 VH	QITLKESGPLVKPTQTLTCTFSGFSLSTSNNMGVGIROPPGKALEWLAHIWWDDDKYYSPS LKSRLTITKDTSKNQVLTMTNMDPVDTATYYCVRSNYGYAWFAYWGQGTIVTVSS
720	PTK7 VL	DIQMTQSPSSLSASVGDRVTITCKASQDIYPYLNWFQQKPGKAPKTLIYRTNRLDGVP RFGSGSGTDFTLTISSLQPEDIATYYCLQYDEFPLTFGAGTKLEIK
721	PTK7 CDR-H1	DYAVII
722	PTK7 CDR-H2	VISTYNDYTNNQDFKG
723	PTK7 CDR-H3	GNSYPYALDY
724	PTK7 CDR-L1	RASESVDSYKGKSFMH
725	PTK7 CDR-L2	RASNLES
726	PTK7 CDR-L3	QQSNEDPWT
727	PTK7 VH	QVQLVQSGPEVKPGASVKVSCKASGYFTDYAVHWVRQAPGKRLEWIGVISTYNDTY NNQDFKGRVTMTRDTSASTAYMELSRRLSEDTAVYYCARGNSYFYALDYWGQGTIVTVSS
728	PTK7 VL	EIVLTQSPATLSLSPGERATLSCRASESVDSYKGKSFMHYQQKPGQAPRLLIYRASNLES GIPARFSGSGSGTDFTLTISSLQPEDFAVYYCQGSNEDPWTFGGGTKLEIK
729	PTK7 CDR-H1	RYWMS
730	PTK7 CDR-H2	DLNPDSSAINYVDSVKG

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SEQ ID NO	Description	Sequence
731	PTK7 CDR-H3	ITTLVPTYTMDF
732	PTK7 CDR-L1	ITNTDIDDDMN
733	PTK7 CDR-L2	EGNGLRP
734	PTK7 CDR-L3	LQSDNLPLT
735	PTK7 VH	EVQLVESGGGLVQPGGSLRLSCAASGFDPSRYMSWVRQAPGKGLEWIGDLNPSSAINY VDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCTLITTLVPTYTMDFWGQGTSTVSS
736	PTK7 VL	ETTLTQSPA FM SATPGDKVNIS CITNTDIDDDMNWYQQKPGEAAILLISEGNGLRPGIPPRFSGS GYGTDFTLTINNIESEDAAYYFCLQSDNLPLTFGSGTKLEIK
737	hLIV22/LIV1 CDR-H1	DYYMH
738	hLIV22/LIV1 CDR-H2	WIDPENG DTEYGPKFQG
739	hLIV22/LIV1 CDR-H3	HNAHYGTWFAY
740	hLIV22/LIV1 CDR-L1	RSSQSLLHSSGNTYLE
741	hLIV22/LIV1 CDR-L2	KISTRFS
742	hLIV22/LIV1 CDR-L3	FQGSHVPYT
743	hLIV22/LIV1 VH	QVQLVQSGAEVKKPGASVKVSCKASGLTIEDYYMHWVRQAPGQGLEWMGWIDPENGDEY GPKFQGRVTMTRDT SINTAYMELSLRSDDTAVYYCAVHN AHYGTWFAYWGQGT LTVSS
744	hLIV22/LIV1 VL	DVVMTQSPLSLPVTLGQPASISCRSSQSLLHSSGNTYLEWYQQRPGQSPRPLIYKISTRFSGVPD RFSGSGSGTDF TLKISRVEAEDVGYYCFQGSHVPYT FGGGT KVEIKRTVAAPS VFI FPPSDEQL
745	hLIV22/LIV1 HC	QVQLVQSGAEVKKPGASVKVSCKASGLTIEDYYMHWVRQAPGQGLEWMGWIDPENGDEY GPKFQGRVTMTRDT SINTAYMELSLRSDDTAVYYCAVHN AHYGTWFAYWGQGT LTVSSA STKGPSVFPLAPSSKTS GGTAA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSL SSVTPVPSLLGTQYICVN H KPNTKV DKKV EPKSCD KTH CPCPAPELLGGPSVFLFPKP KDTLMISRTPEVTCVV DVSHEDPEVKFNWYV DGV E VHN AKT K PREEQYN STYRVV SVLTVL HQDWLNGKEYKCKVSNKALPAPI EKTI SKAKG QPREPQV YTL PPSR DELTKN QVSL T CLVKGF YPSDI AVEWE SNGQ PENNY KTT P PVL DSDGSFF LYSKL T VDKSRW QQGNV FSC VMHEALHN HYTQKSLSLSPG
746	hLIV22/LIV1 LC	DVVMTQSPLSLPVTLGQPASISCRSSQSLLHSSGNTYLEWYQQRPGQSPRPLIYKISTRFSGVPD RFSGSGSGTDF TLKISRVEAEDVGYYCFQGSHVPYT FGGGT KVEIKRTVAAPS VFI FPPSDEQL KSGTASV VCLLN NFY PREAKV QWKVDNALQSGNSQESVTEQDSKD STYLSSTLTL SKADYEK HKVYACEVTHQGLSSPVTKSFNR GEC
747	h15H3/avb6 CDR-H1	GYFMN
748	h15H3/avb6 CDR-H2	LINPYNGDSFY NQKFG
749	h15H3/avb6 CDR-H3	GLRRDFDY
750	h15H3/avb6 CDR-L1	KSSQSLLSDGKTYLN
751	h15H3/avb6 CDR-L2	LVSELDS
752	h15H3/avb6 CDR-L3	WQGTHFPRT

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SEQ ID NO	Description	Sequence
753	h15H3 /avb6 VH	QVQLVQSGAEVKPGASVKVSCKASGYFSGYFMNWRQAPGQGLEWMGLINPYNGDSFY NQKFGRVTMTRQTSTVYMELSSLRSEDTAVYYCVRGLRRDFDYWGQGTIVTSS
754	h15H3 /avb6 VL	DVVMTQSPLSLPVTLGQPASISCKSSQSLLSDDGKTYLNWLQFQPGQSPRRLIYLVSEL SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCWQGTHFPRTFGGGTKLEIK
755	CD48 CDR- H1	DFGMN
756	CD48 CDR- H2	WINTFTGEPSYGNVPKG
757	CD48 CDR- H3	RHGNGNVFDS
758	CD48 CDR- L1	RASQSIGNSNIH
759	CD48 CDR- L2	YTSEISIS
760	CD48 CDR- L3	QQSNSWPLT
761	CD48 VH	QVQLVQSGSELKKPGASVKVSCKASGYFTDFGMNWVRQAPGQGLEWMGWINTFTGEPSYG NVFKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARRHGNGNVFDSWGQGTIVTSS
762	CD48 VL	EIVLTQSPDFQSVTPKEKVITCRASQSIGSNIHWYQQKPDQSPKLLIKYTSESISGVPSRFSGSGS GTDFTLTINSLEAEDAATYYCQGSNSWPLTFGGGTTKVEIKR
763	IGF-1R CDR- H1	SYAIS
764	IGF-1R CDR- H2	GIIPIFGTANYAQKFQG
765	IGF-1R CDR- H3	APLRFLEWSTQDHYYYYYMDV
766	IGF-1R CDR- L1	QGDLSRSYYAT
767	IGF-1R CDR- L2	GENKRPS
768	IGF-1R CDR- L3	KSRDGSGQHLV
769	IGF-1R VH	EVQLVQSGAEVKPGSSVKVSCKASGGTSSYAI SWVRQAPGQGLEWNGGIPIIFGTANY AQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCARAPLRFLEWSTQDHYYYYYMDVWG KGTTIVTSS
770	IGF-1R VL	SSELTQDPAVSVALGQTVRITCQGDSLRSYYATWYQQKPGQAPILVYGENKRPSGIPDR FSGSSSGNTASLTITGAQAEDADYYCKSRDGSGQHLVFGGGTKLTIVL
771	Claudin-18.2 CDR-H1	SYWIN
772	Claudin-18.2 CDR-H2	NIYPSDSYTNYNQKFD
773	Claudin-18.2 CDR-H3	SWRGNSFDY
774	Claudin-18.2 CDR-L1	KSSQSLNNSGNQKNYLT
775	Claudin-18.2 CDR-L2	WASTRES
776	Claudin-18.2 CDR-L3	QNDYSYPFT

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SEQ		
ID		
NO	Description	Sequence
777	Claudin-18.2 VH	QVQLQQPGAAELVRPGASVKLSCKASGYTFTSYWINWVKQRPGQGLEWIGNIYPSDSYTN YNQKFKDKATLTVDKSSSTAYMQLSSPTSEDSA VYYCTRSWRGNSFDYWGCQGTTLVSS
778	Claudin-18.2 VL	DIVMTQSPSSLTVTAGEKVMSCKSSQSLN SGNQKNYL TWYQQKPGQPPKLLIYWA STR ESGPVDRFTGSGSGTDFTLTISSVQAEDLA VYYC QNDYSYPFTFGSGTKLEIK
779	Claudin-18.2 CDR-H1	NYGMN
780	Claudin-18.2 CDR-H2	WINTNTGEPTYAEEFKG
781	Claudin-18.2 CDR-H3	LGFGNAMDY
782	Claudin-18.2 CDR-L1	KSSQSLLNSGNQKNYL T
783	Claudin-18.2 CDR-L2	WASTRES
784	Claudin-18.2 CDR-L3	QNDYSYPLT
785	Claudin-18.2 VH	QIQLVQSGPELKKPGETVKISCKASGYTFTNYGMNWVKQAPGKGLKWMGWINTNTGEPTY AEEFKGRFAFSLETSASTAYLQINNLKNEDTATYFCARLGFGNAMDYWGQGTSVTVSS
786	Claudin-18.2 VL	DIVMTQSPSSLTVTAGEKVMSCKSSQSLN SGNQKNYL TWYQQKPGQPPKLLIYWA STR ESGPVDRFTGSGSGTDFTLTISSVQAEDLA VYYC QNDYSYPLTFGAGTKLELK
787	Nectin-4 CDR-H1	SYNMN
788	Nectin-4 CDR-H2	YISSSSSTIYYADSVKG
789	Nectin-4 CDR-H3	AYYYGMDV
790	Nectin-4 CDR-L1	RASQGISGWLA
791	Nectin-4 CDR-L2	AASTLQS
792	Nectin-4 CDR-L3	QQANSFPPT
793	Nectin-4 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYNMNWVRQAPGKGLEWVS YI SSSSSTIYY ADSVKGRFTISRDNAKNSLSQLQMNSLRDEDTAVYYCARAYYYGMDVWGQGTTTVSS
794	Nectin-4 VL	DIQMTQSPSSVASVGDRVITICRASQGIGWLA WYQQKPGKAPKFLIYA AASTLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQANSFPPTFGGGTKVEIK
795	SLTRK6 CDR-H1	SYGMH
796	SLTRK6 CDR-H2	VIWYDGSNQYYADSVKG
797	SLTRK6 CDR-H3	GLTSGRYGMDV
798	SLTRK6 CDR-L1	RSSQSLLL SHGFNYLD
799	SLTRK6 CDR-L2	LGSSRAS
800	SLTRK6 CDR-L3	MQPLQIPWT

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SEQ ID NO	Description	Sequence
801	SLTRK6 VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAIVYDGSNQYY ADSVKGRFTISRDNSKNTLFLQMHSRAEDTAVYYCARGLTSGRYGMDVWGQGTTVTVSS
802	SLTRK6 VL	DIVMTQSPLSLPVTPGEPA SICR S Q S L L S H G F N Y L D W Y L Q K P G Q S P Q L L I Y L G S S R A S G V P D RFSGSGSGTDFTLKRISRAEDVGLYYCMQPLQIPWTFGQGKVEIK
803	CD142 (TF) CDR-H1	NYAMS
804	CD142 (TF) CDR-H2	SISGSGDYTYYTDSVKG
805	CD142 (TF) CDR-H3	SPWGYYLDS
806	CD142 (TF) CDR-L1	RASQGISSRLA
807	CD142 (TF) CDR-L2	AASSLQS
808	CD142 (TF) CDR-L3	QQYNSYPYT
809	CD142 (TF) VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSNYAMSWVRQAPGKGLEWVSSISGSGDYTY YTDSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPWGYYLDSWGQGTLVTVSS
810	CD142 (TF) VL	DIQMTQSPPLSASAGDRVITTCRASQGISSRLAWYQQKPEAKPKSLIYAASSLQSGVPS RFSGSGSGTDFTLTISLQPEDFATYYCQQYNSYPYTFGQGKLEIK
811	h2G12/STh CDR-H1	DHAIH
812	h2G12/STh CDR-H2	YFSPGNDDIKYNEKFRG
813	h2G12/STh CDR-H3	SLSTPY
814	h2G12/STh CDR-L1	KSSQSLLNRGNHKNYLT
815	h2G12/STh CDR-L2	WASTRES
816	h2G12/STh CDR-L3	QNDYTYPYT
817	h2G12/STh VH	EVQLVQSGAEVKKPGASVKVSCKASGYFTDHAIHWVRQAPGQGLEWMGYFSPGNDDIKY NEKFRGRVTMTADKSSTAYMELRSLSRSDDTAVYFCKRSLSTPYWGQGTLVTVSS
818	h2G12/STh VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNRGHNKNYLTWYQQKPGQPPKLLIYWAST RESGPDRFSGSGSGTDFTLTISLQAEDVAVYYCQNDYTYPYTGFQGKVEIK
819	CD20 CDR- H1	SYNMH
820	CD20 CDR- H2	AIYPGNGDTSYNQKFKG
821	CD20 CDR- H3	STYYGGDWYFPNV
822	CD20 CDR- L1	RASSSVSYIH
823	CD20 CDR- L2	ATSNLAS
824	CD20 CDR- L3	QQWTSNPPT

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SEQ ID NO	Description	Sequence
825	CD20 VH	QVQLQQPGAAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSYNQKFKGKATLTADKSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTTVTVA
826	CD20 VL	QIVLSQLSPAIALSASPGEKVMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGPVRFSGSGSGTYSYSLTISRVEAEDAATYYCQQWTSNPFTFGGGTKLEIK
827	HER2 CDR-H1	DTYIH
828	HER2 CDR-H2	RIYPTNGYTRYADSVKG
829	HER2 CDR-H3	WGGDGFYAMDY
830	HER2 CDR-L1	RASQDVNTAVA
831	HER2 CDR-L2	SASFYLS
832	HER2 CDR-L3	QQHYTTPPT
833	HER2 VH	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTIVTVSS
834	HER2 VL	DIQMTQSPSSLSASVGDRVITICRASQDVNTAVAWYQQKPGKAPKLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKEIK
835	CD79b CDR-H1	SYWIE
836	CD79b CDR-H2	EILPGGGDTNYNEIFKG
837	CD79b CDR-H3	RVPIRLDY
838	CD79b CDR-L1	KASQSVYEGDSFLN
839	CD79b CDR-L2	AASNLES
840	CD79b CDR-L3	QQSNEDPLT
841	CD79b VH	EVQLVESGGGLVQPGGSLRLSCAASGYTFSSYIEWVRQAPGKGLEWIGEILPGGGDTNYNEIFKGRATFSADTSKNTAYLQMNSLRAEDTAVYYCTRVPIRLDYWQGQTLTVSS
842	CD79b VL	DIQMTQSPSSLSASVGDRVITICKASQSVYEGDSFLNWYQQKPGKAPKLIYAASNLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPLTFGQGTKEIK
843	NaPi2B CDR-H1	DFAMS
844	NaPi2B CDR-H2	TIGRVAFHYYPDMSMKG
845	NaPi2B CDR-H3	HRGFDVGHFDF
846	NaPi2B CDR-L1	RSSETLVHSSGNTYLE
847	NaPi2B CDR-L2	RVSNRFS
848	NaPi2B CDR-L3	FQGSFNPLT

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SEQ ID NO	Description	Sequence
849	NaPi2B VH	EVQLVESGGGLVQPGGSLRLSCAASGFSFSDFAMSWVRQAPGKGLEWVATIGRAVFHTYY PDSMKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARHRGFDVGHPDFWGQGTLVTVSS
850	NaPi2B VL	DIQMTQSPSSLSASVGDRV TITCRSSSETLVHSSGNTYLEWYQQKPGKAPKLLIYRVSNRF SGVPSRFSGS GSGTDF TLTISSLQPEDFATYYC PQGSFNPLTFGQGTKVEIK
851	Muc16 CDR-H1	NDYAWN
852	Muc16 CDR-H2	YISYSGYTTYNPSLKS
853	Muc16 CDR-H3	WTSGLDY
854	Muc16 CDR-L1	KASDLIH NWLA
855	Muc16 CDR-L2	GATSLET
856	Muc16 CDR-L3	QQYWTTPFT
857	Muc16 VH	EVQLVESGGGLVQPGGSLRLSCAASGYSITNDYAWN WVRQAPGKGLEWVG YISYSGYTTY NPSLKS RFTISRDT SKNTLYLQMNSLRAEDTAVYYCARW TSGLDYWGQGTLVTVSS
858	Muc16 VL	DIQMTQSPSSLSASVGDRV TITCKASDLIHNWLAWYQQKPGKAPKLLIYGATSLETGVPSRFG SGSGTDFTLTISSLQPEDFATYYC QQYWTTPFTFGQGTKVEIK
859	STEAP1 CDR-H1	SDYAWN
860	STEAP1 CDR-H2	YISNSGSTSYNPSLKS
861	STEAP1 CDR-H3	ERNYDYDDYYAMDY
862	STEAP1 CDR-L1	KSSQSL LYRSNQKNYLA
863	STEAP1 CDR-L2	WASTRES
864	STEAP1 CDR-L3	QQYYNYPRT
865	STEAP1 VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITS DYAWN WVRQAPGKGLEWVG YISNSGSTSYNPS LKS RPTISRDT SKNTLYLQMNSLRAEDTAVYYCARERNYDYDDYYAMDYWGQGTLVTVSS
866	STEAPI VL	DIQMTQSPSSLSASVGDRV TITCKSSQSLLYRSNQKNYLA WYQQKPGKAPKLLIYWASTRESG VPSRFSGS GSGTDF TLTISSLQPEDFATYYC QQYNYNYPRTFGQGTKVEIK
867	BCMA CDR-H1	NYWMH
868	BCMA CDR-H2	ATYRGHSDTYYNQFKKG
869	BCMA CDR-H3	GAIYDGYDVLDN
870	BCMA CDR-L1	SASQDISNYLN
871	BCMA CDR-L2	YTSNLHS
872	BCMA CDR-L3	QQYRKLPWT

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SEQ ID NO	Description	Sequence
873	BCMA VH	QVQLVQSGAEVKPGSSVKVSCKASGGTFSNYWMHWVRQAPGQGLEWMGATYRGHSDTYYNQKFKGRVTITADKSTSTAYMELSSLRSEDTAVYYCARGAIYDGYDVLNDNWGQGTLVTVSS
874	BCMA VL	DIQMTQSPSSLSASVGDRVITICASQDISNYLNWYQQKPGKAKPPLLIIYTSNLHSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYRKLPWTFGQGKLEIK
875	c-Met CDR-H1	AYTMH
876	c-Met CDR-H2	WIKPNNGLANYAQKFQG
877	c-Met CDR-H3	SEITTEFDY
878	c-Met CDR-L1	KSSESVDSYANSFLH
879	c-Met CDR-L2	RASTRES
880	c-Met CDR-L3	QQSKEDPLT
881	c-Met VH	QVQLVQSGAEVKPGASVKVSCKASGYIPTAYTMHWVRQAPGQGLEWMGWIKPNNGLANYAQKFQGRVTMTRDTSISTAYMELSLRSDDTAVYYCARSEITTEFDYWGQGTLVTVSS
882	c-Met VL	DIVMTQSPDSLAVSLGERATINCKSSESVD SYANSFLHWYQQKPGQPPKLLIYRASTRE SGVPDRFSGSGSGTDFTLTISSLQAEDEVAVYYCQSKEDPLTFGGGTKEIK
883	EGFR CDR-H1	SDFAWN
884	EGFR CDR-H2	YISYSGNTRYQPSLKs
885	EGFR CDR-H3	AGRGFPPY
886	EGFR CDR-L1	HSSQDINSNIG
887	EGFR CDR-L2	HGTNLDD
888	EGFR CDR-L3	VQYAQFPWT
889	EGFR VH	QVQLQESGPGLVKPSQTLSLTCTVSGYSISSSDFAWNWIROPPGKGLEWMGYIYSGNTRYQPSLKSRSITISRDTSKNQFFLKLNSVTAADTATYYCVTAGRGFPYWQGQGTLVTVSS
890	EGFR VL	DIQMTQSPSSMSVGDRVITICHSSQDINSNIGWLQQKPGKSFKGLIYHGTNLDDGVPSRFSGSGSGTDYTLTISSLQPEDFATYYCVQYAQFPWTFGGGTKLEIK
891	SLAMF7 CDR-H1	DYYMA
892	SLAMF7 CDR-H2	SINYDGSSTYYVDSVKG
893	SLAMF7 CDR-H3	DRGYYFDY
894	SLAMF7 CDR-L1	RSSQSLVHSNGNTYLH
895	SLAMF7 CDR-L2	KVSNRFS
896	SLAMF7 CDR-L3	SQSTHVPFF

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
897	SLAMF7 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDDYYMAWVRQAPGKGLEWVASINYDGSSTY YVD SVKGRTFISRDNAKNSLYLQMNSLRAEDTAVYYCARDRGYYFDIWGQGTTVTVSS
898	SLAMF7 VL	DVVMTQTPLSLSVTPGQPASISCRSSQSLVHSNGNTYLHWYLQKPGQSPQLLIYKVSNRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCQSSTHVPPTFGGGTKVEIK
899	C4.4a CDR-H1	NAWMS
900	C4.4a CDR-H2	YISSSGSTIYYADSVKG
901	C4.4a CDR-H3	EGLWAFDY
902	C4.4a CDR-L1	TGSSSNIGAGYV VH
903	C4.4a CDR-L2	DNNKRPS
904	C4.4a CDR-L3	AAWDDRLN GPV
905	C4.4a VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSNAWMSWVRQAPGKGLEWVS YISSSGSTIYY ADSVKGRTFISRDN SKNTLYLQMNSLRAEDTAVYYCAREGLWAFDYWGQGTLVTVSS
906	C4.4a VL	ESVLTQPPSVSGAPGQRVTISCTGSSSNIGAGYV VH WYQQLPGTAPKLLIYDNNKRPSGV PDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDDR L NGPVFGGGTKLTVL
907	GCC CDR-H1	GYYWS
908	GCC CDR-H2	EINHRGNTNDNPSLK S
909	GCC CDR-H3	ERGYTYGNFDH
910	GCC CDR-L1	RASQSVSRNL A
911	GCC CDR-L2	GASTRAT
912	GCC CDR-L3	QQYKTWPRT
913	GCC VH	QVQLQQWGAGLLKPSETLSLTCAVFGGSFSGYYWSWIRQPPGKGLEWIGEINHRGNTNDN PSLKS RVTISV DTSKNQFALKLSSVTAADTAVYYCARER GYT GNF DHWGQGTLVTVSS
914	GCC VL	EIVMTQSPATLSVSPGERATLSCRASQSVSRNLAWYQQKPGQAPRLLIYGA STRATGIP ARFSGSGSGTEFTLTIGSLQSEDFAVYYCQYKTWPRTFGQGTNVEIK
915	Ax1 CDR-H1	SYAMN
916	Ax1 CDR-H2	TTSGSGASTYYADSVKG
917	Ax1 CDR-H3	IWIAPDI
918	Ax1 CDR-L1	RASQSVSSSYLA
919	Ax1 CDR-L2	GASSRAT
920	Ax1 CDR-L3	QQYGSSPYT
921	Ax1 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSYYAMNW VRQAPGKGLEWVSTTSGSGASTYY ADSVKGRTFISRDN SKNTLYLQMNSLRAEDTAVYYCAKIWIAFDIWGQGTM VT VSS
922	Ax1 VL	EIVLTQSPGTL SLPGERATLSCRASQSVSSSYLA WYQQKPGQAPRLLIYGA SSRATGIP DRFSGSGSGTDF TL TISRLEPEDFAVYYCQYGTGQGT KLEIK

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
923	CR011/gpNM B CDR-H1	SFNYYWS
924	CR011/gpNM B CDR-H2	YIYYSGSTYSNPSLKS
925	CR011/gpNM B CDR-H3	GYNWNYFDY
926	CR011/gpNM B CDR-L1	RASQSVVDNNLV
927	CR011/gpNM B CDR-L2	GASTRAT
928	CR011/gpNM B CDR-L3	QQYNNWPPWT
929	CR011/gpNM B VH	QVQLQESGPGLVKPSQTLSTCTVSGGSISSFNYYWSIRHHPGKGLEWIGYIYYSGSTYNSPLSKRSRVTSVDTSKNQFSLTLSVTAAADTAVYYCARGYNWNWFDYWGQGTLTVSS
930	CR011/gpNM B VL	EIVMTQSPATLSVSPGERATLSCRASQSVDDNNLVWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTSSLQSEDFAVYYCQYNNWPPWTFGQGTKEIK
931	CR011/gpNM B HC	QVQLQESGPGLVKPSQTLSTCTVSGGSISSFNYYWSIRHHPGKGLEWIGYIYYSGSTYNSPLSKRSRVTSVDTSKNQFSLTLSVTAAADTAVYYCARGYNWNWFDYWGQGTLTVSS FPLAPSSKSTSGGTAALGCLVKDYPPEPVTVSNMSGALTSGVHTFPAPLQSSGLYSLSSVVTP SSSLGTQTYICNVNHKPSNTKVKDKVEPKSCDKTHTCPCCPAPELLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYVGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTIASKAKGQPREPQVTLPPSRDELTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTPVPLSDGSFFLYSKLTVDKSRWQQGNVFCSVMEALHNHYTQKSL SLSPGK
932	CR011/gpNM B LC	EIVMTQSPATLSVSPGERATLSCRASQSVDDNNLVWYQQKPGQAPRLLIYGASTRATGIPARFSG SGSGTEFTLTSSLQSEDFAVYYCQYNNWPPWTFGQGTKEIKRTVAAPSVIDFPPSDEQLKSG TASVCLNNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTSKADYEKHK VYACEVTHQGLSPVTKSFNRGEC
933	Prolactin receptor CDR-H1	TYWMH
934	Prolactin receptor CDR-H2	EIDPSDSYSNYNQFKFD
935	Prolactin receptor CDR-H3	NGGLGPAWFSY
936	Prolactin receptor CDR-L1	KASQYVGTAVA
937	Prolactin receptor CDR-L2	SASNRYT
938	Prolactin receptor CDR-L3	QQYSSYPWT
939	Prolactin receptor VH	EVQLVQSGAEVKKPGSSVKVSCKASGYTFPTTYWMHWVRQAPGQGLEWIGEIDPSDSYSNY NQKFKDRATLTVDKSTSTAYMELSSLRSED TAVYYCARNGGLGPAWF SYWGQGTLTVSS
940	Prolactin receptor VL	DIQMTQSPSSVSASVGDRVITCKASQYVGTAVA WYQQKPGKSPKLLIYSASNRYTGVPS RFSDSGSGTDFTLTSSLQPEDFATYFCQQYSSYPWTFGGGTKEIK
941	FGFR2 CDR- H1	SYAMS
942	FGFR2 CDR- H2	AISGSGTSTYYADSVKG

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
943	FGFR2 CDR-H3	VRYNWNHGDWFDP
944	FGFR2 CDR-L1	SGSSSNIGNNYVS
945	FGFR2 CDR-L2	ENYNRPA
946	FGFR2 CDR-L3	SSWDDSLNYWV
947	FGFR2 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGTSTYYADS VKGRPTISRDNNSKNTLYLQMNSLRAEDTAVYYCARVRYNWNHGDWFDPWGQGTIVTVSS
948	FGFR2 VL	QSVLTQPPSASGTPGQRVTISCGSSSNIGNNYVSWYQQLPGTAPKLLIYENYNRPAGVP DRFSGSKSGTSASLAIISGLRSEDEADYYCSSWDDSLNYWVFGGGTKLTVL
949	CDCP1 CDR-H1	SYGMS
950	CDCP1 CDR-H2	TISSGGSYKYYVDVKG
951	CDCP1 CDR-H3	HPDYDGVWFAY
952	CDCP1 CDR-L1	SVSSSVFYVH
953	CDCP1 CDR-L2	DTSKLAS
954	CDCP1 CDR-L3	QQWNSNPPT
955	CDCP1 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFPNSYGMWSWVRQAPGKGLEWVATISSGGSYKYY VDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHPDYDGVWFAYWGQGTLTVSS
956	CDCP1 VL	DIQMTQSPSSLSASVGDRVITITCVSSSVFYVHWYQQKPGKAPKLLIYDTSKLASGVPSRFSGSG SGTDPTFTISSLQPEDIATYYCQQWNSNPPTFGGGTKVEIK
957	CDCP1 CDR-H1	SYGMS
958	CDCP1 CDR-H2	TISSGGSYTYYPDVKG
959	CDCP1 CDR-H3	HPDYDGVWFAY
960	CDCP1 CDR-L1	SVSSSVFYVH
961	CDCP1 CDR-L2	DTSKLAS
962	CDCP1 CDR-L3	QQWNSNPPT
963	CDCP1 VH	EVQLVESGGDLVKPGGSLKLSCAASGFTFPNSYGMWSWVRQTPDKRLEWVATISSGGSYTY PDSVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHPDYDGVWFAYWGQGTLTVSA
964	CDCP1 VL	QIVLTQSPAIMSASPGEKVMTCSVSSSVFYVHWYQQKSGTSPKRWIYDTSKLASGVPARF SGSGSGTSYSLTISSMEAEDAATYYCQQWNSNPPTFGGGTKLEIK
965	CDCP1 CDR-H1	SYYMH
966	CDCP1 CDR-H2	IINPSGGSTSAYAQKFQG

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
967	CDCP1 CDR-H3	DGVLRYFDWLDDYYYYMDV
968	CDCP1 CDR-L1	RASQSVGSYLA
969	CDCP1 CDR-L2	DASN RAT
970	CDCP1 CDR-L3	QQRANVFT
971	CDCP1 VH	EVQLVQSGAEVKPGASVKVSCKASGYTFTSYMMHWVRQAPGQGLEWNGIINPSGGSTS AQKFQGRVTMTRDTSTSTVYMEMLSED TAVYYCARDGVLYFDWLDDYYYYMDVWGK G TTTVSS
972	CDCP1 VL	EIVLTQSPATLSLSPGERATLSCRASQSVGSYLA WYQQRP GQAPRLLIYDASN RATGIPA RFSGSGSGTDFTLTISLEPEDFAVYYCQQRANVFTFGQGTKVEIK
973	CDCP1 CDR-H1	SYYMH
974	CDCP1 CDR-H2	IINPSGGSTS YAQKFQG
975	CDCP1 CDR-H3	DAELRHFDHLLDYHYMDV
976	CDCP1 CDR-L1	RASQSVGSYLA
977	CDCP1 CDR-L2	DASN RAT
978	CDCP1 CDR-L3	QQRAQEFT
979	CDCP1 VH	EVQLVQSGAEVKPGASVKVSCKASGYTFTSYMMHWVRQAPGQGLEWNGIINPSGGSTS YAQ KFQGRVTMTRDTSTSTVYMEMLSED TAVYYCARD ELRHFDHLLDYHYMDVWGQGTT TVSS
980	CDCP1 VL	EIVMTQSPATLSLSPGERATLSCRASQSVGSYLA WYQQKPG QAPRLLIYDASN RATGIPA RFSGSGSGTDFTLTISLQPEDFAVYYCQRAQEFTFGQGTKVEIK
981	ASCT2 VH	QVQLVQSGSELKKPGAPVKVSCKASGYTFTFGMSWVRQAPGQGLKWMGWIHTYAGVPIYG DFKG R FVFS LDT SV STAYLQISSLKAEDTAVYFCARRSDNRYFFDWGQGTT TVSS
982	ASCT2 VL	DIQM TQSPS LSLASLGDRV TITCRASQDIRNYLNWYQQKPGKAPKLLI YYTSRLHSGVPSRFSGS GSGTDYTLTISLQPEDFATYFCQGHTLPPTFGQGTKLEIK
983	ASCT2 VH	QIQLVQSGPELKPGAPVKISCKASGYTFTFGMSWVKQAPGQGLKWMGWIHTYAGVPIYGD DFKG R FVFS LDT SV STAYLQISSVKAEDTATYFCARRSDNRYFFDWGQGTT TVSS
984	ASCT2 VL	DIQM TQSPS LSLASLGDRV TITCRASQDIRNYLNWYQQKPGKAPKLLI YYTSRLHSGVPS RFSGSGSGTDYTLTISLQPEDFATYFCQGHTLPPTFGQGTKLEIK
985	ASCT2 CDR-H1	NYYMA
986	ASCT2 CDR-H2	SITKGGNTYYRDSVKG
987	ASCT2 CDR-H3	QVTIAAVSTS YFDS
988	ASCT2 CDR-L1	KTNQKV DYYGNSYVY
989	ASCT2 CDR-L2	LASNLAS

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
990 ASCT2 CDR-L3		QQSRNLPYT
991 ASCT2 VH		EVQLVESGGGLVQSGRSIRLSCHAASGFSFSNYYMAWVRQAPSKGLEWVASITKGGGNTYYRD SVKGRTFTSRDNAKSTLYLQMDSLRSEDTATYYCARQVTIAAVTSYFDSWGQGVMTVSS
992 ASCT2 VL		DIVLTQSPALAVSLGQRATISCKTNQKVDDYYGNSYVYWYQQKPGQOPKLLIYLASNLASGIPA RFSGRGSGTDFTLTIDPVEADDTATYYCQQSRNLPYTFGAGTKLELK
993 CD123 CDR-H1		DYYMK
994 CD123 CDR-H2		DIIPNSNGATFYNNQKPKG
995 CD123 CDR-H3		SHLLRASWFAY
996 CD123 CDR-L1		KSSQSLLNSGNQKNYLT
997 CD123 CDR-L2		WASTRES
998 CD123 CDR-L3		QNDYSYPYT
999 CD123 VH		QVQLVQSGAEVKPGASVKMSCKASGYFTDYMMKWKVQAPGQGLEWIGDIIIPNSNGATFYN QKFKGKATLTVDRSISTAYMHLNRLRSDDTAVYYCTRSHLLRASWFAYWGQGTLTVSS
1000 CD123 VL		DFVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLTWYLQKPGQPPKLLIYWASTRESG VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPYTFGQGTLKLEIK
1001 GPC3 CDR-H1		DYEMH
1002 GPC3 CDR-H2		GIDPETGGTAYNQKFKG
1003 GPC3 CDR-H3		YYSFAY
1004 GPC3 CDR-L1		RSSQSIVHSNANTYLO
1005 GPC3 CDR-L2		KVSNRFS
1006 GPC3 CDR-L3		FQVSHVPYT
1007 GPC3 VH		EVQLVQSGAEVKPGATVKISCKVSGYFTDYEMHWVQQAPGKGLEWMGGIDPETGGTAYN QKFGRVTLTADKSTD TAYMELSSLRSEDTAVYYCGRYYSFAYWGQGTLTVSS
1008 GPC3 VL		DVVMTOQSPSLPVTLGQPASISCRSSQSIVHSNANTYLOWFQQRPGQSPRLLIYKVSNRFSGVPD RFSGRGSGTDFTLKISRVEAEDVGVYYCFQVSHVPYTFGQGTLKLEIK
1009 TIGIT CDR-H1		SYAIS
1010 TIGIT CDR-H2		SIIPIFGTANYAQKFQG
1011 TIGIT CDR-H3		GPSEVGAILGYVWFDP
1012 TIGIT CDR-L1		RSSQSLLHSNGNYLD
1013 TIGIT CDR-L2		LGSNRAS

TABLE OF SEQUENCES-continued

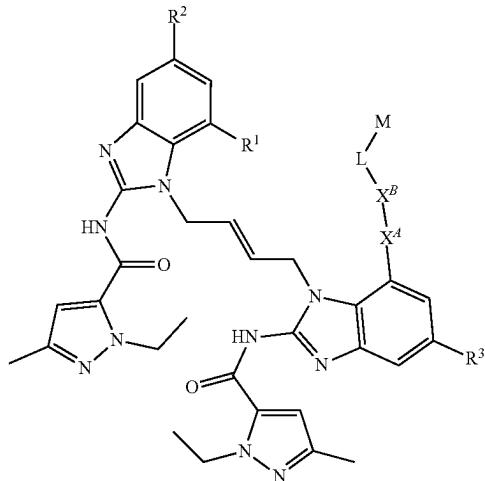
SEQ ID NO	Description	Sequence
1014 TIGIT CDR- L3	MQARRIPIT	
1015 TIGIT VH	QVQLVQSGAEVKPGSSVKVSCKASGGTFSSYAI SWVRQAPGQGLEWMGSIIPIFGTANYAQK FQGRVTITADESTSTAYMELSSLRSEDTAVYYCARGPSEVGA1LGYVWFDPWGQGTIVTVSS	
1016 TIGIT VL	DIVMTQSPLSLPVTPGEPA SICRSSQSLLHSNGNYLDWYLQKPGQSPQLLIYLGSRASGVPD RFSGSGSGTDFTLKISRVEAEDVGVYYCMQARRIPITFGGGTKVEIK	
1017 CD33 CDR- H1	NYDIN	
1018 CD33 CDR- H2	WIYPGDGSTKYNEKFKA	
1019 CD33 CDR- H3	GYEDAMDY	
1020 CD33 CDR- L1	KASQDINSYLS	
1021 CD33 CDR- L2	RANRLVD	
1022 CD33 CDR- L3	LQYDEFPLT	
1023 CD33 VH	QVQLVQSGAE VKPGASVKV SCKASGYTFT NYDINWVRQA PGQGLEWIGW TYPGDSTKY NEFKAKATL TADTSTSTAY MELRSLRSDD TAVYYCASGY EDAMDYWGQG TTIVTVSS	
1024 CD33 VL	DIQMTQSPS SLSASVGDRV T INCKASQDINSYLSWFQQKPGKAPKTL IYRANRLVDGVPS RFSGSGSGQDYTLT ISSLQPEDPATYYCLQYDEFPLTFGGGTKEIK	
1025 BCMA CDR- H1	DYYIH	
1026 BCMA CDR- H2	YINPNNSGYTNYAQKFQG	
1027 BCMA CDR- H3	YMWERVTGFFDF	
1028 BCMA CDR- L1	LASEDISDDLA	
1029 BCMA CDR- L2	TTSSLQS	
1030 BCMA CDR- L3	QQTYKFPPT	
1031 BCMA VH	QVQLVQSGAEVKPGASVKLSCKASGYTFTDYYIHWRQAPGQGLEWIGYINPNNSGYTNYAQ KFQGRATMTADKSINTAYVELSRLSDDTAVYFCTRYMWERVTGFFFWGQGTMVTVSS	
1032 BCMA VL	DIQMTQSPSSVASVGDRV ITCLASED ISDDLAWYQQKPGKAPKVLVYTSSLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATYFCQQTYKFPPTFGGGTKEIK	
1033 <Q13433; protein	MARKLSVILI LTFA LSVTNP LHELKAAFP QTTEKISP NW ESGINV DLA STRQYHLQQL FYRYGENNSL SVEGFRKLLQ NJGIDKIKRI HHHHDHHS DHEHHSDHER HSDHEHHSEH EHHSDDHHS HHNHAASGKN KRKALCPDHD SDSSGKDPRN SQKGGAHRPE HASGRRNVKD SVSASEVTST VYNTVSEGTH FLETIETPRP GKLFPKDVS STPPSVTSKS RVSRLAGRK NESVSEPRKG FMYSRNTEN PQECFNASKL LTSHGMGIQV PLNATEFNYL CPAIINQIDA RSCLIHTSEK KAEI PPKTYS LQIAWVGFFI AISIISFLSL LGVILVPLMN RVFFKFLSF LVAI AVGTL SDAFLHLLPH SHASHHHSHS HEEPAMEMK GPLFSHLSSQ NIEESAYFDS TWKGLTALGG LYFMFLVHEH LT LIKQFKDK KKKNQKKPEN DDDVEIKQL SKYESQLSTN EEKVDTDDR EGYL RADSQE PSHFD SQPA VLEEEEVVIA HAHQEVYNE YVPRGCKNKC HSHFHDTLGQ SDDLIHHHH YHHILHHHH QNHPHSHSQ RYSREELKDA GVATLAWMVI MGDGLHNFS D GLAIGA AFTE GLS SGLL TSV AVFC HELPHE LGDFAVLLKA GMTVKQAVLY NAL SAM LAYL GMATGIFIGH YAENVSMWIF ALTAGLFM YV ALVDMVPEML HNDASDHGCS RWG YFFLQNA GMILLGF GIML LISIFEHKIV PRINF	

TABLE OF SEQUENCES-continued

SEQ ID NO	Description	Sequence
1034 hLIV22 epitope		KGAHRPEH

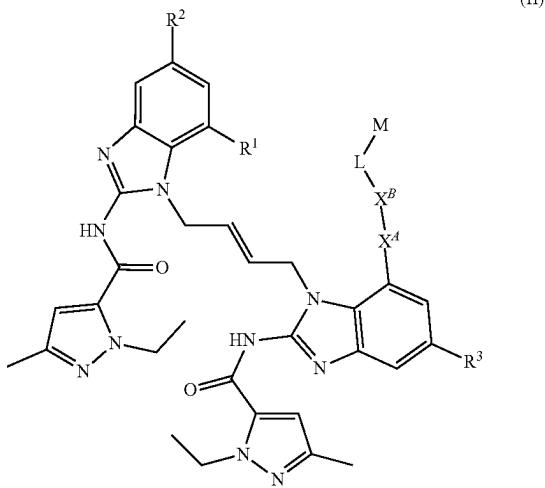
Compounds of Formula (II)

[0334] Some embodiments provide compounds of Formula (II):



(II)

[0347] In some embodiments, the compound of Formula (II) has the structure:



or a pharmaceutically acceptable salt thereof, wherein:

- [0335] or a pharmaceutically acceptable salt thereof, wherein:
- [0336] M is a succinimide or a hydrolyzed succinimide;
- [0337] R¹ is hydrogen, hydroxyl, C₁₋₆ alkoxy, —(C₁₋₆ alkyl)C₁₋₆ alkoxy, —(CH₂)_n—NR⁴R^B, or PEG2 to PEG4;
- [0338] each R² and R³ are independently —CO₂H, —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F;
- [0339] each R^A, R^B, R^C, R^D, R^E, and R^F are independently hydrogen or C₁₋₃ alkyl;
- [0340] each subscript n is independently an integer from 0 to 6;
- [0341] each subscript m is independently 0 or 1;
- [0342] each subscript q is independently an integer from 0 to 6;
- [0343] X^A is —CH₂—, —O—, —S—, —NH—, or —N(CH₃)—;
- [0344] X^B is absent or a 2-16 membered heteroalkylene;
- [0345] X^B, M, and L are each independently optionally substituted with a PEG Unit from PEG2 to PEG 72; and
- [0346] L is an optional linker as described herein.

[0348] R¹ is hydrogen, hydroxyl, C₁₋₆ alkoxy, —(C₁₋₆ alkyl)C₁₋₆ alkoxy, —(CH₂)_n—NR⁴R^B, or PEG2 to PEG4;

[0349] each R² and R³ are independently —CO₂H, —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F;

[0350] each R^A, R^B, R^C, R^D, R^E, and R^F are independently hydrogen or C₁₋₃ alkyl;

[0351] each subscript n is independently an integer from 0 to 6;

[0352] each subscript m is independently 0 or 1;

[0353] each subscript q is independently an integer from 0 to 6;

[0354] X^A is —CH₂—, —O—, —S—, —NH—, or —N(CH₃)—;

[0355] X^B is absent or 2-16 membered heteroalkylene;

[0356] L is a linker having the formula (A)_a—(W)_w—(Y)_y—, wherein:

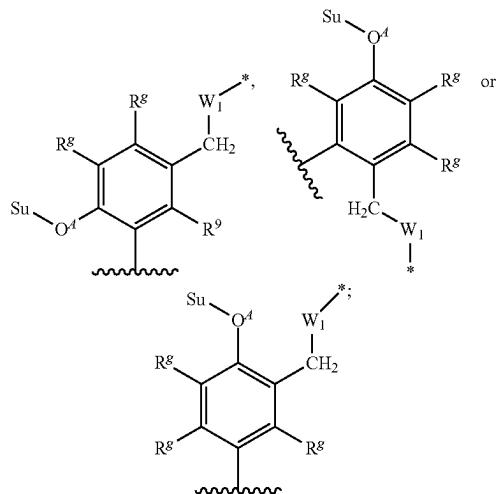
[0357] A is a C₂₋₂₀ alkylene optionally substituted with 1-3 Rai; or a 2 to 40 membered heteroalkylene optionally substituted with 1-3 R^{b1};

[0358] each R^{a1} is independently selected from the group consisting of: C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, halogen, —OH, —O, —NR^{d1}R^{e1}, —C(O)NR^{d1}R^{e1}, —C(O)(C₁₋₆ alkyl), and —C(O)O(C₁₋₆ alkyl);

[0359] each R^{b1} is independently selected from the group consisting of: C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, halogen, —OH, —NR^{d1}R^{e1}, —C(O)NR^{d1}R^{e1}, —C(O)(C₁₋₆ alkyl), and —C(O)O(C₁₋₆ alkyl);

[0360] each R^{d1} and R^{e1} are independently hydrogen or C₁₋₃ alkyl;

[0361] W is from 1-12 amino acids or has the structure:



[0362] wherein Su is a Sugar moiety;

[0363] —O⁴— represents a glycosidic bond;

[0364] each R⁹ is independently hydrogen, halogen, —CN, or —NO₂;

[0365] W₁ is absent or —O—C(=O)—;

[0366] ~~~~ represents covalent attachment to A or M; and * represents covalent attachment to Y, X^A, or X^B.

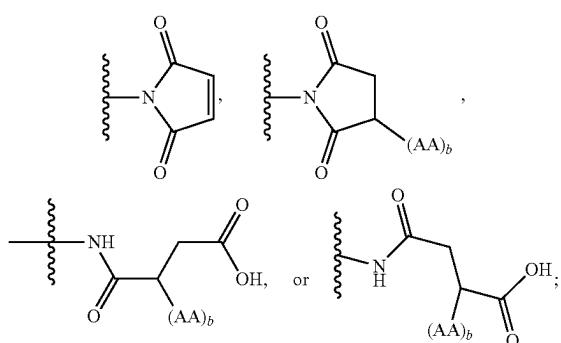
[0367] Y is a self-immolative moiety, a non-self-immolative releasable moiety, or a non-cleavable moiety;

[0368] subscript a is 0 or 1;

[0369] subscript y is 0 or 1;

[0370] subscript w is 0 or 1;

[0371] M is



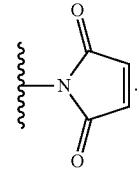
[0372] each AA is an independently selected amino acid, wherein (AA)_b is connected to the succinimide or hydrolyzed succinimide via a sulfur atom;

[0373] each subscript b is independently an integer from 1 to 6; and

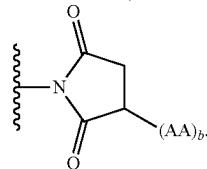
[0374] X^B and L are each independently optionally substituted with a PEG Unit from PEG2 to PEG 72.

[0375] As used herein, A, when present is covalently attached to M or M¹, and Y, when present is attached to X^B or to X^A (when X^B is absent).

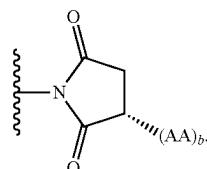
[0376] In some embodiments, M is



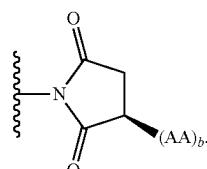
[0377] In some embodiments, M is



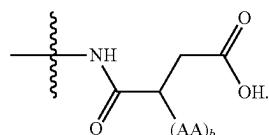
In some aspects, M is



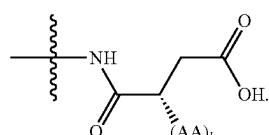
In some aspects, M is



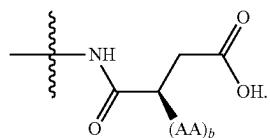
[0378] In some embodiments, M is



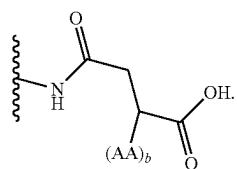
In some aspects, M is



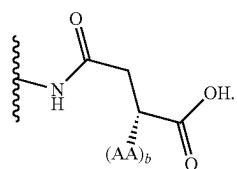
In some aspects, M is



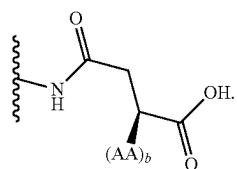
[0379] In some embodiments, M is



In some aspects, M is



In some aspects, M is

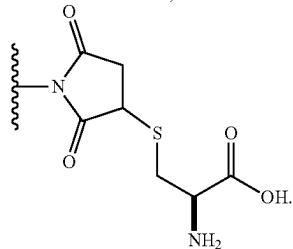


[0380] In some embodiments, each AA is independently a natural amino acid; wherein $(\text{AA})_b$ is connected to the succinimide or hydrolyzed succinimide via a sulfur atom. In some embodiments, each AA is independently a natural amino acid; wherein $(\text{AA})_b$ is connected to the succinimide or hydrolyzed succinimide via a sulfur atom of a cysteine residue.

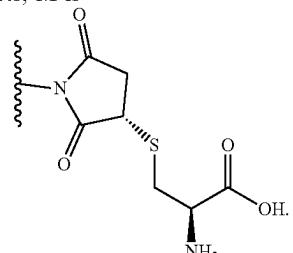
[0381] In some embodiments, each AA is independently a natural amino acid; wherein $(\text{AA})_b$ is connected to the succinimide or hydrolyzed succinimide via a nitrogen atom. In some embodiments, each AA is independently a natural amino acid; wherein $(\text{AA})_b$ is connected to the succinimide or hydrolyzed succinimide via the ϵ -nitrogen atom of a lysine residue.

[0382] In some embodiments, each subscript b is 1, 2, or 3. In some embodiments, each subscript b is 1. In some embodiments, each subscript b is 2. In some embodiments, each subscript b is 3. In some embodiments, each subscript b is 3, 4, 5, or 6. In some embodiments, each subscript b is 4. In some embodiments, each subscript b is 5. In some embodiments, each subscript b is 6.

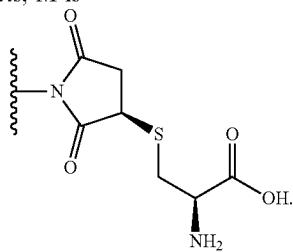
[0383] In some embodiments, M is



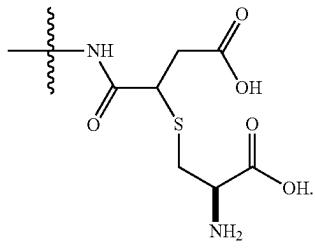
In some aspects, M is



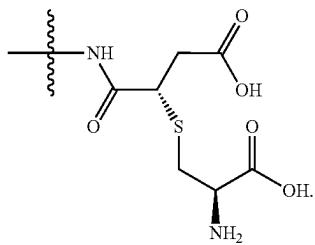
In some aspects, M is



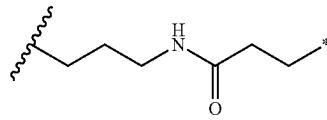
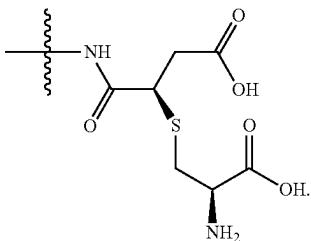
[0384] In some embodiments, M is



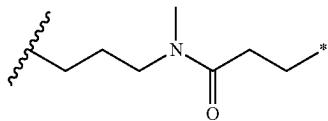
In some aspects, M is



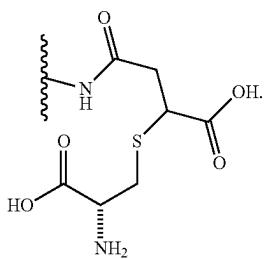
In some aspects, M is



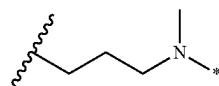
wherein represents covalent linkage to X^A , and * represents covalent linkage to L, when present, or M. In some embodiments, R^1 is methoxy; R^2 and R^3 are both $-C(=O)NH_2$; X^A is $-O-$; and X^B is



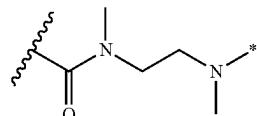
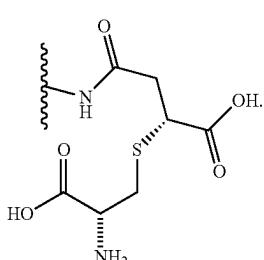
[0385] In some embodiments, M is



wherein represents covalent linkage to X^A , and * represents covalent linkage to L, when present, or M. In some such embodiments, L is absent. In some embodiments, R^1 is methoxy; R^2 and R^3 are both $-C(=O)NH_2$; X^A is $-O-$; X^B is

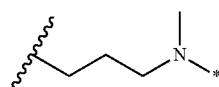
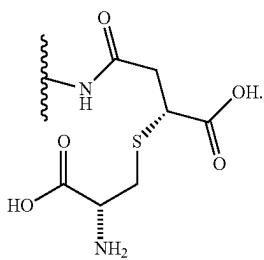


wherein represents covalent linkage to X^A , and * represents covalent linkage to L; and subscript a and subscript y are both 0 (i.e., X^B is covalently attached to W). In some embodiments, X^A is $-O-$; X^B is



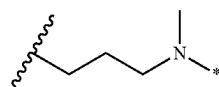
wherein represents covalent linkage to X^A , and * represents covalent linkage to L. In some embodiments, R^1 is methoxy; R^2 and R^3 are both $-C(=O)NH_2$; X^A is $-O-$; and X^B is

In some aspects, M is



wherein represents covalent linkage to X^A , and * represents covalent linkage to L; and subscript a and subscript w are both 0.

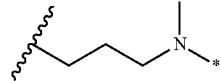
[0387] In some embodiments, R^1 is methoxy; R^2 and R^3 are both $-C(=O)NH_2$; X^A is $-O-$; and X^B is



[0386] In some embodiments, R^1 is methoxy and R^2 and R^3 are both $-C(=O)NH_2$. In some embodiments, X^A is $-O-$ and X^B is

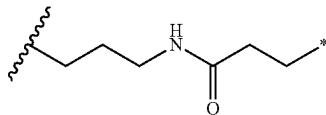
wherein represents covalent linkage to X^A , and * represents covalent linkage to L; and subscript y and subscript w are both 0.

[0388] In some embodiments, R^1 is methoxy; R^2 and R^3 are both $-C(=O)NH_2$; X^A is $-O-$; and X^B is

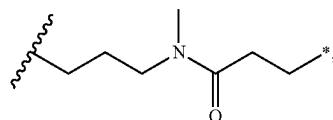


wherein represents covalent linkage to X^A , and * represents covalent linkage to L; and subscript y is 0.

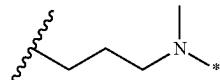
[0389] In some embodiments, R^1 is methoxy and R^2 and R^3 are both $-C(=O)NH_2$. In some embodiments, X^A is $-CH_2-$; and X^B is



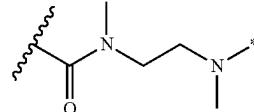
wherein represents covalent linkage to X^A , and * represents covalent linkage to L, when present, or M. In some embodiments, R^1 is methoxy; R^2 and R^3 are both $-C(=O)NH_2$; X^A is $-CH_2-$; and X^B is



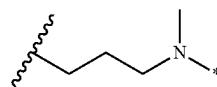
wherein represents covalent linkage to X^A , and * represents covalent linkage to L, when present, or M. In some embodiments, R^1 is methoxy; R^2 and R^3 are both $-C(=O)NH_2$; X^A is $-CH_2-$; and X^B is



wherein represents covalent linkage to X^A , and * represents covalent linkage to L; and subscript a and subscript y are both 0 (i.e., X^B is covalently attached to W). In some embodiments, X^A is $-CH_2-$; and X^B is



wherein represents covalent linkage to X^A , and * represents covalent linkage to L. In some embodiments, R^1 is methoxy; R^2 and R^3 are both $-C(=O)NH_2$; X^A is $-CH_2-$; and X^B is



wherein represents covalent linkage to X^A , and * represents covalent linkage to L; and subscript a and subscript w are both 0 (i.e., X^B is covalently bound to Y).

[0390] In some such embodiments, L is a linker having the formula $-(A)_a-(W)_w-(Y)_y-$.

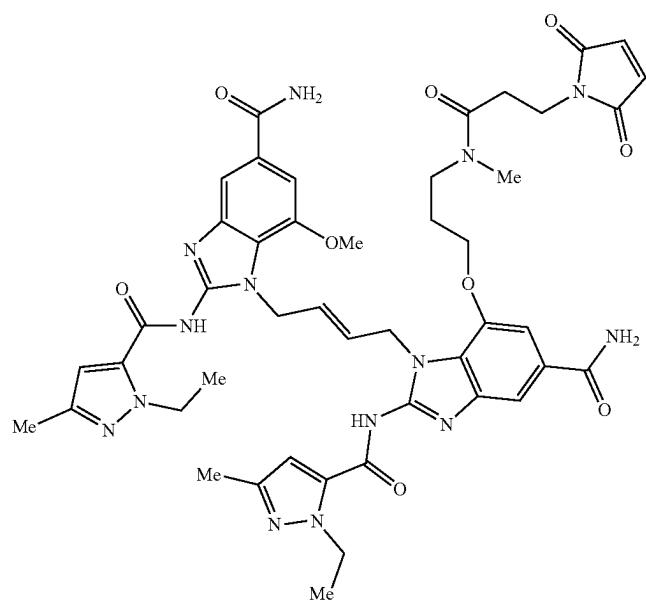
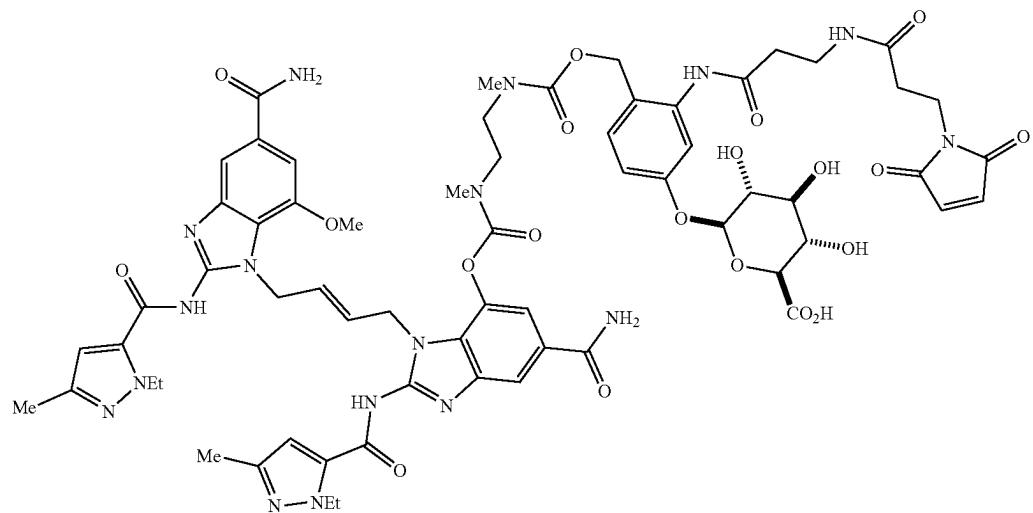
[0391] In some embodiments: X^B is absent and L is covalently attached to X^A . In some embodiments: X^B is absent and Y is covalently attached to X^A . In some embodiments: X^B is absent and Y is absent, and W is covalently attached to X^A . In some embodiments: X^B is absent, Y is absent, W is absent, and A is covalently attached to X^A .

[0392] In some embodiments: X^B is a 2-16 membered heteroalkylene and L is covalently attached to X^B . In some embodiments: X^B is a 2-16 membered heteroalkylene and Y is covalently attached to X^B . In some embodiments: X^B is a 2-16 membered heteroalkylene, Y is absent, and W is covalently attached to X^B . In some embodiments: X^B is a 2-16 membered heteroalkylene, Y is absent, W is absent, and A is covalently attached to X^B .

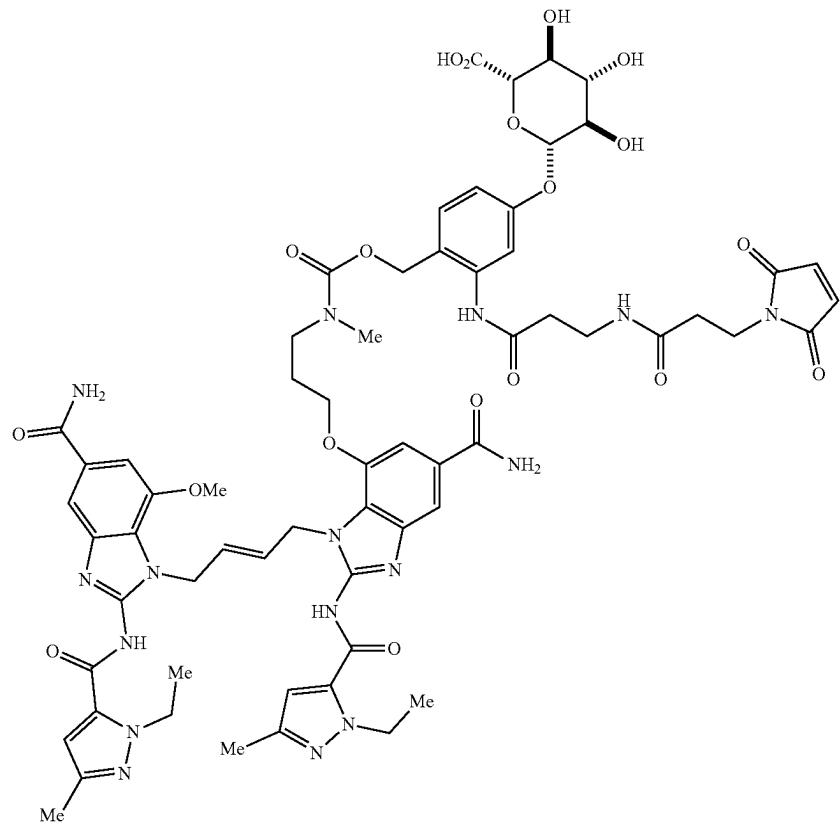
[0393] In some embodiments, W_1 is $-OC(=O)-$ and subscript y is 1. In some embodiments, X^A is $-O-$ and X^B and W are absent. In some embodiments, X^A is NH or $-O-$, X^B is absent, and W_1 is $-OC(=O)$. In some embodiments, X^A is $-N(CH_3)-$, X^B is absent, and W_1 is $-OC(=O)$. In some embodiments, X^A is $-S-$, X^B is absent, and W_1 is $-OC(=O)$. In some embodiments, W_1 is $-OC(=O)-$ and X^B is covalently attached to W via $-O-$ or $-NH-$.

[0394] In some embodiments, A is covalently attached to M. In some embodiments, when subscript a is 0 and subscript w is 0, Y is covalently attached to M. In some embodiments, when subscripts a, y, and w, are each 0, X^B is covalently attached to M.

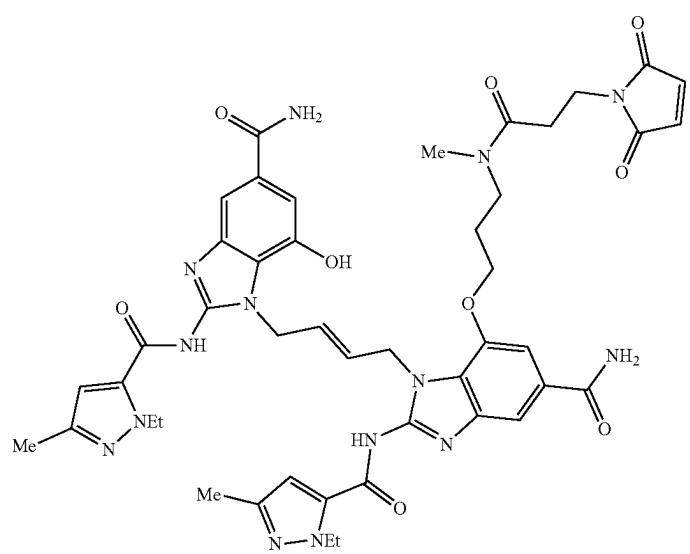
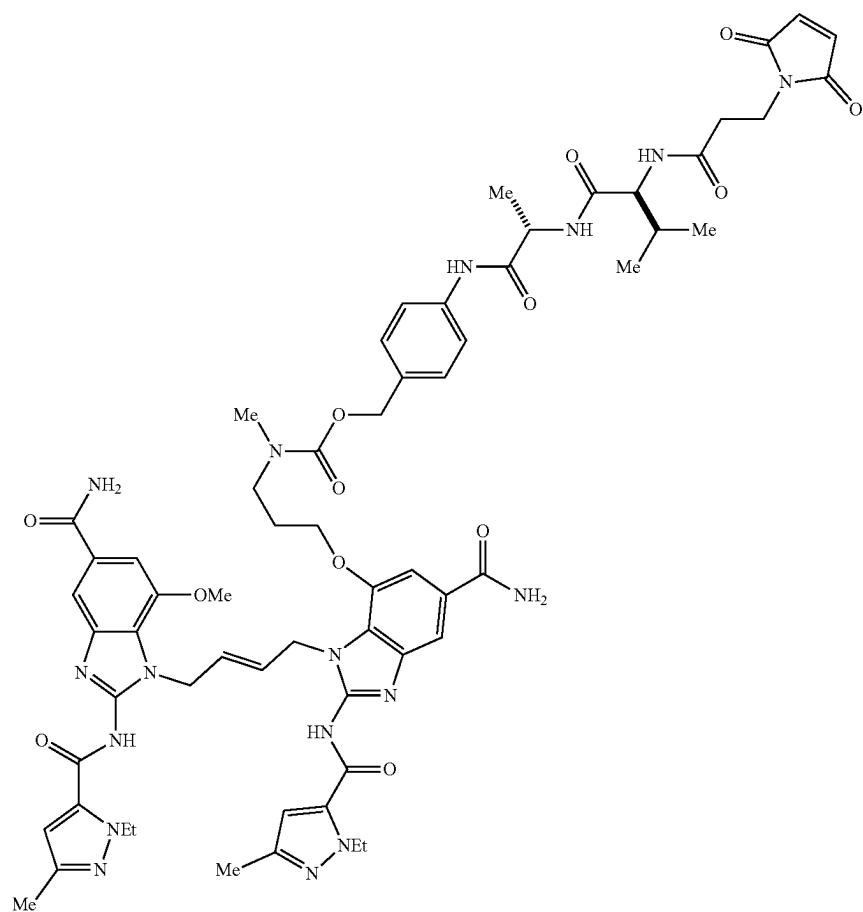
[0395] In some embodiments, the compound of Formula (II) is selected from the group consisting of:



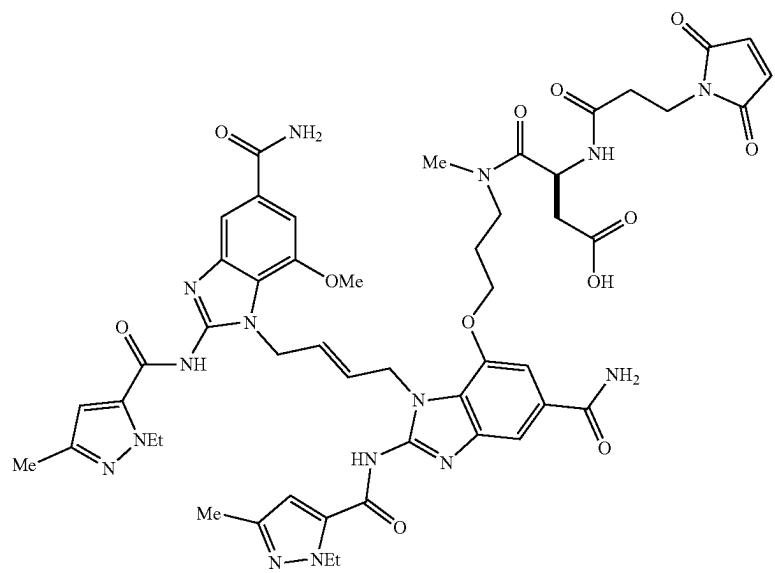
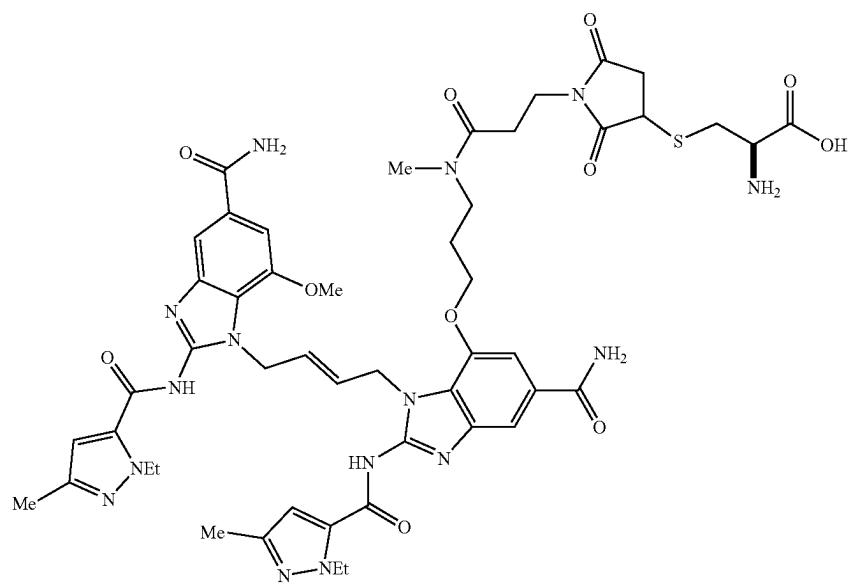
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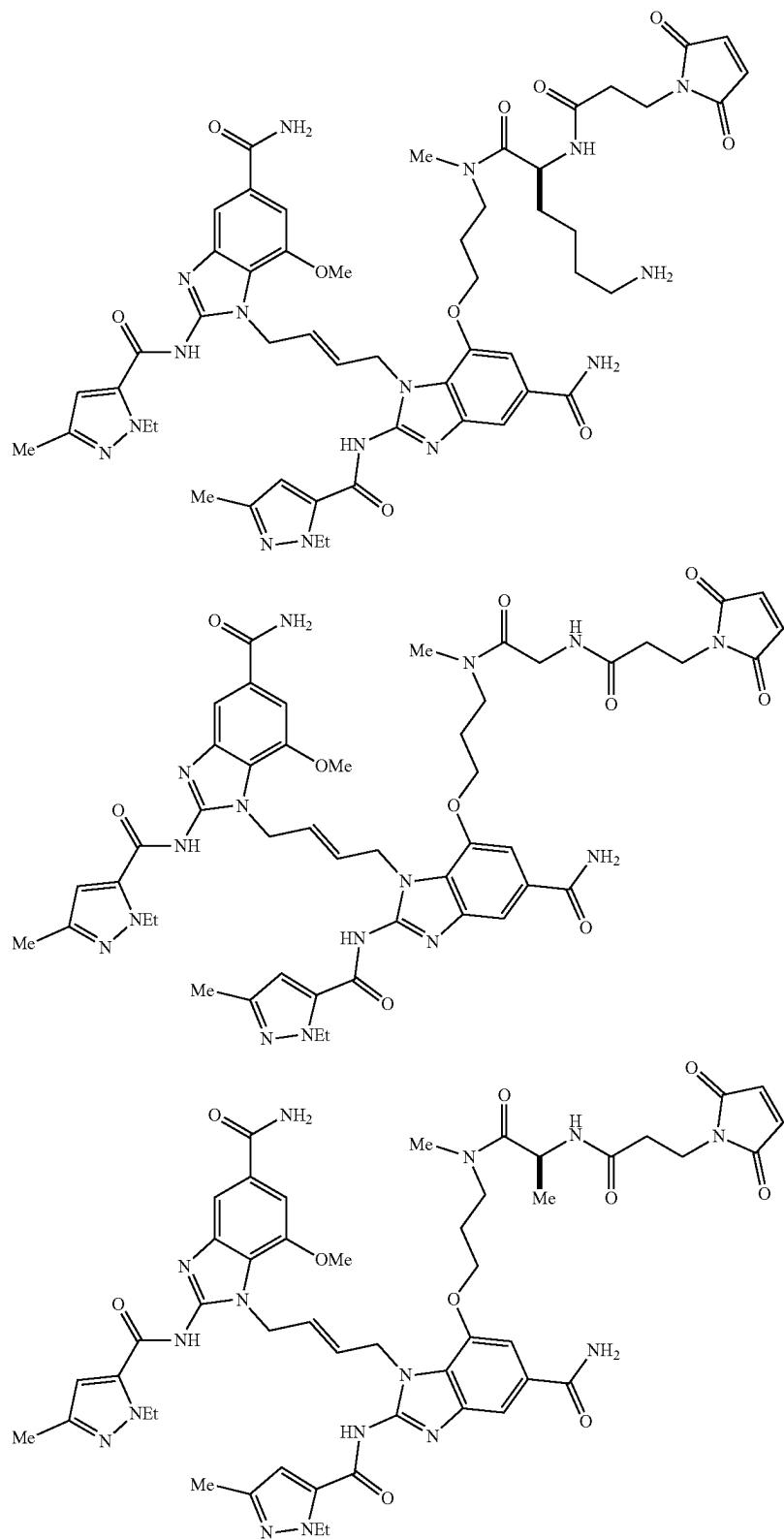
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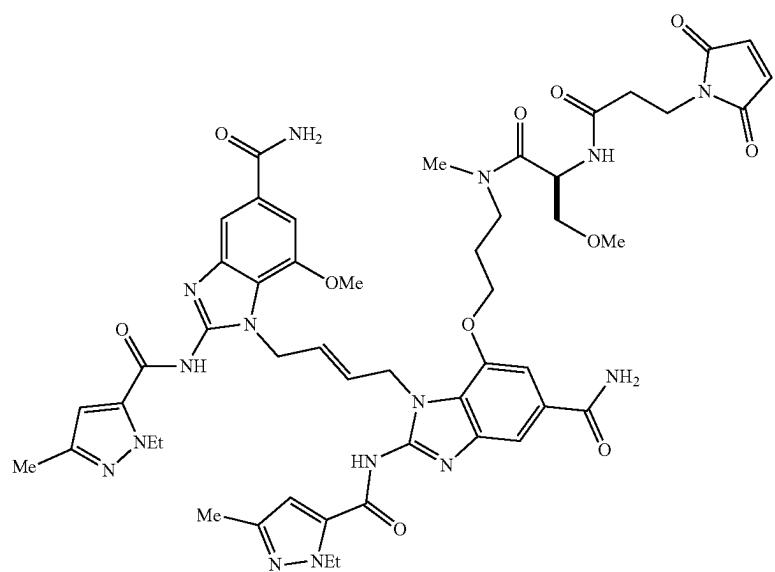
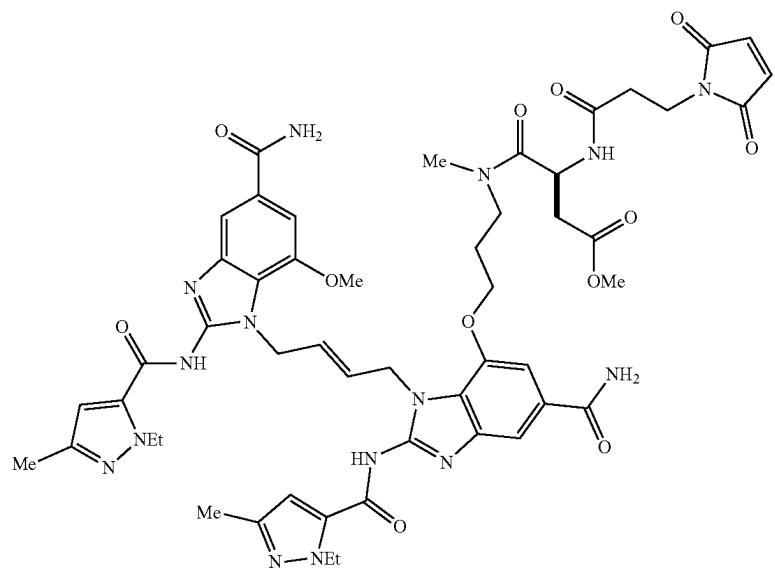
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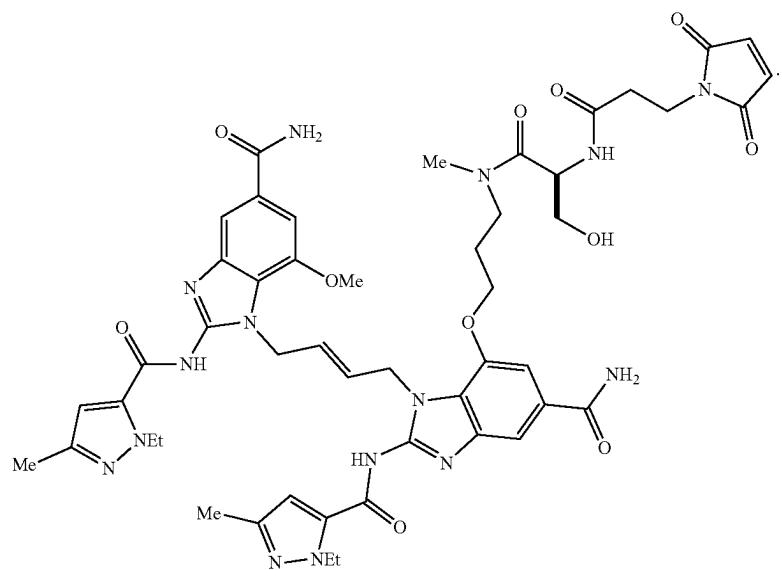
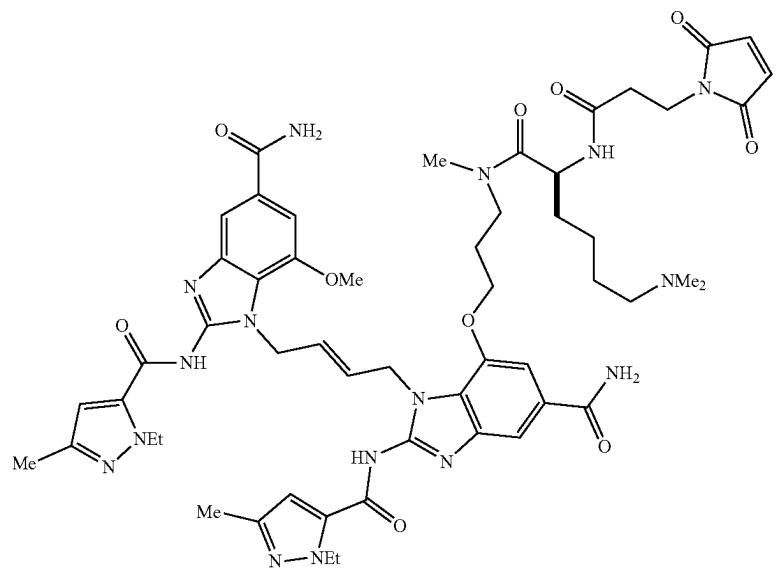
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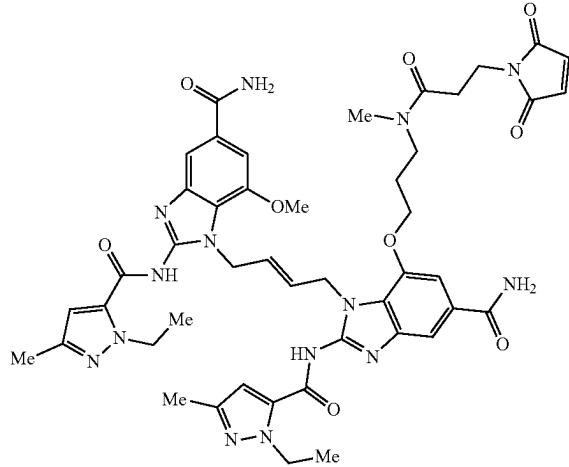
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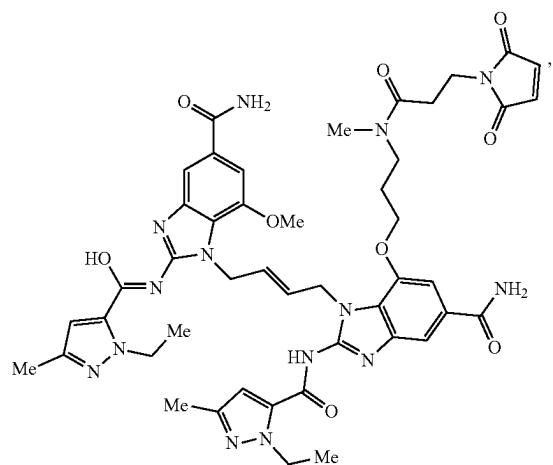
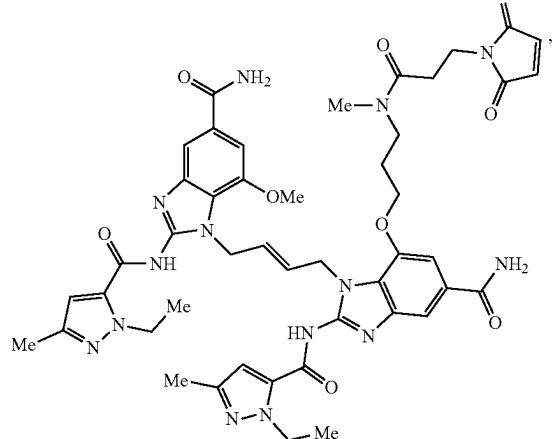
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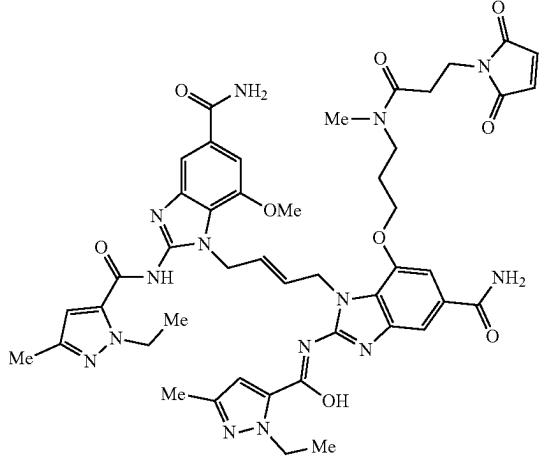
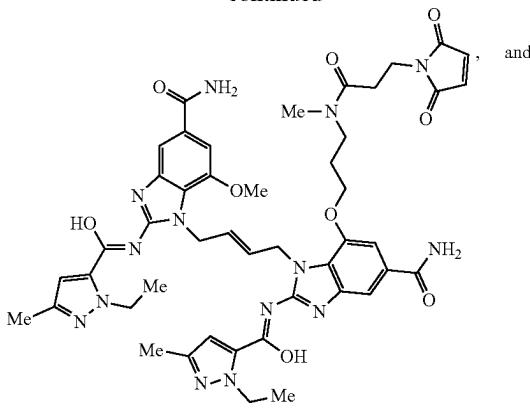
[0396] The structures shown above include all tautomeric forms. Thus, for example, the structure:



is to be understood as encompassing the following tautomeric forms:



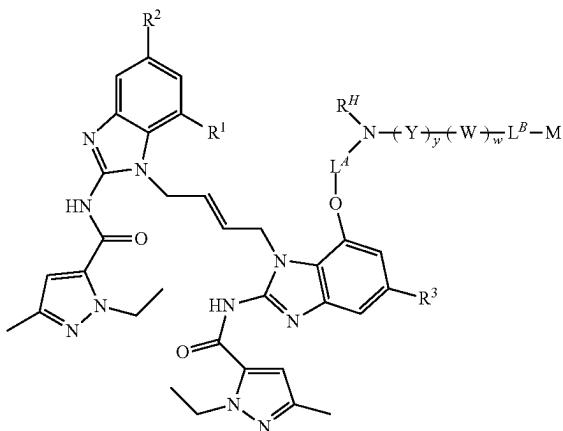
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Compounds of Formula (II-A)

[0397] In some embodiments, the compound of Formula (II) has the structure of Formula (II-A):

(II-A)

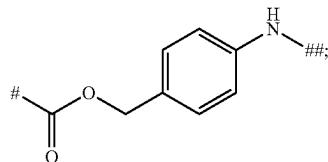


or a pharmaceutically acceptable salt thereof, wherein:

[0398] L^A is $-(CH_2)_{1-6}-$, $-C(O)(CH_2)_{1-6}-$, or $-C(O)NR^H(CH_2)_{1-6}-$;

[0399] each R^H is independently hydrogen or C_{1-3} alkyl;

[0400] Y is

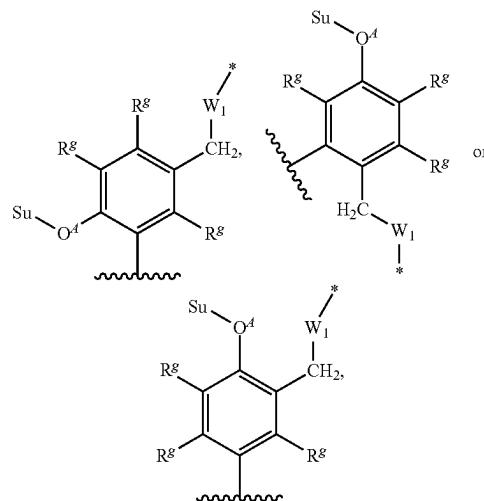


[0401] # represents covalent attachment to NR^HL^A ;
 [0402] ## represents covalent attachment to W or L^B .
 [0403] L^B is $-(\text{CH}_2)_{1-6}-$, $-\text{C}(\text{O})(\text{CH}_2)_{1-6}-$, or
 $-[\text{NHC}(\text{O})(\text{CH}_2)_{1-4}]_{1-3}-$; and
 [0404] the remaining variables are as defined above in connection of Formula (II).

[0405] In some embodiments, R^H is C_{1-3} alkyl. In some embodiments, R^H is methyl. In some embodiments, R^H is not hydrogen. In some embodiments, L^A is $-(CH_2)_{2-6}-$. In some embodiments, L^A is $-(CH_2)_3-$. In some embodiments, subscript y is 0. In some embodiments, subscript y is 1. In some embodiments, subscript w is 0. In some embodiments, subscript w is 1. In some embodiments, subscript y and subscript w are both 1. In some embodiments, subscript y and subscript w are both 0. When subscript y and subscript w are both 0, the compound of Formula (II) has the structure of Formula (II-B):

lysine, histidine, arginine, glycine, serine, threonine, phenylalanine, O-methylserine, O-methyleaspartic acid, O-methylglutamic acid, N-methyllysine, O-methyltyrosine, O-methylhistidine, and O-methylthreonine.

[0410] In some embodiments, W is:

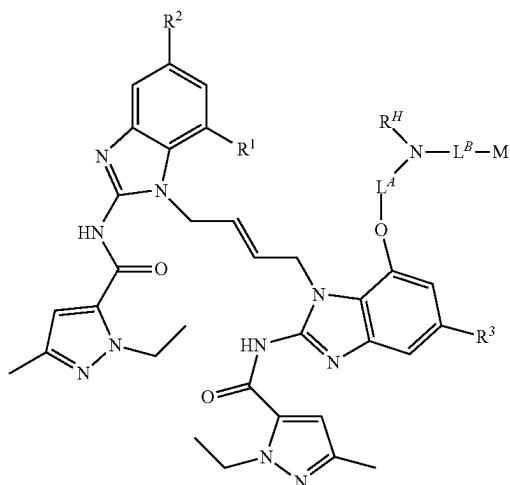


wherein:

[0411] represents covalent attachment to L^B;
and

[0412] * represents covalent attachment to Y or NR^H .

[0413] In some embodiments, L^B is $-C(O)(CH_2)_{2-6}-$. In some embodiments, L^B is $-C(O)(CH_2)_2-$. In some embodiments, L^B is $-C(O)(CH_2)_3-$. In some embodiments, L^B is $-C(O)(CH_2)_4-$. In some embodiments, L^B is $-C(O)(CH_2)_5-$. In some embodiments, L^B is $-C(O)(CH_2)_6-$. In some embodiments, L^B is $-[NHC(O)(CH_2)_2]_2-$. In some embodiments, M is



or a pharmaceutically acceptable salt thereof, wherein:

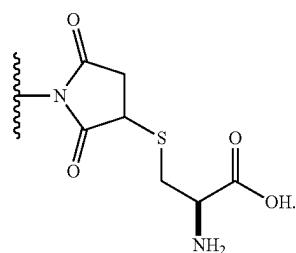
[0406] L^A is $-(CH_2)_{1-6}-$, $-C(O)(CH_2)_{1-6}-$, or $-C(O)NR^H(CH_2)_{1-6}-$;

[0407] each R^H is independently hydrogen or C₁₋₃ alkyl;

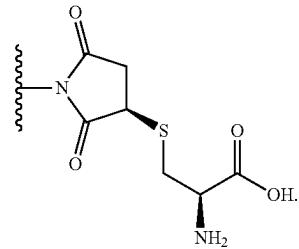
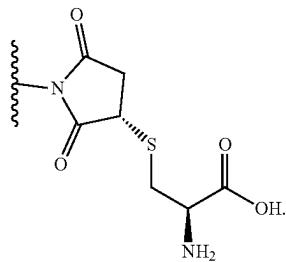
[0408] L^B is $-(\text{CH}_2)_{1-6}-$, $-\text{C}(\text{O})(\text{CH}_2)_{1-6}-$, or $-[\text{NHC}(\text{O})(\text{CH}_2)_{1-4}]_{1-3}-$; and the remaining variables are as defined above in connection of Formula (II).

[0409] In some embodiments, W is a chain of 1-6 amino acids. In some embodiments, W is a chain of 1-4 amino acids. In some embodiments, W is a chain of 1-3 amino acids. In some embodiments, each amino acid of W is independently selected from the group consisting of alanine, valine, isoleucine, leucine, aspartic acid, glutamic acid,

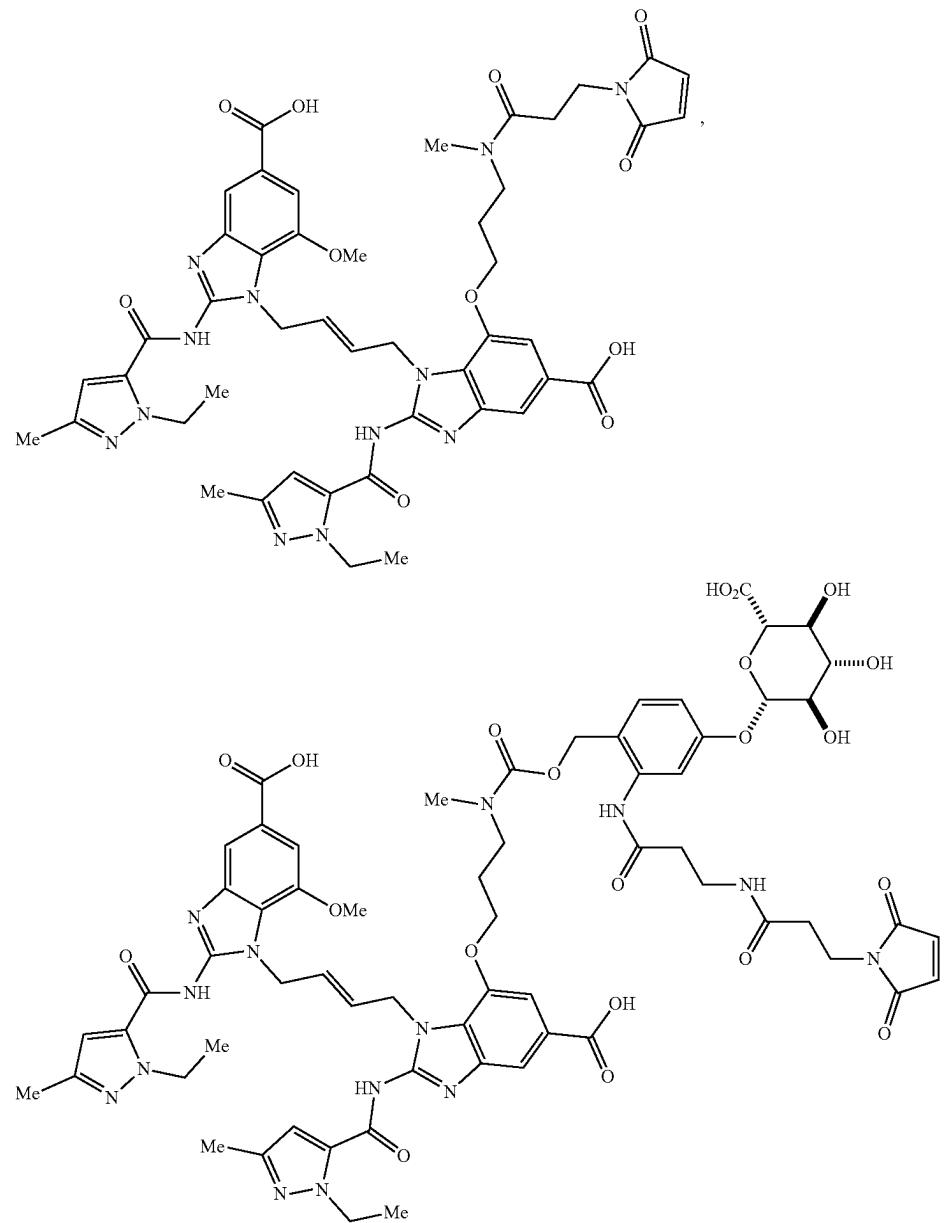
In some embodiments, M is



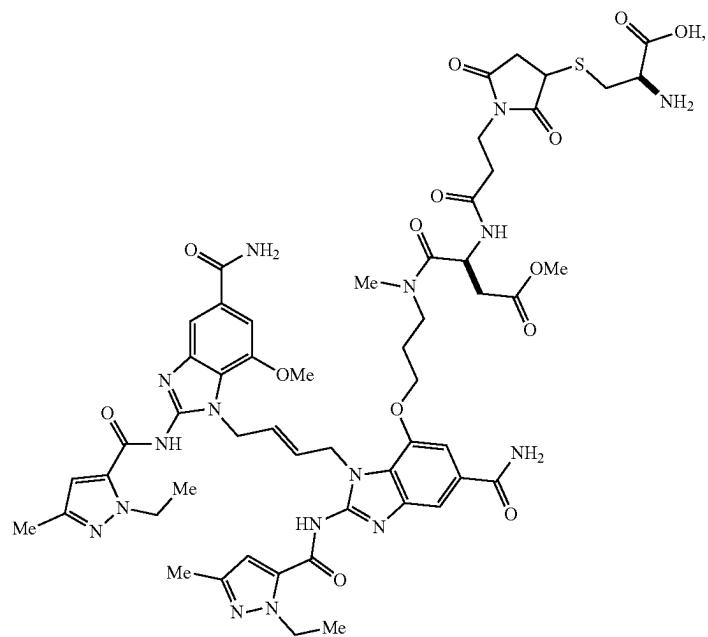
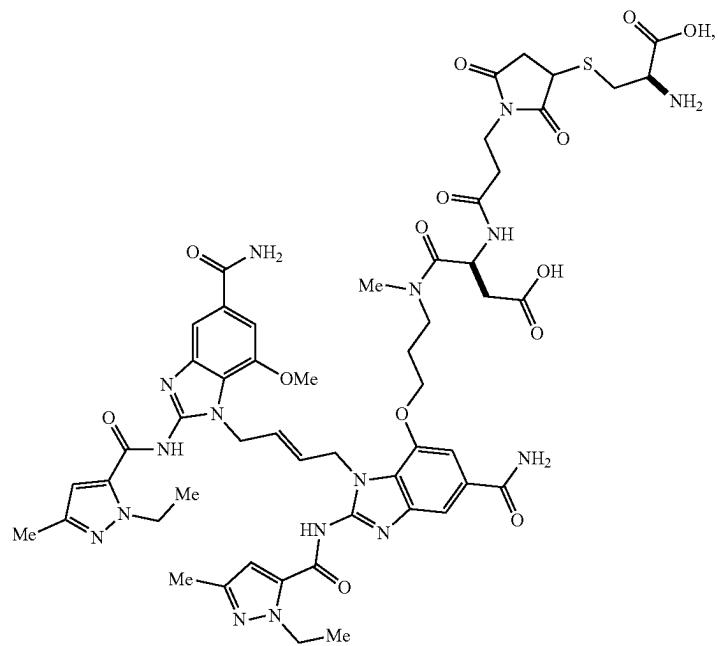
In some aspects, M is

In some aspects, M is NH₂

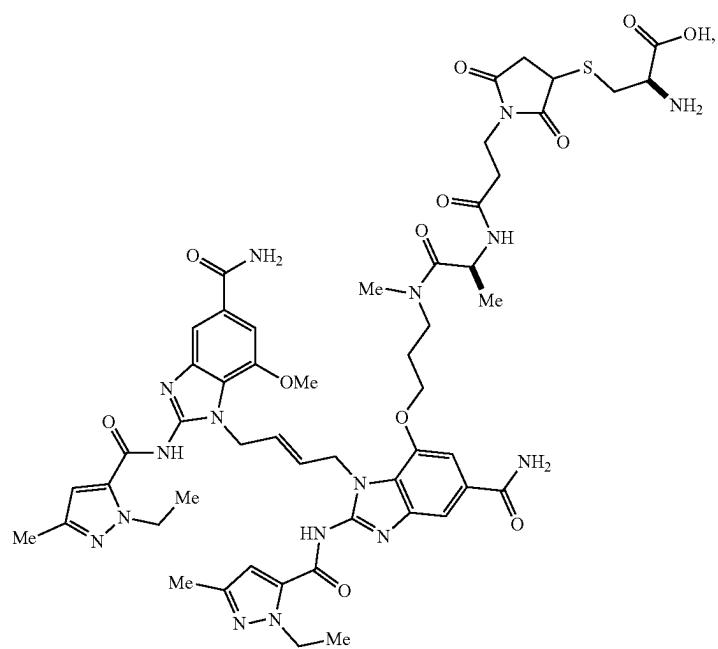
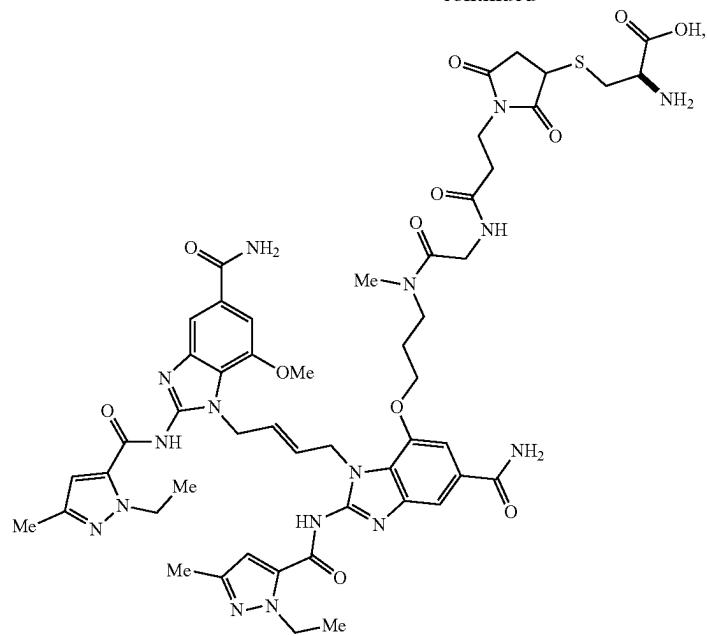
[0414] In some embodiments, the compound of Formula (II-A) is selected from the group consisting of:



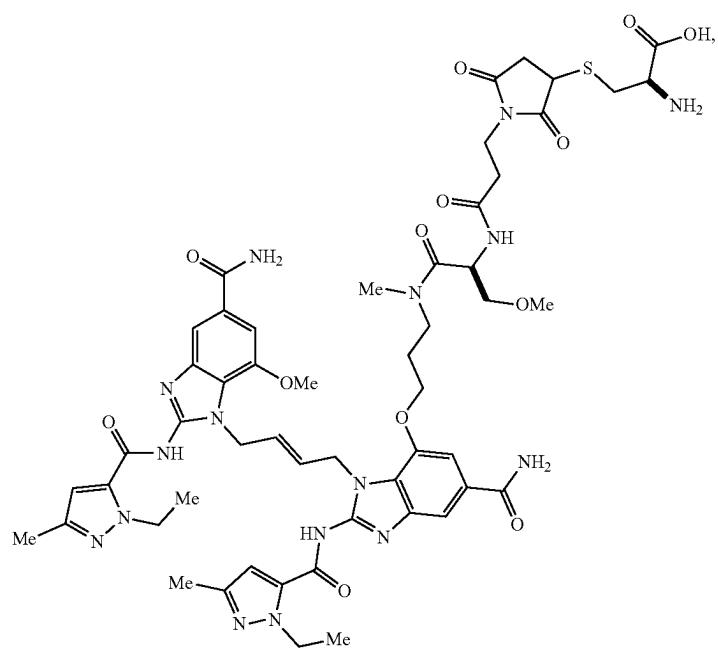
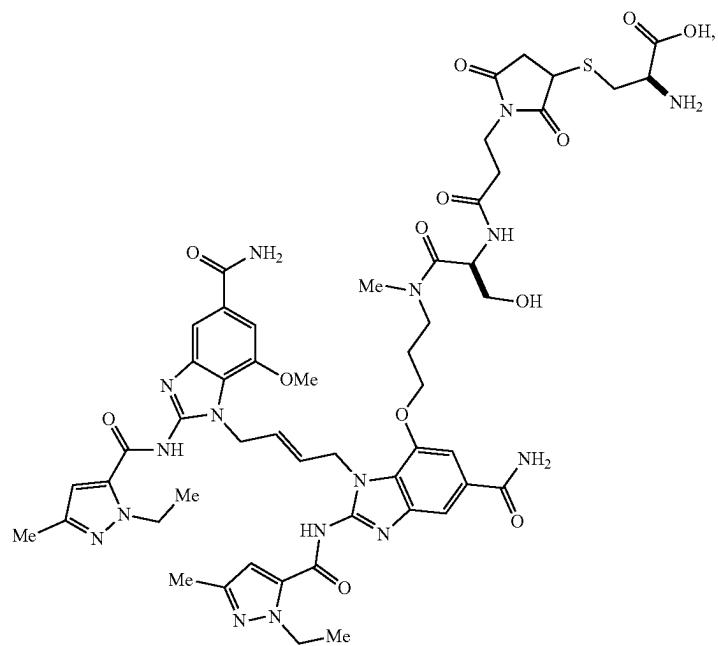
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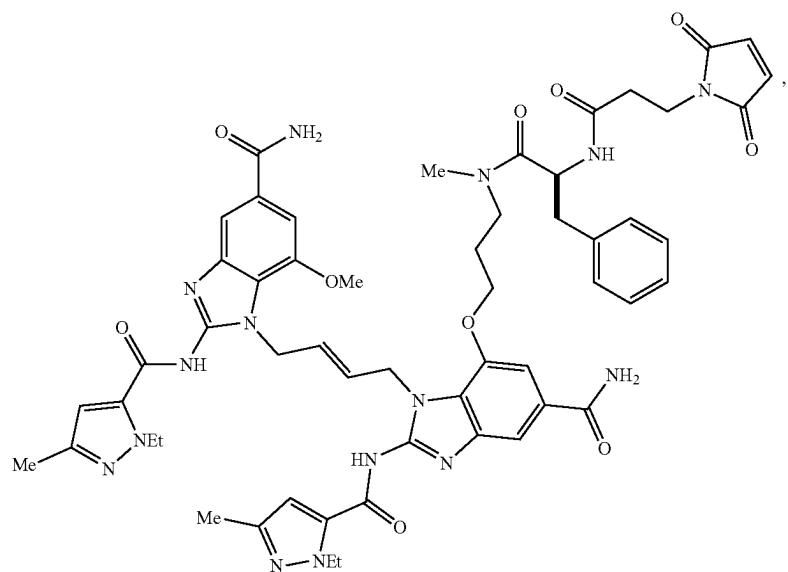
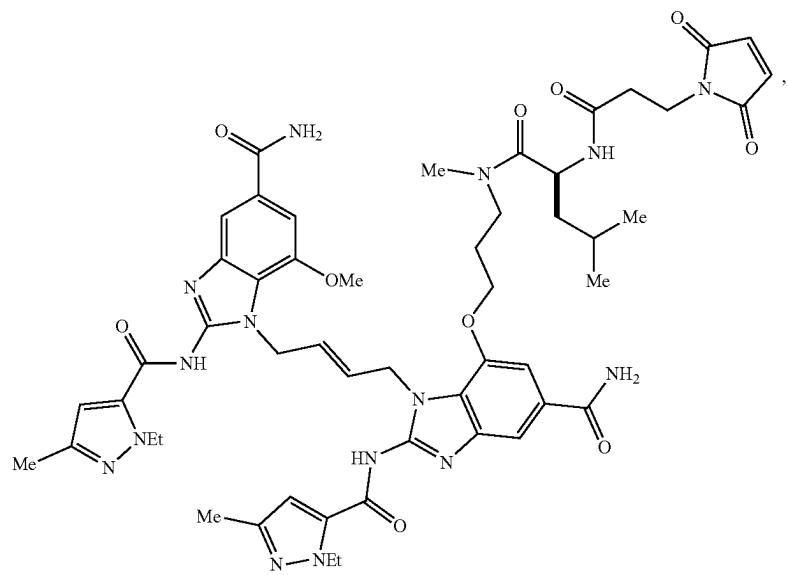
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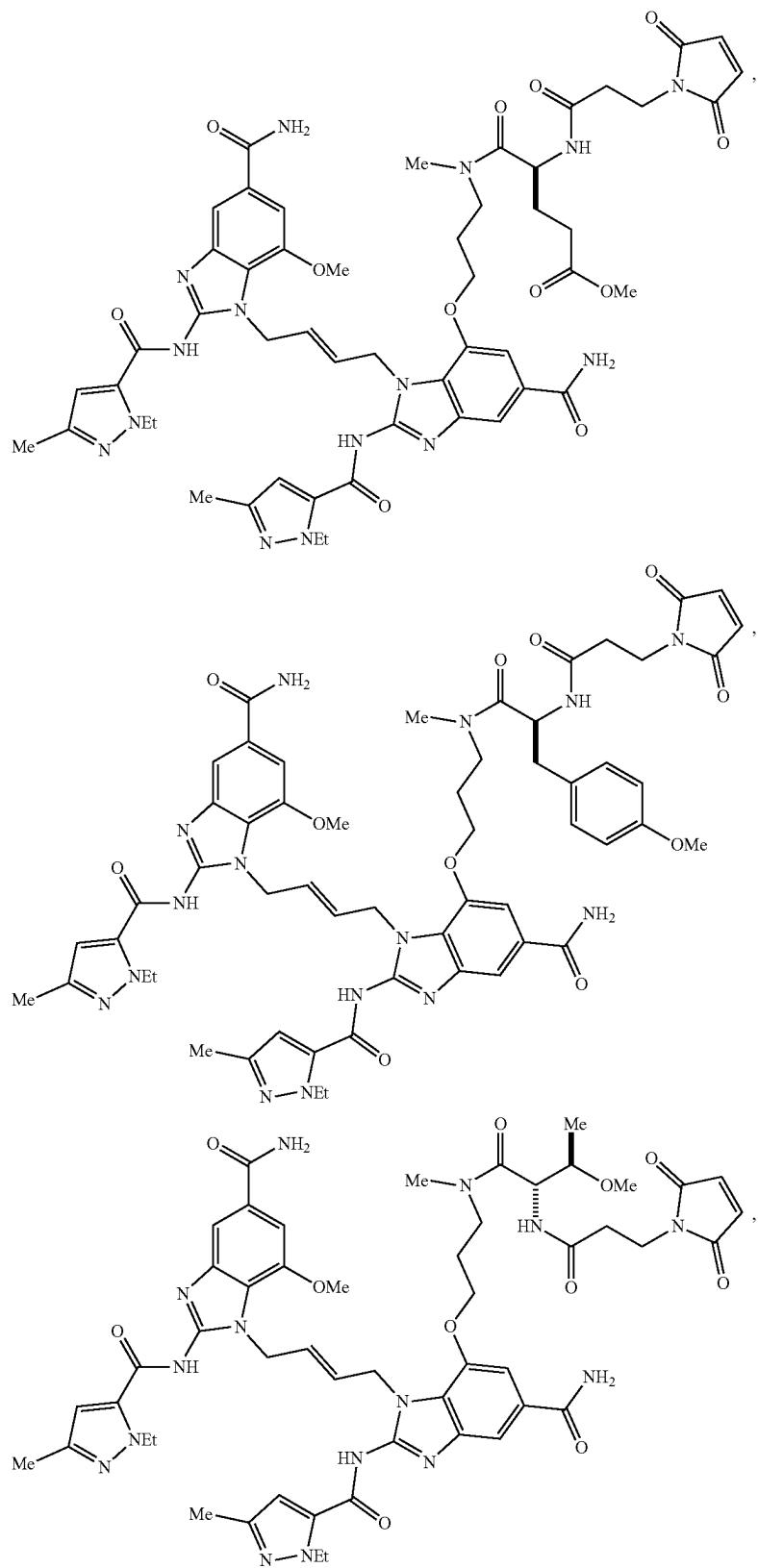
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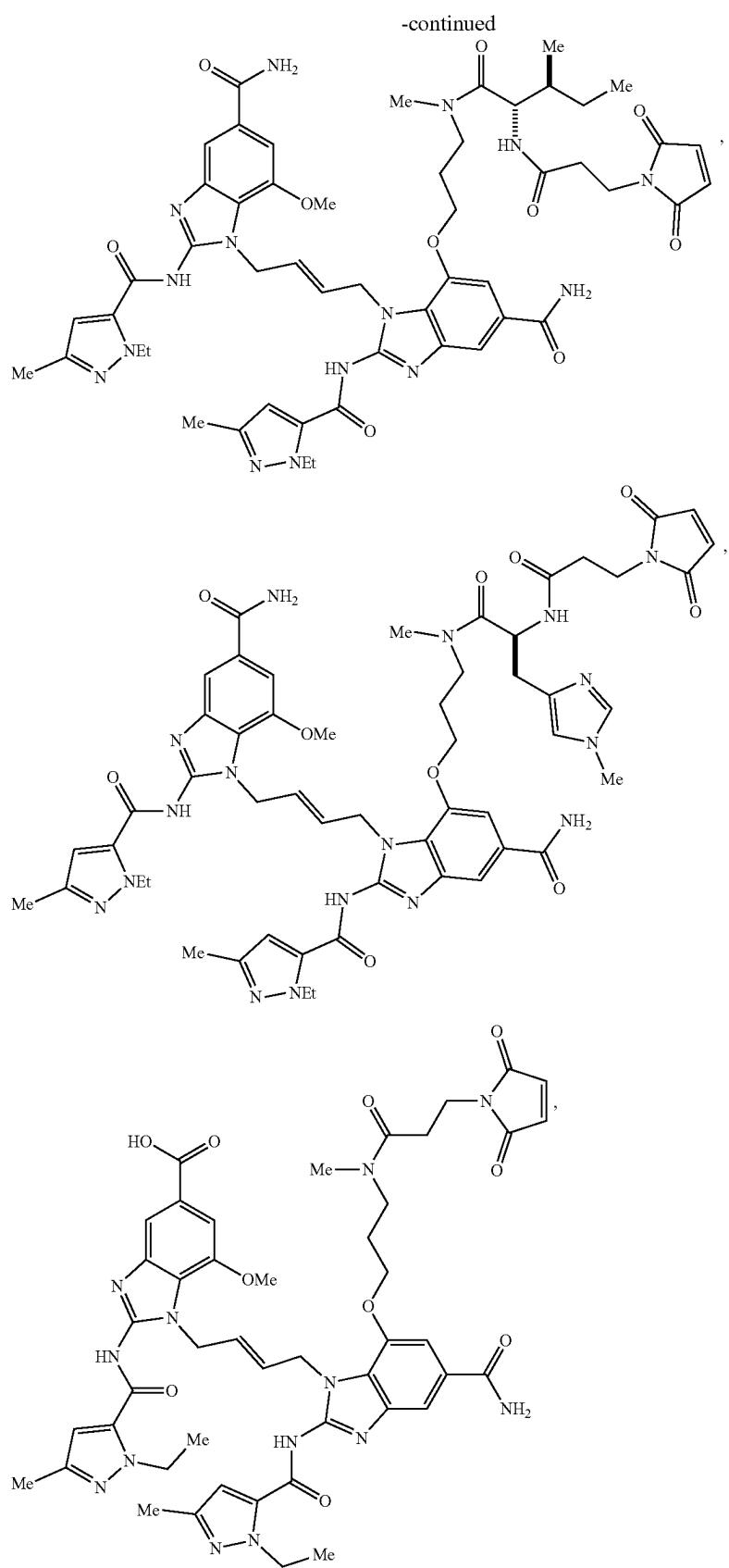


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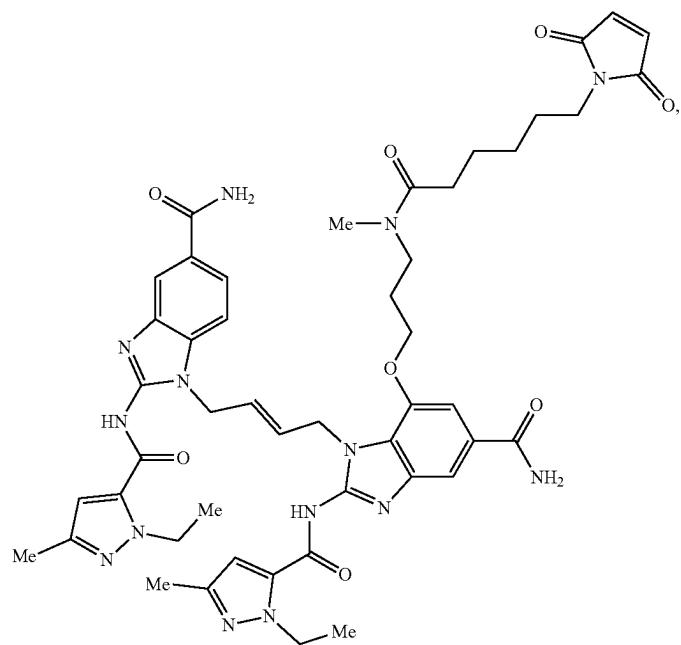
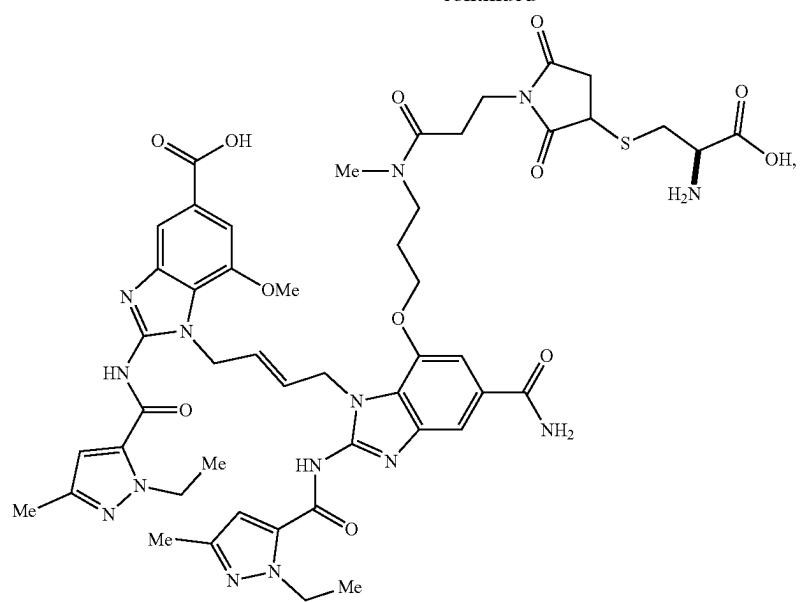


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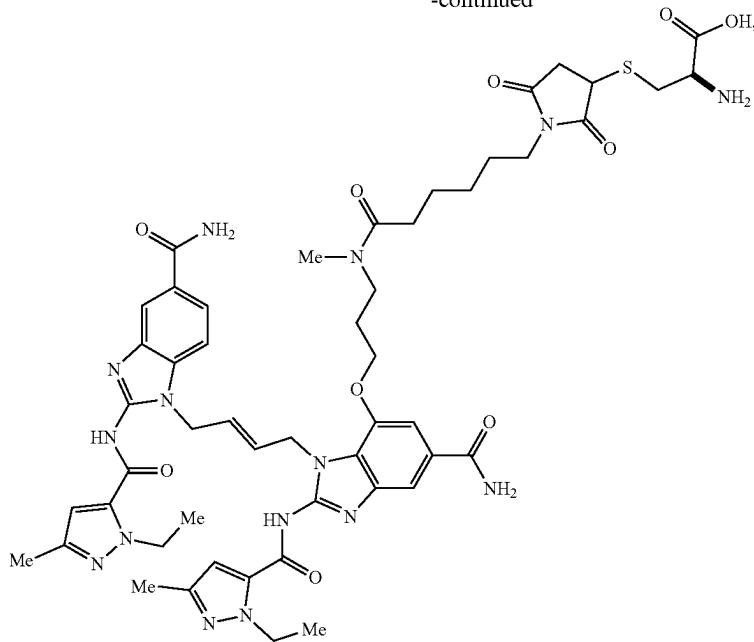




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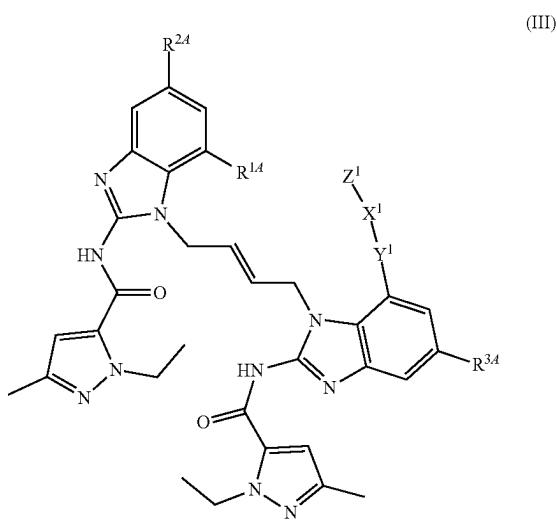
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and pharmaceutically acceptable salts thereof.

Compounds of Formula (III)

[0415] Some embodiments provide compounds of Formula (III):



or a pharmaceutically acceptable salt thereof, wherein:

- [0416]** R^{1A} is hydrogen, hydroxyl, C₁₋₆ alkoxy, -(C₁₋₆ alkyl)C₁₋₆ alkoxy, -(CH₂)_{mm}-NR^{AA}R^{BB};
- [0417]** each R^{2A} and R^{3A} are independently -CO₂H, -(C=O)_{mm}-NR^{CC}R^{DD}, or -(CH₂)_{qq}-NR^{EE}R^{FF};
- [0418]** each subscript nn is independently an integer from 0 to 6;
- [0419]** each subscript mm is independently 0 or 1;

[0420] each subscript qq is independently an integer from 0 to 6;

[0421] Y¹ is -CH₂-, -O-, -S-, -NH-, or -N(CH₃)-;

[0422] X¹ is a C₂-C₆ alkylene;

[0423] Z¹ is -NR^{EE}R^{FF}, -C(=O)NR^{GG}R^{HH}, or -CO₂H;

[0424] each R^{AA}, R^{BB}, R^{CC}, R^{DD}, R^{EE}₁, and R^{FF}₁ are independently hydrogen or C₁₋₃ alkyl; and

[0425] each R^{EE}, R^{FF}, R^{GG}, and R^{HH} are independently hydrogen or C₁₋₆ alkyl.

[0426] In some embodiments, R^{1A} is hydrogen. In some embodiments, R^{1A} is hydroxyl. In some embodiments, R^{1A} is C₁₋₆ alkoxy. In some embodiments, R¹ is methoxy. In some embodiments, R^{1A} is -(C₁₋₆ alkyl)C₁₋₆ alkoxy. In some embodiments, R^{1A} is methoxyethyl.

[0427] In some embodiments, R¹ is -(CH₂)_{nn}-NR^{AA}R^{BB}. In some embodiments, R^{AA} and R^{BB} are both hydrogen. In some embodiments, R^{AA} and R^{BB} are independently C₁₋₃ alkyl. In some embodiments, one of R^{AA} and R^{BB} is hydrogen and the other of R^{AA} and R^{BB} is C₁₋₃ alkyl. In some embodiments, the C₁₋₃ alkyl is methyl. In some embodiments, each subscript nn is 0. In some embodiments, each subscript nn is 1. In some embodiments, each subscript nn is 2. In some embodiments, each subscript nn is 3. In some embodiments, each subscript nn is 4, 5, or 6. In some embodiments, each subscript nn is 4. In some embodiments, each subscript nn is 5. In some embodiments, each subscript nn is 6.

[0428] In some embodiments, each R^{2A} and R^{3A} are independently -CO₂H, -(C=O)_m-NR^{CC}R^{DD}, or -(CH₂)_{qq}-NR^{EE}R^{FF}; and R^{2A} and R^{3A} are the same. In some embodiments, each R^{2A} and R^{3A} are independently -CO₂H, -(C=O)_{mm}-NR^{CC}R^{DD}, or -(CH₂)_{qq}-NR^{EE}R^{FF}; and R^{2A} and R^{3A} are different.

[0429] In some embodiments, R^{2A} is (C=O)_{mm}NR^CR^{DD}. In some embodiments, R^{3A} is -(C=O)_{mm}NR^C-

cR^{DD} . In some embodiments, each R^{CC} and each R^{DD} is hydrogen. In some embodiments, each R^{CC} and each R^{DD} is independently C_{1-3} alkyl. In some embodiments, one of each R^{CC} and R^{DD} is hydrogen and the other of each R^{CC} and R^{DD} is C_{1-3} alkyl. In some embodiments, the C_{1-3} alkyl is methyl. In some embodiments, each subscript mm is 0. In some embodiments, each subscript mm is 1.

[0430] In some embodiments, R^{2A} is $-(CH_2)_{qq}-NR^{EE1}R^{FF1}$. In some embodiments, R^{3A} is $-(CH_2)_{qq}-NR^{EE1}R^{FF1}$. In some embodiments, each R^{EE1} and each R^{FF1} is hydrogen. In some embodiments, each R^{EE1} and each R^{FF1} is independently C_{1-3} alkyl. In some embodiments, one of each R^{EE1} and R^{FF1} is hydrogen and the other of each R^{EE1} and R^{FF1} is C_{1-3} alkyl. In some embodiments, the C_{1-3} alkyl is methyl. In some embodiments, each subscript q is 0. In some embodiments, each subscript q is an integer from 1 to 6. In some embodiments, each subscript qq is 1. In some embodiments, each subscript qq is 2. In some embodiments, each subscript qq is 3, 4, 5, or 6.

[0431] In some embodiments, R^{3A} is $-CO_2H$. In some embodiments, R^{2A} is $-CO_2H$.

[0432] In some embodiments, Y^1 is $-CH_2-$. In some embodiments, Y^1 is $-O-$. In some embodiments, Y^1 is $-S-$. In some embodiments, Y^1 is $-NH-$. In some embodiments, Y^1 is $-N(CH_3)-$.

[0433] In some embodiments, X^1 is a C_2-C_5 alkylene. In some embodiments, X^1 is a C_2-C_4 alkylene. In some embodiments, X^1 is ethylene or n-propylene. In some embodiments, X^1 is ethylene. In some embodiments, X^1 is n-propylene.

[0434] In some embodiments, Z^1 is $-NR^{E1}R^{F1}$. In some embodiments, R^{EE} and R^{FF} are both hydrogen. In some embodiments, R^{EE} and R^{FF} are independently C_{1-6} alkyl. In some embodiments, one of R^{EE} and R^{FF} is hydrogen and the other of R^{EE} and R^{FF} is C_{1-6} alkyl. In some embodiments, the C_{1-6} alkyl is a C_{1-3} alkyl. In some embodiments, the C_{1-3} alkyl is methyl.

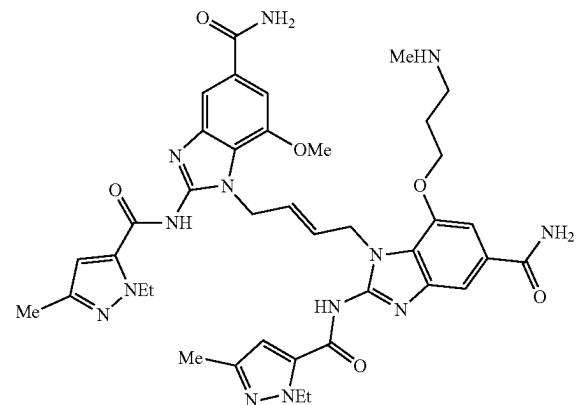
[0435] In some embodiments, Z^1 is $-C(=O)NR^{GG}R^{HH}$. In some embodiments, R^{GG} and R^{HH} are both hydrogen. In some embodiments, R^{GG} and R^{HH} are independently C_{1-6} alkyl. In some embodiments, one of R^{GG} and R^{HH} is hydrogen and the other of R^{GG} and R^{HH} is C_{1-6} alkyl. In some

embodiments, the C_{1-6} alkyl is a C_{1-3} alkyl. In some embodiments, the C_{1-3} alkyl is methyl. In some embodiments, Z^1 is $-CO_2H$. In some embodiments, Z^1 is $-NR^{EE}R^{FF}$. In some embodiments, R^{EE} is hydrogen and R^{FF} is methyl.

[0436] In some embodiments, R^{1A} is methoxy and R^{2A} and R^{3A} are both $-C(=O)NH_2$. In some embodiments, Y^1 is $-O-$ and X^1 is a C_3 alkylene. In some embodiments, Y^1 is $-O-$ and X^1 is n-propylene. In some embodiments, Y^1 is $-O-$, X^1 is n-propylene, and Z^1 is $-NH_2$. In some embodiments, Y^1 is $-O-$, X^1 is n-propylene, and Z^1 is $-NHCH_3$. In some embodiments, Y^1 is $-O-X^1$ is n-propylene, and Z^1 is $-N(CH_3)_2$.

[0437] In some embodiments, R^{1A} is methoxy; R^{2A} and R^{3A} are both $-C(=O)NH_2$; Y^1 is $-O-$; X^1 is n-propylene; and Z^1 is $-NH_2$. In some embodiments, R^{1A} is methoxy; R^{2A} and R^{3A} are both $-C(=O)NH_2$; Y^1 is $-O-$; X^1 is n-propylene; and Z^1 is $-NHCH_3$. In some embodiments, R^{1A} is methoxy; R^{2A} and R^{3A} are both $-C(=O)NH_2$; Y^1 is $-O-$; X^1 is n-propylene; and Z^1 is $-N(CH_3)_2$.

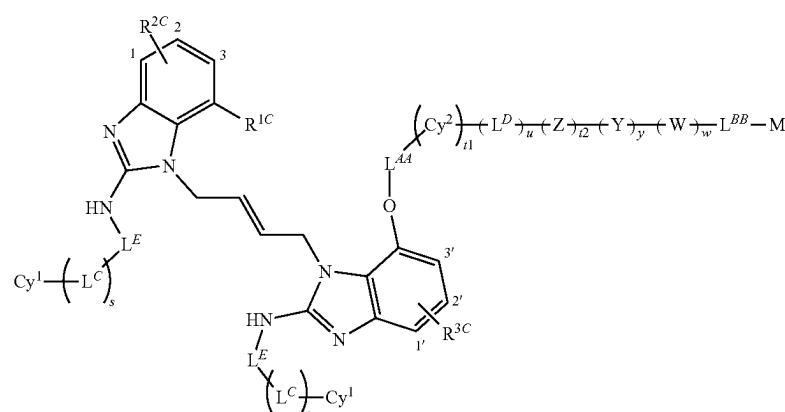
[0438] In some embodiments, the compound of Formula (III) is



Compounds of Formula (IV)

[0439] Some embodiments include a compound of Formula (IV):

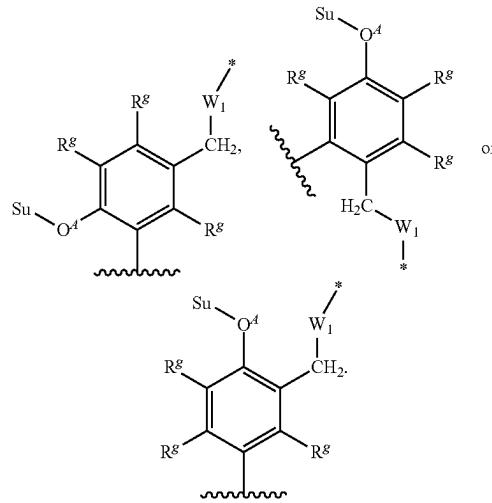
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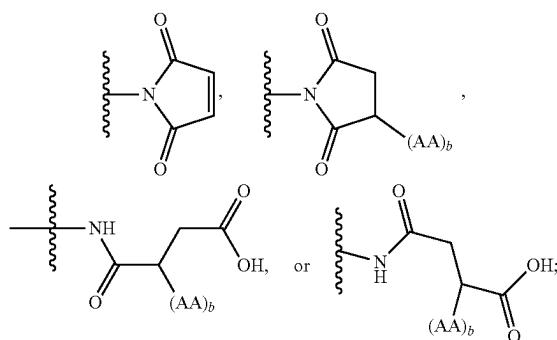
or a pharmaceutically acceptable salt thereof, wherein:

- [0440] R^{1C} is hydrogen, hydroxyl, C_{1-6} alkoxy, $-(C_{1-6} \text{ alkyl})C_{1-6}$ alkoxy, $-(CH_2)_n-NR^A R^B$, or PEG2 to PEG4;
- [0441] R^{2C} is $-CO_2 R^M$, $-(C=O)NR^C R^D$, $-S(O)_2 NR^C R^D$, $-S(O)_2 R^M$, $-(CH_2)_q-NR^E R^F$, $-(CH_2)_q-OR^M$, $-O(C=O)-NR^E R^F$, or $-NR^M(C=O)-NR^E R^F$, wherein R^{2C} is attached at any one of positions labeled 1, 2, or 3;
- [0442] R^{3C} is $-CO_2 R^M$, $-(C=O)NR^C R^D$, $-S(O)_2 NR^C R^D$, $-S(O)_2 R^M$, $-(CH_2)_q-NR^E R^F$, $-(CH_2)_q-OR^M$, $-O(C=O)-NR^E R^F$, or $-NR^M(C=O)-NR^E R^F$, wherein R^{3C} is attached at any one of positions labeled 1', 2', or 3';
- [0443] each R^A , R^B , R^C , R^D , R^E , R^F , and R^M are independently hydrogen or C_{1-6} alkyl;
- [0444] each subscript n is independently an integer from 0 to 6;
- [0445] each subscript q is independently an integer from 0 to 6;
- [0446] L^E is $-(C=O)-$ or $-S(0)_2-$;
- [0447] L^C is $-(CR^I R^J)_{1-3}-$
- [0448] each R^I and R^J are independently hydrogen or C_{1-3} alkyl;
- [0449] subscript s is 0 or 1;
- [0450] each Cy^1 is independently a 4-6 membered heterocycle, a 5-6 membered heteroaryl, or a C_{3-6} cycloalkyl, each optionally substituted with one or more R^K ;
- [0451] each R^K is independently selected from the group consisting of: C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, $-OH$, $=O$, $-NR^{d2} R^{e2}$, $-C(O)NR^{d2} R^{e2}$, $-C(O)(C_{1-6} \text{ alkyl})$, and $-C(O)O(C_{1-6} \text{ alkyl})$;
- [0452] each R^{d2} and R^{e2} are independently hydrogen or C_{1-3} alkyl;
- [0453] L^{4A} is $-(CH_2)_{1-6}-$, $-C(O)(CH_2)_{1-6}-$, $-C(O)NR^L(CH_2)_{1-6}-$, $-(CH_2)_{1-6}O-$, $-C(O)(CH_2)_{1-6}O-$, or $-C(O)NR^L(CH_2)_{1-6}O-$;
- [0454] R^L is hydrogen or C_{1-3} alkyl;
- [0455] Cy^2 is C_{3-6} cycloalkyl, 4-6 membered heterocycle, 5-6 membered heteroaryl, or phenyl, each optionally substituted with one or more R^U ;
- [0456] each R^U is independently selected from the group consisting of $-CO_2 R^{j1}$, $-(C=O)NR^{d3} R^{e3}$, $-S(O)_2 NR^{d3} R^{e3}$, $-(CH_2)_{g1}-NR^{g1} R^{h1}$, $-(CH_2)_{q1}-OR^{j1}$, and $-(CH_2)^{q1}-(OCH_2 CH_2)_{1-8} OH$;
- [0457] each R^{d3} , R^{e3} , R^{g1} , R^{h1} , and R^{j1} are independently hydrogen or C_{1-6} alkyl;
- [0458] subscript q1 is an integer from 0 to 6;
- [0459] subscripts t1 and t2 are independently 0 or 1, wherein at least one of t1 and t2 is 1;
- [0460] L^D is $-(CH_2)_{1-6}-$;
- [0461] subscript u is 0 or 1;
- [0462] Z is $-N(R^{HH})-$ or $-N^+(C_{1-6} \text{ alkyl})(R^{HH})-$;
- [0463] R^{HH} is hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, $-(CH_2)_{1-3} C_{3-6}$ cycloalkyl, $-(CH_2)_{1-3} C_{1-3}$ alkoxy, $-(CH_2)_{1-3}$ 4-6 membered heterocycle, or $-(CH_2)_{1-3}$ 5-6 membered heteroaryl;
- [0464] Y is a self-immolative moiety, a non-self-immolative releasable moiety, or a non-cleavable moiety;
- [0465] subscript y is 0 or 1;

- [0466] W is a chain of 1-12 amino acids or has the structure:



- [0467] wherein Su is a Sugar moiety;
- [0468] $-O^4-$ represents a glycosidic bond;
- [0469] each R^g is independently hydrogen, halogen, $-CN$, or $-NO_2$;
- [0470] W^1 is absent or $-O-C(=O)-$;
- [0471] $\sim\sim\sim$ represents covalent attachment to L^{BB} ;
- [0472] * represents covalent attachment to Y, L^D , NR^{HH} , or Cy^2 ;
- [0473] subscript w is 0 or 1;
- [0474] L^{BB} is $-(CH_2)_{1-6}-$, $-C(O)(CH_2)_{1-6}-$, or $-[NHC(O)(CH_2)_{1-4}]1-3-$; and
- [0475] M is



- [0476] each AA is an independently selected amino acid, wherein $(AA)_b$ is connected to the succinimide or hydrolyzed succinimide via a sulfur atom; and
- [0477] each subscript b is independently an integer from 1 to 6.
- [0478] In some embodiments, R^{1C} is hydrogen. In some embodiments, R^{1C} is hydroxyl. In some embodiments, R^{1C} is C_{1-6} alkoxy. In some embodiments, R^{1C} is methoxy. In some embodiments, R^{1C} is $-(C_{1-6} \text{ alkyl})C_{1-6}$ alkoxy. In some embodiments, R^{1C} is methoxyethyl. In some embodiments, R^{1C} is PEG2 to PEG4. In some embodiments, R^{1C} is $-(CH_2)_n-NR^A R^B$.

[0479] In some embodiments, R^A and R^B are both hydrogen. In some embodiments, R^A and R^B are independently C_{1-3} alkyl. In some embodiments, one of R^A and R^B is hydrogen and the other of R^A and R^B is C_{1-3} alkyl.

[0480] In some embodiments, each subscript n is 0. In some embodiments, each subscript n is 1. In some embodiments, each subscript n is 2. In some embodiments, each subscript n is 3, 4, 5, or 6.

[0481] In some embodiments, R^{2C} and R^{3C} are independently $-CO_2H$, $-(C=O)_m$, $-NR^CR^D$, or $-(CH_2)_qNR^ER^F$; and R^{2C} and R^{3C} are the same. In some embodiments, R^{2C} and R^{3C} are independently $-CO_2H$, $-(C=O)_m-NR^CR^D$, or $-(CH_2)_q-NR^ER^F$; and R^{2C} and R^{3C} are different. In some embodiments, R^{2C} is $-(C=O)_m-NR^CR^D$. In some embodiments, R^{3C} is $-(C=O)_m-NR^CR^D$. In some embodiments, R^C and R^D are both hydrogen. In some embodiments, R^C and R^D are each independently C₁₋₃ alkyl. In some embodiments, one of R^C and R^D is hydrogen and the other of R^C and R^D is C₁₋₃ alkyl. In some embodiments, each subscript m is 0. In some embodiments, each subscript m is 1.

[0482] In some embodiments, R^{2C} is $-(CH_2)_q-NR^E R^F$. In some embodiments, R^{3C} is $-(CH_2)_q-NR^E R^F$. In some embodiments, R^E and R^F are both hydrogen. In some embodiments, R^E and R^F are each independently C_{1-3} alkyl. In some embodiments, one of R^E and R^F is hydrogen and the other of R^E and R^F is C_{1-3} alkyl. In some embodiments, each subscript q is 0. In some embodiments, each subscript q is an integer from 1 to 6.

[0483] In some embodiments, R^{2C} is $-CO_2R^M$. In some embodiments, R^{3C} is $-CO_2R^M$. In some embodiments, R^M is hydrogen. In some embodiments, R^M is C_{1-3} alkyl.

[0484] In some embodiments, R^{2C} is $(CH_2)_q-OR^M$.

[0485] In some embodiments, R^{3C} is $-(CH_2)_q-OR^M$. In some embodiments, R^M is hydrogen. In some embodiments, q is 0. In some embodiments, q is 1.

[0486] In some embodiments, R^{2C} is $-\text{O}(\text{C}=\text{O})-\text{NR}^E\text{R}^F$. In some embodiments, R^{3C} is $-\text{O}(\text{C}=\text{O})-\text{NR}^E\text{R}^F$. In some embodiments, R^E and R^F are both hydrogen. In some embodiments, R^E and R^F are each independently C_{1-3} alkyl. In some embodiments, R^E and R^F is hydrogen and the other is R^{2E} , R^{3E} , C_6H_4 , C_6H_5 .

of R^G and R^F is C_{1-3} alkyl.

[0487] In some embodiments, R^{2C} is $-\text{NR}^M(\text{C}=\text{O})-$ NR^ER^F . In some embodiments, R^{3C} is $-\text{NR}^M(\text{C}=\text{O})-$ NR^ER^F . In some embodiments, R^E , R^F , and R^M are all hydrogen. In some embodiments, R^E , R^F , and R^M are each independently C_{1-3} alkyl. In some embodiments, one of R^E , R^F , and R^M is C_{1-3} alkyl and the rest of R^E , R^F , and R^M is hydrogen.

[0488] In some embodiments, R^{2C} is $-\text{S}(\text{O})_2\text{NR}^CR^D$. In some embodiments, R^{3C} is $-\text{S}(\text{O})_2\text{NR}^CR^D$. In some embodiments, R^C and R^D are both hydrogen. In some embodiments, R^C and R^D are each independently C_{1-3} alkyl. In some embodiments, one of R^C and R^D is hydrogen and the other of R^C and R^D is C_{1-3} alkyl.

[0489] In some embodiments, R^{2C} is $-\text{S}(\text{O})_2\text{R}^M$. In some embodiments, R^{3C} is $-\text{S}(\text{O})_2\text{R}^M$. In some embodiments, R^M is hydrogen. In some embodiments, R^M is C_{1-3} alkyl.

[0490] In some embodiments, R^{2C} is attached at position 1. In some embodiments, R^{2C} is attached at position 2. In some embodiments, R^{2C} is attached at position 3. In some embodiments, R^{3C} is attached at position 1'. In some embodiments, R^{3C} is attached at position 2'. In some embodiments, R^{3C} is attached at position 3'.

[0491] In some embodiments, L^E is $-(C=O)-$. In some embodiments, L^E is $-S(O)_2-$.

[0492] In some embodiments, each R^I and R^J is hydrogen. In some embodiments, each R^I and R^J is C₁₋₃ alkyl. In some embodiments, one of R^I and R^J is hydrogen and the other of R^I and R^J is C₁₋₃ alkyl.

[0493] In some embodiments, L^C is —(CR^IR^J)—.

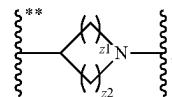
[0494] In some embodiments, s is 0. In some embodiments, s is 1.

[0495] In some embodiments, each Cy¹ is independently a 5-6 membered heteroaryl. In some embodiments, each Cy¹ is pyrazole optionally substituted with one or more R^K. In some embodiments, each Cy¹ is independently selected from the group consisting of pyrazole, imidazole, furan, thiophene, thiazole, isothiazole, oxazole, isoxazole, pyrrole, pyridazine, pyridine, pyrimidine, and pyrazine, each optionally substituted with one or more R^K. In some embodiments, each Cy¹ is independently selected from the group consisting of imidazole, furan, thiophene, thiazole, isothiazole, oxazole, isoxazole, pyrrole, pyridazine, pyridine, pyrimidine, and pyrazine, each optionally substituted with one or more R^K. In some embodiments, each Cy¹ is independently a C₄₋₅ cycloalkyl optionally substituted with one or more R^K. In some embodiments, each R^K is independently selected from the group consisting of C₁₋₃ alkyl, C₁₋₃ haloalkyl, and halogen. In some embodiments, each R^K is independently selected from the group consisting of methyl, ethyl, —CF₃, and halogen.

[0496] In some embodiments, each Cy¹ is the same. In some embodiments, each Cy¹ is different.

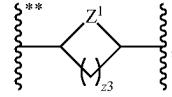
[0497] In some embodiments, L^{A4} is $-(CH_2)_{1-6}-$. In some embodiments, L^{A4} is $-(CH_2)_{1-3}-$. In some embodiments, L^{A4} is $-(CH_2)_{1-6}O-$. In some embodiments, L^{A4} is $-(CH_2)_{1-3}O-$.

[0498] In some embodiments, Cy² is a 4-6 membered heterocycle. In some embodiments, Cy² has the structure:



wherein each of subscripts z1 and z2 is independently an integer from 1 to 3 and ** indicates attachment to L⁴⁴. In some embodiments, z1 and z2 are 1. In some embodiments, z1 and z2 are 2. In some embodiments, z1 is 1 and z2 is 2.

[0499] In some embodiments, Cy² has the structure:



wherein

[0500] Z^1 is selected from the group consisting of $-\text{O}-$, $-\text{S}-$, $-\text{CR}^N\text{R}^O-$, and $-\text{NR}^P-$;

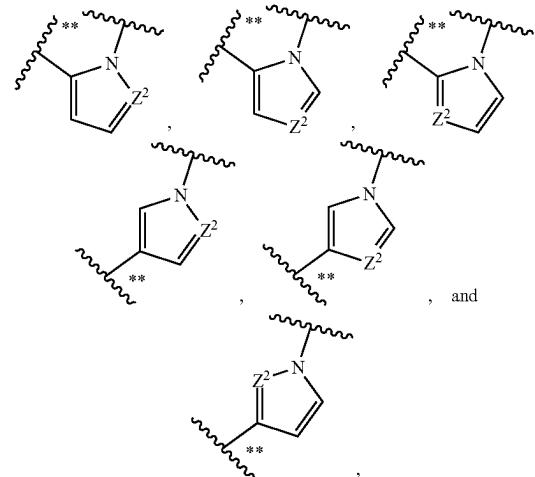
[0501] R^N, R^O, and R^P are independently hydrogen or C₁₋₆ alkyl;

[0502] subscript z3 is an integer from 1 to 3; and

[0503] ** indicates attachment to L^{AA}.

[0504] In some embodiments, R^N and R^O are hydrogen. In some embodiments, R^P is hydrogen. In some embodiments, R^P is methyl.

[0505] In some embodiments, Cy^2 is a 5-6 membered heteroaryl. In some embodiments, Cy^2 is selected from the group consisting of:



wherein

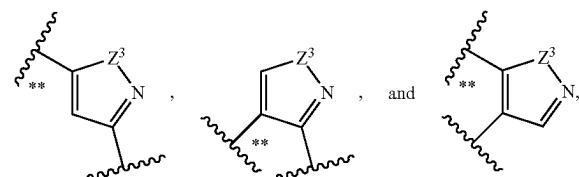
[0506] Z^2 is $=CR^N-$ or $=N-$;

[0507] R^N is hydrogen or C_{1-6} alkyl; and

[0508] ** indicates attachment to L^AA .

[0509] In some embodiments, Z^2 is $=CR^N-$ and R^N is hydrogen. In some embodiments, Z^2 is $=N-$.

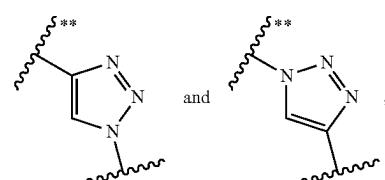
[0510] In some embodiments, Cy^2 is selected from the group consisting of:



wherein Z^3 is $-O-$ or $-S-$ and ** indicates attachment to L^AA , L^D , NR^{HH} , Y , W , or L^{BB} .

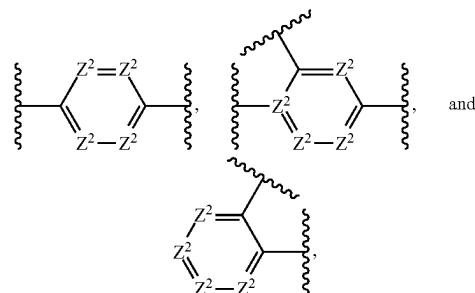
[0511] In some embodiments, ** indicates attachment to L^AA . In some embodiments, ** indicates attachment to L^D , NR^{HH} , Y , W , or L^{BB} .

[0512] In some embodiments, Cy^2 is selected from the group consisting of:



wherein ** indicates attachment to L^AA .

[0513] In some embodiments, Cy^2 is selected from the group consisting of:



wherein

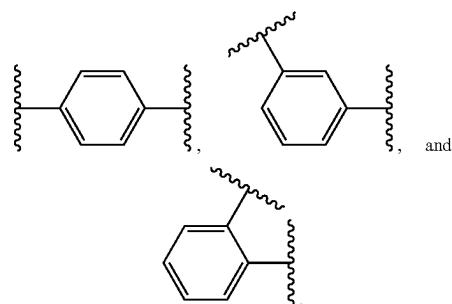
[0514] each Z^2 is independently $=CR^N-$ or $=N-$;

[0515] each R^N is hydrogen or C_{1-6} alkyl.

[0516] In some embodiments, at least one Z^2 is $=N-$. In some embodiments, one Z^2 is $=N-$ and the remaining Z^2 are $=CR^N-$. In some embodiments, two Z^2 are $=N-$ and the remaining Z^2 are $=CR^N-$.

[0517] In some embodiments, R^N is hydrogen.

[0518] In some embodiments, Cy^2 is selected from the group consisting of:



[0519] In some embodiments, Cy^2 is cyclobutyl.

[0520] In some embodiments, each R^{d3} , R^{e3} , R^{g1} , R^{h1} , and R^{j1} are independently hydrogen or $-CH_3$.

[0521] In some embodiments, each R^U is independently selected from $-CO_2H$, $-(C=O)NH_2$, $-S(O)_2NH_2$, $-CH_2NH_2$, and $-CH_2OH$.

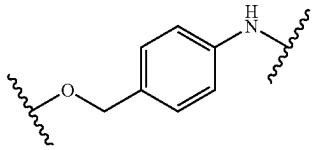
[0522] In some embodiments, t_1 is 0 and t_2 is 1. In some embodiments, t_1 is 1 and t_2 is 0. In some embodiments, t_1 is 1 and t_2 is 1.

[0523] In some embodiments, u is 1 and L^D is $-(CH_2)_{1-3}$. In some embodiments, u is 0.

[0524] In some embodiments, t_2 is 1 and R^{HH} is hydrogen. In some embodiments, t_2 is 1 and R^{HH} is C_{1-3} alkyl. In some embodiments, t_2 is 1 and R^{HH} is C_{3-4} cycloalkyl. In some embodiments, t_2 is 1 and R^{HH} is $-(CH_2)C_{3-4}$ cycloalkyl. In some embodiments, t_2 is 1 and R^{HH} is $-(CH_2)4-5$ membered heterocycle. In some embodiments, t_2 is 1 and R^{HH} is $-(CH_2)5$ -membered heteroaryl.

[0525] In some embodiments, Z is $-N(R^{HH})-$. In other embodiments, Z is $-N^+(C_{1-6} \text{ alkyl})(R^{HH})-$.

[0526] In some embodiments, Y is

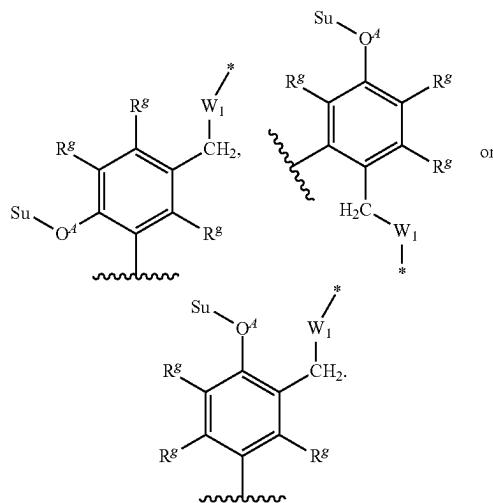


[0527] In some embodiments, Y is a cyclohexanecarboxyl, undecanoyl, caproyl, hexanoyl, butanoyl or propionyl group. In some embodiments, Y is PEG4 to PEG12. In some embodiments, y is 0. In some embodiments, y is 1.

[0528] In some embodiments, W is a chain of 1-12 amino acids. In some embodiments, W is a chain of 1-6 amino acids. In some embodiments, W is a chain of 1-3 amino acids.

[0529] In some embodiments, W is independently selected from the group consisting of alanine, valine, isoleucine, leucine, aspartic acid, glutamic acid, lysine, histidine, arginine, glycine, serine, threonine, phenylalanine, O-methylserine, O-methylaspartic acid, O-methylglutamic acid, N-methyllysine, O-methyltyrosine, O-methylhistidine, and O-methylthreonine. In some embodiments, each amino acid in W is independently selected from the group consisting of alanine, glycine, lysine, serine, aspartic acid, aspartate methyl ester, N,N-dimethyl-lysine, phenylalanine, citrulline, valine-alanine, valine-citrulline, phenylalanine-lysine or homoserine methyl ether.

[0530] In some embodiments, W has the structure:



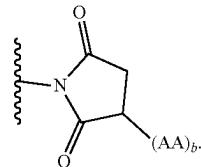
[0531] In some embodiments, W¹ is $-\text{O}-\text{C}(=\text{O})-$. In some embodiments, one R^g is halogen, —CN, or $-\text{NO}_2$, and the remaining R^g are hydrogen. In some embodiments, each R^g is hydrogen.

[0532] In some embodiments, w is 0. In some embodiments, w is 1.

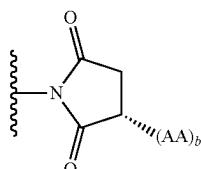
[0533] In some embodiments, L^{BB} is $-(\text{CH}_2)_{1-3}-$. In some embodiments, L^{RR} is $-\text{C}(\text{O})(\text{CH}_2)_{1-2}-$.

[0534] In some embodiments, L^{BB} is $-\text{C}(\text{O})(\text{CH}_2)_2-$. In some embodiments, L^{BB} is $-[\text{NHC}(\text{O})(\text{CH}_2)_2]_1-2-$. In some embodiments, L^{BB} is $-[\text{NHC}(\text{O})(\text{CH}_2)_2]_2-$.

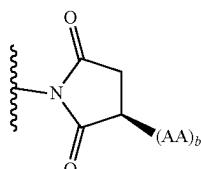
[0535] In some embodiments, M is



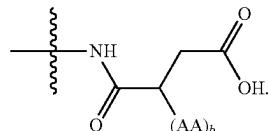
In some aspects, M is



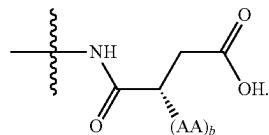
In some aspects, M is



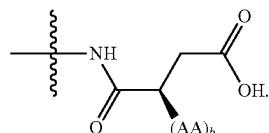
[0536] In some embodiments, M is



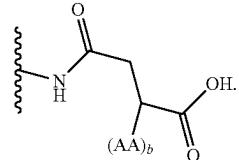
In some aspects, M is



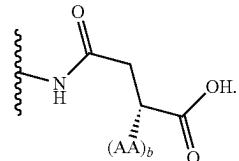
In some aspects, M is



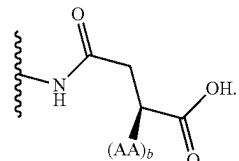
[0537] In some embodiments, M is



In some aspects, M is

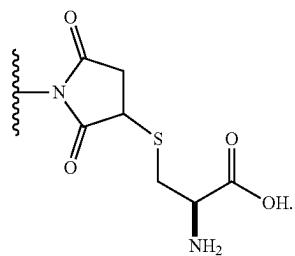


In some aspects, M is

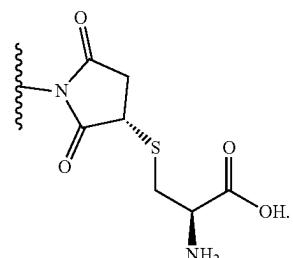


[0538] In some embodiments, each AA is independently a natural amino acid; wherein (AA)_b is connected to the succinimide or hydrolyzed succinimide via a sulfur atom. In some embodiments, each AA is independently a natural amino acid; wherein (AA)_b is connected to the succinimide or hydrolyzed succinimide via a nitrogen atom. In some embodiments, each subscript b is 1. In some embodiments, each subscript b is 2. In some embodiments, each subscript b is 3, 4, 5, or 6.

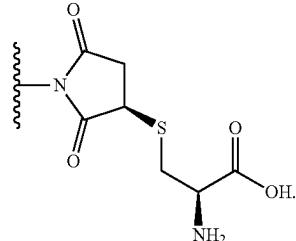
[0539] In some embodiments, M is



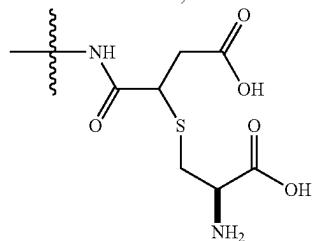
In some aspects, M is



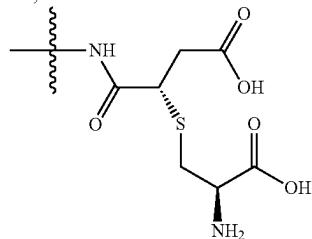
In some aspects, M is



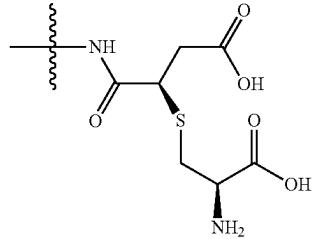
[0540] In some embodiments, M is



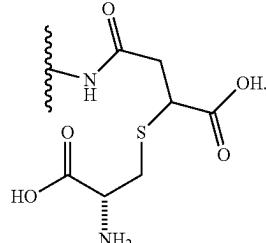
In some aspects, M is



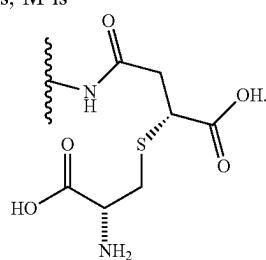
In some aspects, M is



[0541] In some embodiments, M is

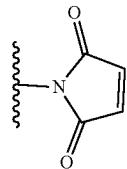
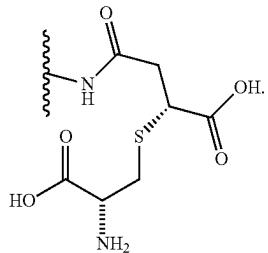


In some aspects, M is

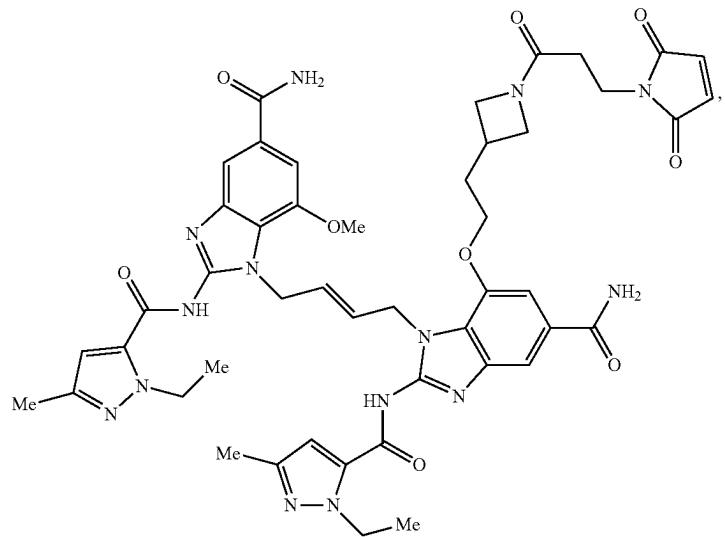
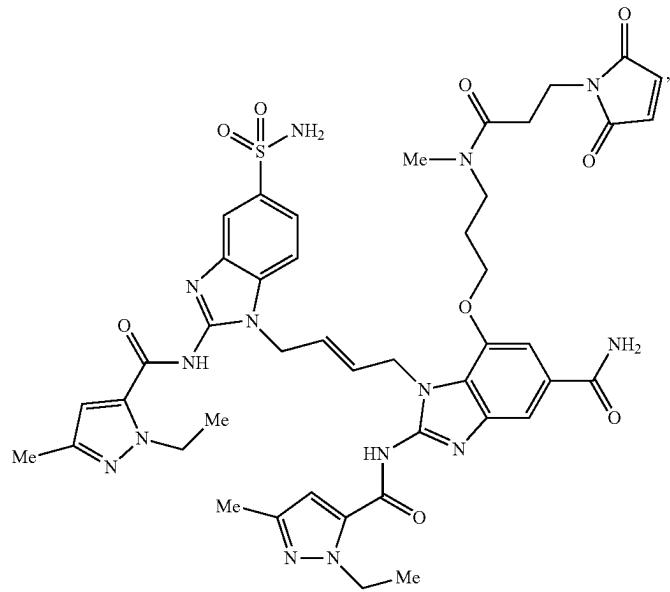


In some aspects, M is

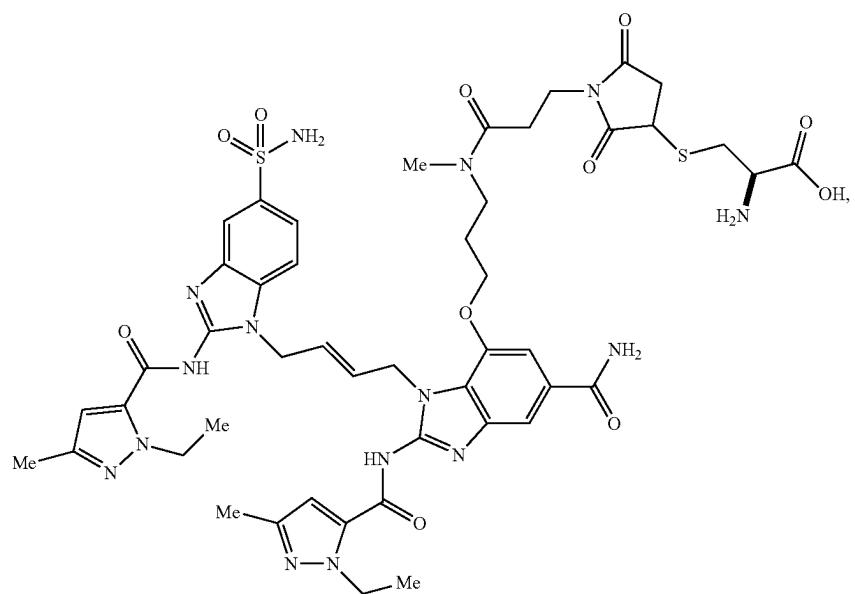
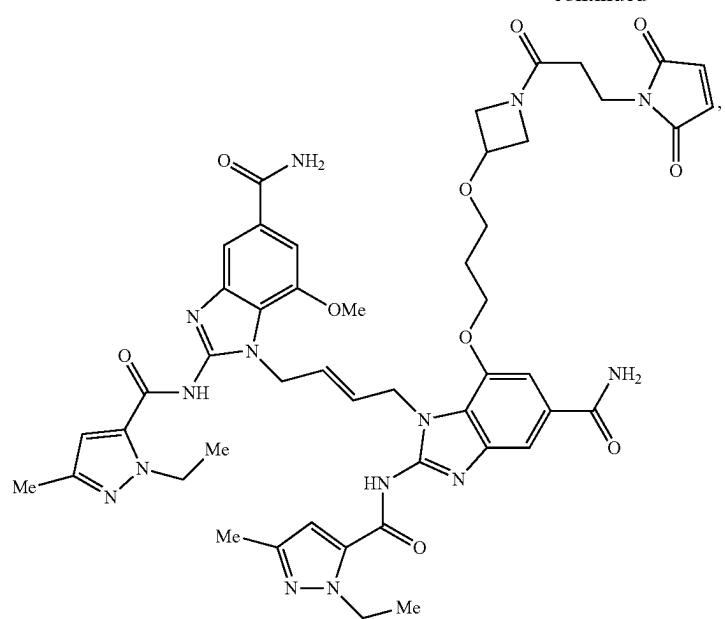
[0542] In some embodiments, M is



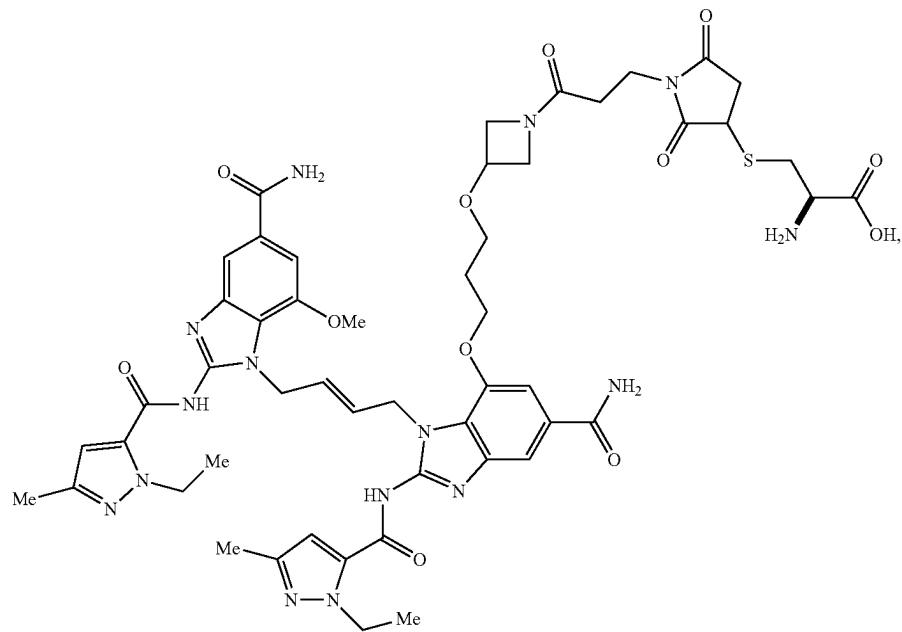
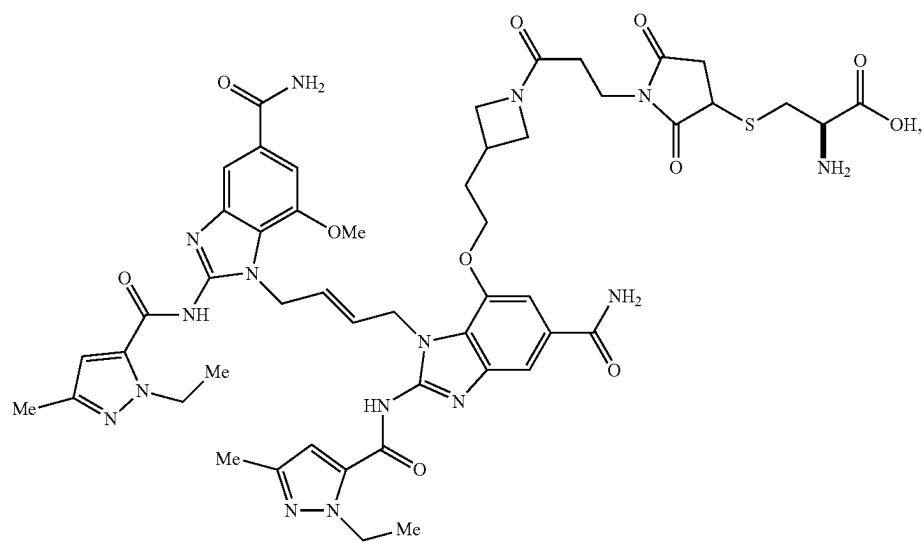
[0543] Some embodiments of the compound of Formula (IV) include a compound selected from the group consisting of:



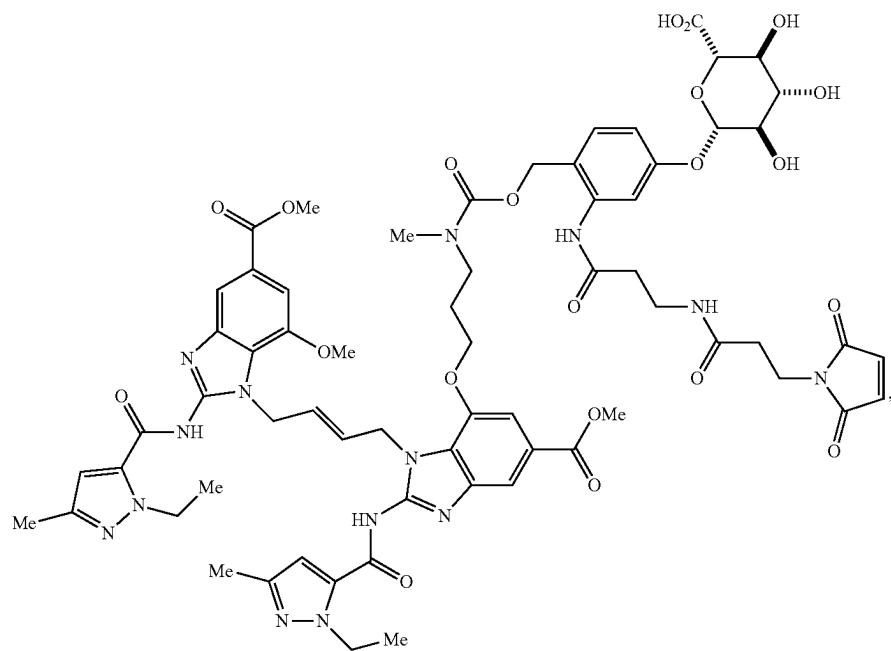
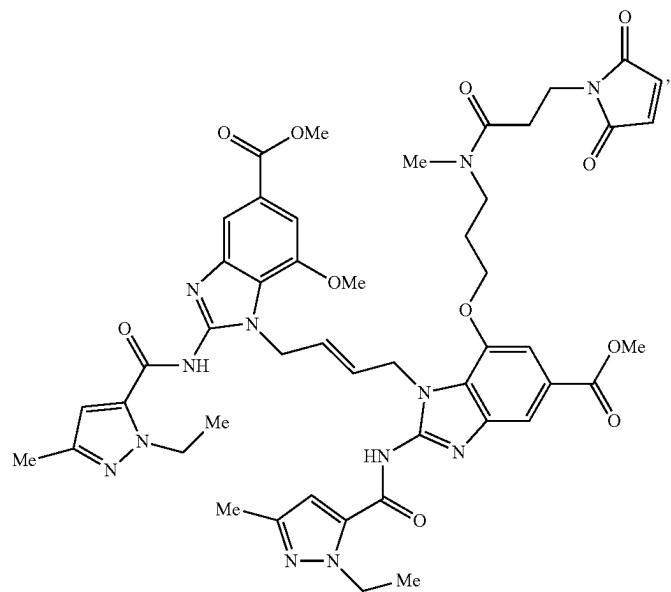
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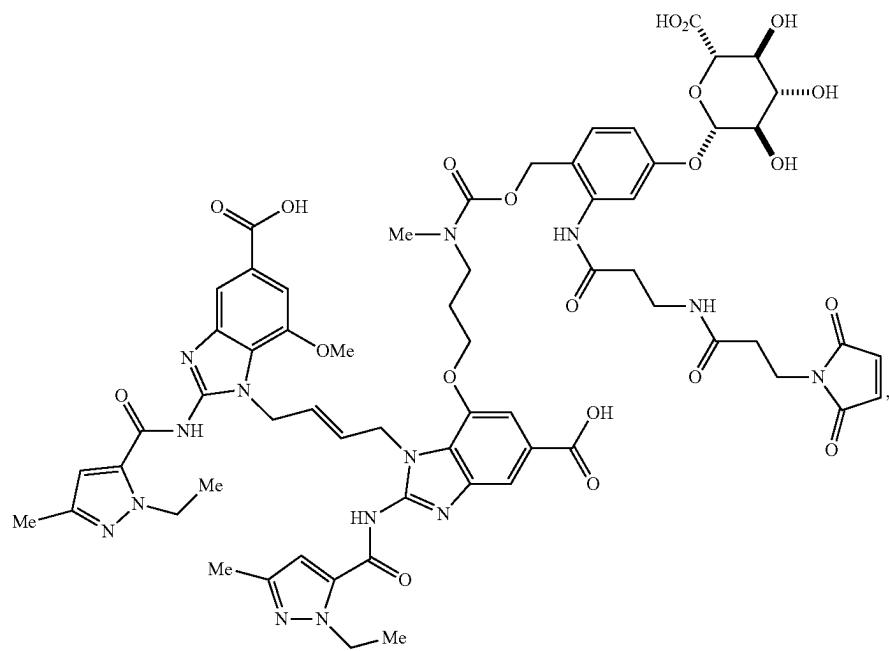
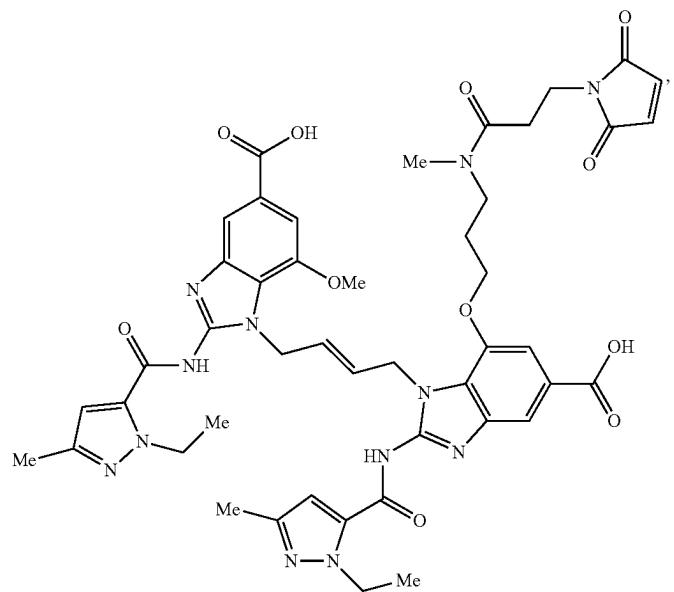
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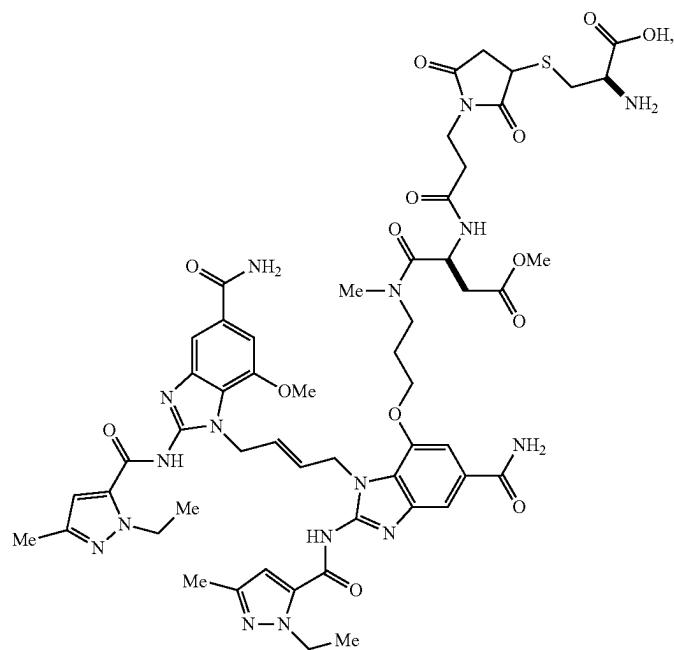
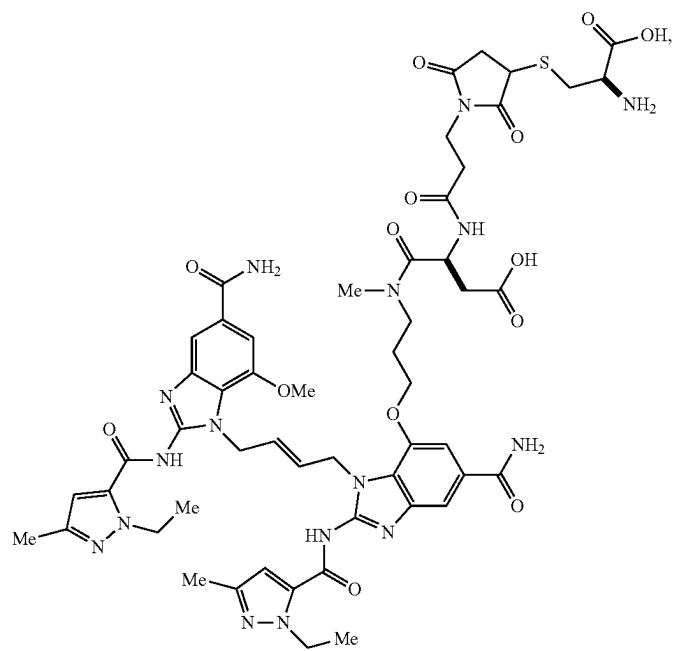
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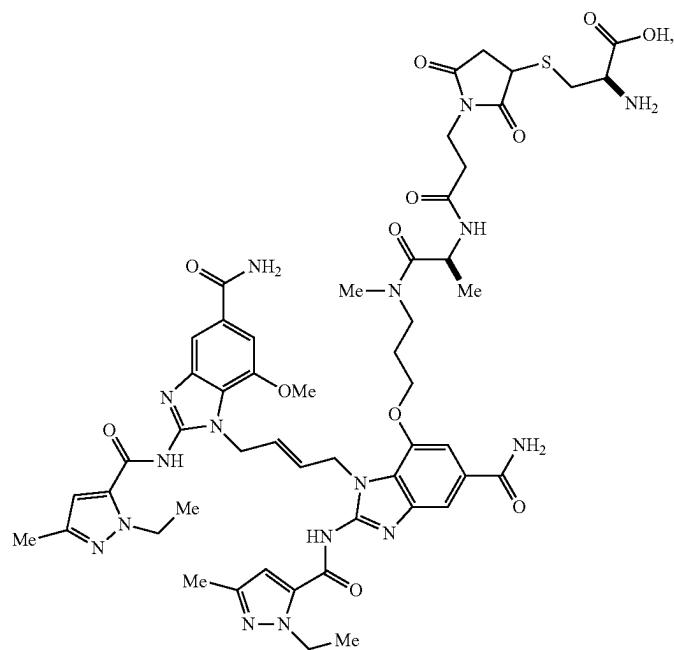
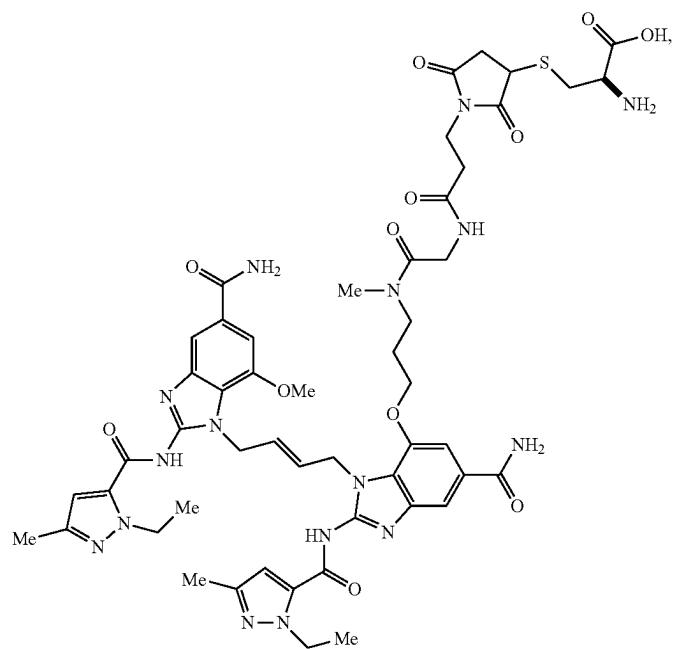
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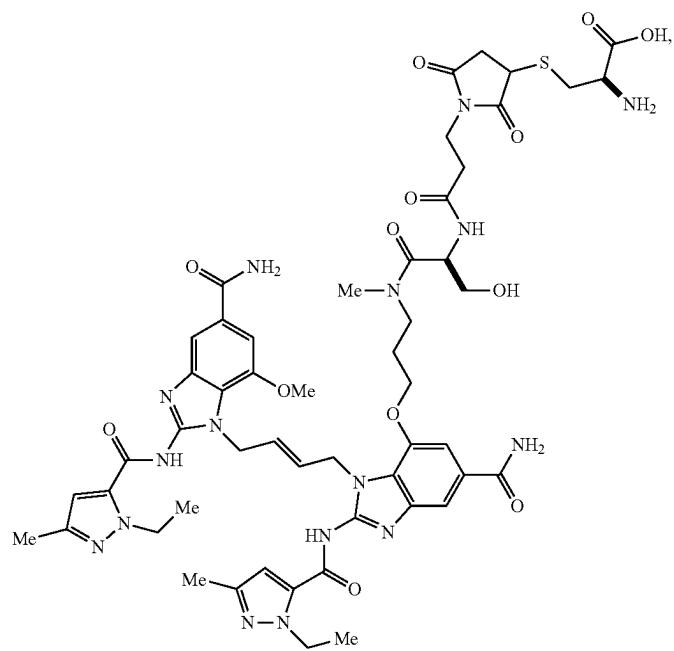
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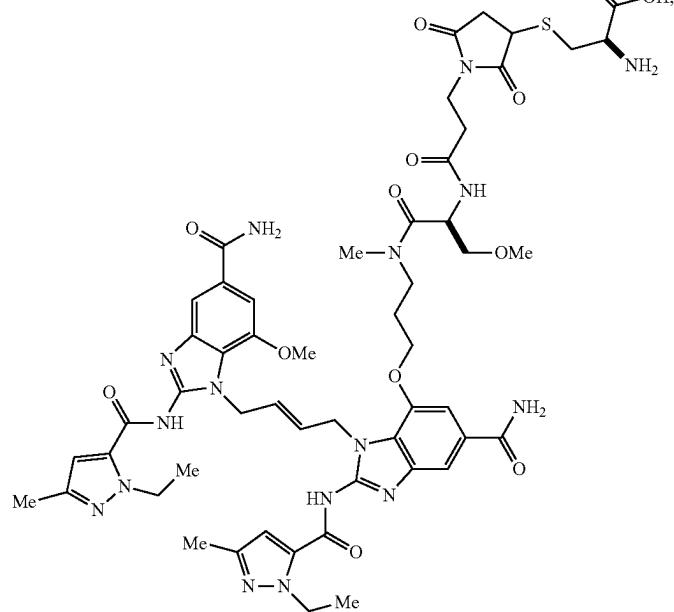
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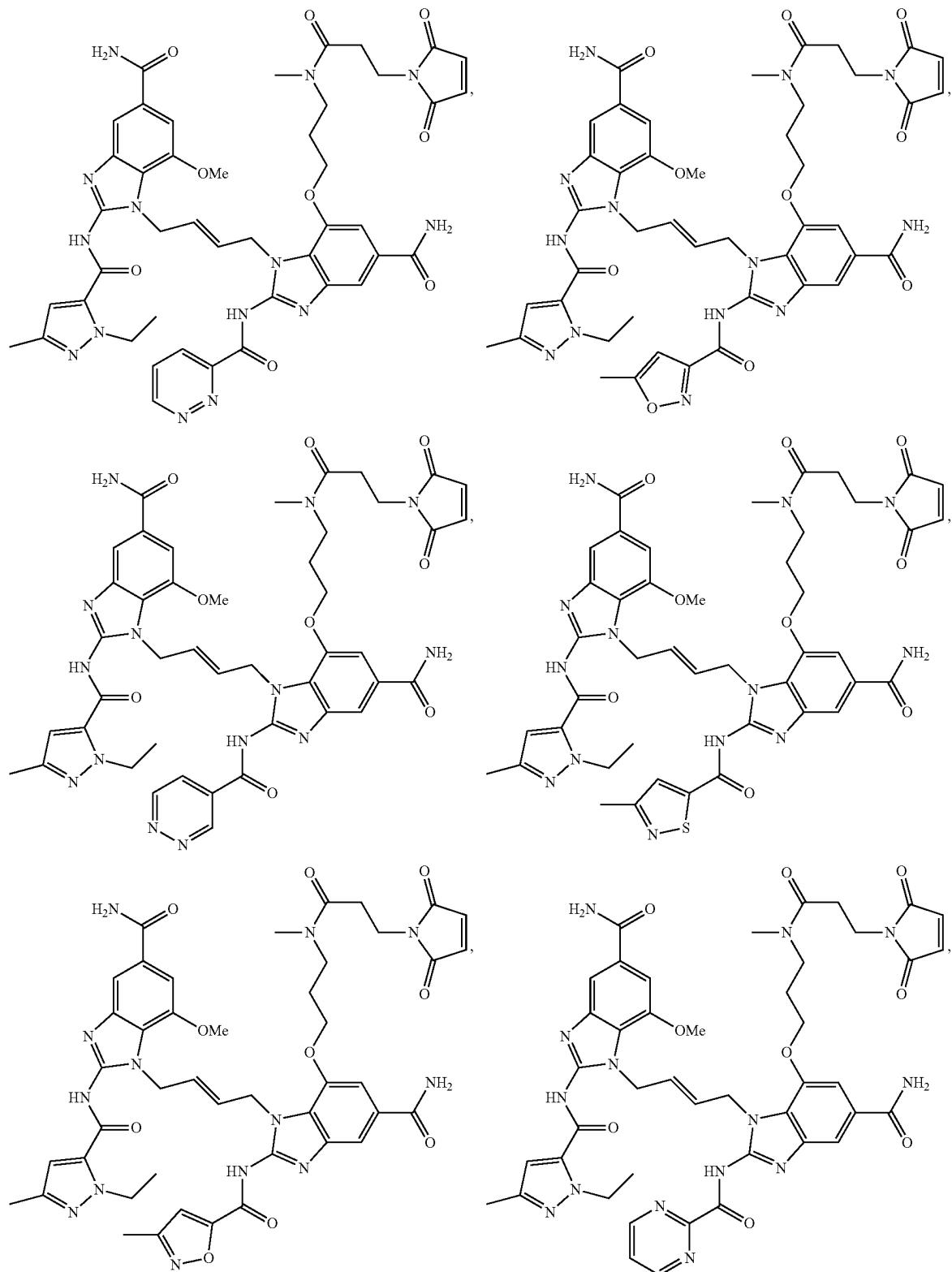
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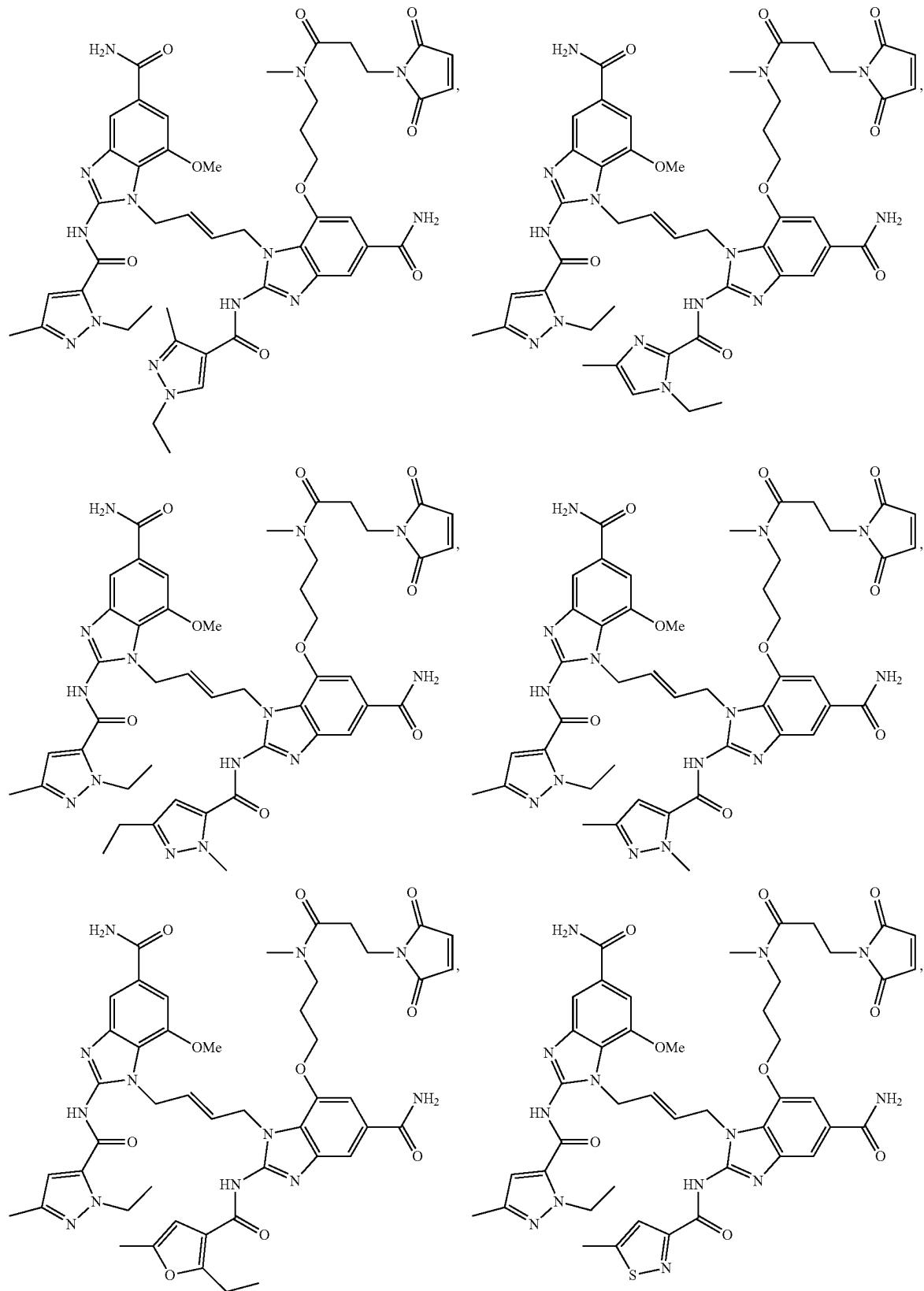
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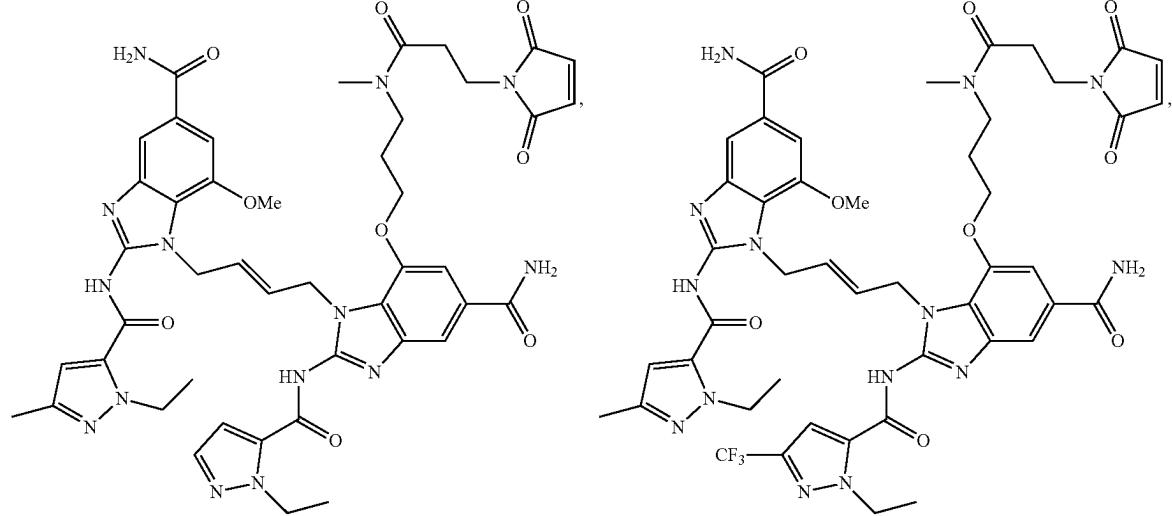
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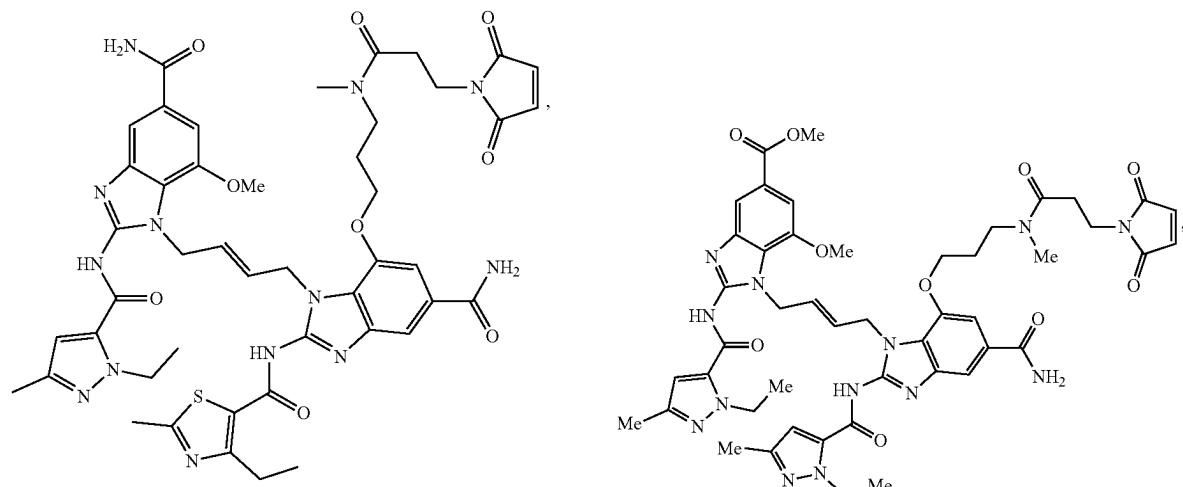
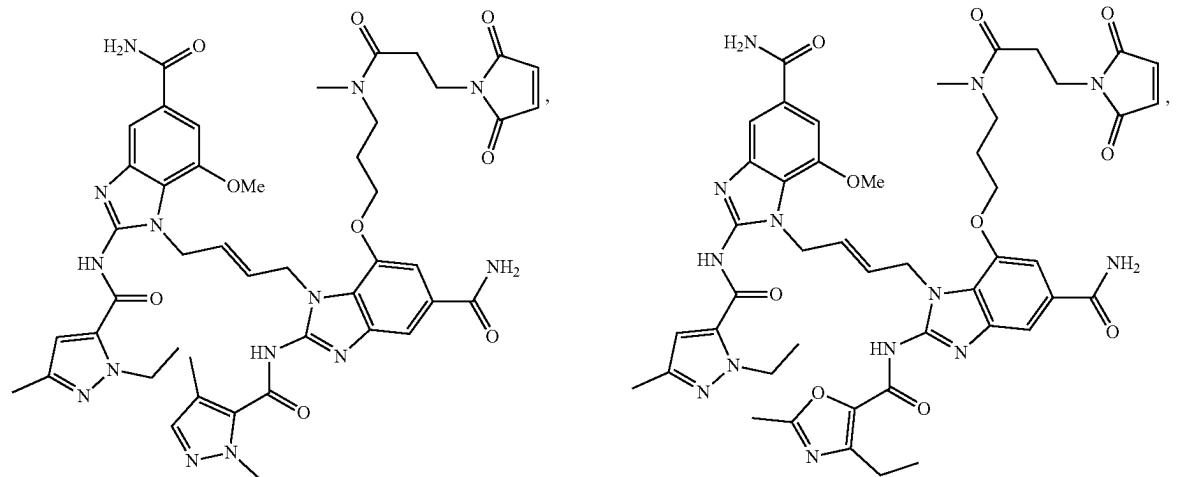
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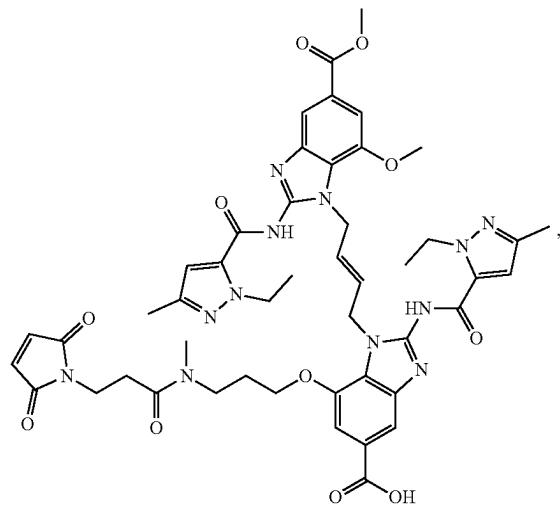
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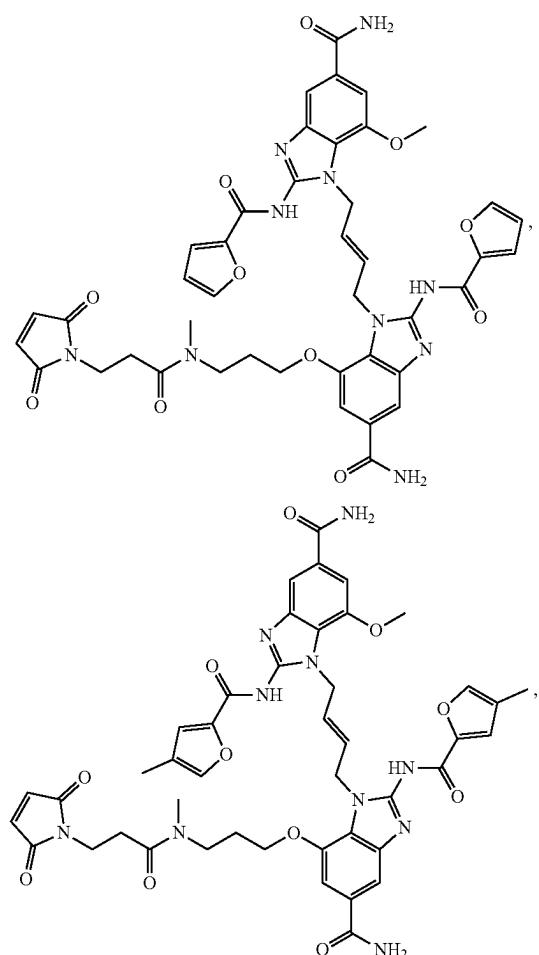
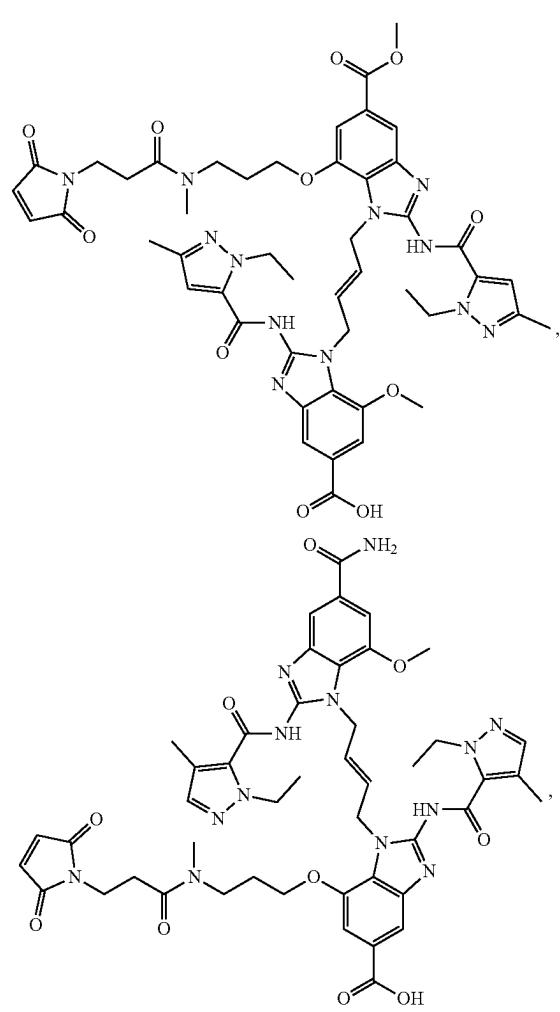
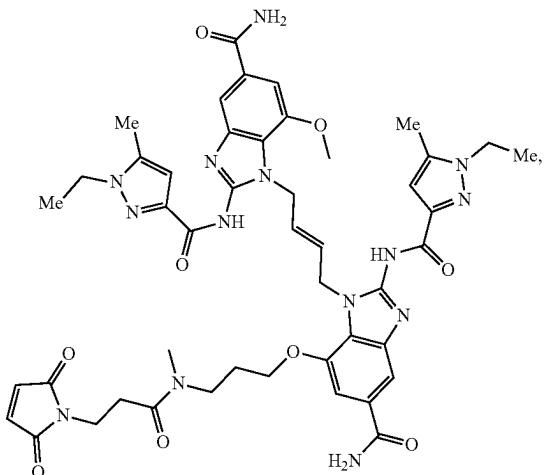
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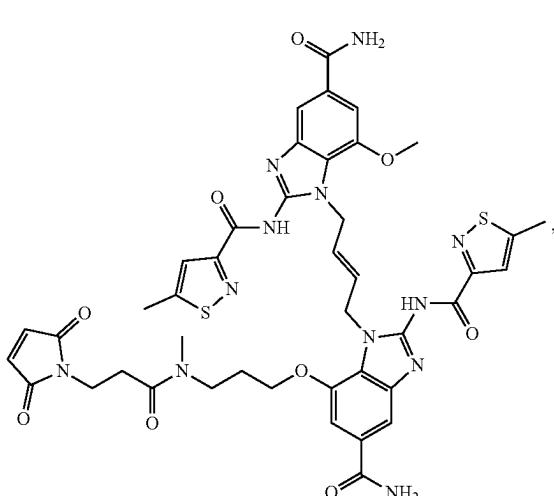
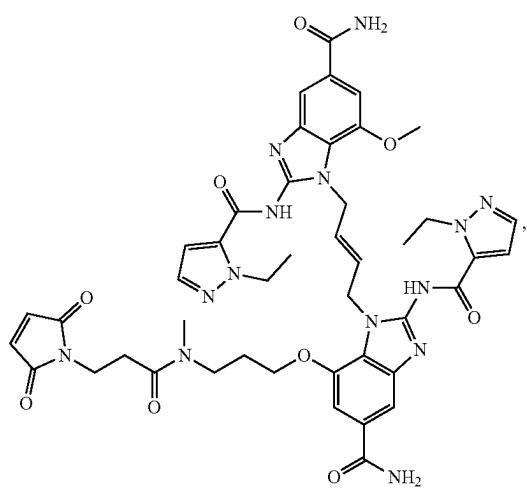
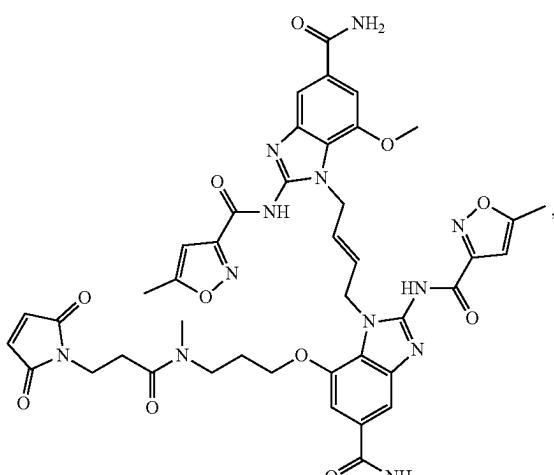
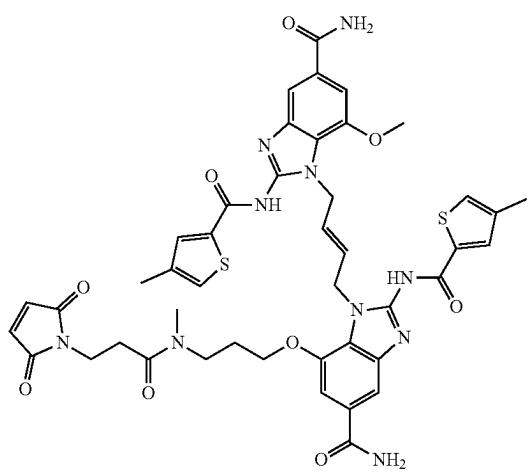
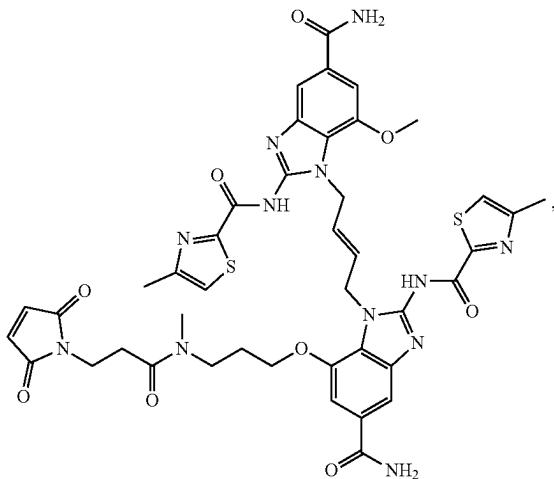
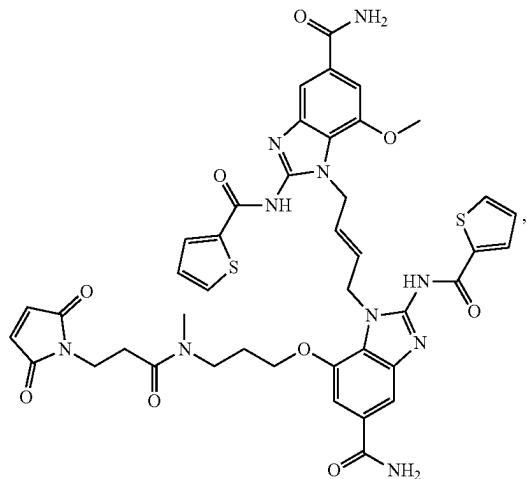


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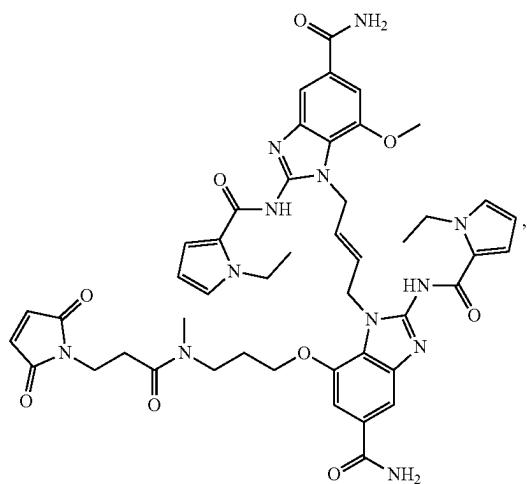


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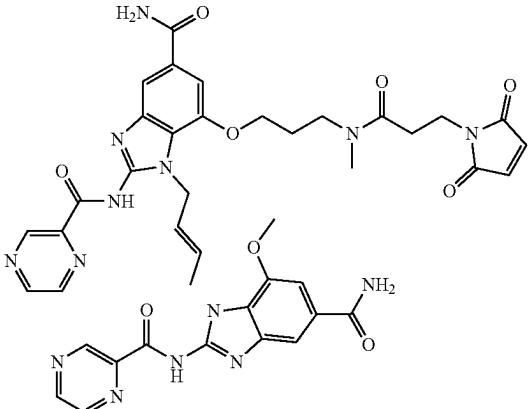
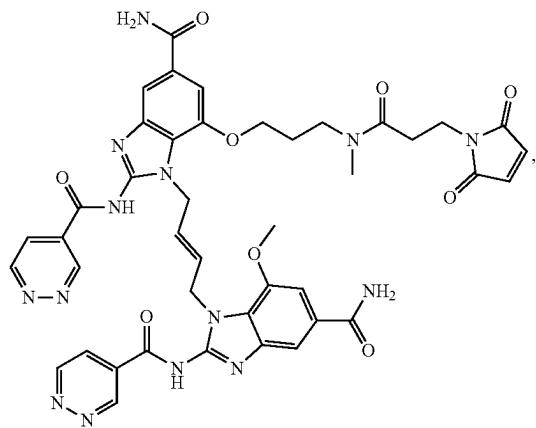
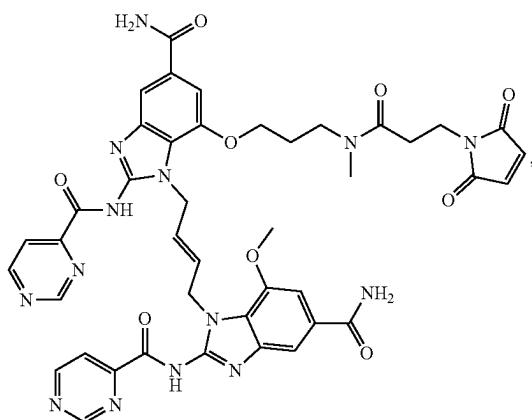
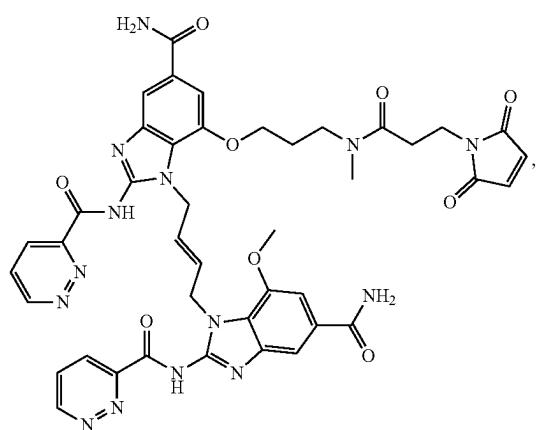
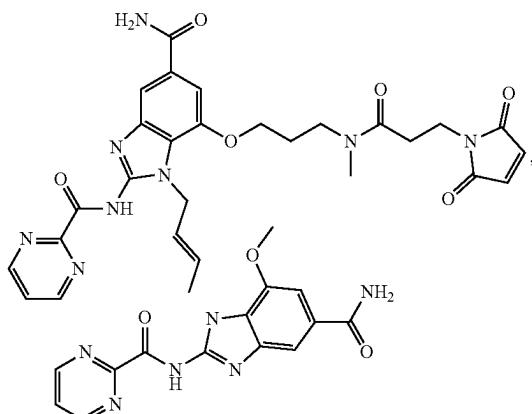
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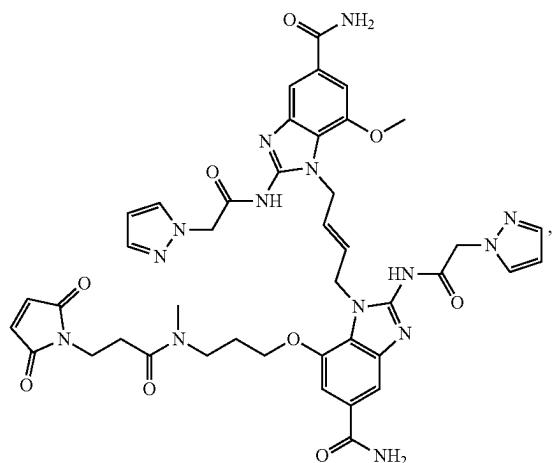
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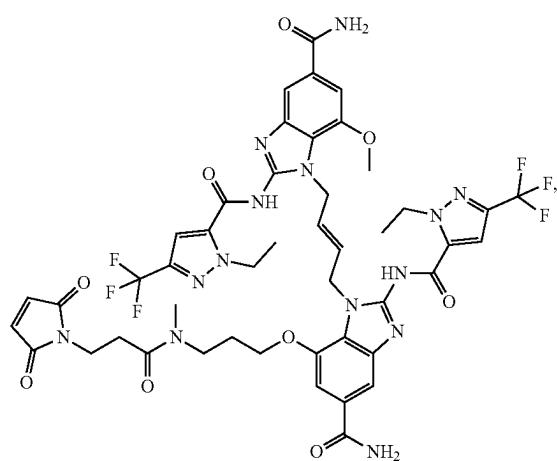
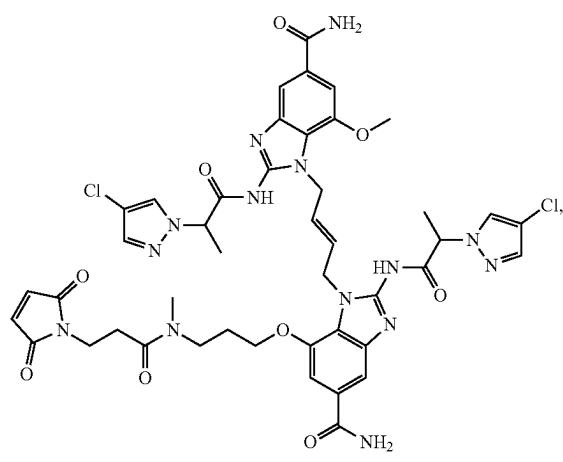
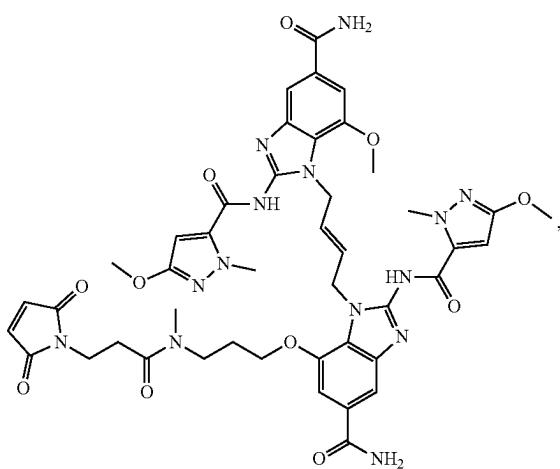
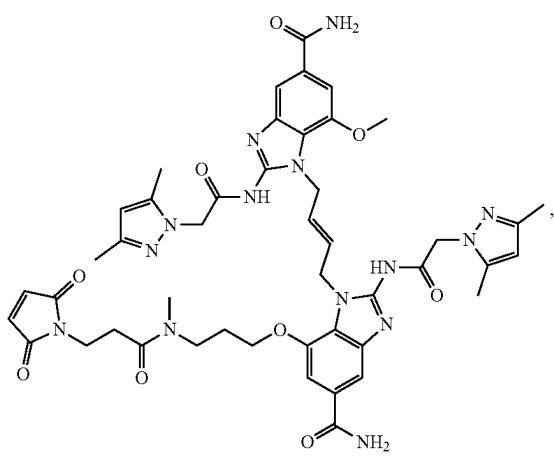
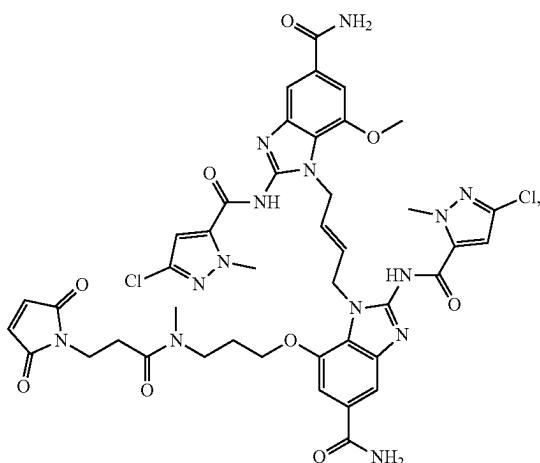
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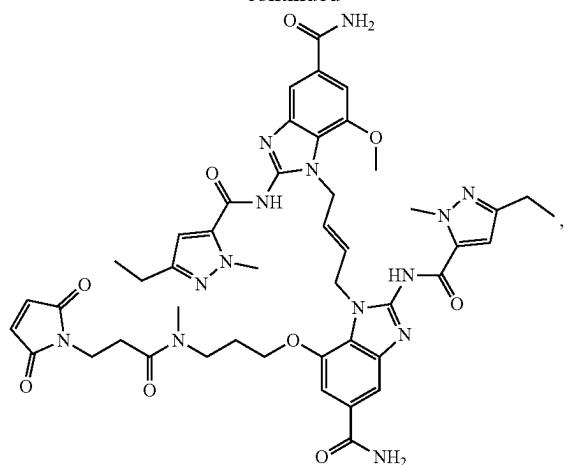
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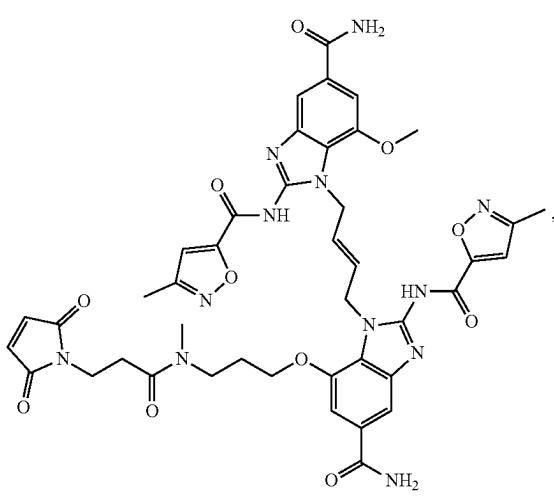
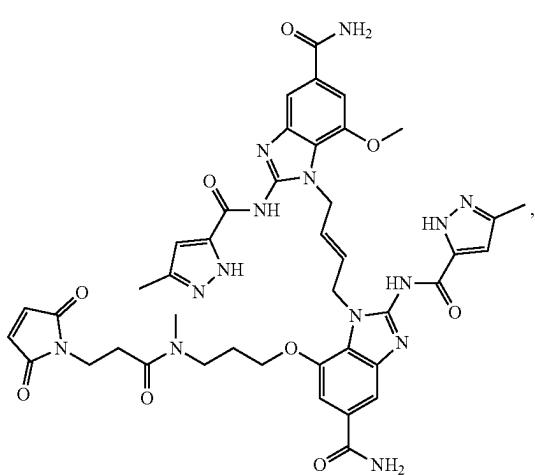
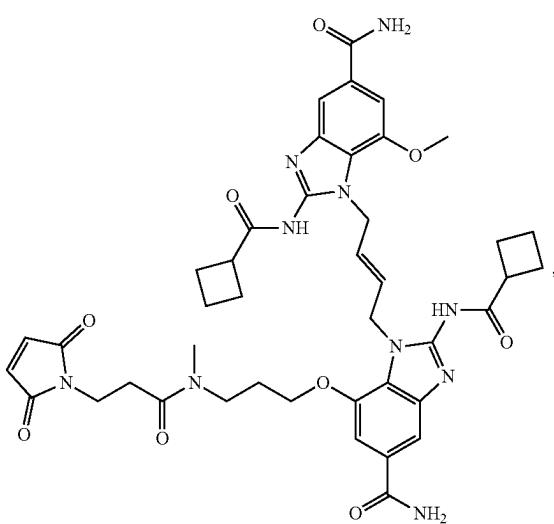
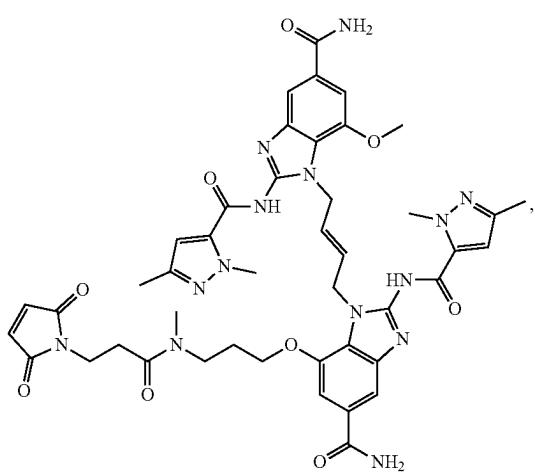
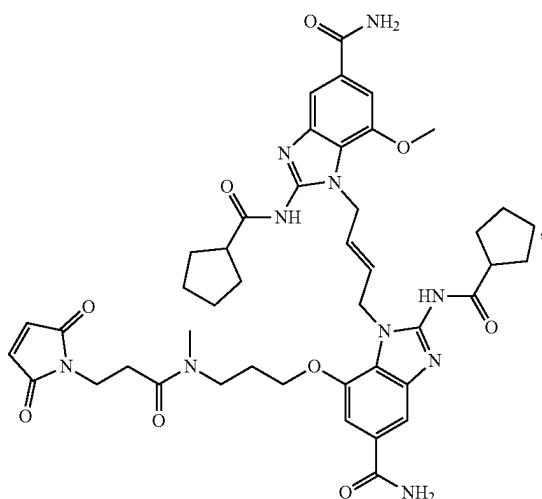
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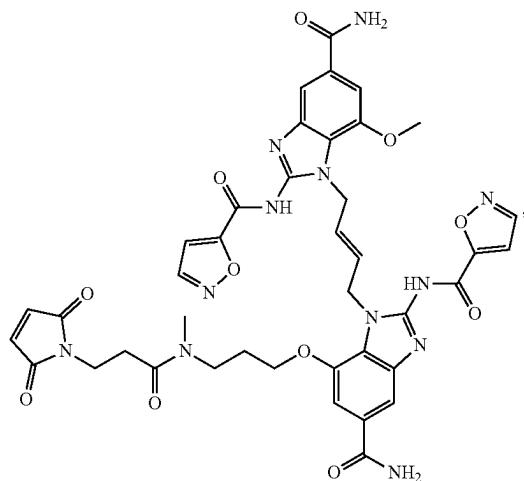
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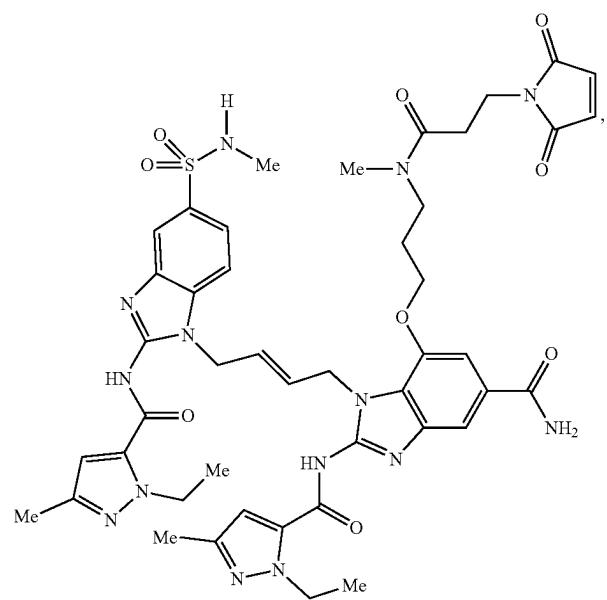
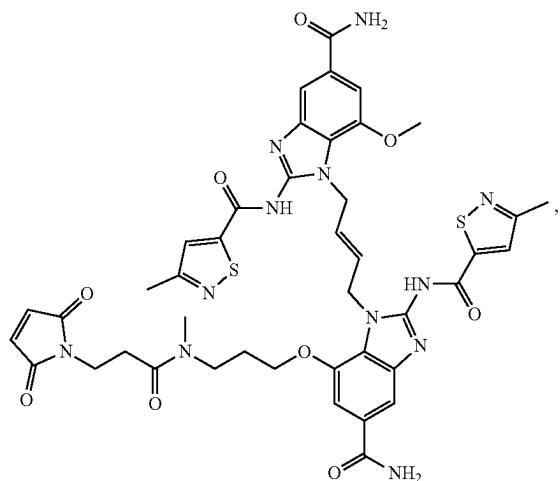
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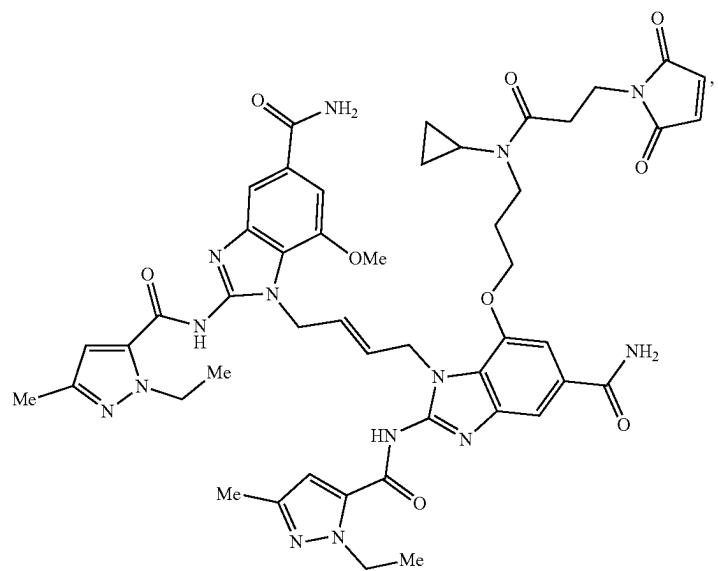
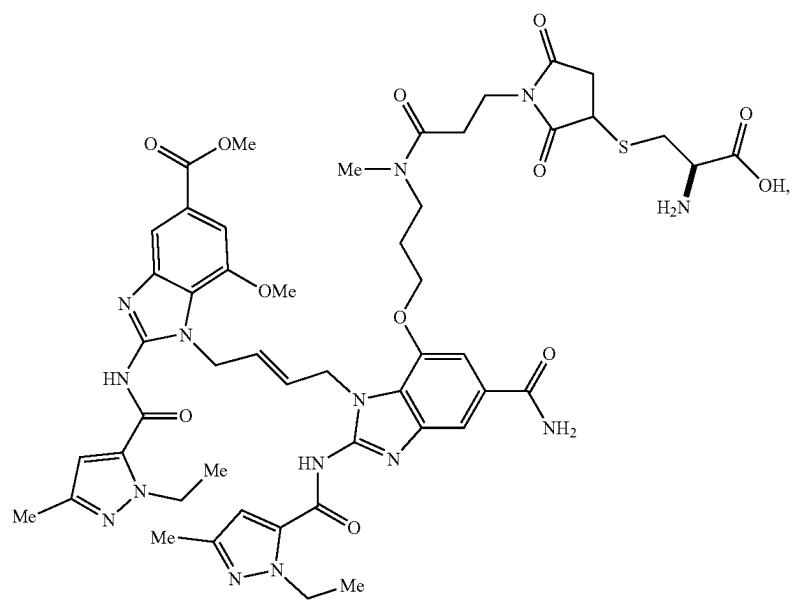
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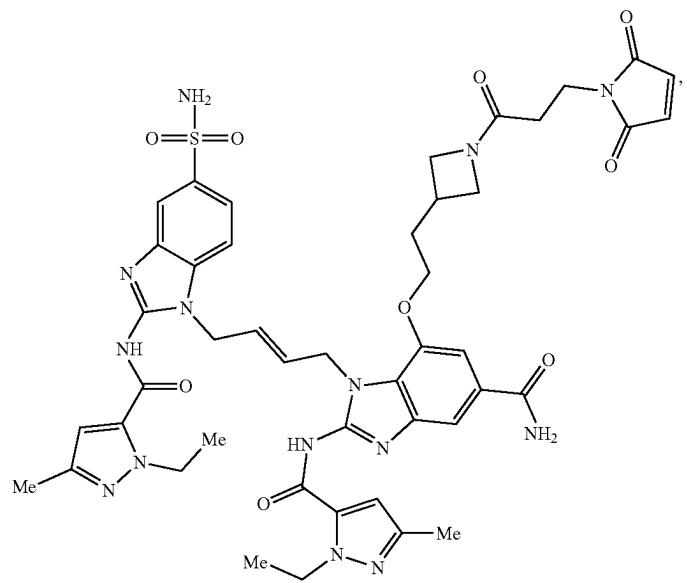
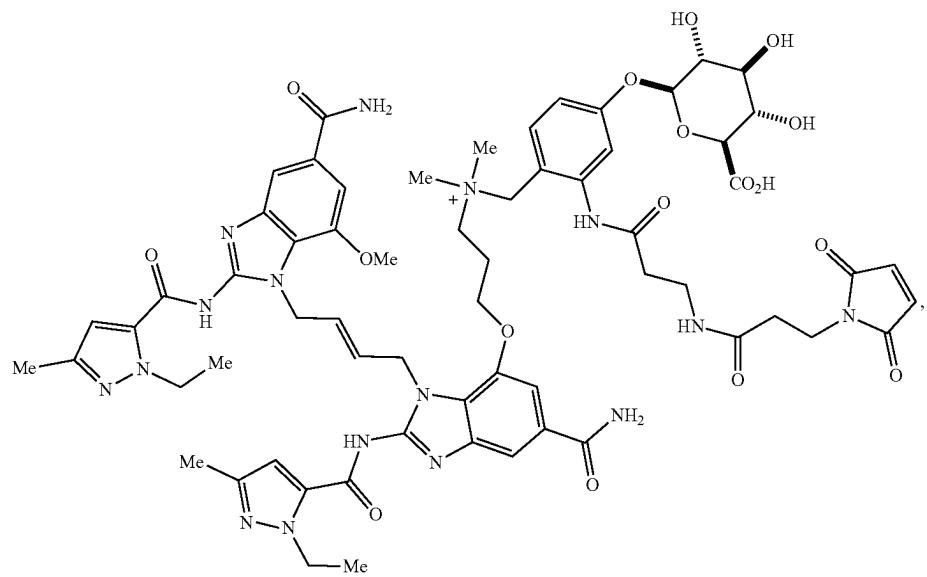
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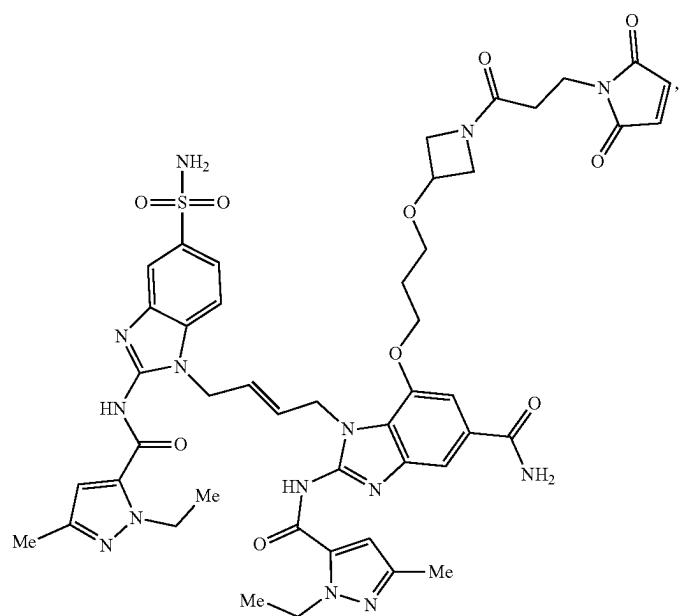
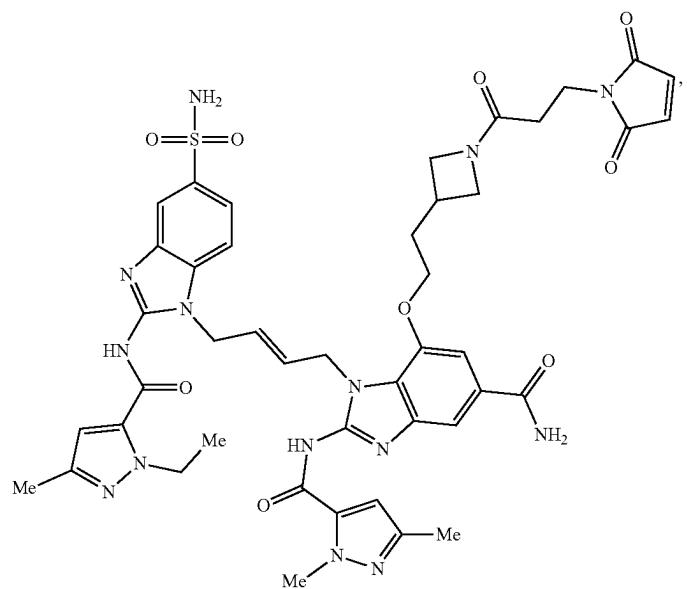
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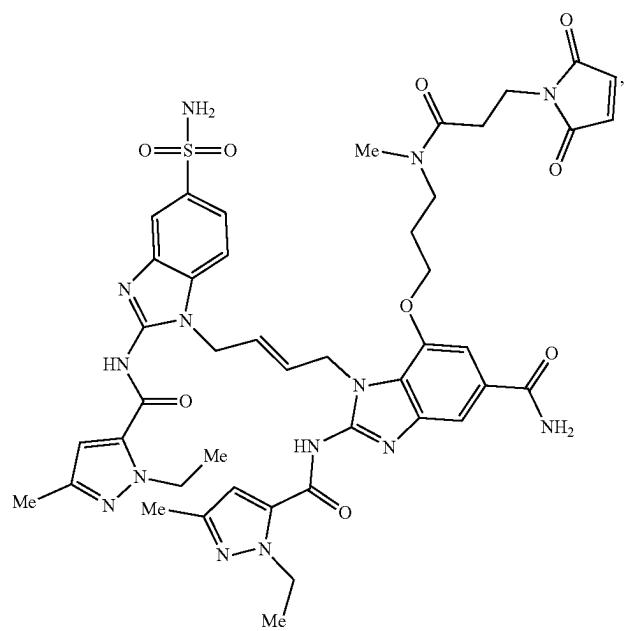
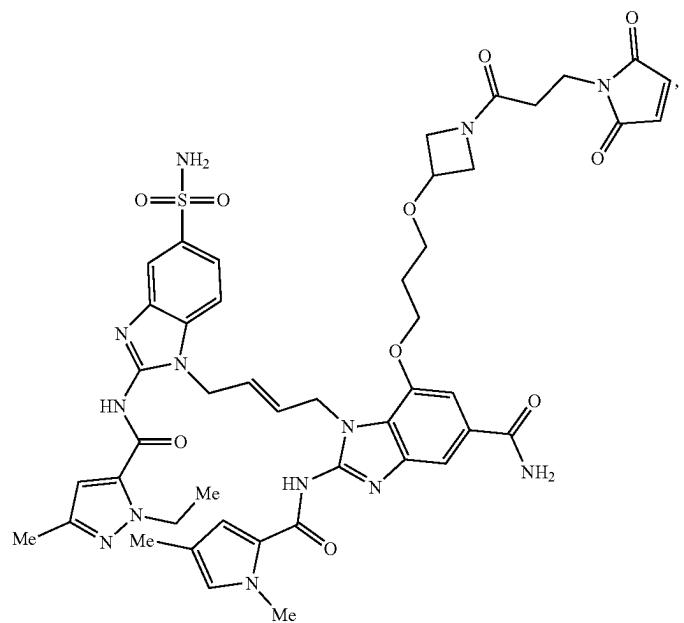
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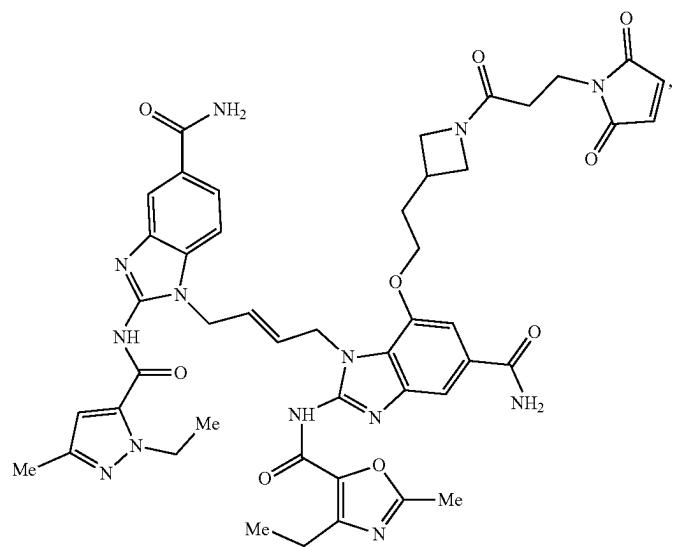
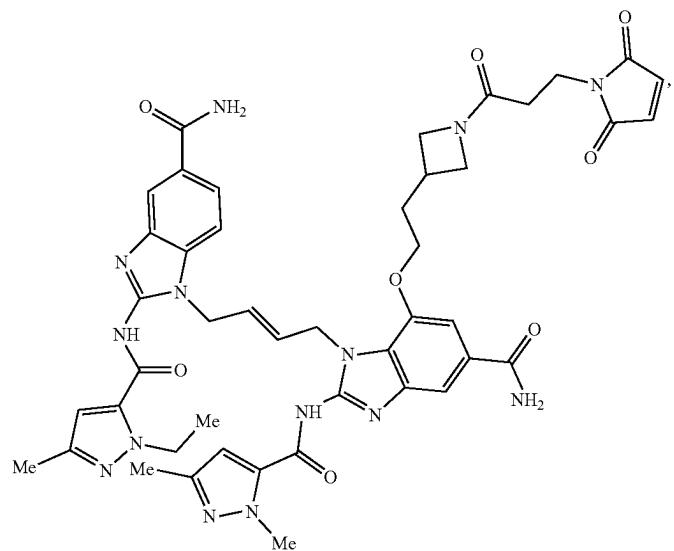
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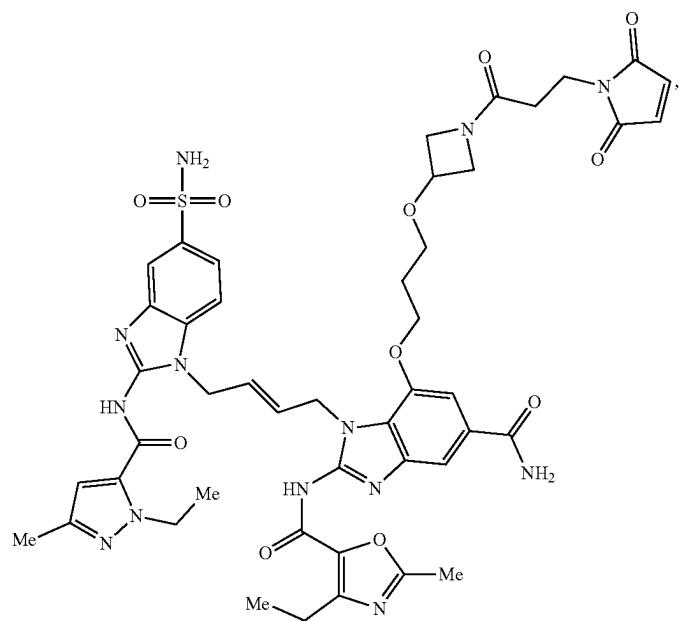
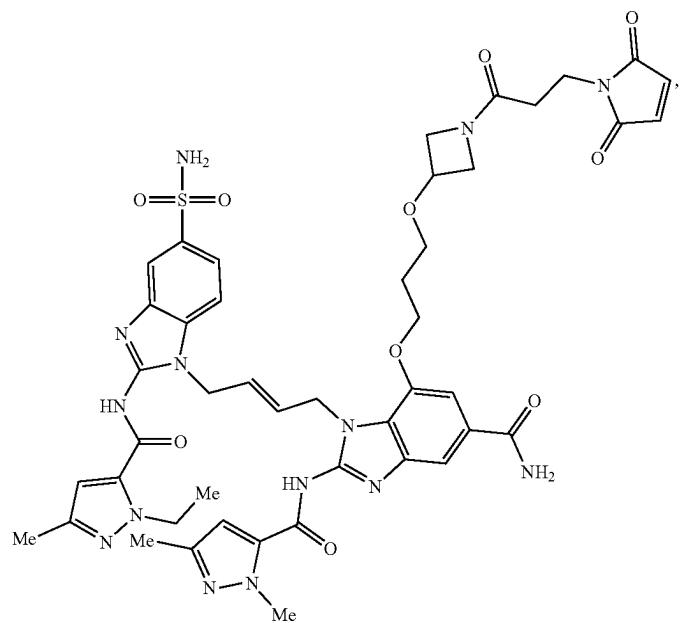
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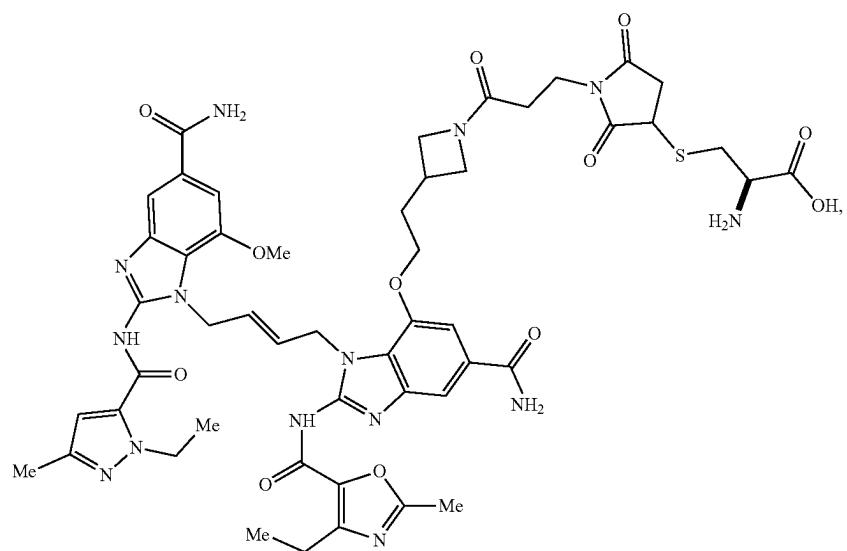
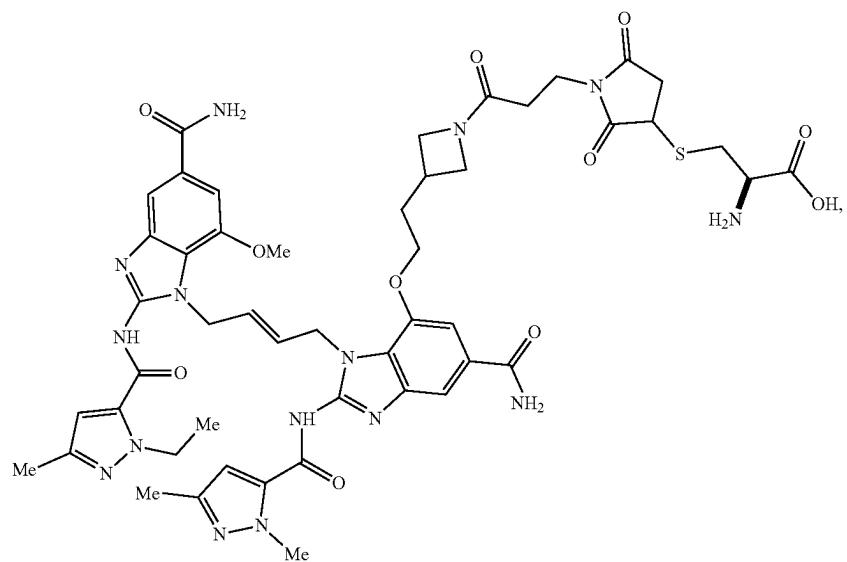
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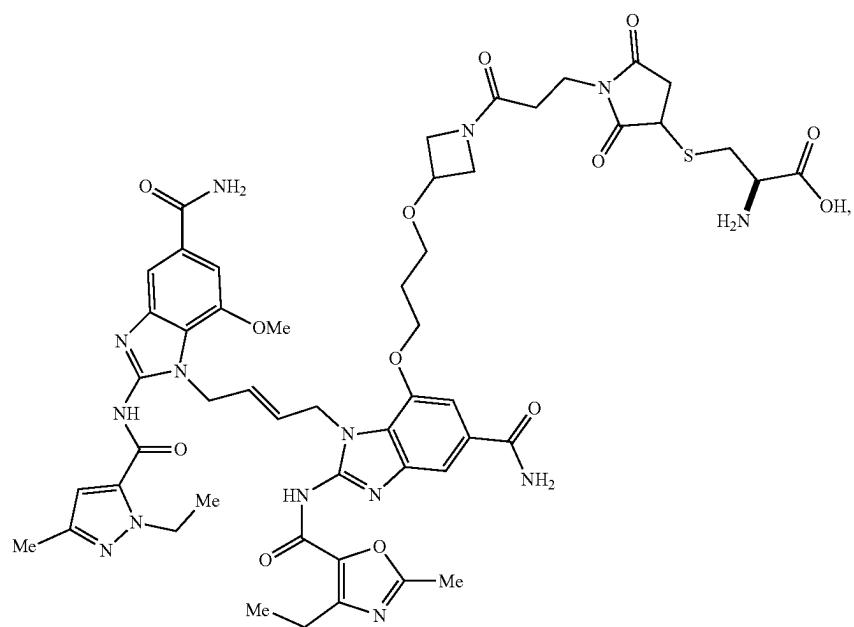
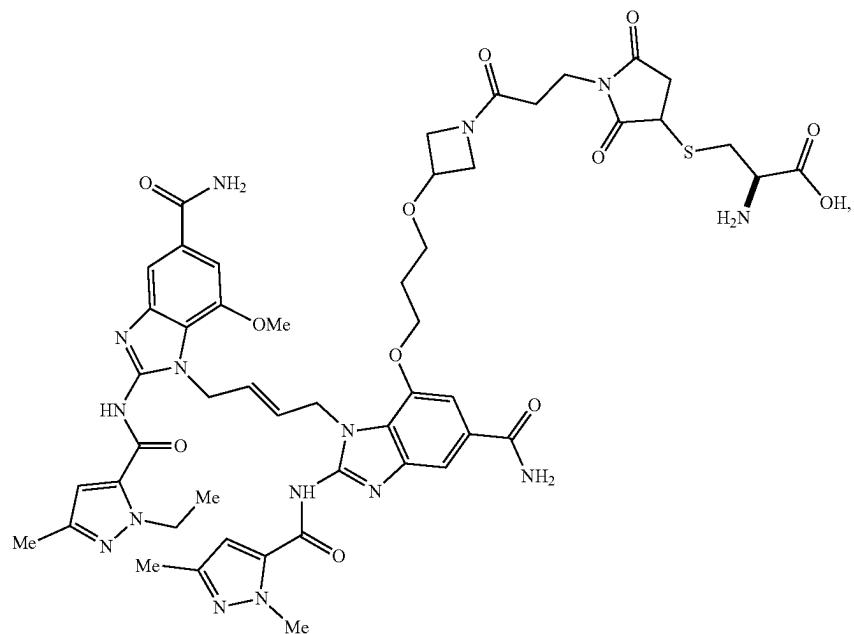
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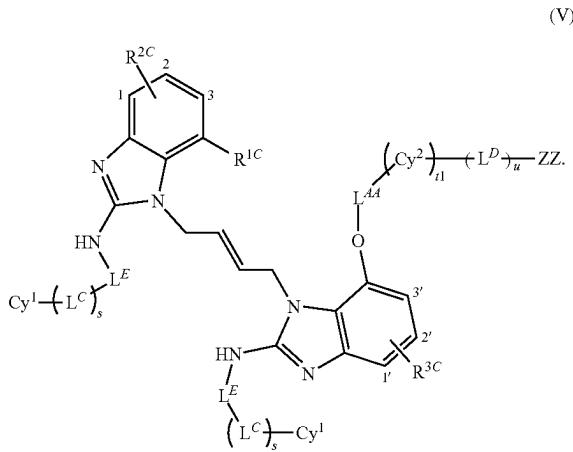
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and pharmaceutically acceptable salts thereof.

Compounds of Formula (V)

[0544] Some embodiments include a compound of Formula (V):



or a pharmaceutically acceptable salt thereof, wherein:

[0545] R^{1C} is hydrogen, hydroxyl, C₁₋₆ alkoxy, —(C₁₋₆ alkyl) C₁₋₆ alkoxy, —(CH₂)_nNR^AR^B, or PEG2 to PEG4;

[0546] R^{2C} is —CO₂R^M, —(C=O)NR^CR^D, —S(O)₂NR^CR^D, —S(O)₂R^M, —(CH₂)_qNR^ER^F, —(CH₂)_qOR^M, —O(C=O)—NR^ER^F, or —NR^M(C=O)—NR^ER^F, wherein R^{2C} is attached at any one of positions labeled 1, 2, or 3;

[0547] R^{3C} is —CO₂R^M, —(C=O)NR^CR^D, —S(O)₂NR^CR^D, —S(O)₂R^M, —(CH₂)_qNR^ER^F, —(CH₂)_qOR^M, —O(C=O)—NR^ER^F, or —NR^M(C=O)—NR^ER^F, wherein R^{3C} is attached at any one of positions labeled 1', 2', or 3';

[0548] each R^A, R^B, R^C, R^D, R^E, R^F, and R^M are independently hydrogen or C₁₋₆ alkyl;

[0549] each subscript n is independently an integer from 0 to 6;

[0550] each subscript q is independently an integer from 0 to 6;

[0551] L^E is —(C=O)— or —S(O)₂—;

[0552] L^C is —(CR^IR^J)₁₋₃—

[0553] each R^I and R^J are independently hydrogen or C₁₋₃ alkyl;

[0554] subscript s is 0 or 1;

[0555] each Cy¹ is independently a 4-6 membered heterocycle, a 5-6 membered heteroaryl, or a C₃₋₆ cycloalkyl, each optionally substituted with one or more R^K;

[0556] each R^K is independently selected from the group consisting of: C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, halogen, —OH, —O, —NR^DR^E, —C(O)NR^DR^E, —C(O)(C₁₋₆ alkyl), and —C(O)O(C₁₋₆ alkyl);

[0557] each R^{d2} and R^{e2} are independently hydrogen or C₁₋₃ alkyl;

[0558] L^{A4} is —(CH₂)₁₋₆—, —C(O)(CH₂)₁₋₆—, —C(O)NR^L(CH₂)₁₋₆—, —(CH₂)₁₋₆O—, —C(O)(CH₂)₁₋₆O—, or —C(O)NR^L(CH₂)₁₋₆O—;

[0559] R^L is hydrogen or C₁₋₃ alkyl;

[0560] Cy² is C₃₋₆ cycloalkyl, 4-6 membered heterocycle, 5-6 membered heteroaryl, or phenyl, each optionally substituted with one or more R^U;

[0561] each R^U is independently selected from the group consisting of —CO₂R^I, —(C=O)NR^{D3}R^{E3}, —S(O)₂NR^{D3}R^{E3}, —(CH₂)_{q1}NR^{g1}R^{H1}, —(CH₂)_{q1}OR^I, and —(CH₂)_{q1}—(OCH₂)₁₋₈OH;

[0562] each R^{D3}, R^{E3}, R^{g1}, R^{H1}, and R^I are independently hydrogen or C₁₋₆ alkyl;

[0563] subscript q1 is an integer from 0 to 6;

[0564] subscript t1 is 0 or 1;

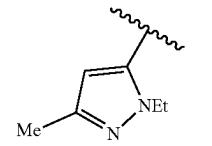
[0565] L^D is —(CH₂)₁₋₆—;

[0566] subscript u is 0 or 1;

[0567] when t1 is 0, ZZ is —NR^QR^R, —N<sup>+(C₁₋₆ alkyl)R^QR^R, —C(=O)N^SR^T, —C(O)O(C₁₋₆ alkyl), —CO₂H, or an amino acid, or when t1 is 1, ZZ is hydrogen, —NR^QR^R, —N<sup>+(C₁₋₆ alkyl)R^QR^R, —C(=O)N^SR^T, —C(O)O(C₁₋₆ alkyl), —CO₂H, or an amino acid;

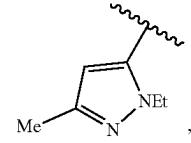
[0568] R^Q is hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, —(CH₂)₁₋₃C₃₋₆ alkoxy, —(CH₂)₁₋₃ 4-6 membered heterocycle, or —(CH₂)₁₋₃ 5-6 membered heteroaryl, provided that

[0569] if t1 is 0 and both Cy¹ are



then R^Q is C₂₋₆ alkyl, C₃₋₆ cycloalkyl, —(CH₂)₁₋₃C₃₋₆ cycloalkyl, —(CH₂)₁₋₃C₁₋₃ alkoxy, —(CH₂)₁₋₃ 4-6 membered heterocycle, or —(CH₂)₁₋₃ 5-6 membered heteroaryl, and

[0570] if t1 is 0 and at least one Cy¹ is not



then ZZ is —NR^QR^R, —N<sup>+(C₁₋₆ alkyl)R^QR^R, or —C(=O)N^SR^T, and R^Q is C₁₋₆ alkyl, C₃₋₆ cycloalkyl, —(CH₂)₁₋₃C₃₋₆ cycloalkyl, —(CH₂)₁₋₃C₁₋₃ alkoxy, —(CH₂)₁₋₃ 4-6 membered heterocycle, or —(CH₂)₁₋₃ 5-6 membered heteroaryl; and

[0571] each R^R, R^S, and R^T are independently hydrogen or C₁₋₆ alkyl.

[0572] In some embodiments, R^{1C} is hydrogen. In some embodiments, R^{1C} is hydroxyl. In some embodiments, R^{1C} is C₁₋₆ alkoxy. In some embodiments, R^{1C} is methoxy. In some embodiments, R^{1C} is —(C₁₋₆ alkyl)C₁₋₆ alkoxy. In some embodiments, R^{1C} is methoxyethyl. In some embodiments, R^{1C} is PEG2 to PEG4. In some embodiments, R^{1C} is —(CH₂)_nNR^AR^B. In some embodiments, R^A and R^B are both hydrogen. In some embodiments, R^A and R^B are independently C₁₋₃ alkyl. In some embodiments, one of R^A and R^B is hydrogen and the other of R^A and R^B is C₁₋₃ alkyl. In some embodiments, each subscript n is 0. In some embodiments,

ments, each subscript n is 1. In some embodiments, each subscript n is 2. In some embodiments, each subscript n is 3, 4, 5, or 6.

[0573] In some embodiments, R^{2C} and R^{3C} are —CO₂H, —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F; and R^{2C} and R^{3C} are the same. In some embodiments, R^{2C} and R^{3C} are independently —CO₂H, —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F; and R^{2C} and R^{3C} are different.

[0574] In some embodiments, R^{2C} is —(C=O)_m—NR^CR^D. In some embodiments, R^{3C} is —(C=O)_m—NR^CR^D. In some embodiments, R^C and R^D are both hydrogen. In some embodiments, R^C and R^D are each independently C₁₋₃ alkyl. In some embodiments, one of R^C and R^D is hydrogen and the other of R^C and R^D is C₁₋₃ alkyl. In some embodiments, each subscript m is 0. In some embodiments, each subscript m is 1.

[0575] In some embodiments, R^{2C} is —(CH₂)_q—NR^ER^F. In some embodiments, R^{3C} is —(CH₂)_q—NR^ER^F. In some embodiments, R^E and R^F are both hydrogen. In some embodiments, R^E and R^F are each independently C₁₋₃ alkyl. In some embodiments, one of R^E and R^F is hydrogen and the other of R^E and R^F is C₁₋₃ alkyl.

[0576] In some embodiments, each subscript q is 0. In some embodiments, each subscript q is an integer from 1 to 6.

[0577] In some embodiments, R^{2C} is —CO₂R^M. In some embodiments, R^{3C} is —CO₂R^M.

[0578] In some embodiments, R^M is hydrogen. In some embodiments, R^M is C₁₋₃ alkyl.

[0579] In some embodiments, R^{2C} is —(CH₂)_q—OR^M. In some embodiments, R^{3C} is —(CH₂)_q—OR^M.

[0580] In some embodiments, R^M is hydrogen. In some embodiments, subscript q is 0. In some embodiments, subscript q is 1.

[0581] In some embodiments, R^{2C} is —O(C=O)—NR^ER^F. In some embodiments, R^{3C} is —O(C=O)—NR^ER^F. In some embodiments, R^E and R^F are both hydrogen. In some embodiments, R^E and R^F are each independently C₁₋₃ alkyl. In some embodiments, one of R^E and R^F is hydrogen and the other of R^E and R^F is C₁₋₃ alkyl.

[0582] In some embodiments, R^{2C} is —NR^M(C=O)—NR^ER^F. In some embodiments, R^{3C} is —NR^M(C=O)—NR^ER^F. In some embodiments, R^E, R^F, and R^M are all hydrogen. In some embodiments, R^E, R^F, and R^M are each independently C₁₋₃ alkyl. In some embodiments, one of R^E, R^F, and R^M is C₁₋₃ alkyl and the rest of R^E, R^F, and R^M is hydrogen.

[0583] In some embodiments, R^{2C} is —S(O)₂NR^CR^D.

[0584] In some embodiments, R^{3C} is —S(O)₂NR^CR^D. In some embodiments, R^C and R^D are both hydrogen. In some embodiments, R^C and R^D are each independently C₁₋₃ alkyl. In some embodiments, one of R^C and R^D is hydrogen and the other of R^C and R^D is C₁₋₃ alkyl.

[0585] In some embodiments, R^{2C} is —S(O)₂R^M. In some embodiments, R^{3C} is —S(O)₂R^M. In some embodiments, R^M is hydrogen. In some embodiments, R^M is C₁₋₃ alkyl.

[0586] In some embodiments, R^{2C} is attached at position 1. In some embodiments, R^{2C} is attached at position 2. In some embodiments, R^{2C} is attached at position 3. In some embodiments, R^{3C} is attached at position 1'. In some embodiments, R^{3C} is attached at position 2'. In some embodiments, R^{3C} is attached at position 3'.

[0587] In some embodiments, L^E is —(C=O)—. In some embodiments L^E is —S(O)₂—.

[0588] In some embodiments, each R^I and R^J is hydrogen. In some embodiments, each R^I and R^J is C₁₋₃ alkyl. In some embodiments, one of R^I and R^J is hydrogen and the other of R^I and R^J is C₁₋₃ alkyl.

[0589] In some embodiments, L^C is —(CR'^IR'^J)—.

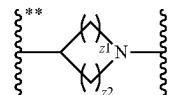
[0590] In some embodiments, subscript s is 0. In some embodiments, subscript s is 1.

[0591] In some embodiments, each Cy¹ is independently a 5-6 membered heteroaryl. In some embodiments, each Cy¹ is pyrazole optionally substituted with one or more R^K. In some embodiments, each Cy¹ is independently selected from the group consisting of pyrazole, imidazole, furan, thiophene, thiazole, isothiazole, oxazole, isoxazole, pyrrole, pyridazine, pyridine, pyrimidine, and pyrazine, each optionally substituted with one or more R^K. In some embodiments, each Cy¹ is independently selected from the group consisting of imidazole, furan, thiophene, thiazole, isothiazole, oxazole, isoxazole, pyrrole, pyridazine, pyridine, pyrimidine, and pyrazine, each optionally substituted with one or more R^K. In some embodiments, each Cy¹ is independently selected from the group consisting of C₄₋₅ cycloalkyl optionally substituted with one or more R^K. In some embodiments, each R^K is independently selected from the group consisting of methyl, ethyl, —CF₃, and halogen.

[0592] In some embodiments, each Cy¹ is the same. In some embodiments, each Cy¹ is different.

[0593] In some embodiments, L^{A4} is —(CH₂)₁₋₆—. In some embodiments, L^{A4} is —(CH₂)₁₋₃—. In some embodiments, L^{A4} is —(CH₂)₁₋₆O—. In some embodiments, L^{A4} is —(CH₂)₁₋₃₀—.

[0594] In some embodiments, Cy² is a 4-6 membered heterocycle. In some embodiments, Cy² has the structure:

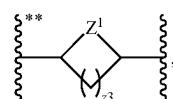


wherein each of subscripts z1 and z2 is independently an integer from 1 to 3 and ** indicates attachment to L^{A4}.

[0595] In some embodiments, subscript z1 and subscript z2 are 1. In some embodiments, subscript z1 and subscript z2 are 2.

[0596] In some embodiments, subscript z1 is 1 and subscript z2 is 2.

[0597] In some embodiments, Cy² has the structure:



wherein

[0598] Z¹ is selected from the group consisting of —O—, —S—, —CR^NR^O—, and —NR^P—;

[0599] R^N, R^O, and R^P are independently hydrogen or C₁₋₆ alkyl;

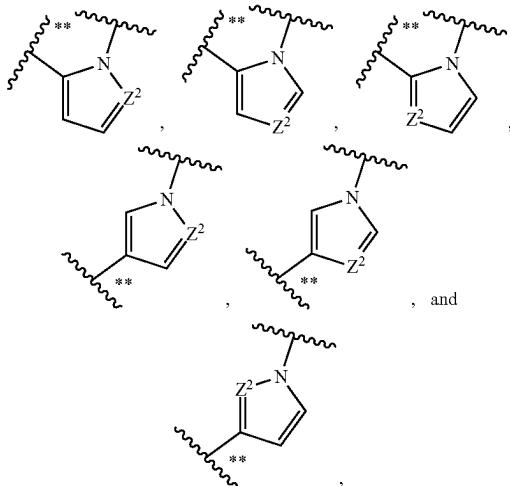
[0600] subscript z3 is an integer from 1 to 3; and

[0601] ** indicates attachment to L^{A4}.

[0602] In some embodiments, R^N and R^O are hydrogen. In some embodiments, R^P is hydrogen. In some embodiments, R^P is methyl.

[0603] In some embodiments, Cy^2 is a 5-6 membered heteroaryl.

[0604] In some embodiments, Cy^2 is selected from the group consisting of:



wherein

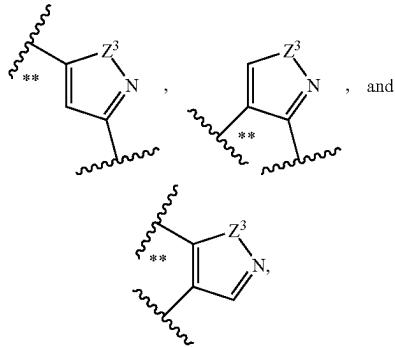
[0605] Z^2 is $=CR^N-$ or $=N-$;

[0606] R^N is hydrogen or C_{1-6} alkyl; and

[0607] ** indicates attachment to L^{AA} .

[0608] In some embodiments, Z^2 is $=CR^N-$ and R^N is hydrogen. In some embodiments, Z^2 is $=N-$.

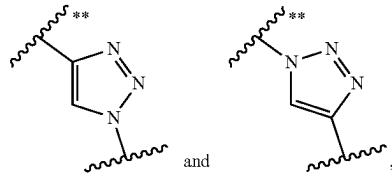
[0609] In some embodiments, Cy^2 is selected from the group consisting of:



wherein Z^3 is $-O-$ or $-S-$ and ** indicates attachment to L^{AA} , L^D , NR^{HH} , Y , W , or L^{BB} .

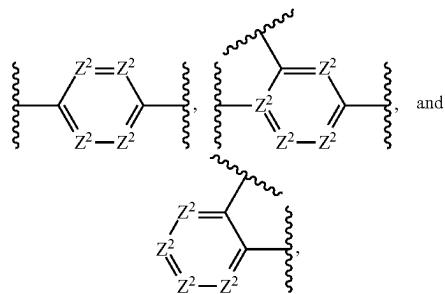
[0610] In some embodiments, ** indicates attachment to L^{AA} . In some embodiments, ** indicates attachment to L^D , NR^{HH} , Y , W , or L^{BB} .

[0611] In some embodiments, Cy^2 is selected from the group consisting of:



wherein ** indicates attachment to L^{AA} .

[0612] In some embodiments, Cy^2 is selected from the group consisting of:



wherein

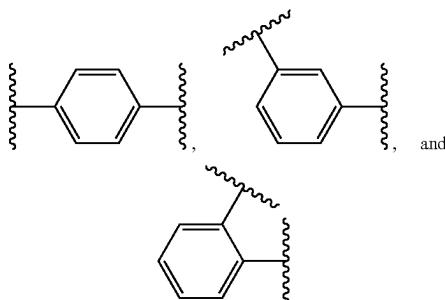
[0613] each Z^2 is independently $=CR^N-$ or $=N-$; and

[0614] each R^N is hydrogen or C_{1-6} alkyl.

[0615] In some embodiments, at least one Z^2 is $=N-$. In some embodiments, one Z^2 is $=N-$ and the remaining Z^2 are $=CR^N-$. In some embodiments, two Z^2 are $=NR^P-$ and the remaining Z^2 are $=CR^N-$.

[0616] In some embodiments, R^N is hydrogen.

[0617] In some embodiments, Cy^2 is selected from the group consisting of:



and

[0618] In some embodiments, Cy^2 is cyclobutyl.

[0619] In some embodiments, R^3 , R^{e3} , R^{g1} , R^{h1} , and R^{j1} are independently hydrogen or $-CH_3$.

[0620] In some embodiments, each RU is independently selected from $-CO_2H$, $-(C=O)NH_2$, $-S(O)_2NH_2$, $-CH_2NH_2$, and $-CH_2OH$.

[0621] In some embodiments, t_1 is 0. In some embodiments, t_1 is 1.

[0622] In some embodiments, u is 1 and L^D is —(CH₂)₁₋₃.
In some embodiments, u is 0.

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[0623] In some embodiments, ZZ is —NR^QR^R. In some embodiments, R^Q is C₁₋₆ alkyl. In some embodiments, R^Q is C₃₋₆ cycloalkyl. In some embodiments, R^Q is cyclopropyl. In some embodiments, R^Q is —(CH₂)₁₋₃C₃₋₆ cycloalkyl. In some embodiments, R^R is hydrogen.

[0624] In some embodiments, ZZ is —N*(C₁₋₆ alkyl)R^QR^R.

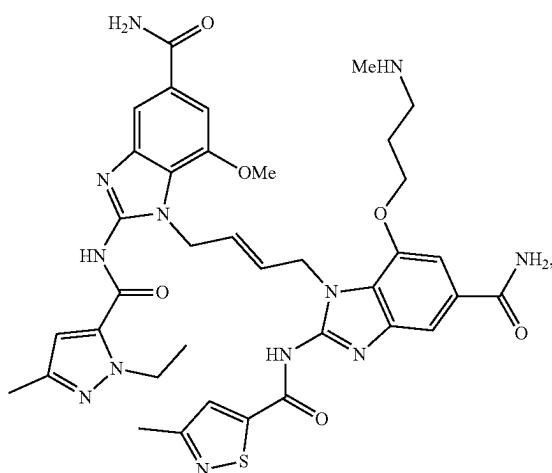
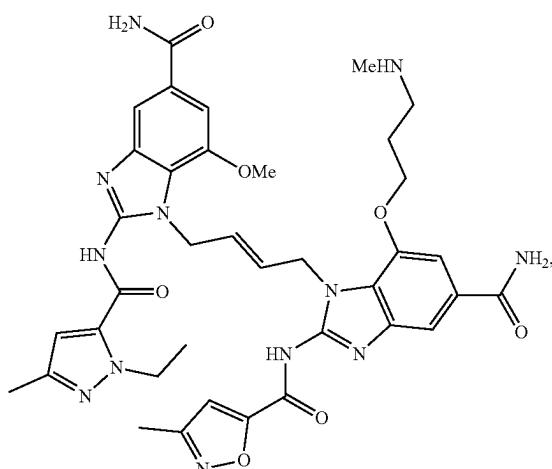
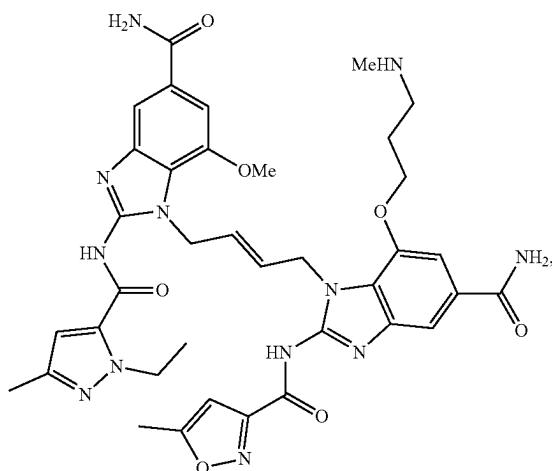
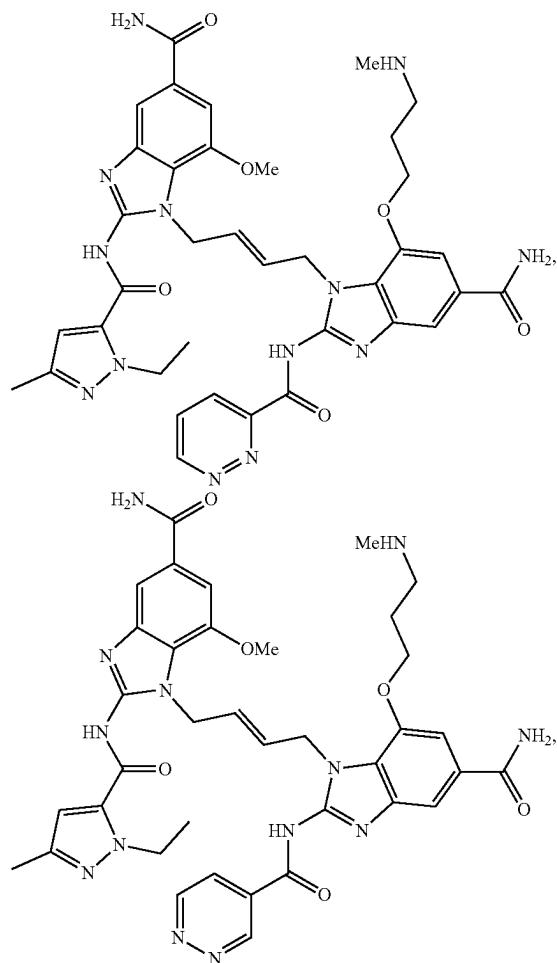
[0625] In some embodiments, ZZ is —C(=O)N^SR^T.

[0626] In some embodiments, ZZ is —C(O)O(t-butyl).

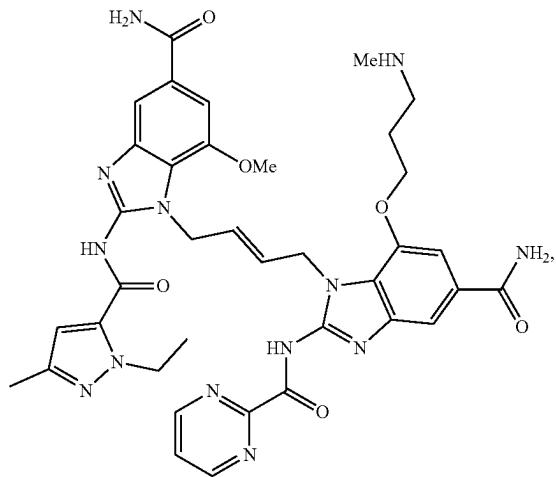
[0627] In some embodiments, ZZ is —CO₂H.

[0628] In some embodiments, ZZ is an amino acid selected from the group consisting of alanine, valine, isoleucine, leucine, aspartic acid, glutamic acid, lysine, histidine, arginine, glycine, serine, threonine, phenylalanine, O-methylserine, O-methylethionic acid, O-methylglutamic acid, N-methyllysine, O-methyltyrosine, O-methylhistidine, and O-methylthreonine.

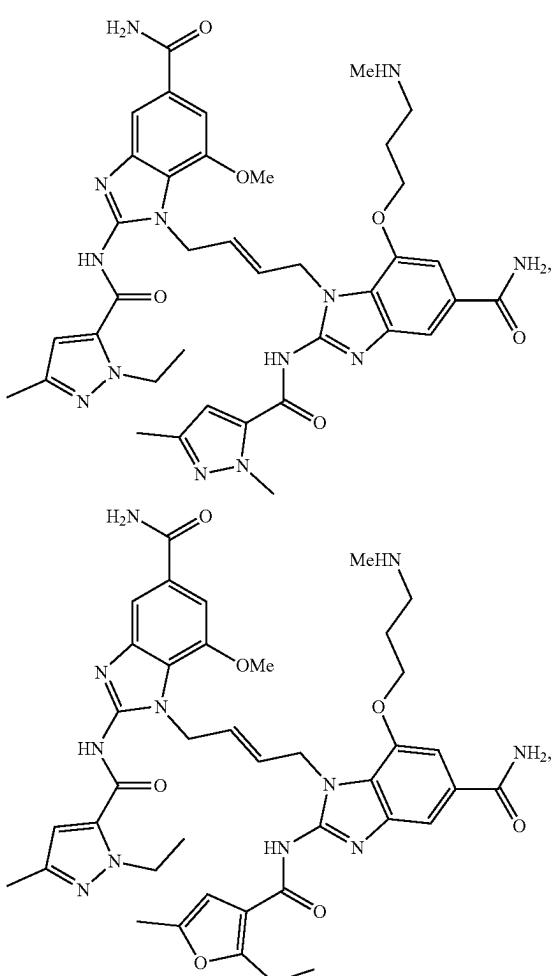
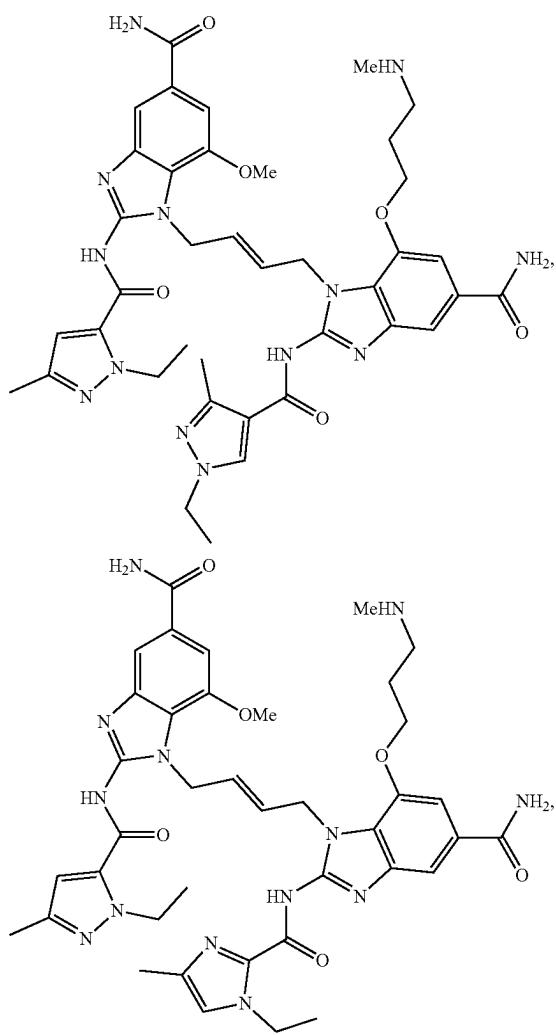
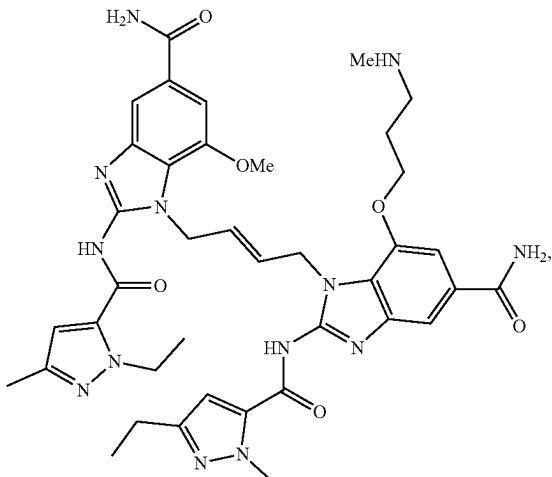
[0629] Some embodiments of Formula (V) include compounds selected from the group consisting of:



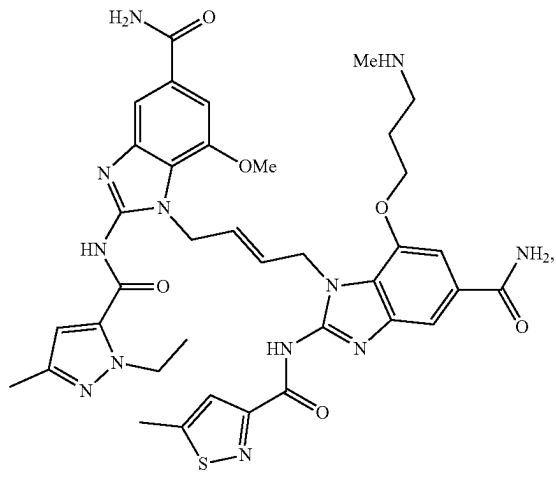
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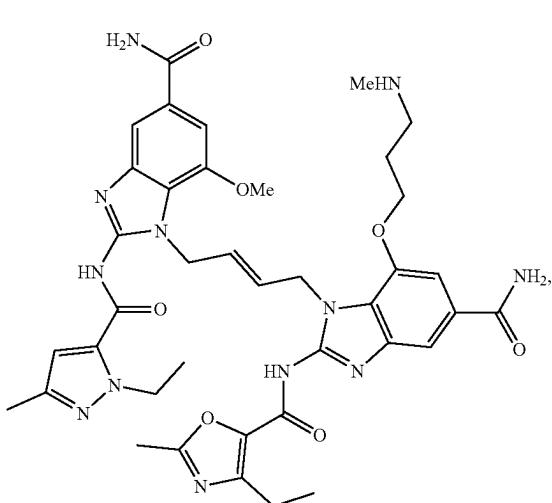
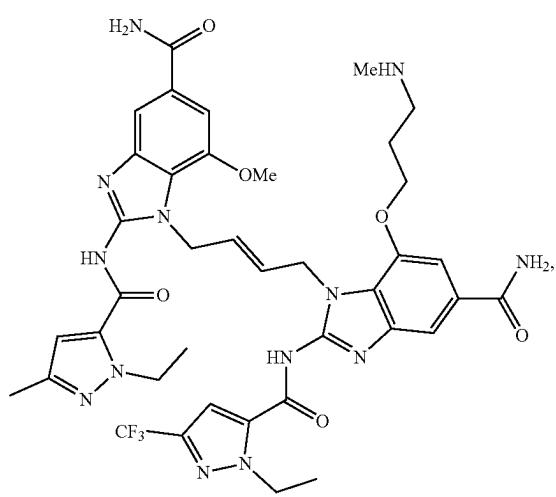
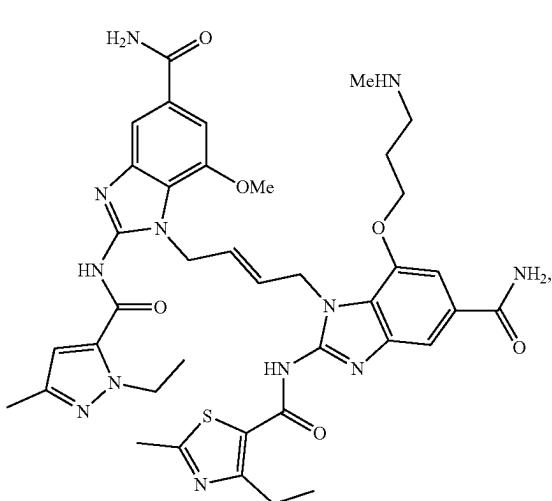
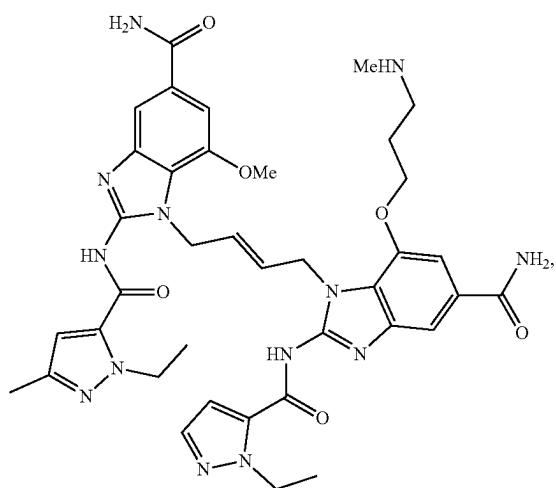
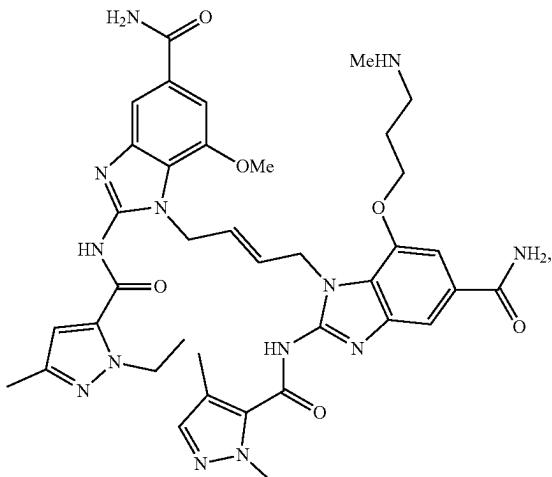
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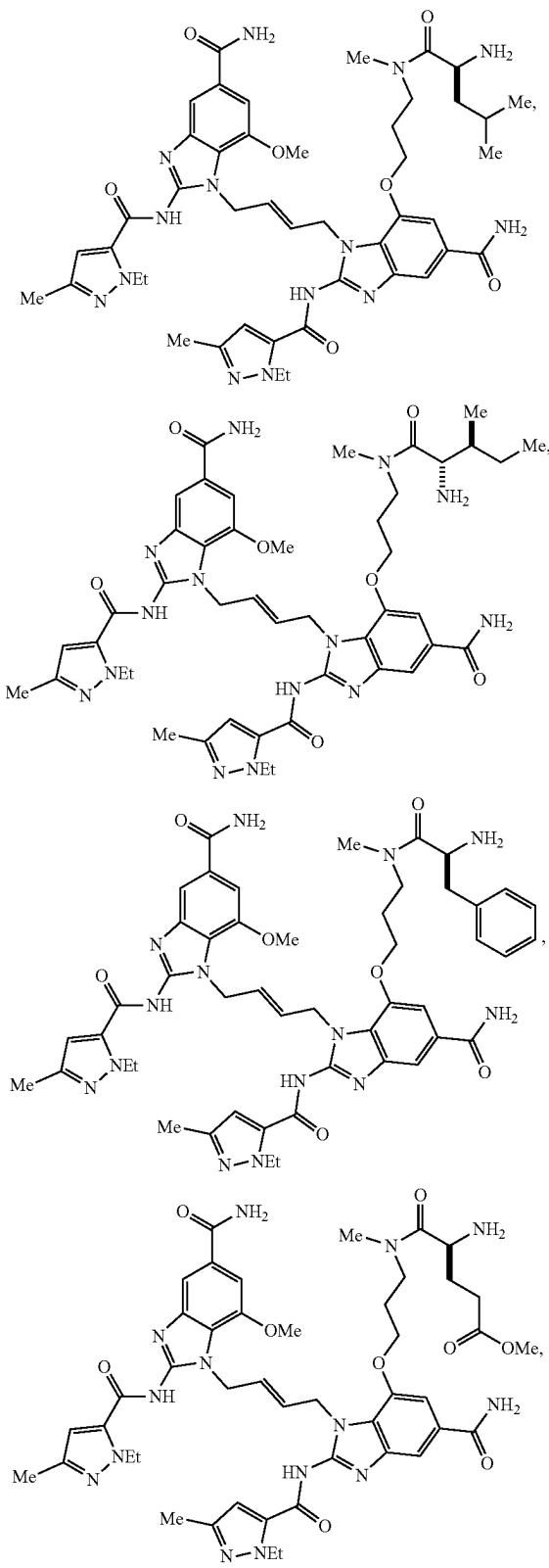
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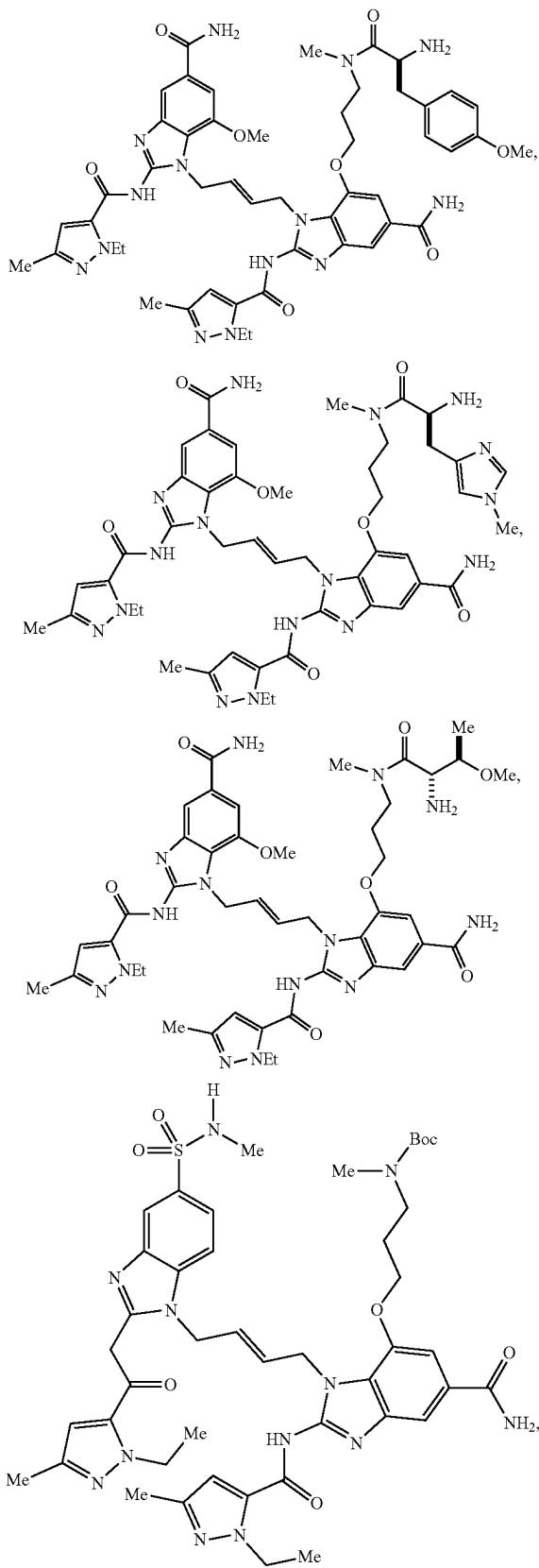
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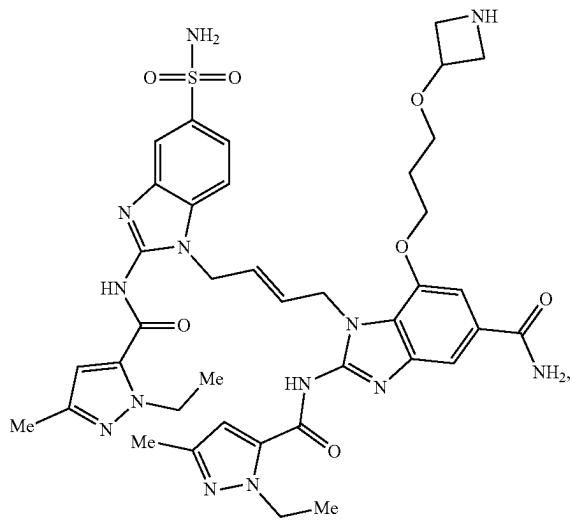
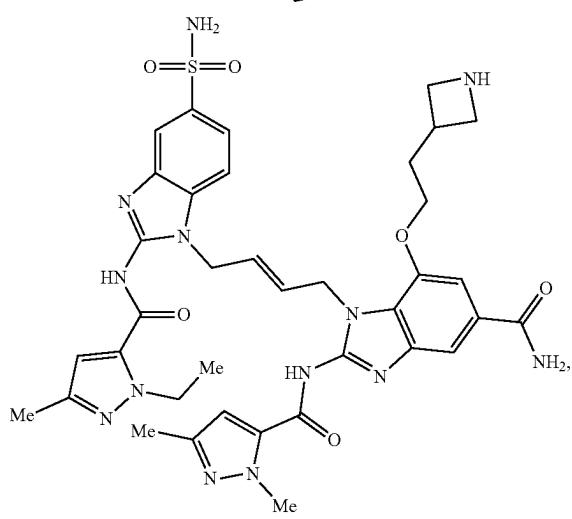
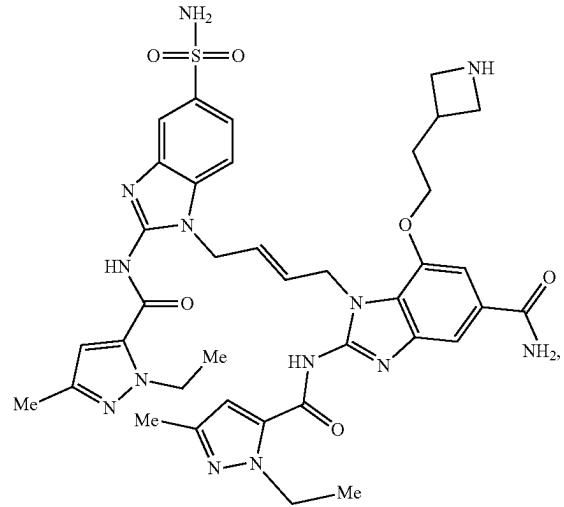
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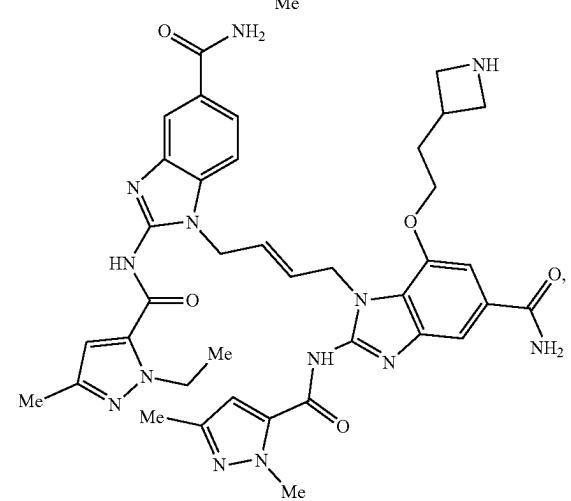
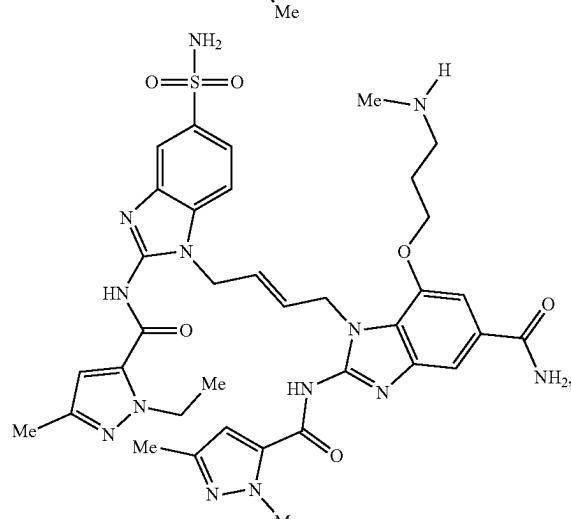
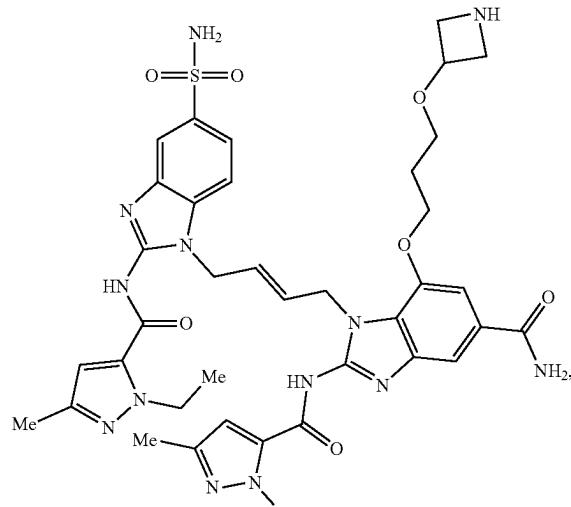
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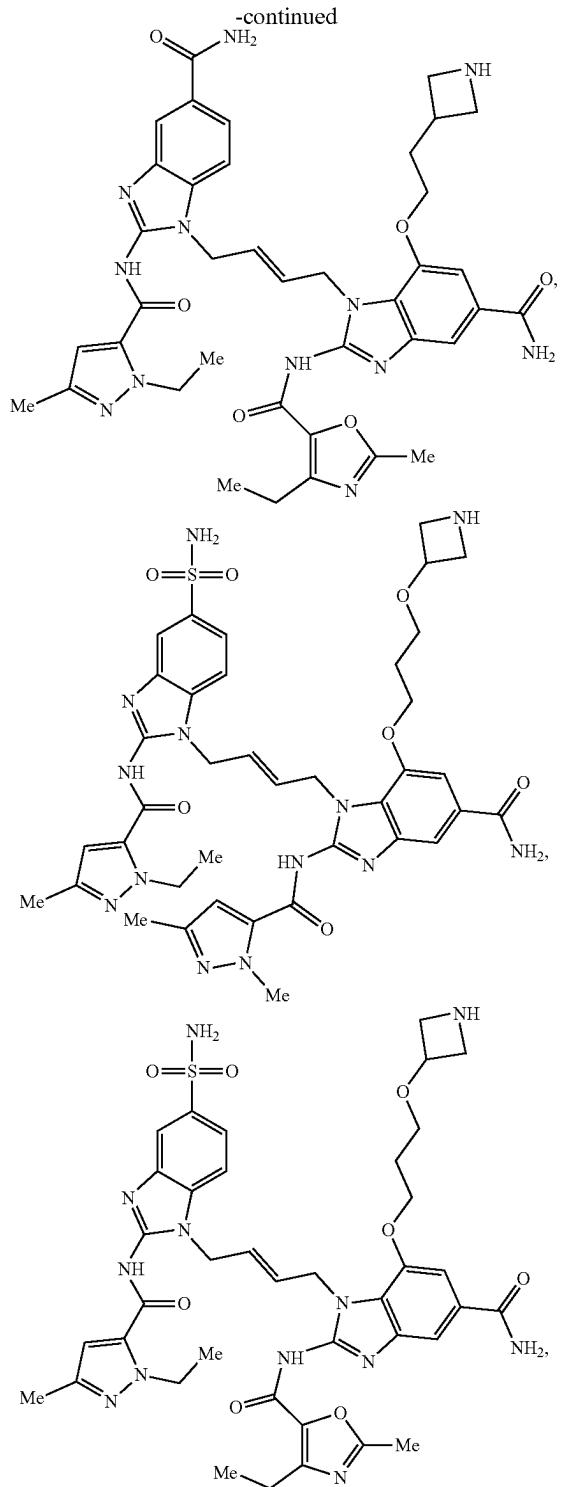


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and pharmaceutically acceptable salts thereof.

Linkers

[0630] As described herein, linkers (L) as defined in connection with Formulae (I), (II), and (II-A) are optional groups that connect X^A or X^B , when present, with M or M^1 .

For example, A, when present, is covalently attached to M or M^1 , and Y, when present, is attached to X^B or to X^A (when X^B is absent). In some embodiments, the linker (L) has the formula $-(A)_a-(W)_w-(Y)_y$, wherein:

[0631] A is a C_{2-20} alkylene optionally substituted with 1-3 Rai; or a 2 to 40 membered heteroalkylene optionally substituted with 1-3 R^{b1} ;

[0632] each R^{a1} is independently selected from the group consisting of:

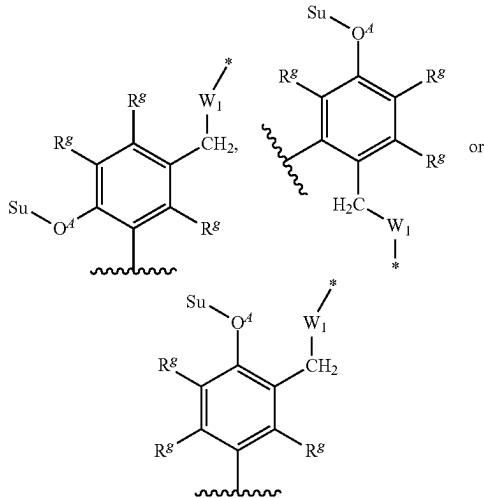
[0633] C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, $-OH$, $=O$, $-NR^{d1}R^{e1}$, $-C(O)NR^{d1}R^{e1}$, $-C(O)(C_{1-6}$ alkyl), and $-C(O)O(C_{1-6}$ alkyl);

[0634] each R^{b1} is independently selected from the group consisting of:

[0635] C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, $-OH$, $=O$, $-NR^{d1}R^{e1}$, $-C(O)NR^{d1}R^{e1}$, $-C(O)(C_{1-6}$ alkyl), and $-C(O)O(C_{1-6}$ alkyl);

[0636] each R^{a1} and R^{e1} are independently hydrogen or C_{1-3} alkyl;

[0637] a is 0 or 1; W is from 1-12 amino acids or has the structure:



[0638] wherein Su is a Sugar moiety;

[0639] $-O^4-$ represents a glycosidic bond;

[0640] each R^g is independently hydrogen, halogen, $-CN$, or $-NO_2$;

[0641] W_1 is absent or $O-C(=O)$;

[0642] $\sim\sim\sim$ represents covalent attachment to A, when present, or M in compounds of Formula (II) and covalent attachment to A, M, or M^1 in the ADCs and compounds described herein;

[0643] * represents covalent attachment to Y, X^A , or X^B in compounds of Formula (II) and to Y, X^A , or X^B in the ADCs described herein;

[0644] w is 0 or 1;

[0645] Y is a self-immolative moiety, a non-self-immolative releasable moiety, or a non-cleavable moiety; and

[0646] y is 0 or 1.

[0647] In some embodiments, $-O^4-$ represents a glycosidic bond. In some embodiments, the glycosidic bond provides a β -glucuronidase or a β -mannosidase-cleavage

site. In some embodiments, the β -glucuronidase-cleavage site is cleavable by human lysosomal β -glucuronidase. In some embodiments, the β -mannosidase-cleavage site is cleavable by human lysosomal β -mannosidase.

[0648] In some embodiments, a is 0. In some embodiments, a is 1. In some embodiments, w is 0. In some embodiments, w is 1. In some embodiments, y is 0. In some embodiments, y is 1. In some embodiments, $a+y+w=1$. In some embodiments, $a+y+w=2$. In some embodiments, $a+y+w=3$. In some embodiments, $a+y+w=0$ (i.e., the linker (L) is absent).

[0649] In some embodiments, A is a C_{2-20} alkylene optionally substituted with 1-3 R^{a1} . In some embodiments, A is a C_{2-10} alkylene optionally substituted with 1-3 R^{a1} . In some embodiments, A is a C_{4-10} alkylene optionally substituted with 1-3 R^{a1} . In some embodiments, A is a C_{2-20} alkylene substituted with R^{a1} . In some embodiments, A is a C_{2-10} alkylene substituted with R^{a1} . In some embodiments, A is a C_{2-10} alkylene substituted with R^{a1} .

[0650] In some embodiments, each R^{a1} is independently selected from the group consisting of: C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, $-\text{OH}$, $=\text{O}$, $-\text{NR}^{d1}\text{R}^{e1}$, $-\text{C}(\text{O})\text{NR}^{d1}\text{R}^{e1}$, $-\text{C}(\text{O})(\text{C}_{1-6}\text{ alkyl})$, and $-\text{C}(\text{O})\text{O}(\text{C}_{1-6}\text{ alkyl})$. In some embodiments, each R^{a1} is C_{1-6} alkyl. In some embodiments, each R^{a1} is C_{1-6} haloalkyl. In some embodiments, each R^{a1} is C_{1-6} alkoxy. In some embodiments, each R^{a1} is C_{1-6} haloalkoxy. In some embodiments, each R^{a1} is halogen. In some embodiments, each R^{a1} is $-\text{OH}$. In some embodiments, each R^{a1} is $=\text{O}$. In some embodiments, each R^{a1} is $-\text{NR}^{d1}\text{R}^{e1}$. In some embodiments, each R^{a1} is $\text{C}(\text{O})\text{NR}^{d1}\text{R}^{e1}$. In some embodiments, each R^{a1} is $-\text{C}(\text{O})(\text{C}_{1-6}\text{ C}_6\text{ alkyl})$. In some embodiments, each R^{a1} is $-\text{C}(\text{O})\text{O}(\text{C}_{1-6}\text{ C}_6\text{ alkyl})$. In some embodiments, one occurrence of R^{a1} is $-\text{NR}^{d1}\text{R}^{e1}$. In some embodiments, A is a C_{2-20} alkylene substituted with 1 or 2 R^{a1} , each of which is $=\text{O}$.

[0651] In some embodiments, R^{d1} and R^{e1} are independently hydrogen or C_{1-3} alkyl. In some embodiments, one of R^{d1} and R^{e1} is hydrogen, and the other of R^{d1} and R^{e1} is C_{1-3} alkyl. In some embodiments, R^{d1} and R^{e1} are both hydrogen or C_{1-3} alkyl. In some embodiments, R^{d1} and R^{e1} are both C_{1-3} alkyl. In some embodiments, R^{d1} and R^{e1} are both methyl.

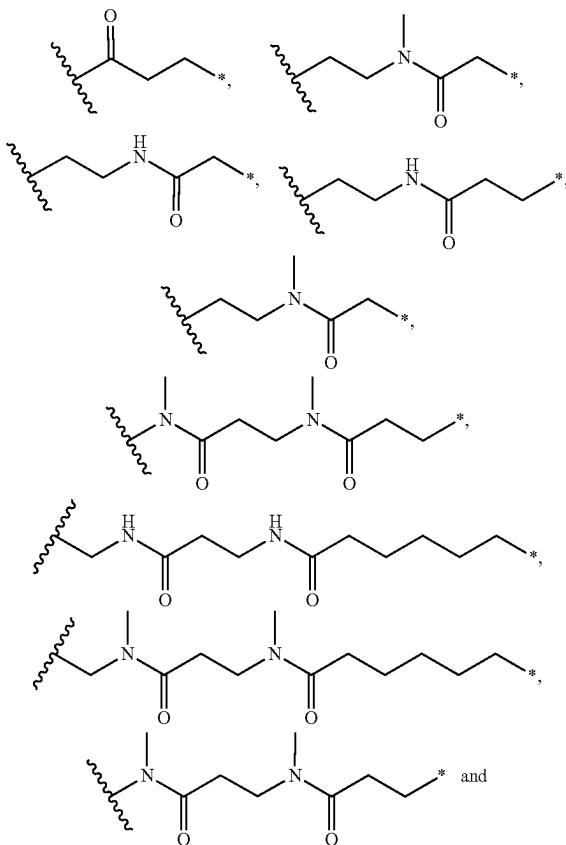
[0652] In some embodiments, A is a C_{2-20} alkylene. In some embodiments, A is a C_{2-10} alkylene. In some embodiments, A is a C_{2-10} alkylene. In some embodiments, A is a C_{2-6} alkylene. In some embodiments, A is a C_{4-10} alkylene.

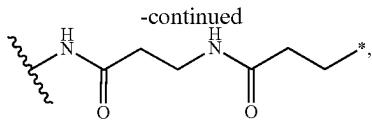
[0653] In some embodiments, A is a 2 to 40 membered heteroalkylene optionally substituted with 1-3 R^{b1} . In some embodiments, A is a 2 to 20 membered heteroalkylene optionally substituted with 1-3 R^{b1} . In some embodiments, A is a 2 to 12 membered heteroalkylene optionally substituted with 1-3 R^{b1} . In some embodiments, A is a 4 to 12 membered heteroalkylene optionally substituted with 1-3 R^{b1} . In some embodiments, A is a 4 to 8 membered heteroalkylene optionally substituted with 1-3 R^{b1} . In some embodiments, A is a 2 to 40 membered heteroalkylene substituted with R^{b1} . In some embodiments, A is a 2 to 20 membered heteroalkylene substituted with R^{b1} . In some embodiments, A is a 2 to 12 membered heteroalkylene substituted with R^{b1} . In some embodiments, A is a 4 to 12 membered heteroalkylene substituted with R^{b1} . In some embodiments, A is a 4 to 8 membered heteroalkylene substituted with R^{b1} . In some embodiments, A is a 4 to 12 membered heteroalkylene substituted with R^{b1} . In some embodiments, A is a 4 to 8 membered heteroalkylene substituted with R^{b1} .

[0654] In some embodiments, each R^{b1} is independently selected from the group consisting of: C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, $-\text{OH}$, $-\text{NR}^{d1}\text{R}^{e1}$, $-\text{C}(\text{O})\text{NR}^{d1}\text{R}^{e1}$, $-\text{C}(\text{O})(\text{C}_{1-6}\text{ alkyl})$, and $-\text{C}(\text{O})\text{O}(\text{C}_{1-6}\text{ alkyl})$. In some embodiments, each R^{b1} is C_{1-6} alkyl. In some embodiments, each R^{b1} is C_{1-6} haloalkyl. In some embodiments, each R^{b1} is C_{1-6} alkoxy. In some embodiments, each R^{b1} is C_{1-6} haloalkoxy. In some embodiments, each R^{b1} is halogen. In some embodiments, each R^{b1} is $-\text{OH}$. In some embodiments, each R^{b1} is $-\text{NR}^{d1}\text{R}^{e1}$. In some embodiments, each R^{b1} is $\text{C}(\text{O})\text{NR}^{d1}\text{R}^{e1}$. In some embodiments, each R^{b1} is $-\text{C}(\text{O})(\text{C}_{1-6}\text{ alkyl})$. In some embodiments, each R^{b1} is $-\text{C}(\text{O})\text{O}(\text{C}_{1-6}\text{ alkyl})$. In some embodiments, one occurrence of R^{b1} is $-\text{NR}^{d1}\text{R}^{e1}$.

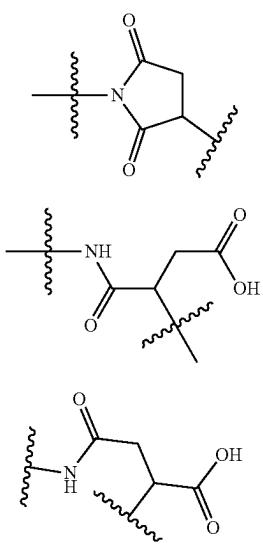
[0655] In some embodiments, R^{d1} and R^{e1} are independently hydrogen or C_{1-3} alkyl. In some embodiments, one of R^{d1} and R^{e1} is hydrogen, and the other of R^{d1} and R^{e1} is C_{1-3} alkyl. In some embodiments, R^{d1} and R^{e1} are both hydrogen or C_{1-3} alkyl. In some embodiments, R^{d1} and R^{e1} are both C_{1-3} alkyl. In some embodiments, R^{d1} and R^{e1} are both methyl.

[0656] In some embodiments, A is a 2 to 40 membered heteroalkylene. In some embodiments, A is a 2 to 20 membered heteroalkylene. In some embodiments, A is a 2 to 12 membered heteroalkylene. In some embodiments, A is a 4 to 12 membered heteroalkylene. In some embodiments, A is a 4 to 8 membered heteroalkylene. In some embodiments, A is selected from the group consisting of:

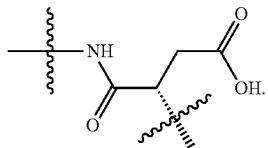




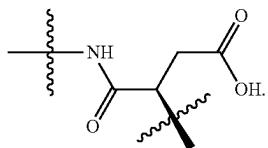
wherein represents covalent attachment to W or Y, and * represents covalent linkage to M¹ or M (e.g., in compounds of Formula (I) or (II), respectively). In some embodiments, M is a succinimide. In some embodiments, M is a hydrolyzed succinimide. In some embodiments, M¹ is a succinimide. In some embodiments, M¹ is a hydrolyzed succinimide. It will be understood that a hydrolyzed succinimide may exist in two regioisomeric form(s). Those forms are exemplified below for hydrolysis of M, wherein the structures representing the regioisomers from that hydrolysis are formula M' and M"; wherein the wavy lines adjacent to the bonds are as defined for A.



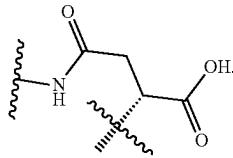
[0657] In some embodiments, M' is



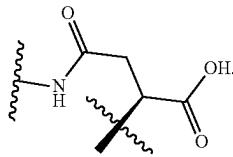
In some embodiments, M' is



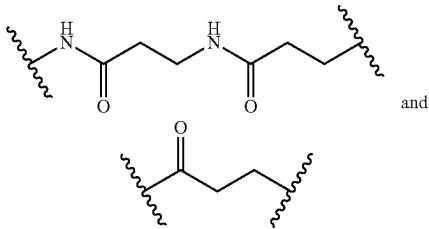
In some embodiments, M" is



In some embodiments, M" is



[0658] In some embodiments, A is a PEG4 to PEG12. In some embodiments, A is a PEG4 to PEG8. Representative A groups include, but are not limited to:



M"

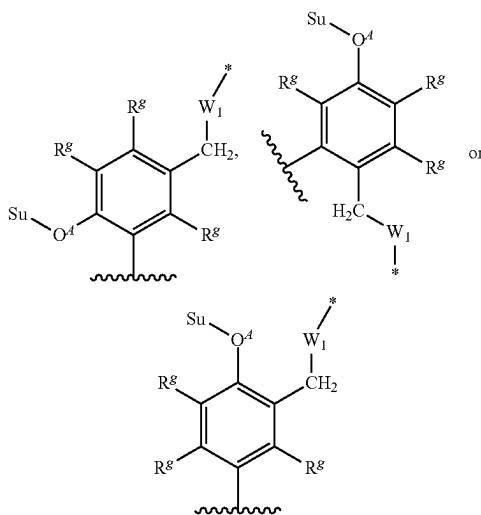
[0659] In some embodiments, w is 0. In some embodiments w is 1.

[0660] In some embodiments, W is a single amino acid. In some embodiments, W is a single natural amino acid. In some embodiments, W is a peptide including from 2-12 amino acids, wherein each amino acid is independently a natural or unnatural amino acid. In some embodiments, the natural or unnatural amino acid is a D or L isomer. In some embodiments, each amino acid is independently a natural amino acid. In some embodiments, each W is independently an alpha, beta, or gamma amino acid that is natural or unnatural. In some embodiments, W comprises a natural amino acid linked to an unnatural amino acid. In some embodiments, W comprises a natural or unnatural amino acid linked to a D-isomer of a natural or unnatural amino acid. In some embodiments, W is a dipeptide. In some embodiments, W is a tripeptide. In some embodiments, W is a tetrapeptide. In some embodiments, W is a pentapeptide. In some embodiments, W is a hexapeptide. In some embodiments, W is 7, 8, 9, 10, 11, or 12 amino acids. In some embodiments, each amino acid of W is independently selected from the group consisting of valine, alanine, β -alanine, glycine, lysine, leucine, phenylalanine, proline, aspartic acid, serine, glutamic acid, homoserine methyl ether, aspartate methyl ester, N,N-dimethyl lysine, arginine, valine-alanine, valine-citrulline, phenylalanine-lysine, and citrulline. In some embodiments, W is an aspartic acid. In some embodiments, W is a lysine. In some embodiments, W is a glycine. In some embodiments, W is an alanine. In some embodiments, W is aspartate methyl ester. In some embodiments,

ments, W is a N,N-dimethyl lysine. In some embodiments, W is a homoserine methyl ether. In some embodiments, W is a serine. In some embodiments, W is a valine-alanine.

[0661] In some embodiments, w is 1; W is from 1-12 amino acids; and the bond between W and the X^B or between W and Y is enzymatically cleavable by a tumor-associated protease. In some embodiments, the tumor-associated protease is a cathepsin. In some embodiments, the tumor-associated protease is cathepsin B, C, or D.

[0662] In some embodiments, w is 1; and W has the structure of:



[0663] wherein Su is a Sugar moiety;

[0664] —O⁴— represents a glycosidic bond;

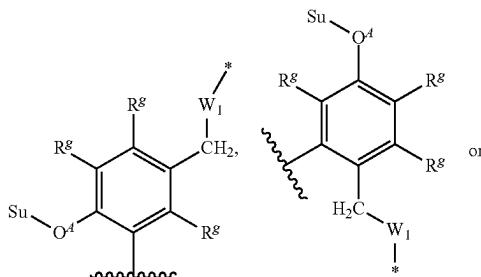
[0665] each R⁹ is independently hydrogen, halogen, —CN, or —NO₂;

[0666] W₁ is absent or —O—C(=O)—;

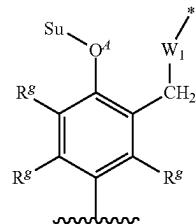
[0667] ~~~~ represents covalent attachment to A or M in compounds of Formula (II); and

[0668] the * represents covalent attachment to Y, X^A, or X^B in compounds of Formula (II);

[0669] In some embodiments, w is 1; and W has the structure of:



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[0670] wherein Su is a Sugar moiety;

[0671] —O⁴— represents a glycosidic bond;

[0672] each R⁹ is independently hydrogen, halogen, —CN, or —NO₂;

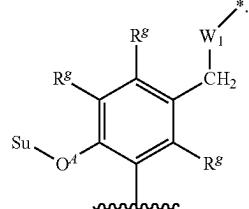
[0673] W₁ is absent or —O—C(=O)—;

[0674] ~~~~ represents covalent attachment to A or M in the ADCs described herein; and

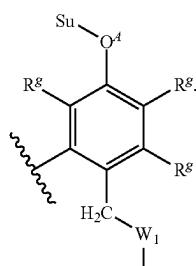
[0675] the * represents covalent attachment to Y, X^A, or X^B in the ADCs described herein;

[0676] In some embodiments, —O⁴— represents a glycosidic bond. In some embodiments, the glycosidic bond provides a β-glucuronidase or a β-mannosidase-cleavage site. In some embodiments, the β-glucuronidase or a α-mannosidase-cleavage site is cleavable by human lysosomal β-glucuronidase or by human lysosomal β-mannosidase.

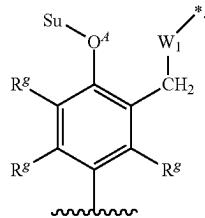
[0677] In some embodiments, W is



In some embodiments, W is



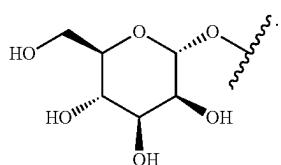
In some embodiments, W is



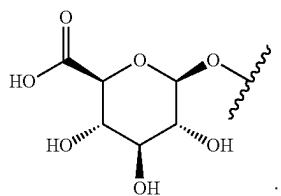
[0678] In some embodiments, each R^g is hydrogen. In some embodiments, one R^g is hydrogen, and the remaining R^g are independently halo, —CN, or —NO₂. In some embodiments, two R^g are hydrogen, and the remaining R^g is halo, —CN, or —NO₂.

[0679] In some embodiments, one R^g is halogen, —CN, or —NO₂, and the other R^g are hydrogen. In some embodiments, each R^g is hydrogen.

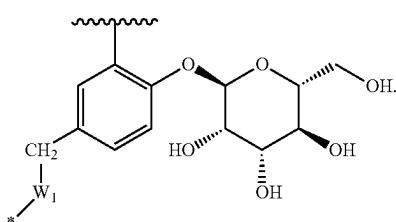
[0680] In some embodiments, O⁴—Su is charged neutral at physiological pH. In some embodiments, O⁴—Su is mannose. In some embodiments, O⁴—Su is



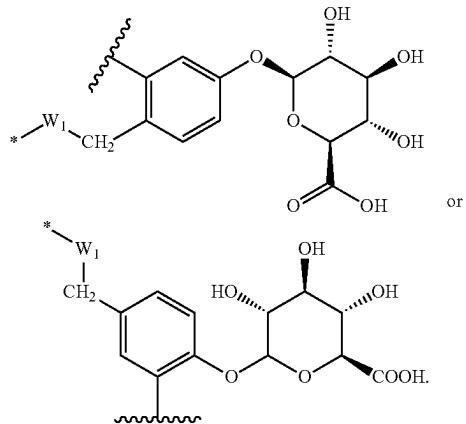
In some embodiments, O⁴—Su comprises a carboxylate moiety. In some embodiments, O⁴—Su is glucuronic acid. In some embodiments, O⁴—Su is



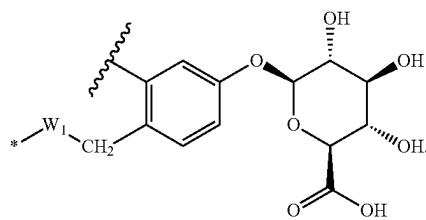
[0681] In some embodiments, W is



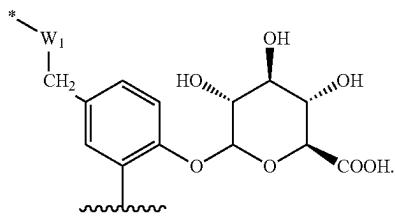
In some embodiments, W is



In some embodiments, W is



In some embodiments, W is



[0682] In some embodiments, a is 0.

[0683] In some embodiments, y is 0. In some embodiments y is 1.

[0684] In some embodiments, Y is a self-immolative moiety, a non-self-immolative releasable moiety, or a non-cleavable moiety. In some embodiments, Y is a self-immolative moiety or a non-self-immolative releasable moiety. In some embodiments, Y is a self-immolative moiety. In some embodiments, Y is a non-self-immolative moiety.

[0685] A non-self-immolative moiety is one which requires enzymatic cleavage, and in which part or all of the group remains bound to the Drug Unit after cleavage from the ADC, thereby forming free drug. Examples of a non-self-immolative moiety include, but are not limited to: -glycine-; and -glycine-glycine. When an ADC having Y is -glycine- or -glycine-glycine undergoes enzymatic cleavage (for example, via a cancer-cell-associated protease or a lymphocyte-associated protease), the Drug Unit is cleaved from the ADC such that the free drug includes the glycine or

glycine-glycine group from Y. In some embodiments, an independent hydrolysis reaction takes place within, or in proximity to, the target cell, further cleaving the glycine or glycine-glycine group from the free drug. In some embodiments, enzymatic cleavage of the non-self-immolative moiety, as described herein, does not result in any further hydrolysis step(s).

[0686] A self-immolative moiety refers to a bifunctional chemical moiety that is capable of covalently linking together two spaced chemical moieties into a normally stable tripartite molecule. The self-immolative group will spontaneously separate from the second chemical moiety if its bond to the first moiety is cleaved. For example, a self-immolative moiety includes a p-aminobenzyl alcohol (PAB) optionally substituted with one or more alkyl, alkoxy, halogen, cyano, or nitro groups. Other examples of self-immolative moieties include, but are not limited to, aromatic compounds that are electronically similar to the PAB group such as 2-aminoimidazol-5-methanol derivatives (see, e.g., Hay et al., 1999, *Bioorg. Med. Chem. Lett.* 9:2237), ortho or para-aminobenzylacetals, substituted and unsubstituted 4-aminobutyric acid amides (see, e.g., Rodrigues et al., 1995, *Chemistry Biology* 2:223), appropriately substituted bicyclo[2.2.1] and bicyclo[2.2.2] ring systems (see, e.g., Storm et al., 1972, *J. Amer. Chem. Soc.* 94:5815), 2-amino-phenylpropionic acid amides (see, e.g., Amsberry et al., 1990, *J. Org. Chem.* 55:5867), and elimination of amine-containing drugs that are substituted at the α -position of glycine (see, e.g., Kingsbury et al., 1984, *J. Med. Chem.* 27:1447).

[0687] In some embodiments, Y is a PAB group, optionally substituted with one or more alkyl, alkoxy, halogen, cyano, or nitro groups; a para-aminobenzyloxy-carbonyl (PABC) group optionally substituted with a sugar moiety; -glycine-; -glycine-glycine-; or a branched bis(hydroxymethyl)styrene (BHMS) unit, which is capable of incorporating (and releasing) multiple Drug Units.

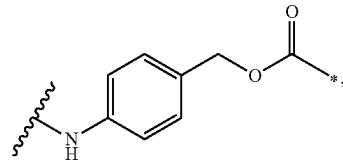
[0688] In some embodiments, -(A)_a-(W)_w—(Y)_y comprises a non-self-immolative releasable linker, which provides release of the free drug once the ADC has been internalized into the target cell. In some embodiments, -(A)_a-(W)_w—(Y)_y comprises a releasable linker, which provides release of the free Drug with, or in the vicinity, of targeted cells. Releasable linkers possess a recognition site, such as a peptide cleavage site, sugar cleavage site, or disulfide cleavage side. In some embodiments, each releasable linker is a di-peptide. In some embodiments, each releasable linker is a disulfide. In some embodiments, each releasable linker is a hydrazone. In some embodiments, each releasable linker is independently Val-Cit-, -Phe-Lys-, or -Val-Ala-. In some embodiments, each releasable linker, when bound to a succinimide or hydrolyzed succinimide, is independently succinimido-caproyl (mc), succinimido-caproyl-valine-citrulline (sc-ve), succinimido-caproyl-valine-citrulline-paraaminobenzylloxycarbonyl (sc-vc-PABC), or SDPr-vc (where "S" refers to succinimido).

[0689] In some embodiments, -(A)_a-(W)_w—(Y)_y comprises a non-cleavable linker. Non-cleavable linkers are known in the art and, in some embodiments, are adapted for use with the ADCs described herein as the "Y" group. A non-cleavable linker is capable of linking a Drug Unit to an antibody in a generally stable and covalent manner and is substantially resistant to acid-induced cleavage, light-induced cleavage, peptidase- or esterase-induced cleavage,

and disulfide bond cleavage. In some embodiments, the free drug is released from the ADCs containing non-cleavable linkers via alternative mechanisms, such as proteolytic antibody degradation. In some embodiments, the Drug Unit can exert a biological effect as a part of the ADC (i.e., while still conjugated to the antibody via a linker).

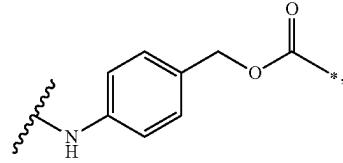
[0690] Reagents that form non-cleavable linker-maleimide and non-cleavable linker-succinimide compounds are known in the art and can be adapted for use herein. Exemplary reagents comprise a maleimido or haloacetyl-based moiety, such as 6-maleimidocaprylic acid N-hydroxy succinimide ester (MCC), N-succinimidyl 4-(maleimidomethyl)cyclohexanecarboxylate (SMCC), N-succinimidyl-4-(N-maleimidomethyl)-cyclohexane-1-carboxy-(6-amidocaproate) (LC-SMCC), maleimidoundecanoic acid N-succinimidyl ester (KMUA), γ -maleimidobutyric acid N-succinimidyl ester (GMBS), c-maleimidocaprylic acid N-hydroxysuccinimide ester (EMCS), m-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS), N-(α -maleimidooctyloxy)-succinimide ester [AMAS], succinimidyl-6-(β -maleimidopropionamido) hexanoate (SMPH), N-succinimidyl 4-(p-maleimidophenyl)-butyrate (SMPB), and N-(p-maleimidophenyl)isocyanate (PMPI), N-succinimidyl-4-(iodoacetyl)-aminobenzoate (STAB), N-succinimidyl iodoacetate (SIA), N-succinimidyl bromoacetate (SBA) and N-succinimidyl 3-(bromoacetamido)propionate (SBAP). Additional "A-M" and "A-M¹" groups for use in the ADCs described herein are found, for example, in U.S. Pat. No. 8,142,784, incorporated herein by reference in its entirety.

[0691] In some embodiments, y is 1; and Y is



wherein represents connection to W, A, or M in compounds of Formula (II); and the * represents connection to X^A or X^B, in compounds of Formula (II).

[0692] In some embodiments, y is 1; and Y is



wherein represents connection to W, A, M or M¹ in the ADCs described herein; and the * represents connection to X^A or X^B, in the ADCs described herein.

[0693] In some embodiments, -(A)_a-(W)_w—(Y)_y comprises a non-releasable linker, wherein the Drug is released after the ADC has been internalized into the target cell and degraded, liberating the Drug.

[0694] In some embodiments, the linker (L) is substituted with a polyethylene glycol moiety selected from the group consisting of PEG2 to PEG20. In some embodiments, L is substituted with a polyethylene glycol moiety selected from

the group consisting of PEG2, PEG4, PEG6, PEG8, PEG10, PEG12, PEG16, and PEG20. In some embodiments, L is not substituted with a polyethylene glycol moiety selected from the group consisting of PEG2 to PEG20.

[0695] In some embodiments, polydisperse PEGs, monodisperse PEGs or discrete PEGs are used to make the ADCs and intermediates thereof. Polydisperse PEGs are a heterogeneous mixture of sizes and molecular weights whereas monodisperse PEGs are typically purified from heterogeneous mixtures and therefore provide a single chain length and molecular weight. Discrete PEGs are synthesized in step-wise fashion and not via a polymerization process. Discrete PEGs provide a single molecule with defined and specified chain length. The number of —CH₂CH₂O— subunits of a PEG Unit ranges, for example, from 8 to 24 or from 12 to 24, referred to as PEG8 to PEG24 and PEG12 to PEG24, respectively.

[0696] The PEG moieties provided herein, which are also referred to as PEG Units, comprise one or multiple polyethylene glycol chains. The polyethylene glycol chains are linked together, for example, in a linear, branched or star shaped configuration. Typically, at least one of the polyethylene glycol chains of a PEG Unit is derivatized at one end for covalent attachment to an appropriate site on a component of the ADC (e.g., L). Exemplary attachments to ADCs 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 to the Formula (I) ADC is by means of a non-conditionally cleavable linkage. In some embodiments, attachment to the ADC is not via an ester linkage, hydrazone linkage, oxime linkage, or disulfide linkage. In some embodiments, attachment to the ADC is not via a hydrazone linkage.

[0697] A conditionally cleavable linkage refers to a linkage that is not substantially sensitive to cleavage while circulating in 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 biologically relevant environment in a subject that is administered the ADC. Chemical hydrolysis of a hydrazone, reduction of a disulfide bond, and enzymatic cleavage of a peptide bond or glycosidic bond of a Glucuronide Unit as described by WO 2007/011968 (which is incorporated by reference in its entirety) are examples of conditionally cleavable linkages.

[0698] In some embodiments, the PEG Unit is directly attached to the ADC (or an intermediate thereof) at L. In those embodiments, the other terminus (or termini) of the PEG Unit is free and untethered (i.e., not covalently attached), and in some embodiments, is 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 polyethylene glycol subunit of the PEG Unit. By untethered, it is meant that the PEG Unit will not be covalently attached at that untethered site to a Drug Unit, to an antibody, or to a linking component to a Drug Unit and/or an antibody. Such an arrangement can allow a PEG Unit of sufficient length to assume a parallel orientation with respect to the drug in conjugated form, i.e., as a Drug Unit (D). For those embodiments in which the PEG Unit comprises more than one

Polyethylene glycol chain, the multiple polyethylene glycol chains are independently chosen, e.g., are the same or different chemical moieties (e.g., polyethylene glycol chains of different molecular weight or number of —CH₂CH₂O— subunits). A PEG Unit having multiple polyethylene glycol chains is attached to the ADC at a single attachment site. The skilled artisan will understand that the PEG Unit, in addition to comprising repeating polyethylene glycol subunits, may also contain non-PEG material (e.g., to facilitate coupling of multiple polyethylene glycol chains to each other or to facilitate coupling to the ADC). Non-PEG material refers to the atoms in the PEG Unit that are not part of the repeating —CH₂CH₂O— subunits. In some embodiments provided herein, the PEG Unit comprises two monomeric polyethylene glycol chains attached to each other via non-PEG elements. In other embodiments provided herein, the PEG Unit comprises two linear polyethylene glycol chains attached to a central core that is attached to the ADC (i.e., the PEG Unit itself is branched).

[0699] There are a number of PEG attachment methods available to those skilled in the art: see, for example: 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); ACT 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. Biootechnol.* 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).

[0700] For example, in some embodiments, a PEG Unit is covalently bound to an amino acid residue via reactive groups of a polyethylene glycol-containing compound and the amino acid residue. Reactive groups of the amino acid residue include those that are reactive to an activated PEG molecule (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) are also useful as a reactive group for forming a covalent attachment to a 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.

[0701] In some embodiments, a polyethylene glycol-containing compound forms a covalent attachment to an amino group 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 chlo-

ride. 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 (mPEG-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.

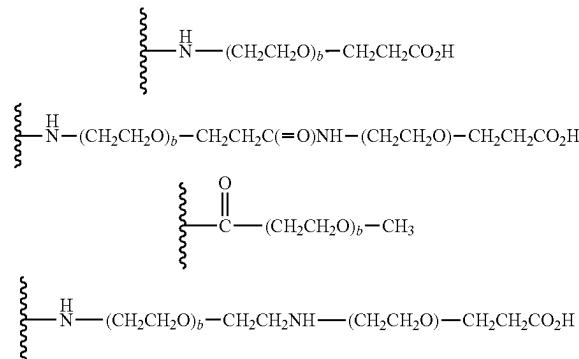
[0702] Generally, at least one of the polyethylene glycol chains that make up the PEG is functionalized to provide covalent attachment to the ADC. Functionalization of the polyethylene glycol-containing compound that is the precursor to the PEG includes, for example, via an amine, thiol, NHS ester, maleimide, alkyne, azide, carbonyl, or other functional group. In some embodiments, the PEG further comprises non-PEG material (i.e., material not comprised of —CH₂CH₂O—) that provides coupling to the ADC or in constructing the polyethylene glycol-containing compound or PEG facilitates coupling of two or more polyethylene glycol chains.

[0703] In some embodiments, the presence of the PEG Unit in an ADC is capable of having two potential impacts upon the pharmacokinetics of the resulting ADC. One 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 Drug Unit. The second impact is a decrease in volume and rate of distribution that sometimes arises from the increase in the molecular weight of the ADC. Increasing the number of polyethylene glycol subunits increases the hydrodynamic radius of a conjugate, typically resulting in decreased diffusivity. In turn, decreased diffusivity typically diminishes the ability of the ADC to penetrate into a tumor. See Schmidt and Wittrup, *Mol Cancer Ther* 2009; 8:2861-2871. Because of these two competing pharmacokinetic effects, it can be desirable to use a PEG Unit that is sufficiently large to decrease the ADC 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 ADC to reach the intended target cell population. See, e.g., Examples 1, 18, and 21 of US 2016/0310612, which is incorporated by reference herein (e.g., for methodology for selecting an optimal size of a PEG Unit for a particular Drug Unit, Linker, and/or drug-linker compound).

[0704] In one group of embodiments, the PEG Unit comprises one or more linear polyethylene glycol chains each having at 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 some embodiments, the PEG comprises a combined total of at least 8 subunits, at least 10 subunits, or at least 12 subunits. In some such embodiments, the PEG comprises no more than a combined total of about 72 subunits. In some such embodiments, the PEG comprises no more than a combined total of about 36 subunits. In some embodiments, the PEG comprises about 8 to about 24 subunits (referred to as PEG8 to PEG24).

[0705] In another group of embodiments, the PEG Unit comprises a combined total of 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.

[0706] In some embodiments, illustrative linear PEGs used in any of the embodiments provided herein are as follows:



[0707] wherein the wavy line indicates the site of attachment to the ADC, and each subscript b is independently selected from the group consisting of 7 to 72, 8 to 72, 10 to 72, 12 to 72, 6 to 24, or 8 to 24. In some embodiments, each subscript b is about 8, about 12, or about 24.

[0708] As described herein, in some embodiments, the PEG Unit is selected such that it improves clearance of the resultant ADC but does not significantly impact the ability of the ADC to penetrate into the tumor.

[0709] In some embodiments, the PEG 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; from about 300 daltons to about 1 kilodalton; or any value in between. In some embodiments, the PEG has at least 8, 10 or 12 subunits. In some embodiments, the PEG Unit is PEG8 to PEG72, for example, PEG8, PEG10, PEG12, PEG16, PEG20, PEG24, PEG28, PEG32, PEG36, PEG48, or PEG72.

[0710] In some embodiments, apart from the PEGylation of the ADC, there are no other PEG subunits present in the ADC (i.e., no PEG subunits are present as part of any of the other components of the conjugates and linkers provided

herein, such as A and X^B). In some embodiments, apart from the PEG, there are no more than 8, no more than 7, no more than 6, no more than 5, no more than 4, no more than 3, no more than 2 or no more than 1 other polyethylene glycol (—CH₂CH₂O—) subunits present in the ADC, or intermediate thereof (i.e., no more than 8, 7, 6, 5, 4, 3, 2, or 1 other polyethylene glycol subunits in other components of the ADCs (or intermediates thereof) provided herein).

[0711] It will be appreciated that when referring to polyethylene glycol subunits of a PEG Unit, and depending on context, the number of subunits can represent an average number, e.g., when referring to a population of ADCs or intermediates thereto and/or using polydisperse PEGs.

Methods of Use

[0712] In some embodiments, the ADCs or ADC compositions described herein, or pharmaceutically acceptable salts thereof, are used to deliver the conjugated drug to a target cell. Without being bound by theory, in some embodiments, an ADC associates with an antigen on the surface of a target cell. The Drug Unit can then be released as free drug to induce its biological effect (such as an immunostimulatory effect). The Drug Unit can also remain attached to the antibody, or a portion of the antibody and/or linker, and induce its biological effect.

[0713] Some embodiments provide a method of treating cancer in a subject in need thereof, comprising administering a therapeutically effective amount of an ADC or ADC composition described herein, or a pharmaceutically acceptable salt thereof, to the subject.

[0714] Some embodiments provide a method of treating cancer in a subject in need thereof, comprising administering a therapeutically effective amount of a composition comprising an ADC or ADC composition described herein, or a pharmaceutically acceptable salt thereof, to the subject.

[0715] Some embodiments provide a method of inducing an anti-tumor immune response in a subject in need thereof, comprising administering a therapeutically effective amount of a composition comprising an ADC or ADC composition described herein, or a pharmaceutically acceptable salt thereof, to the subject.

[0716] Some embodiments provide a method of inducing an anti-tumor immune response in a subject in need thereof, comprising administering a therapeutically effective amount of an ADC or ADC composition described herein, or a pharmaceutically acceptable salt thereof, to the subject.

[0717] Some embodiments provide a method of treating cancer in a subject in need thereof, comprising administering a therapeutically effective amount of an ADC or ADC composition as described herein, or a pharmaceutically acceptable salt thereof, to the subject in combination with another anticancer therapy (e.g., surgery and radiation therapy) and/or anticancer agent (e.g., an immunotherapy such as nivolumab or pembrolizumab). In some embodiments, the ADCs or ADC compositions described herein is administered before, during, or after administration of the anticancer therapy and/or anticancer agent to the subject. In some embodiments, the ADCs or ADC compositions described herein is administered to the subject following treatment with radiation and/or after surgery.

[0718] Some embodiments provide a method for delaying or preventing acquired resistance to an anticancer agent, comprising administering a therapeutically effective amount of an ADC as described herein, or a pharmaceutically acceptable salt thereof, to a patient at risk for developing or having acquired resistance to an anticancer agent. In some embodiments, the patient is administered a dose of the anticancer agent (e.g., at substantially the same time as a dose of an ADC or ADC composition as described herein, or a pharmaceutically acceptable salt thereof) is administered to the patient).

[0719] Some embodiments provide a method of delaying and/or preventing development of cancer resistant to an anticancer agent in a subject, comprising administering to the subject a therapeutically effective amount of an ADC or ADC composition as described herein, or a pharmaceutically acceptable salt thereof, before, during, or after administration of a therapeutically effective amount of the anti-cancer agent.

[0720] The ADCs and/or ADC compositions described herein are useful for inhibiting the multiplication of a cancer cell, causing apoptosis in a cancer cell, for increasing phagocytosis of a cancer cell, and/or for treating cancer in a subject in need thereof. In some embodiments, the ADCs or ADC compositions are used accordingly in a variety of settings for the treatment of cancers. In some embodiments, the ADCs or ADC compositions are used to deliver a drug to a cancer cell. Without being bound by theory, in some embodiments, the antibody of an ADC binds to or associates with a cancer-cell-associated antigen. In some embodiments, the antigen is attached to a cancer cell or an extracellular matrix protein associated with the cancer cell. In some embodiments, the drug is released in proximity to the cancer cell, thus recruiting/activating immune cells to attack the cancer cell. In some embodiments, the Drug Unit is cleaved from the ADC outside the cancer cell. In some embodiments, the Drug Unit remains attached to the antibody bound to the antigen.

[0721] In some embodiments, the antibody binds to the cancer cell. In some embodiments, the antibody binds to a cancer cell antigen which is on the surface of the cancer cell. In some embodiments, the antibody binds to a cancer cell antigen which is an extracellular matrix protein associated with the tumor cell or cancer cell. In some embodiments, the antibody of an ADC binds to or associates with a cancer-associated cell or an antigen on a cancer-associated cell. In some embodiments, the cancer-associated cell is a stromal cell in a tumor, for example, a cancer-associated fibroblast (CAF).

[0722] In some embodiments, the antibody of an ADC binds to or associates with an immune cell or an immune-cell-associated antigen. In some embodiments, the antigen is attached to an immune cell or is an extracellular matrix protein associated with the immune cell. In some embodiments, the drug is released in proximity to the immune cell, thus recruiting/activating the immune cell to attack a cancer cell. In some embodiments, the Drug Unit is cleaved from the ADC outside the immune cell. In some embodiments, the Drug Unit remains attached to the antibody bound to the antigen. In some embodiments, the immune cell is a lymphocyte, an antigen-presenting cell, a natural killer (NK) cell, a neutrophil, an eosinophil, a basophil, a mast cell, innate lymphoid cells or a combination of any of the foregoing. In some embodiments, the immune cell is selected from the group consisting of B cells, plasma cells, T cells, NKT cells, gamma delta T (76T) cells, monocytes, macrophages, dendritic cells, natural killer (NK) cells, neu-

trophils, eosinophils, basophils, mast cells, innate lymphoid cells and a combination of any of the foregoing.

[0723] The specificity of the antibody for a particular cancer cell can be important for determining those tumors or cancers that are most effectively treated. For example, ADCs that target a cancer cell antigen present on hematopoietic cancer cells in some embodiments treat hematologic malignancies. In some embodiments, ADCs target a cancer cell antigen present on abnormal cells of solid tumors for treating such solid tumors. In some embodiments an ADC are directed against abnormal cells of hematopoietic cancers such as, for example, lymphomas (Hodgkin Lymphoma and Non-Hodgkin Lymphomas) and leukemias.

[0724] Cancers, including, but not limited to, a tumor, metastasis, or other disease or disorder characterized by abnormal cells that are characterized by uncontrolled cell growth in some embodiments are treated or inhibited by administration of an ADC or ADC composition.

[0725] In some embodiments, the subject has previously undergone treatment for the cancer. In some embodiments, the prior treatment is surgery, radiation therapy, administration of one or more anticancer agents, or a combination of any of the foregoing.

[0726] In any of the methods described herein, the cancer is selected from the group consisting of: adenocarcinoma, adrenal gland cortical carcinoma, adrenal gland neuroblastoma, anus squamous cell carcinoma, appendix adenocarcinoma, bladder urothelial carcinoma, bile duct adenocarcinoma, bladder carcinoma, bladder urothelial carcinoma, bone chordoma, bone marrow leukemia lymphocytic chronic, bone marrow leukemia non-lymphocytic acute myelocytic, bone marrow lymph proliferative disease, bone marrow multiple myeloma, bone sarcoma, brain astrocytoma, brain glioblastoma, brain medulloblastoma, brain meningioma, brain oligodendrogloma, breast adenoid cystic carcinoma, breast carcinoma, breast ductal carcinoma *in situ*, breast invasive ductal carcinoma, breast invasive lobular carcinoma, breast metaplastic carcinoma, cervix neuroendocrine carcinoma, cervix squamous cell carcinoma, colon adenocarcinoma, colon carcinoid tumor, duodenum adenocarcinoma, endometrioid tumor, esophagus adenocarcinoma, esophagus and stomach carcinoma, eye intraocular melanoma, eye intraocular squamous cell carcinoma, eye lacrimal duct carcinoma, fallopian tube serous carcinoma, gallbladder adenocarcinoma, gallbladder *glomus* tumor, gasteresophageal junction adenocarcinoma, head and neck adenoid cystic carcinoma, head and neck carcinoma, head and neck neuroblastoma, head and neck squamous cell carcinoma, kidney chromophore carcinoma, kidney medullary carcinoma, kidney renal cell carcinoma, kidney renal papillary carcinoma, kidney sarcomatoid carcinoma, kidney urothelial carcinoma, kidney carcinoma, leukemia lymphocytic, leukemia lymphocytic chronic, liver cholangiocarcinoma, liver hepatocellular carcinoma, liver carcinoma, lung adenocarcinoma, lung adenosquamous carcinoma, lung atypical carcinoid, lung carcinosarcoma, lung large cell neuroendocrine carcinoma, lung non-small cell lung carcinoma, lung sarcoma, lung sarcomatoid carcinoma, lung small cell carcinoma, lung small cell undifferentiated carcinoma, lung squamous cell carcinoma, upper aerodigestive tract squamous cell carcinoma, upper aerodigestive tract carcinoma, lymph node lymphoma diffuse large B cell, lymph node lymphoma follicular lymphoma, lymph node lymphoma mediastinal B-cell, lymph node lymphoma

plasmablastic lung adenocarcinoma, lymphoma follicular lymphoma, lymphoma, non-Hodgkins, nasopharynx and paranasal sinuses undifferentiated carcinoma, ovary carcinoma, ovary carcinosarcoma, ovary clear cell carcinoma, ovary epithelial carcinoma, ovary granulosa cell tumor, ovary serous carcinoma, pancreas carcinoma, pancreas ductal adenocarcinoma, pancreas neuroendocrine carcinoma, peritoneum mesothelioma, peritoneum serous carcinoma, placenta choriocarcinoma, pleura mesothelioma, prostate acinar adenocarcinoma, prostate carcinoma, rectum adenocarcinoma, rectum squamous cell carcinoma, skin adnexal carcinoma, skin basal cell carcinoma, skin melanoma, skin Merkel cell carcinoma, skin squamous cell carcinoma, small intestine adenocarcinoma, small intestine gastrointestinal stromal tumors (GTSTs), large intestine/colon carcinoma, large intestine adenocarcinoma, soft tissue angiosarcoma, soft tissue Ewing sarcoma, soft tissue hemangioendothelioma, soft tissue inflammatory myofibroblastic tumor, soft tissue leiomyosarcoma, soft tissue liposarcoma, soft tissue neuroblastoma, soft tissue paraganglioma, soft tissue perivascular epithelioid cell tumor, soft tissue sarcoma, soft tissue synovial sarcoma, stomach adenocarcinoma, stomach adenocarcinoma diffuse-type, stomach adenocarcinoma intestinal type, stomach adenocarcinoma intestinal type, stomach leiomyosarcoma, thymus carcinoma, thymus thymoma lymphocytic, thyroid papillary carcinoma, unknown primary adenocarcinoma, unknown primary carcinoma, unknown primary malignant neoplasm, lymphoid neoplasm, unknown primary melanoma, unknown primary sarcomatoid carcinoma, unknown primary squamous cell carcinoma, unknown undifferentiated neuroendocrine carcinoma, unknown primary undifferentiated small cell carcinoma, uterus carcinosarcoma, uterus endometrial adenocarcinoma, uterus endometrial adenocarcinoma endometrioid, uterus endometrial adenocarcinoma papillary serous, and uterus leiomyosarcoma.

[0727] In some embodiments, the subject is concurrently administered one or more additional anticancer agents with the ADCs or ADC compositions described herein, or a pharmaceutically acceptable salt thereof. In some embodiments, the subject is concurrently receiving radiation therapy with the ADCs or ADC compositions described herein, or a pharmaceutically acceptable salt thereof. In some embodiments, the subject is administered one or more additional anticancer agents after administration of the ADCs or ADC compositions described herein, or a pharmaceutically acceptable salt thereof. In some embodiments, the subject receives radiation therapy after administration of the ADCs or ADC compositions described herein, or a pharmaceutically acceptable salt thereof.

[0728] In some embodiments, the subject has discontinued a prior therapy, for example, due to unacceptable or unbearable side effects, wherein the prior therapy was too toxic, or wherein the subject developed resistance to the prior therapy.

[0729] Some embodiments provide a method for delaying or preventing a disease or disorder, comprising administering a therapeutically effective amount of an ADC or ADC composition as described herein, or a pharmaceutically acceptable salt thereof, and a vaccine against the disease or disorder, to a patient at risk for developing the disease or disorder. In some embodiments, the disease or disorder is cancer, as described herein. In some embodiments, the disease or disorder is a viral pathogen. In some embodi-

ments, the vaccine is administered subcutaneously. In some embodiments, the vaccine is administered intramuscularly. In some embodiments, the ADC or ADC composition and the vaccine are administered via the same route (for example, the ADC and the vaccine are both administered subcutaneously). In some embodiments, the ADC or ADC composition, or a pharmaceutically acceptable salt thereof, and the vaccine are administered via different routes. In some embodiments, the vaccine and the ADC or ADC composition, or a pharmaceutically acceptable salt thereof, are provided in a single formulation. In some embodiments, the vaccine and the ADC or ADC composition, or a pharmaceutically acceptable salt thereof, are provided in separate formulations.

Compositions and Methods of Administration

[0730] Some embodiments provide a composition comprising a distribution of ADCs, as described herein (i.e., an ADC composition). In some embodiments, the composition comprises a distribution of ADCs, as described herein and at least one pharmaceutically acceptable carrier. In some embodiments, the route of administration is parenteral. Parenteral administration includes subcutaneous injections, intravenous, intramuscular, intrasternal injection or infusion techniques. In some embodiments, the compositions are administered parenterally. In one of those embodiments, the ADCs are administered intravenously. Administration is typically through any convenient route, for example by infusion or bolus injection.

[0731] Compositions of an ADC are formulated so as to allow the ADC to be bioavailable upon administration of the composition to a subject. In some embodiments, compositions are in the form of one or more injectable dosage units.

[0732] In some embodiments, materials used in preparing the compositions are 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 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.

[0733] In some embodiments, the ADC composition is a solid, for example, as a lyophilized powder, suitable for reconstitution into a liquid prior to administration. In some embodiments, the ADC composition is a liquid composition, such as a solution or a suspension. A liquid composition or suspension is useful for delivery by injection and a lyophilized solid is suitable for reconstitution as a liquid or suspension using a diluent suitable for injection. In a composition administered by injection, one or more of a surfactant, preservative, wetting agent, dispersing agent, suspending agent, buffer, stabilizer and isotonic agent is typically included.

[0734] In some embodiments, the liquid compositions, whether they are solutions, suspensions or other like form, can also include one or more of the following: sterile diluents such as water for injection, saline solution, 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 ethylenediamine-

netetraacetic 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 typically enclosed in ampoule, a disposable syringe or a multiple-dose vial made of glass, plastic or other material. In some embodiments, the sterile diluent comprises physiological saline. In some embodiments, the sterile diluent is physiological saline. In some embodiments, the composition described herein are liquid injectable compositions that are sterile.

[0735] The amount of the ADC or ADC composition that is effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, which is usually determined by standard clinical techniques. In addition, *in vitro* or *in vivo* assays are sometimes employed to help identify optimal dosage ranges. The precise dose to be employed in the compositions will also depend on the route of parenteral administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each subject's circumstances.

[0736] In some embodiments, the compositions comprise an effective amount of an ADC such that a suitable dosage will be obtained. Typically, this amount is at least about 0.01% of the ADC by weight of the composition.

[0737] In some embodiments, the compositions dosage of an ADC or ADC composition administered to a subject is from about 0.01 mg/kg to about 100 mg/kg, from about 1 to about 100 mg of a per kg or from about 0.1 to about 25 mg/kg of the subject's body weight. In some embodiments, the dosage administered to a subject is about 0.01 mg/kg to about 15 mg/kg of the subject's body weight. In some embodiments, the dosage administered to a subject is about 0.1 mg/kg to about 15 mg/kg of the subject's body weight. In some embodiments, the dosage administered to a subject is about 0.1 mg/kg to about 20 mg/kg of the subject's body weight. In some embodiments, the dosage administered is 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 about 1 mg/kg to about 15 mg/kg of the subject's body weight. In some embodiments, the dosage administered is about 1 mg/kg to about 10 mg/kg of the subject's body weight. In some embodiments, the dosage administered is about 0.1 to about 4 mg/kg, about 0.1 to about 3.2 mg/kg, or about 0.1 to about 2.7 mg/kg of the subject's body weight over a treatment cycle.

[0738] The term "carrier" refers to a diluent, adjuvant or excipient, with which a compound is administered. Such pharmaceutical carriers are liquids. Water is an exemplary carrier when the compounds are administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are also useful as liquid carriers for injectable solutions. Suitable pharmaceutical carriers also include glycerol, propylene, glycol, or ethanol. The present compositions, if desired, will in some embodiments also contain minor amounts of wetting or emulsifying agents, and/or pH buffering agents.

[0739] In some embodiments, the ADCs or ADC compositions are formulated in accordance with routine procedures as a composition adapted for intravenous administration to animals, particularly human beings. Typically, the carriers or vehicles for intravenous administration are sterile isotonic

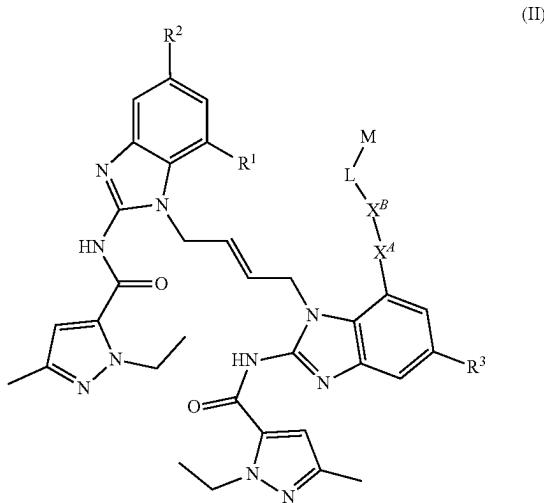
aqueous buffer solutions. In some embodiments, the composition further comprises a local anesthetic, such as lignocaine, to ease pain at the site of the injection. In some embodiments, the ADC or ADC composition and the remainder of the formulation are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where an ADC or ADC composition is to be administered by infusion, it is sometimes dispensed, for example, with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the ADCs or ADC compositions are administered by injection, an ampoule of sterile water for injection or saline is typically provided so that the ingredients can be mixed prior to administration.

[0740] The 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.

Various Embodiments

[0741] Various embodiments disclosed herein include the following:

[0742] 1. A compound of Formula (II):



or a pharmaceutically acceptable salt thereof, wherein:

[0743] R¹ is hydrogen, hydroxyl, C₁₋₆ alkoxy, —(C₁₋₆ alkyl) C₁₋₆ alkoxy, —(CH₂)_n—NR^AR^B, or PEG2 to PEG4;

[0744] each R² and R³ are independently —CO₂H, —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F;

[0745] each R^A, R^B, R^C, R^D, R^E, and R^F are independently hydrogen or C₁₋₃ alkyl;

[0746] each subscript n is independently an integer from 0 to 6;

[0747] each subscript m is independently 0 or 1;

[0748] each subscript q is independently an integer from 0 to 6;

[0749] X^A is —CH₂—, —O—, —S—, —NH—, or —N(CH₃)—;

[0750] X^B is absent or a 2-16 membered heteroalkylene;

[0751] L is a linker having the formula -(A)_a-(W)_w—(Y)_y—, wherein:

[0752] subscript a is 0 or 1;

[0753] subscript y is 0 or 1;

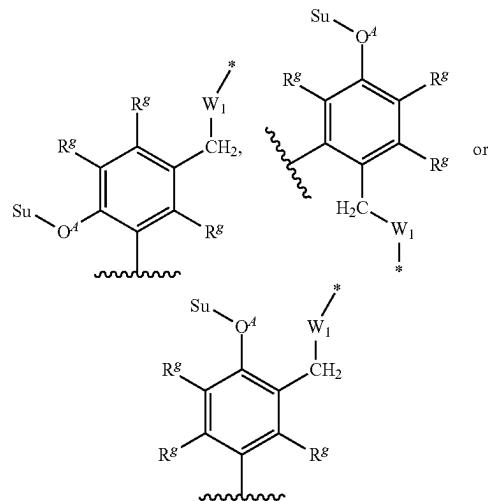
[0754] subscript w is 0 or 1;

[0755] A is a C₂-20 alkylene optionally substituted with 1-3 R^{a1}; or a 2 to 40 membered heteroalkylene optionally substituted with 1-3 R^{b1};

[0756] each R^{a1} is independently selected from the group consisting of: C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, halogen, —OH, —O—, —NR^{d1}R^{e1}, —C(O)NR^{d1}R^{e1}, —C(O)(C₁₋₆ alkyl), and —C(O)O(C₁₋₆ alkyl);

[0757] each R^{b1} is independently selected from the group consisting of: C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, halogen, —OH, —NR^{d1}R^{e1}, —C(O)NR^{d1}R^{e1}, —C(O)(C₁₋₆ alkyl), and —C(O)O(C₁₋₆ alkyl);

[0758] each R^{d1} and R^{e1} are independently hydrogen or C₁₋₃ alkyl; W is from 1-12 amino acids or has the structure:



[0759] wherein Su is a Sugar moiety;

[0760] —O⁴— represents a glycosidic bond;

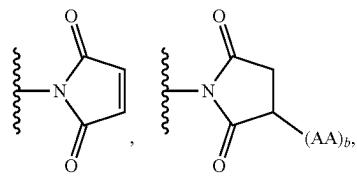
[0761] each R^g is independently hydrogen, halogen, —CN, or —NO₂;

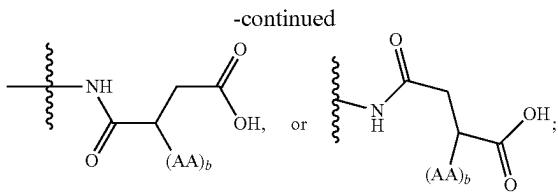
[0762] W¹ is absent or —O—C(=O)—; ~~~~~ represents covalent attachment to A or M;

[0763] * represents covalent attachment to Y, X^A, or X^B; and

[0764] Y is a self-immolative moiety, a non-self-immolative releasable moiety, or a non-cleavable moiety;

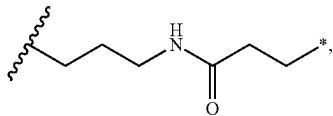
[0765] M is





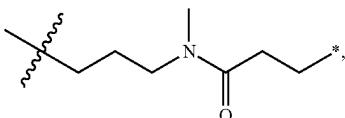
- [0766] each AA is an independently selected amino acid, wherein (AA)_b is connected to the succinimide or hydrolyzed succinimide via a sulfur atom;
- [0767] each subscript b is independently an integer from 1 to 6; and
- [0768] X^B and L are each independently optionally substituted with a PEG Unit from PEG2 to PEG 72.
- [0769] 2. The compound of Embodiment 1, wherein R¹ is hydrogen.
- [0770] 3. The compound of Embodiment 1, wherein R¹ is hydroxyl.
- [0771] 4. The compound of Embodiment 1, wherein R¹ is C₁₋₆ alkoxy.
- [0772] 5. The compound of Embodiment 1 or 4, wherein R¹ is methoxy.
- [0773] 6. The compound of Embodiment 1, wherein R¹ is —(C₁₋₆ alkyl)C₁₋₆ alkoxy.
- [0774] 7. The compound of Embodiment 1 or 6, wherein R¹ is methoxyethyl.
- [0775] 8. The compound of Embodiment 1, wherein R¹ is PEG2 to PEG4.
- [0776] 9. The compound of Embodiment 1, wherein R¹ is —(CH₂)_n—NR⁴R^B.
- [0777] 10. The compound of Embodiment 1 or 9, wherein R^A and R^B are both hydrogen.
- [0778] 11. The compound of Embodiment 1 or 9, wherein R^A and R^B are independently C₁₋₃ alkyl.
- [0779] 12. The compound of Embodiment 1 or 9, wherein one of R^A and R^B is hydrogen and the other of R^A and R^B is C₁₋₃ alkyl.
- [0780] 13. The compound of any one of Embodiments 1 or 9-12, wherein each subscript n is 0.
- [0781] 14. The compound of any one of Embodiments 1 or 9-12, wherein each subscript n is 1.
- [0782] 15. The compound of any one of Embodiments 1 or 9-12, wherein each subscript n is 2.
- [0783] 16. The compound of any one of Embodiments 1 or 9-12, wherein each subscript n is 3, 4, 5, or 6.
- [0784] 17. The compound of any one of Embodiments 1-16, wherein R² and R³ are independently —CO₂H, —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F; and R² and R³ are the same.
- [0785] 18. The compound of any one of Embodiments 1-16, wherein R² and R³ are independently —C₀₂H, —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F; and R² and R³ are different.
- [0786] 19. The compound of any one of Embodiments 1-18, wherein R² is —(C=O)_m—NR^CR^D.
- [0787] 20. The compound of any one of Embodiments 1-18, wherein R³ is —(C=O)_m—NR^CR^D.
- [0788] 21. The compound of any one of Embodiments 1-20, wherein R^C and R^D are both hydrogen.
- [0789] 22. The compound of any one of Embodiments 1-20, wherein R^C and R^D are each independently C₁₋₃ alkyl.

- [0790] 23. The compound of any one of Embodiments 1-20, wherein one of R^C and R^D is hydrogen and the other of R^C and R^D is C₁₋₃ alkyl.
- [0791] 24. The compound of any one of Embodiments 1-20, wherein each subscript m is 0.
- [0792] 25. The compound of any one of Embodiments 1-20, wherein each subscript m is 1.
- [0793] 26. The compound of any one of Embodiments 1-18, wherein R² is —(CH₂)_q—NR^ER^F.
- [0794] 27. The compound of any one of Embodiments 1-18, wherein R³ is —(CH₂)_q—NR^ER^F.
- [0795] 28. The compound of any one of Embodiments 1-18, 26, or 27, wherein R^E and R^F are both hydrogen.
- [0796] 29. The compound of any one of Embodiments 1-18, 26, or 27, wherein R^E and R^F are each independently C₁₋₃ alkyl.
- [0797] 30. The compound of any one of Embodiments 1-18, 26, or 27, wherein one of R^E and R^F is hydrogen and the other of R^E and R^F is C₁₋₃ alkyl.
- [0798] 31. The compound of any one of Embodiments 1-18, 26, or 27, wherein each subscript q is 0.
- [0799] 32. The compound of any one of Embodiments 1-18, 26, or 27, wherein each subscript q is an integer from 1 to 6.
- [0800] 33. The compound of any one of Embodiments 1-18, wherein R³ is —CO₂H.
- [0801] 34. The compound of any one of Embodiments 1-18, wherein R² is —CO₂H.
- [0802] 35. The compound of any one of Embodiments 1-34, wherein X^A is —CH₂—.
- [0803] 36. The compound of any one of Embodiments 1-34, wherein X^A is —O—.
- [0804] 37. The compound of any one of Embodiments 1-34, wherein X^A is —S—.
- [0805] 38. The compound of any one of Embodiments 1-34, wherein X^A is —NH—.
- [0806] 39. The compound of any one of Embodiments 1-38, wherein X^B is a 2-16 membered heteroalkylene.
- [0807] 40. The compound of any one of Embodiments 1-39, wherein X^B is a 2-12 membered heteroalkylene.
- [0808] 41. The compound of any one of Embodiments 1-40, wherein X^B is a 2-8 membered heteroalkylene.
- [0809] 42. The compound of any one of Embodiments 39-41, wherein the heteroalkylene is branched, having 1-4 methyl groups.
- [0810] 43. The compound of any one of Embodiments 39-42, wherein the heteroalkylene is branched, having 1 or 2 methyl groups.
- [0811] 44. The compound of any one of Embodiments 39-43, wherein the heteroalkylene is substituted with 1-3 fluoro groups.
- [0812] 45. The compound of any one of Embodiments 1-44, wherein X^B comprises one or two nitrogen atoms.
- [0813] 46. The compound of any one of Embodiments 1-45, wherein X^B comprises one or two oxo groups.
- [0814] 47. The compound of any one of Embodiments 1-46, wherein X^B Comprises one nitrogen atom and one oxo group.
- [0815] 48. The compound of any one of Embodiments 1-47, wherein X^B comprises two nitrogen atoms and one oxo group.
- [0816] 49. The compound of any one of Embodiments 1-41 or 45-47, wherein X^B is



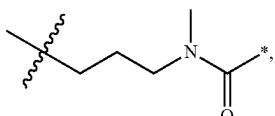
wherein represents covalent attachment to X^A , and * represents covalent attachment to L or M.

[0817] 50. The compound of any one of Embodiments 1-41 or 45-47, wherein X^B



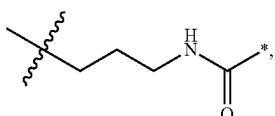
wherein represents covalent attachment to X^A , and * represents covalent attachment to L or M.

[0818] 51. The compound of any one of Embodiments 1-41 or 45-47, wherein X^B is



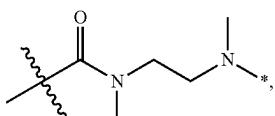
wherein represents covalent attachment to X^A , and * represents covalent attachment to L or M.

[0819] 52. The compound of any one of Embodiments 1-41 or 45-47, wherein X^B is



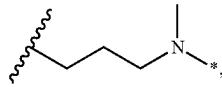
wherein represents covalent attachment to X^A , and * represents covalent attachment to L or M.

[0820] 53. The compound of any one of Embodiments 1-43 or 48, wherein X^B is



wherein represents covalent attachment to X^A , and * represents covalent attachment to L.

[0821] 54. The compound of any one of Embodiments 1-43 or 45, wherein X^B is



wherein represents covalent attachment to X^A , and * represents covalent attachment to L or M.

[0822] 55. The compound of any one of Embodiments 1-38, wherein X^B is absent.

[0823] 56. The compound of any one of Embodiments 1-55, wherein subscript a is 1.

[0824] 57. The compound of any one of Embodiments 1-56, wherein subscript y is 1.

[0825] 58. The compound of any one of Embodiments 1-57, wherein subscript w is 1.

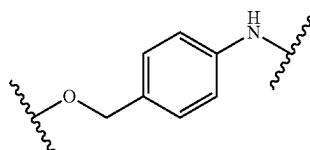
[0826] 59. The compound of any one of Embodiments 1-55, wherein the sum of subscript a, subscript y, and subscript w is 1.

[0827] 60. The compound of any one of Embodiments 1-55, wherein the sum of subscript a, subscript y, and subscript w is 2.

[0828] 61. The compound of any one of Embodiments 1-58, wherein the sum of subscript a, subscript y, and subscript w is 3.

[0829] 62. The compound of any one of Embodiments 1-61, wherein Y is a self-immolative moiety.

[0830] 63. The compound of any one of Embodiments 1-61, wherein Y is



[0831] 64. The compound of any one of Embodiments 1-54 or 56-61, wherein Y is a non-cleavable moiety and a is 0.

[0832] 65. The compound of any one of Embodiments 1-54, 56-61, or 64, wherein Y is a cyclohexanecarboxyl, undecanoyl, caproyl, hexanoyl, butanoyl or propionyl group.

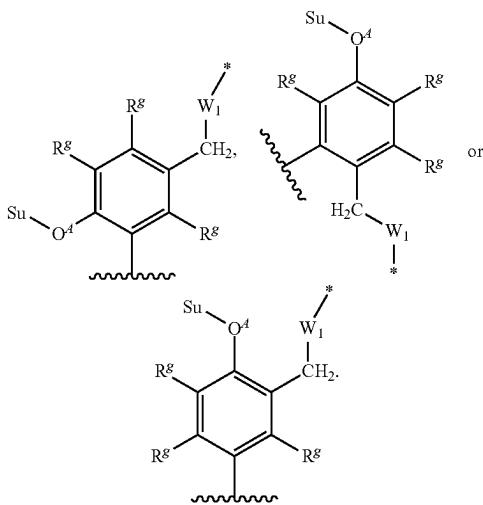
[0833] 66. The compound of any one of Embodiments 1-54, 56-61, or 64, wherein Y is PEG4 to PEG12.

[0834] 67. The compound of any one of Embodiments 1-66, wherein W is from 1-12 amino acids.

[0835] 68. The compound of any one of Embodiments 1-67, wherein W is from 1-6 amino acids.

[0836] 69. The compound of any one of Embodiments 1-68, wherein each amino acid in W is independently selected from the group consisting of alanine, glycine, lysine, serine, aspartic acid, aspartate methyl ester, N,N-dimethyl-lysine, phenylalanine, citrulline, valine-alanine, valine-citrulline, phenylalanine-lysine or homoserine methyl ether.

[0837] 70. The compound of any one of Embodiments 1-66, wherein W has the structure:



[0838] wherein Su is a Sugar moiety;

[0839] —O⁴— represents a glycosidic bond;

[0840] each R⁹ is independently hydrogen, halogen, —CN, or —NO₂;

[0841] W¹ is absent or O—C(=O);

[0842] ~~~~~ represents covalent attachment to A or M; and

[0843] * represents covalent attachment to Y, X^A, or X^B.

[0844] 71. The compound of any one of Embodiments 1-66 or 70, wherein W¹ is —O—C(=O)—.

[0845] 72. The compound of any one of Embodiments 1-66 or 70-71, wherein one R⁹ is halogen, —CN, or —NO₂, and the remaining R⁹ are hydrogen.

[0846] 73. The compound of any one of Embodiments 1-66 or 70-71, wherein each R⁹ is hydrogen.

[0847] 74. The compound of any one of Embodiments 1-73, wherein A is C₂₋₂₀ alkylene optionally substituted with 1-3 R^{a1}

[0848] 75. The compound of any one of Embodiments 1-74, wherein A is C₄₋₁₀ alkylene optionally substituted with 1-3 R^{a1}.

[0849] 76. The compound of any one of Embodiments 1-75, wherein A is C₂₋₂₀ alkylene substituted with R^{a1}.

[0850] 77. The compound of any one of Embodiments 1-76, wherein A is C₄₋₁₀ alkylene substituted with R^{a1}.

[0851] 78. The compound of any one of Embodiments 1-75, wherein A is C₂₋₂₀ alkylene.

[0852] 79. The compound of any one of Embodiments 1-75, wherein A is C₄₋₁₀ alkylene.

[0853] 80. The compound of any one of Embodiments 1-73, wherein A is a 2 to 40 membered heteroalkylene optionally substituted with 1-3 R^{b1}.

[0854] 81. The compound of any one of Embodiments 1-72, wherein A is a 4 to 12 membered heteroalkylene optionally substituted with 1-3 R^{b1}.

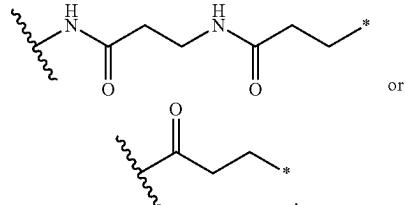
[0855] 82. The compound of any one of Embodiments 1-73 or 80, wherein A is a 2 to 40 membered heteroalkylene optionally substituted with one R^{b1}.

[0856] 83. The compound of any one of Embodiments 1-73 or 80, wherein A is a 4 to 12 membered heteroalkylene optionally substituted with one R^{b1}.

[0857] 84. The compound of any one of Embodiments 1-73 or 80, wherein A is a 2 to 40 membered heteroalkylene.

[0858] 85. The compound of any one of Embodiments 1-73 or 80, wherein A is a 4 to 12 membered heteroalkylene.

[0859] 86. The compound of any one of Embodiments 1-73 or 84-85, wherein A is



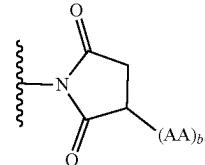
wherein ~~~~~ represents covalent attachment to W, and * represents covalent linkage to M.

[0860] 87. The compound of any one of Embodiments 1-54 or 61-73, wherein subscript a is 0.

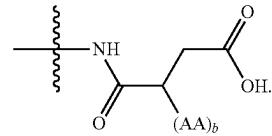
[0861] 88. The compound of any one of Embodiments 1-54 or 67-79, wherein subscript y is 0.

[0862] 89. The compound of any one of Embodiments 1-54, 58-66, or 79-80, wherein subscript w is 0.

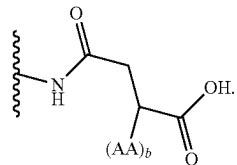
[0863] 90. The compound of any one of Embodiments 1-54, wherein the sum of subscript a, subscript y, and subscript w is 0.



[0864] 91. The compound of any one of Embodiments 1-90, wherein M is



[0865] 92. The compound of any one of Embodiments 1-90, wherein M is



[0866] 93. The compound of any one of Embodiments 1-90, wherein M is b 94. The compound of any one of Embodiments 1-93, wherein each AA is independently a natural amino acid; wherein $(AA)_b$ is connected to the succinimide or hydrolyzed succinimide via a sulfur atom.

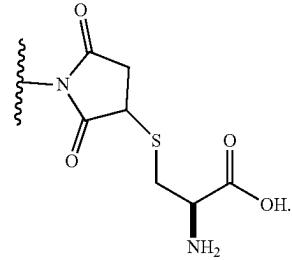
[0867] 95. The compound of any one of Embodiments 1-93, wherein each AA is independently a natural amino acid; wherein $(AA)_b$ is connected to the succinimide or hydrolyzed succinimide via a nitrogen atom.

[0868] 96. The compound of any one of Embodiments 1-95, wherein each subscript b is 1.

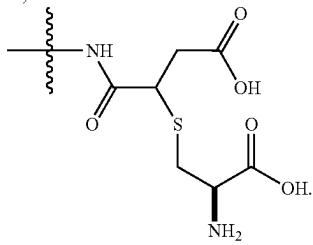
[0869] 97. The compound of any one of Embodiments 1-95, wherein each subscript b is 2.

[0870] 98. The compound of any one of Embodiments 1-95, wherein each subscript b is 3, 4, 5, or 6.

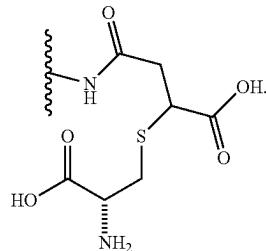
[0871] 99. The compound of any one of Embodiments 1-91, 94, or 96, wherein M is



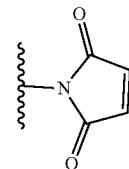
[0872] 100. The compound of any one of Embodiments 1-90, 92, or 96, wherein M is



[0873] 101. The compound of any one of Embodiments 1-90, 93, or 96, wherein M is



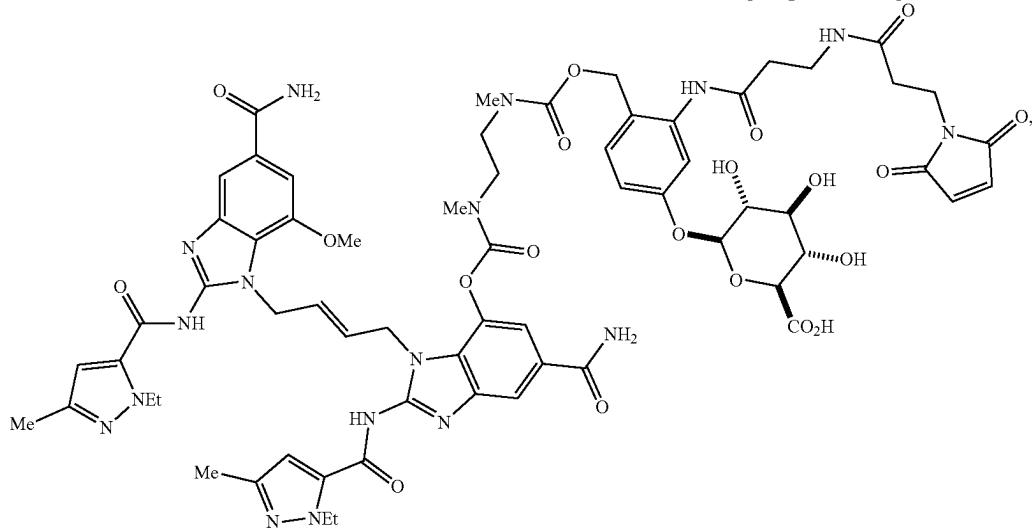
[0874] 102. The compound of any one of Embodiments 1-90, wherein M is



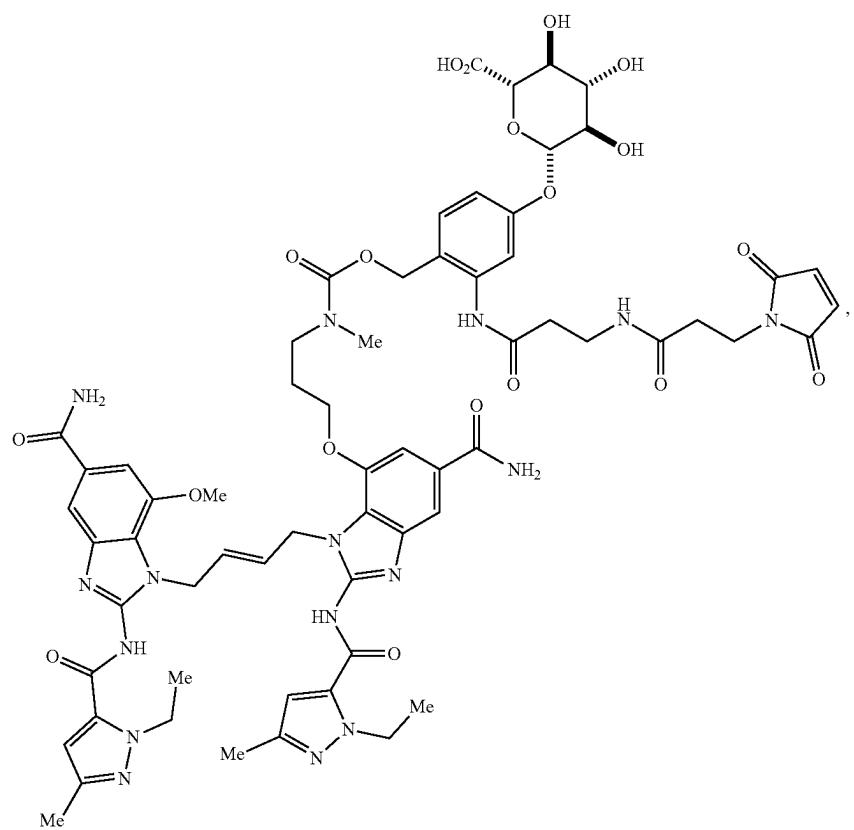
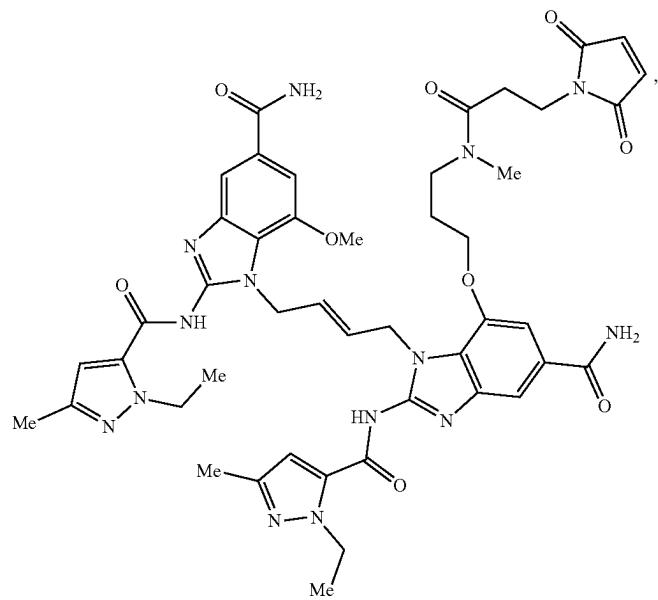
[0875] 103. The compound of any one of Embodiments 1-102, wherein one of X^B and L are substituted with an independently selected PEG Unit from PEG2 to PEG 72.

[0876] 104. The compound of any one of Embodiments 1-102, wherein X^B and L are unsubstituted.

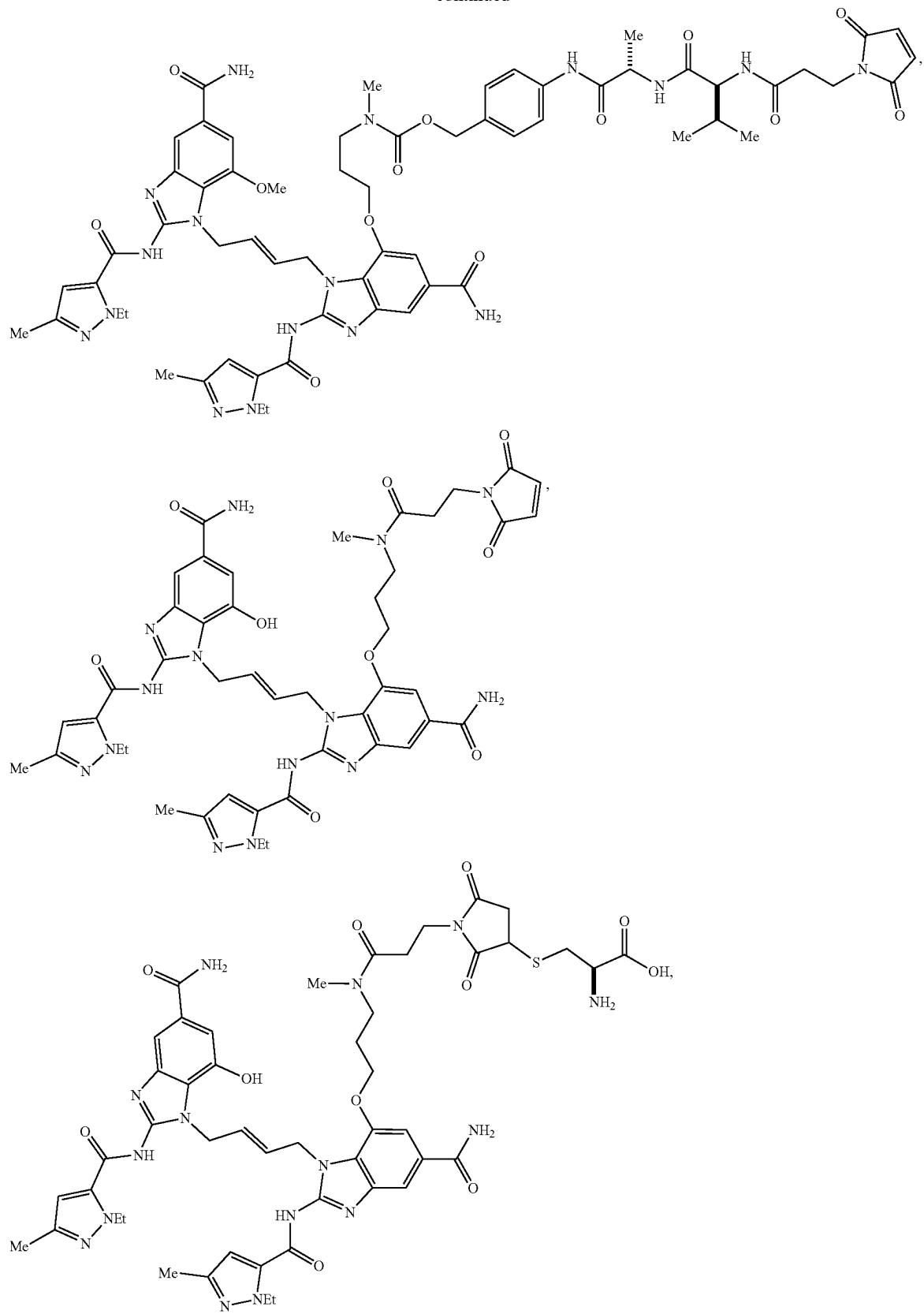
[0877] 105. The compound of Embodiment 1, selected from the group consisting of:



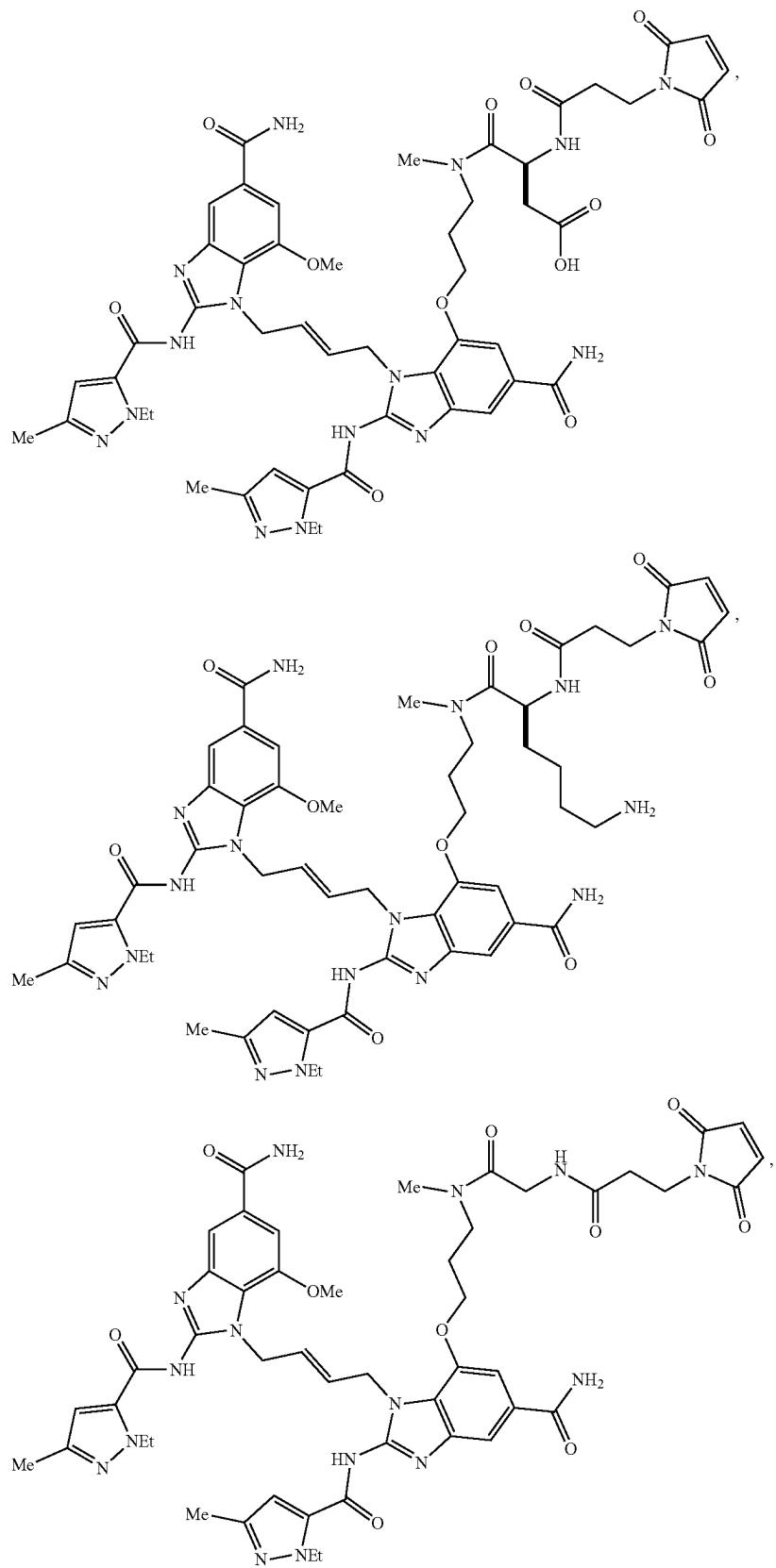
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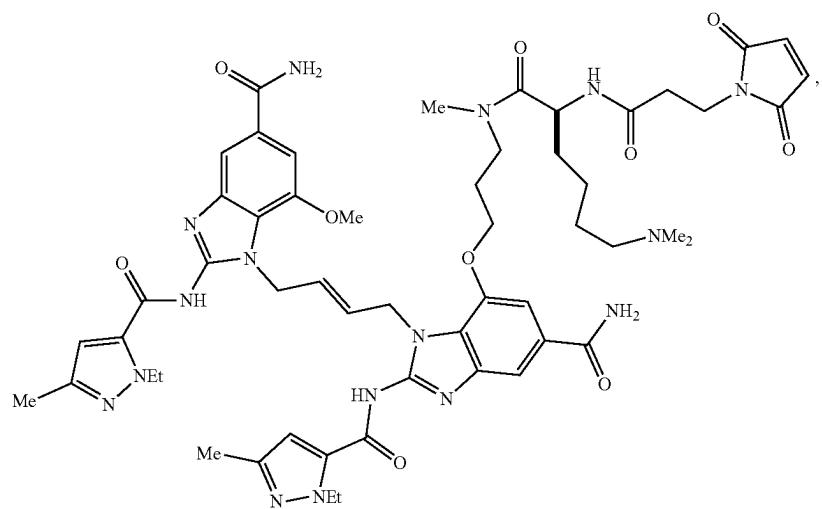
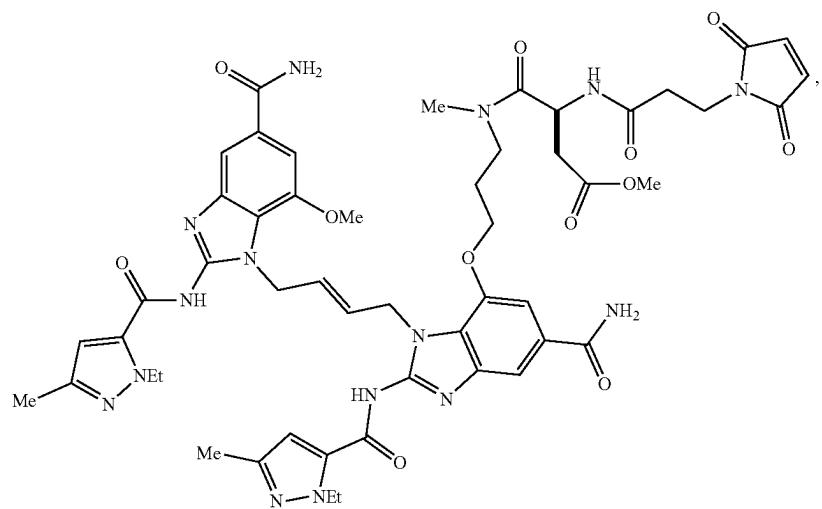
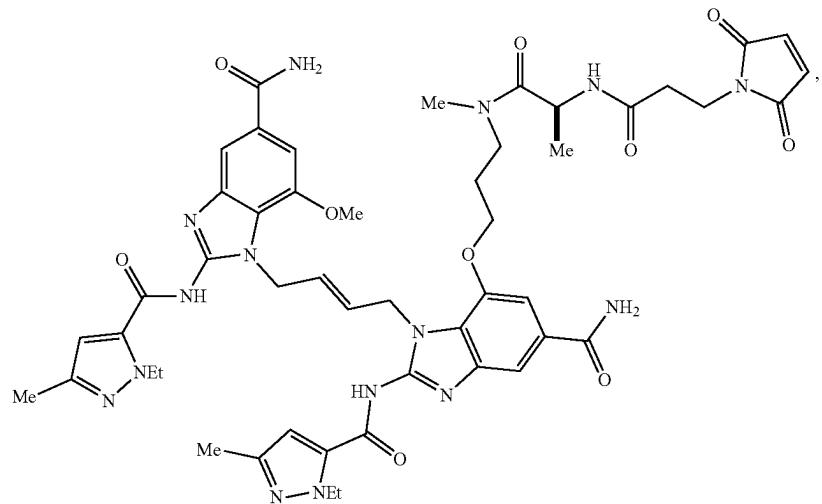
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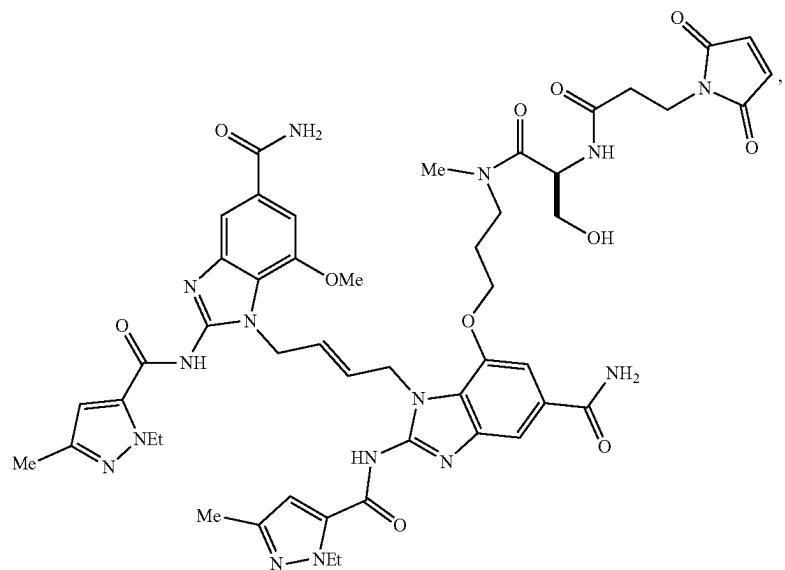
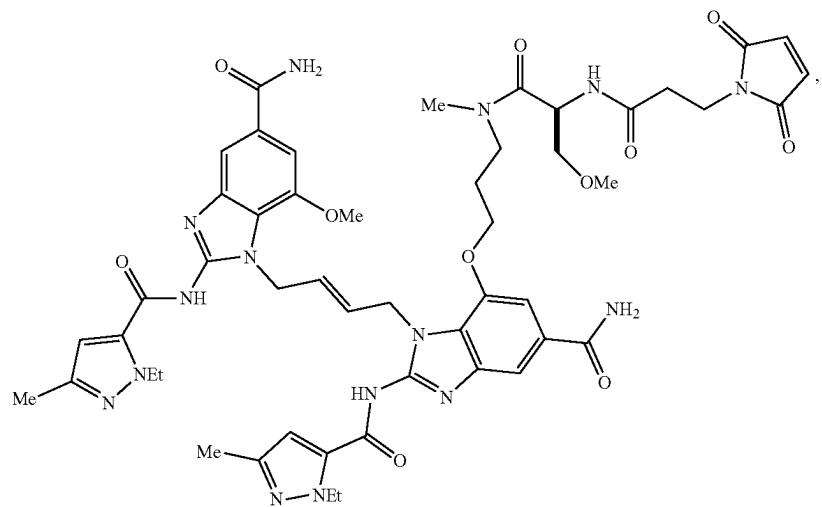
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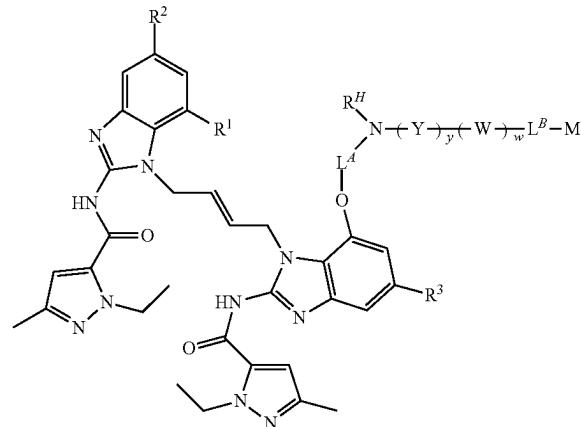
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[0878] and pharmaceutically acceptable salts thereof.

[0879] 106. The compound of Embodiment 1, having the structure of Formula (II-A):

(II-A)



or a pharmaceutically acceptable salt thereof, wherein:

[0880] L^A is $-(CH_2)_{1-6}-$, $-C(O)(CH_2)_{1-6}-$, or $-C(O)NR^H(CH_2)_{1-6}-$;

[0881] each R^H is independently hydrogen or C_{1-3} alkyl;

[0882] Y is

[0887] 108. The compound of Embodiment 106 or 107, wherein L^A is $-(CH_2)_{2-6}-$.

[0888] 109. The compound of Embodiment 106 or 107, wherein L^A is $(CH_2)_3-$.

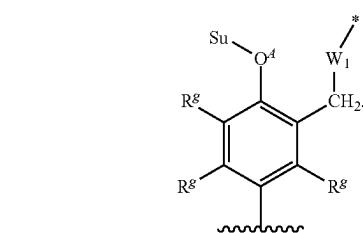
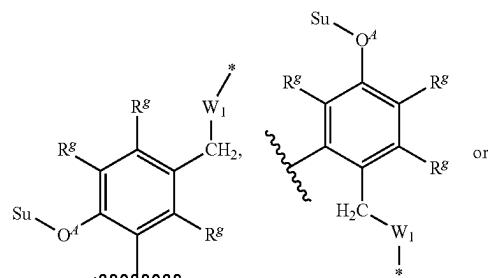
[0889] 110. The compound of any one of Embodiments 106-109, wherein y is 0.

[0890] 111. The compound of any one of Embodiments 106-109, wherein y is 1.

[0891] 112. The compound of any one of Embodiments 106-111, wherein W is a chain of 1-3 amino acids.

[0892] 113. The compound of Embodiment 112, wherein each amino acid of W is independently selected from the group consisting of alanine, valine, isoleucine, leucine, aspartic acid, glutamic acid, lysine, histidine, arginine, glycine, serine, threonine, phenylalanine, O-methylserine, O-methylethylserine, O-methylaspartic acid, O-methylglutamic acid, N-methyllysine, O-methyltyrosine, O-methylhistidine, and O-methylthreonine.

[0893] 114. The compound of any one of Embodiments 106-111, wherein W is:



wherein:

[0894] $\sim\sim\sim$ represents covalent attachment to L^B ; and

[0895] * represents covalent attachment to Y or NR^H .

[0896] 115. The compound of any one of Embodiments 106-114, wherein L^B is $-C(O)(CH_2)_2-$

[0897] 116. The compound of any one of Embodiments 106-114, wherein L^B is $-[NHC(O)(CH_2)_2]-$.

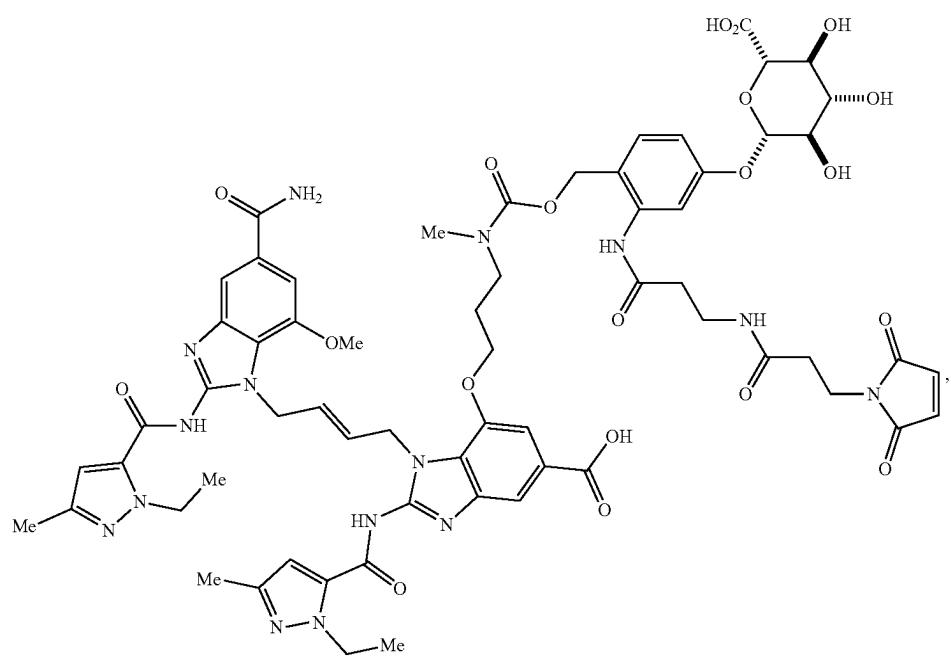
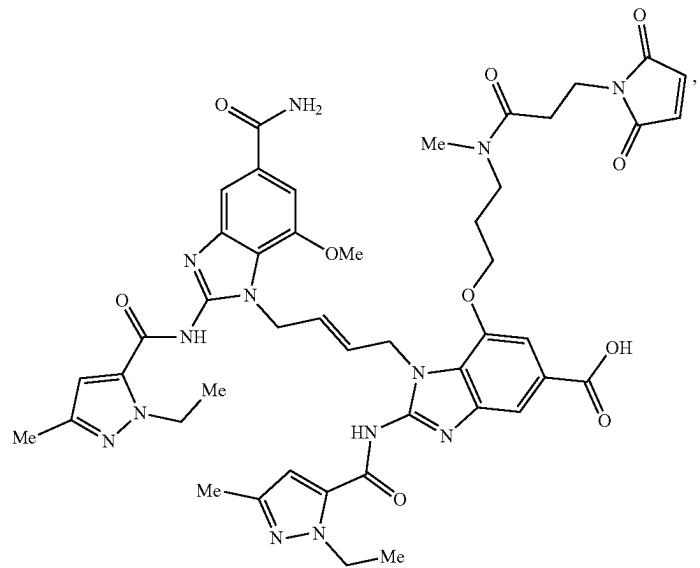
[0883] # represents covalent attachment to $-NR^H L^A$;

[0884] ## represents covalent attachment to W or L^B ; and

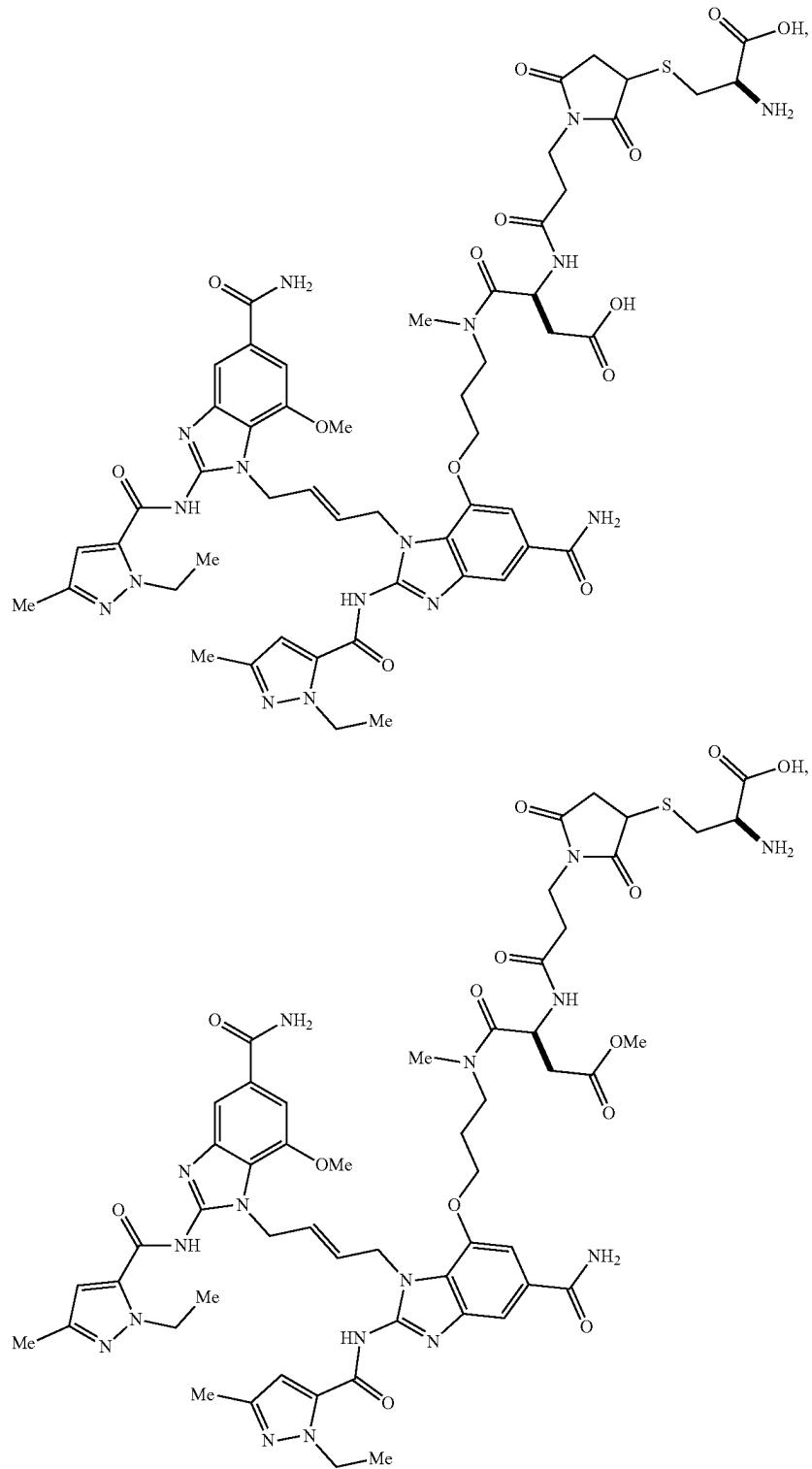
[0885] L^B is $-(CH_2)_{1-6}-$, $-C(O)(CH_2)_{1-6}-$, or $-[NHC(O)(CH_2)_{1-4}]_1-3-$.

[0886] 107. The compound of Embodiment 106, wherein R^H is methyl.

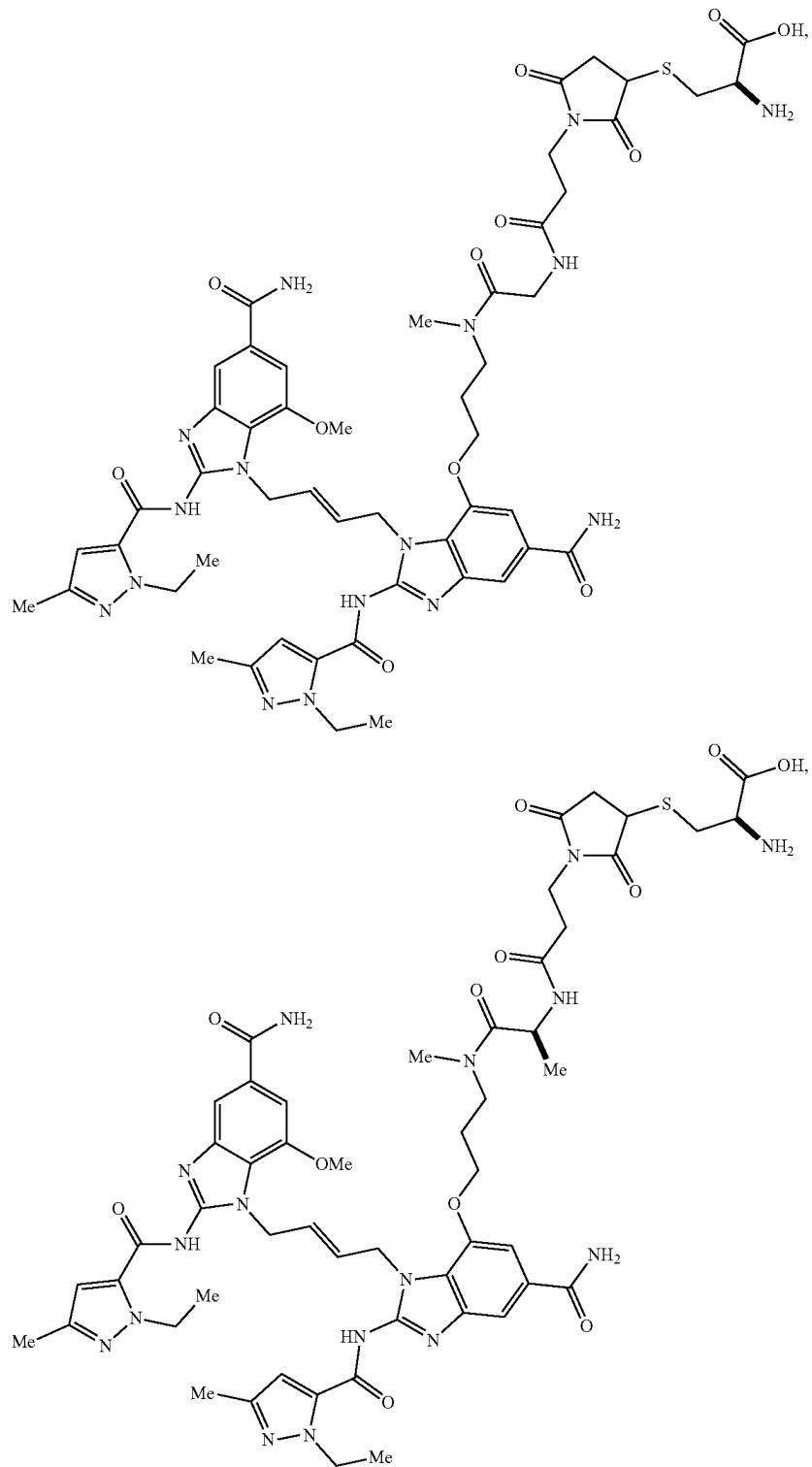
[0898] 117. The compound of Embodiment 106,
selected from the group consisting of:



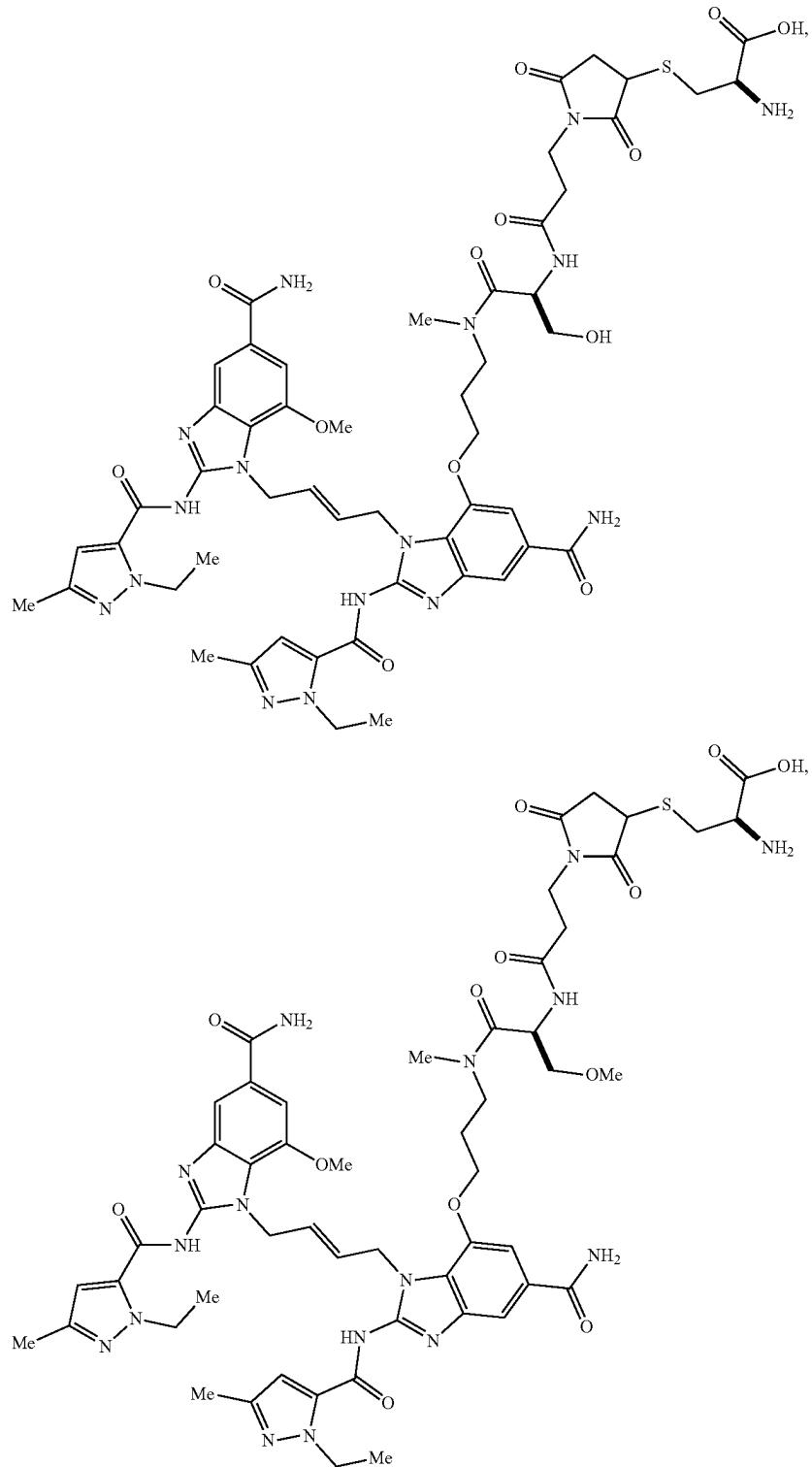
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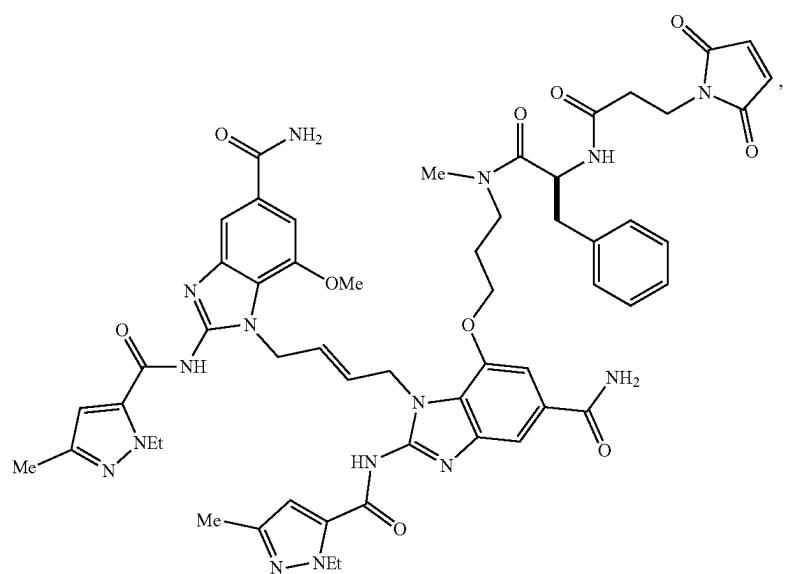
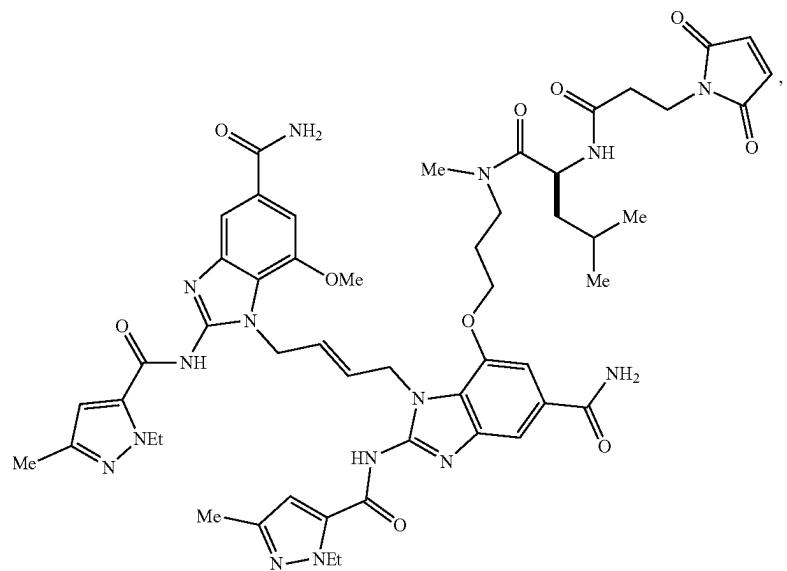
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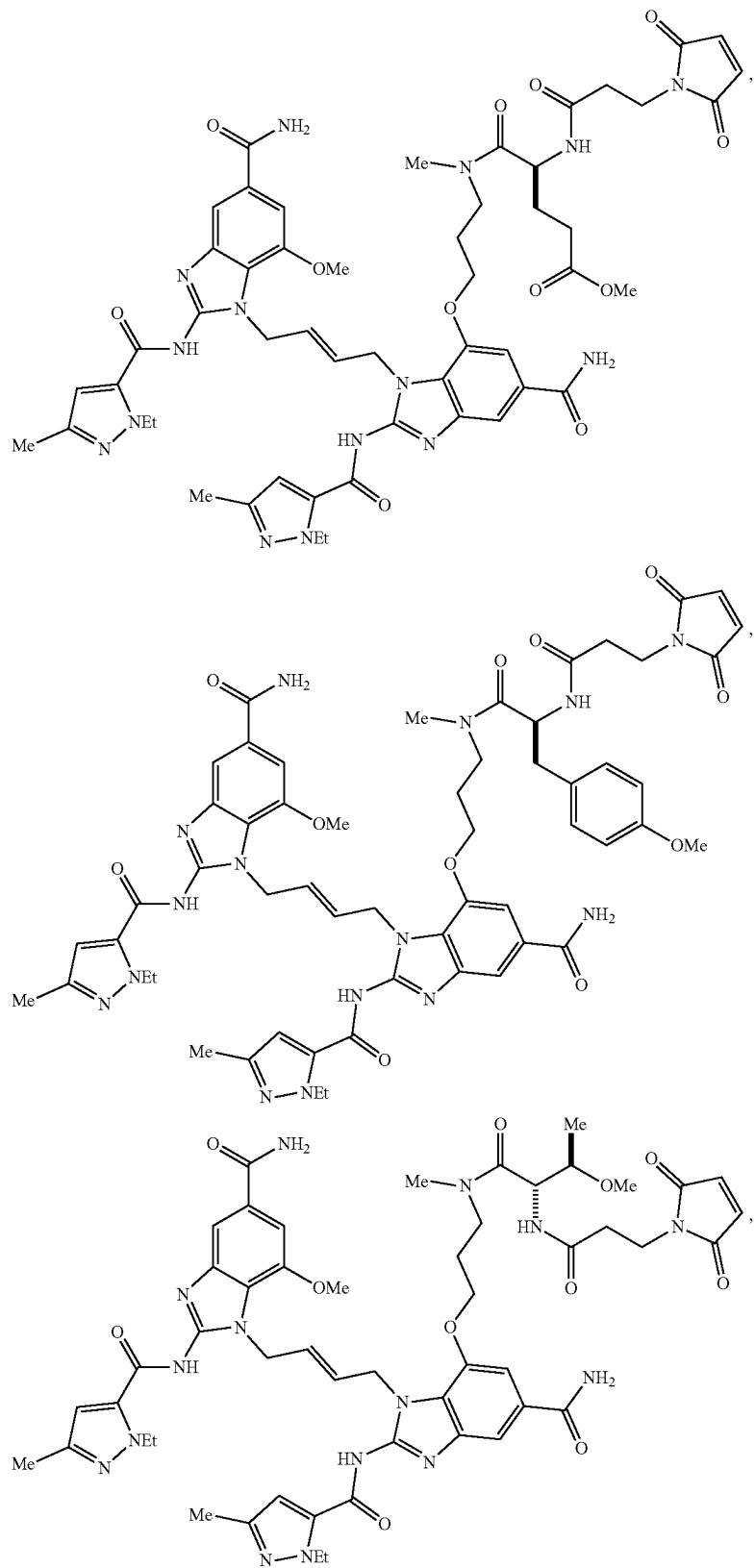
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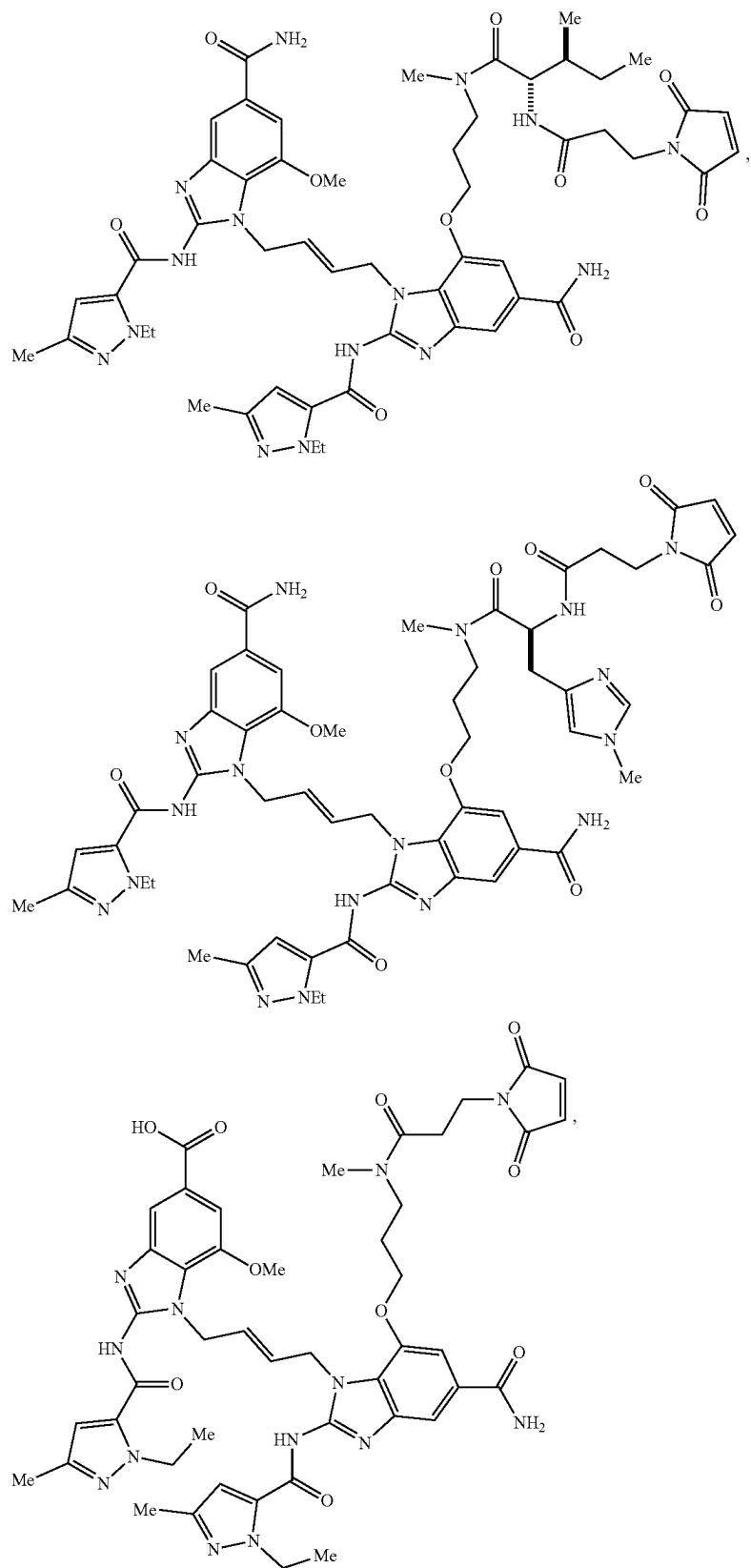
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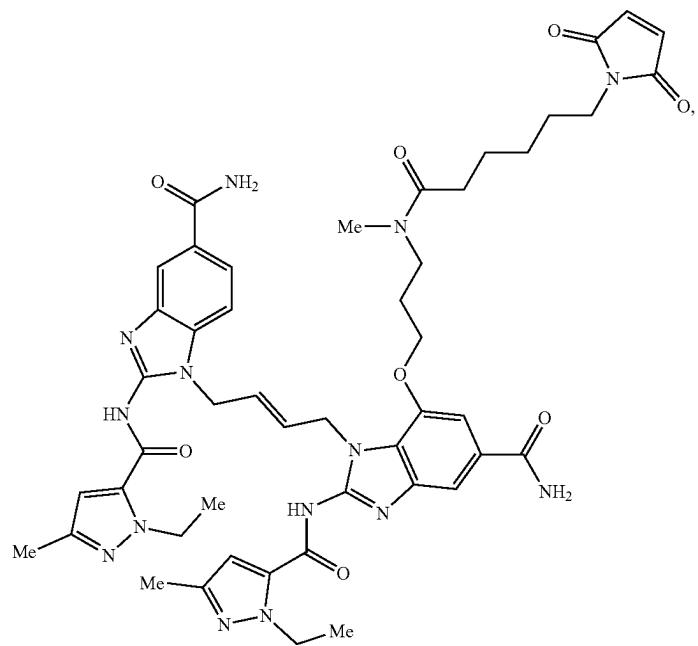
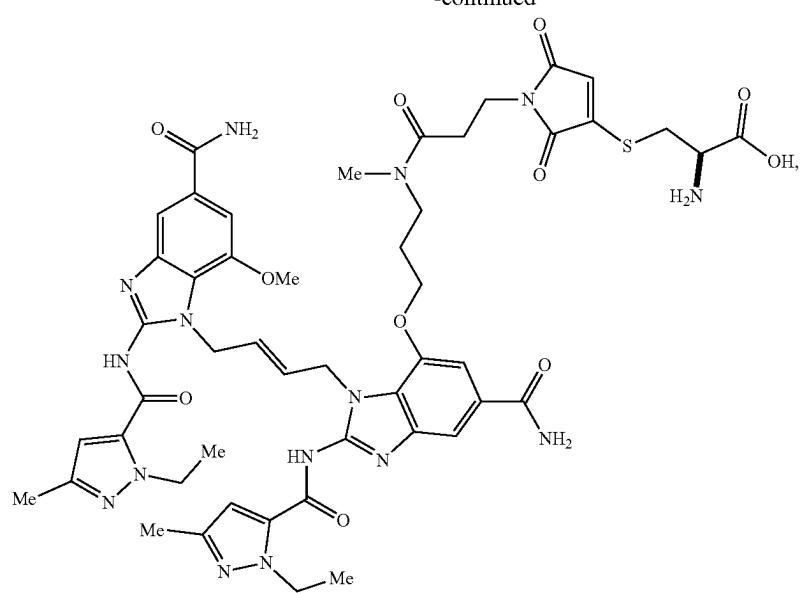
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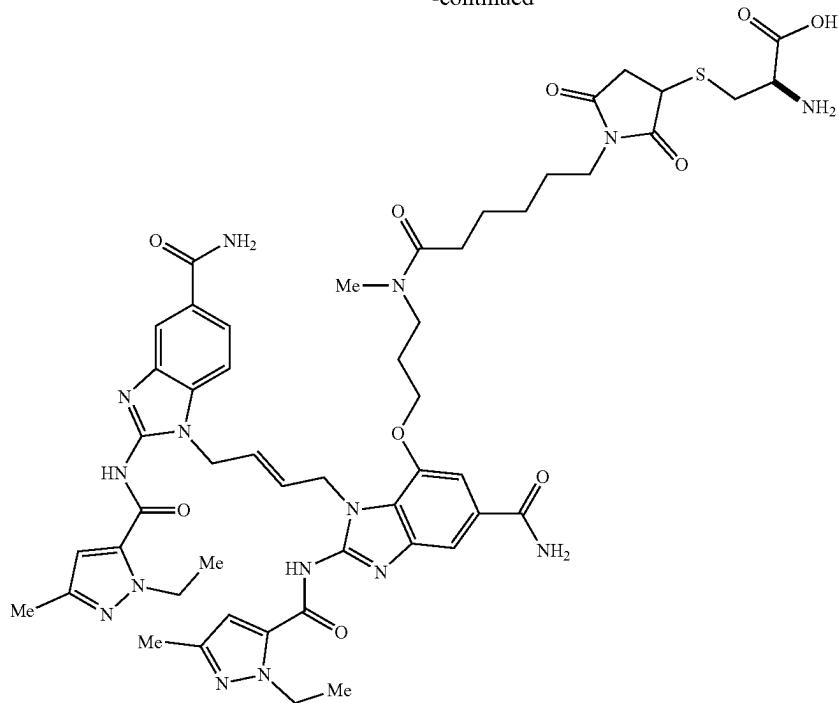
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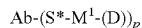


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and pharmaceutically acceptable salts thereof.

[0899] 118. An antibody-drug conjugate (ADC) having the formula:



wherein:

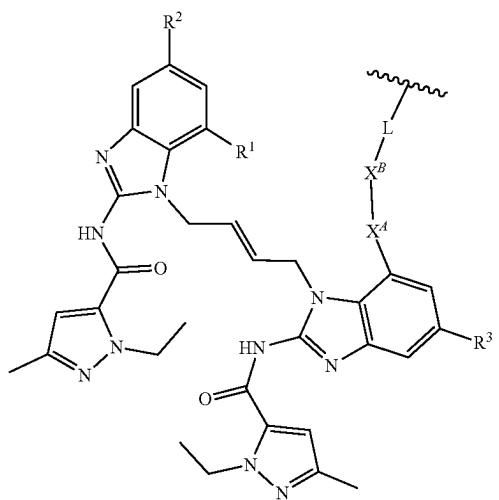
[0900] Ab is an antibody;

[0901] each S* is a sulfur atom from a cysteine residue of the antibody;

[0902] M¹ is a succinimide or a hydrolyzed succinimide;

[0903] subscript p is an integer from 2 to 8; and

[0904] each (D) is a Drug-Linker Unit of Formula (I):



[0905] wherein:

[0906] ~~~~~ represents covalent attachment of L to M¹;

[0907] R¹ is hydrogen, hydroxyl, C₁₋₆ alkoxy, —(C₁₋₆ alkyl)C₁₋₆ alkoxy, —(CH₂)_n—NR⁴R^B, or PEG2 to PEG4;

[0908] R² and R³ are independently —CO₂H, —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F;

[0909] each R⁴, R^B, R^C, R^D, R^E, and R^F are independently hydrogen or C₁₋₃ alkyl;

[0910] each subscript n is independently an integer from 0 to 6;

[0911] each subscript m is independently 0 or 1;

[0912] each subscript q is an integer from 0 to 6;

[0913] X^A is —CH₂—, —O—, —S—, —NH—, or —N(CH₃)—;

[0914] X^R is absent or a 2-16 membered heteroalkylene;

[0915] L has the formula -(A)_a-(W)_w—(Y)_y—, wherein:

[0916] subscript a is 0 or 1;

[0917] subscript y is 0 or 1;

[0918] subscript w is 0 or 1;

[0919] A is a C₂₋₂₀ alkylene optionally substituted with 1-3 R^{a1}; or a 2 to 40 membered heteroalkylene optionally substituted with 1-3 R^{b1};

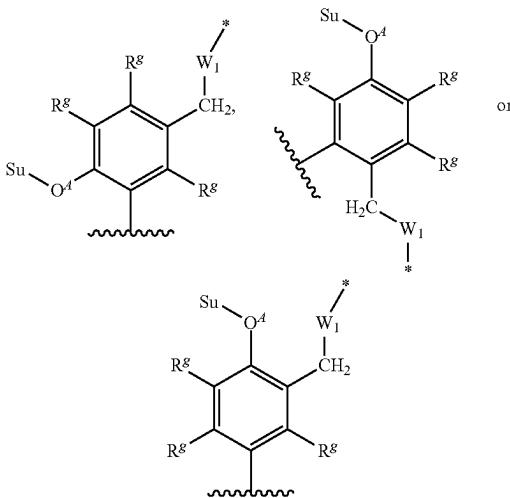
[0920] each R^{a1} is independently selected from the group consisting of: C₁ 6 alkyl, C₁ 6 haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, halogen, —OH, =O, —NR^{d1}R^{e1}, —C(O)NR^{a1}R^{e1}, —C(O)(C₁₋₆ alkyl), and —C(O)O(C₁₋₆ alkyl);

[0921] each R^{b1} is independently selected from the group consisting of: C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆

alkoxy, C_{1-6} haloalkoxy, halogen, —OH, —NR^{d1}R^{e1}, —C(O)NR^{d1}R^{e1}, —C(O)(C₁₋₆ alkyl), and —C(O)O(C₁₋₆ alkyl);

[0922] each R^{d1} and R^{e1} are independently hydrogen or C₁₋₃ alkyl;

[0923] W is from 1-12 amino acids or has the structure:



[0924] wherein Su is a Sugar moiety;

[0925] —O⁴— represents a glycosidic bond;

[0926] each R⁹ is independently hydrogen, halogen, —CN, or —NO₂;

[0927] W¹ is absent or —O—C(=O)—;

[0928] ~~~~~ represents covalent attachment to A or M¹;

[0929] * represents covalent attachment to Y, X¹, or X⁴.

[0930] Y is self-immolative moiety, a non-self-immolative releasable moiety, or a non-cleavable moiety; and

[0931] X^B and L are each independently optionally substituted with a PEG Unit from PEG2 to PEG 72.

[0932] 119. The ADC of Embodiment 118, wherein R¹ is hydrogen.

[0933] 120. The ADC of Embodiment 118, wherein R¹ is hydroxyl.

[0934] 121. The ADC of Embodiment 118, wherein R¹ is C₁₋₆ alkoxy.

[0935] 122. The ADC of Embodiment 118 or 121, wherein R¹ is methoxy.

[0936] 123. The ADC of Embodiment 118, wherein R¹ is —(C₁₋₆ alkyl)C₁₋₆ alkoxy.

[0937] 124. The ADC of Embodiment 118 or 123, wherein R¹ is methoxyethyl.

[0938] 125. The ADC of Embodiment 118, wherein R¹ is PEG2 to PEG4.

[0939] 126. The ADC of Embodiment 118, wherein R¹ is —(CH₂)_n—NR^AR^B.

[0940] 127. The ADC of Embodiment 118 or 126, wherein R^A and R^B are both hydrogen.

[0941] 128. The ADC of Embodiment 118 or 126, wherein R^A and R^B are independently C₁₋₃ alkyl.

[0942] 129. The ADC of Embodiment 118 or 126, wherein one of R^A and R^B is hydrogen and the other of R^A and R^B is C₁₋₃ alkyl.

[0943] 130. The ADC of any one of Embodiments 118 or 126-129, wherein each subscript n is 0.

[0944] 131. The ADC of any one of Embodiments 118 or 126-129, wherein each subscript n is 1.

[0945] 132. The ADC of any one of Embodiments 118 or 126-129, wherein each subscript n is 2.

[0946] 133. The ADC of any one of Embodiments 118 or 126-129, wherein each subscript n is 3,4, 5, or 6.

[0947] 134. The ADC of any one of Embodiments 118-133, wherein R² and R³ are independently —CO₂H or —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F; and R² and R³ are the same.

[0948] 135. The ADC of any one of Embodiments 118-133, wherein R² and R³ are independently —CO₂H or —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F; and R² and R³ are different.

[0949] 136. The ADC of any one of Embodiments 118-135, wherein R² is —(C=O)_m—NR^CR^D.

[0950] 137. The ADC of any one of Embodiments 118-135, wherein R³ is —(C=O)_m—NR^CR^D.

[0951] 138. The ADC of any one of Embodiments 118-137, wherein R^C and R^D are both hydrogen.

[0952] 139. The ADC of any one of Embodiments 118-137, wherein R^C and R^D are each independently C₁₋₃ alkyl.

[0953] 140. The ADC of any one of Embodiments 118-137, wherein one of R^C and R^D is hydrogen and the other of R^C and R^D is C₁₋₃ alkyl.

[0954] 141. The ADC of any one of Embodiments 118-140, wherein each subscript m is 0.

[0955] 142. The ADC of any one of Embodiments 118-140, wherein each subscript m is 1.

[0956] 143. The ADC of any one of Embodiments 118-135, wherein R² is —(CH₂)_q—NR^ER^F.

[0957] 144. The ADC of any one of Embodiments 118-135, wherein R³ is —(CH₂)_q—NR^ER^F.

[0958] 145. The ADC of any one of Embodiments 118-135, 143, or 144, wherein R^E and R^F are both hydrogen.

[0959] 146. The ADC of any one of Embodiments 118-135, 143, or 144, wherein R^E and R^F are each independently C₁₋₃ alkyl.

[0960] 147. The ADC of any one of Embodiments 118-135, 143, or 144, wherein one of R^E and R^F is hydrogen and the other of R^E and R^F is C₁₋₃ alkyl.

[0961] 148. The ADC of any one of Embodiments 118-135, 143, or 144, wherein each subscript q is 0.

[0962] 149. The ADC of any one of Embodiments 118-135, 143, or 144, wherein each subscript q is an integer from 1 to 6.

[0963] 150. The ADC of any one of Embodiments 118-135, wherein R³ is —CO₂H.

[0964] 151. The ADC of any one of Embodiments 118-135, wherein R² is —CO₂H.

[0965] 152. The ADC of any one of Embodiments 118-151, wherein X^A is —CH₂—.

[0966] 153. The ADC of any one of Embodiments 118-151, wherein X^A is —O—.

[0967] 154. The ADC of any one of Embodiments 118-151, wherein X^A is —S—155. The ADC of any one of Embodiments 118-151, wherein X^A is —NH—.

[0968] 156. The ADC of any one of Embodiments 118-155, wherein X^B is a 2-16 membered heteroalkylene.

[0969] 157. The ADC of any one of Embodiments 118-155, wherein X^B is a 2-12 membered heteroalkylene.

[0970] 158. The ADC of any one of Embodiments 118-157, wherein X^B is a 2-8 membered heteroalkylene.

[0971] 159. The ADC of any one of Embodiments 118-158, wherein the heteroalkylene is branched, having 1-4 methyl groups.

[0972] 160. The ADC of any one of Embodiments 118-159, wherein the heteroalkylene is branched, having 1 or 2 methyl groups.

[0973] 161. The ADC of any one of Embodiments 118-160, wherein the heteroalkylene is substituted with 1-3 fluoro groups.

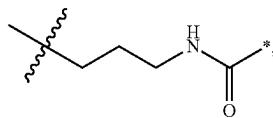
[0974] 162. The ADC of any one of Embodiments 118-161, wherein X^B comprises one or two nitrogen atoms.

[0975] 163. The ADC of any one of Embodiments 118-162, wherein X^B comprises one or two oxo groups.

[0976] 164. The ADC of any one of Embodiments 118-163, wherein X^B comprises one nitrogen atom and one oxo group.

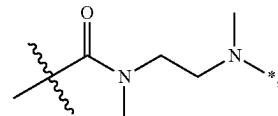
[0977] 165. The ADC of any one of Embodiments 118-163, wherein X^B comprises two nitrogen atoms and one oxo groups.

[0978] 166. The ADC of any one of Embodiments 118-158 or 162-164, wherein X^B is



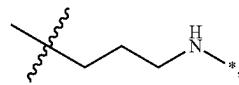
wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L or M^1 .

[0982] 170. The ADC of any one of Embodiments 118-158 or 162-165, wherein X^B is



wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L.

[0983] 171. The ADC of any one of Embodiments 118-158 or 162-165, wherein X^B is



wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L.

[0984] 172. The ADC of any one of Embodiments 118-158, wherein X^B is absent.

[0985] 173. The ADC of any one of Embodiments 118-171, wherein subscript a is 1.

[0986] 174. The ADC of any one of Embodiments 118 to 171 or 173, wherein subscript y is 1.

[0987] 175. The ADC of any one of Embodiments 118-173, wherein subscript w is 1.

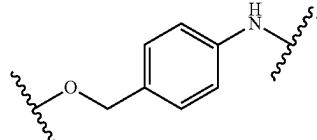
[0988] 176. The ADC of any one of Embodiments 118-171, wherein the sum of subscript a, subscript y, and subscript w is 1.

[0989] 177. The ADC of any one of Embodiments 118-171, wherein the sum of subscript a, subscript y, and subscript w is 2.

[0990] 178. The ADC of any one of Embodiments 118-171, wherein the sum of subscript a, subscript y, and subscript w is 3.

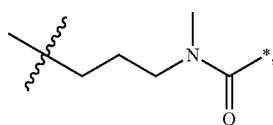
[0991] 179. The ADC of any one of Embodiments 118-178, wherein Y is a self-immolative moiety.

[0992] 180. The ADC of any one of Embodiments 118-178, wherein Y is



wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L or M^1 .

[0980] 168. The ADC of any one of Embodiments 118-158 or 162-163, wherein X^B is



wherein $\sim\sim\sim$ represents covalent attachment to X^A , and * represents covalent attachment to L or M^1 .

[0981] 169. The ADC of any one of Embodiments 118-158 or 162-164, wherein X^B is

[0993] 181. The ADC of any one of Embodiments 118-172, wherein Y is a non-cleavable moiety and a is 0.

[0994] 182. The ADC of any one of Embodiments 118-178 or 181, wherein Y is MCC or SMCC.

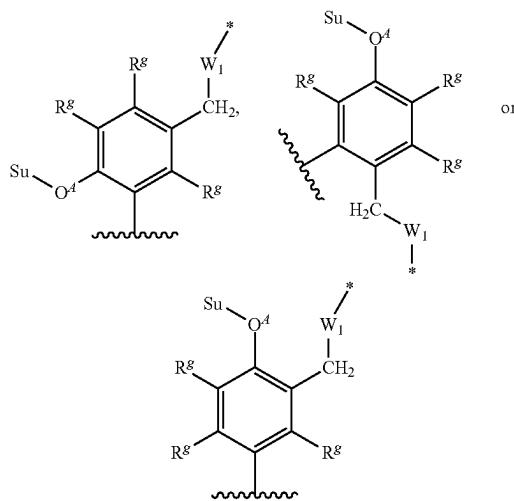
[0995] 183. The ADC of any one of Embodiments 118-178 or 181, wherein Y is PEG4 to PEG12.

[0996] 184. The ADC of any one of Embodiments 118-183, wherein W is from 1-12 amino acids.

[0997] 185. The ADC of any one of Embodiments 118-184, wherein W is from 1-6 amino acids.

[0998] 186. The ADC of any one of Embodiments 118-185, wherein each amino acid in W is selected from the group consisting of alanine, glycine, lysine, serine, aspartic acid, aspartate methyl ester, N,N-dimethyl-lysine, phenylalanine, citrulline, valine-alanine, valine-citrulline, phenylalanine-lysine or homoserine methyl ether.

[0999] 187. The ADC of any one of Embodiments 118-183, wherein W has the structure:



[1000] wherein Su is a Sugar moiety;

[1001] —O⁴— represents a glycosidic bond;

[1002] each R⁹ is independently hydrogen, halogen, —CN, or —NO₂;

[1003] W¹ is absent or —O—C(=O)—;

[1004] ~~~~ represents covalent attachment to A or M¹; and

[1005] * represents covalent attachment to Y, X^B, or X^A.

[1006] 188. The ADC of any one of Embodiments 118-187, wherein W¹ is —O—C(=O)—.

[1007] 189. The ADC of any one of Embodiments 118-187, wherein W¹ is absent.

[1008] 190. The ADC of any one of Embodiments 118-188, wherein one R⁹ is halogen, —CN, or —NO₂, and the remaining R^G are hydrogen.

[1009] 191. The ADC of any one of Embodiments 118-188, wherein each R⁹ is hydrogen.

[1010] 192. The ADC of any one of Embodiments 118-191, wherein A is C₂₋₂₀ alkylene optionally substituted with 1-3 R^{a1}

[1011] 193. The ADC of any one of Embodiments 118-192, wherein A is C₄₋₁₀ alkylene optionally substituted with 1-3 R^{a1}

[1012] 194. The ADC of any one of Embodiments 118-191, wherein A is C₂₋₂₀ alkylene substituted with R^{a1}.

[1013] 195. The ADC of any one of Embodiments 118-192, wherein A is C₄₋₁₀ alkylene substituted with R^{a1}.

[1014] 196. The ADC of any one of Embodiments 118-191, wherein A is C₂₋₂₀ alkylene.

[1015] 197. The ADC of any one of Embodiments 118-192, wherein A is C₄₋₁₀ alkylene.

[1016] 198. The ADC of any one of Embodiments 118-191, wherein A is a 2 to 40 membered heteroalkylene optionally substituted with 1-3 R^{b1}.

[1017] 199. The ADC of any one of Embodiments 118-191, wherein A is a 4 to 12 membered heteroalkylene optionally substituted with 1-3 R^{b1}.

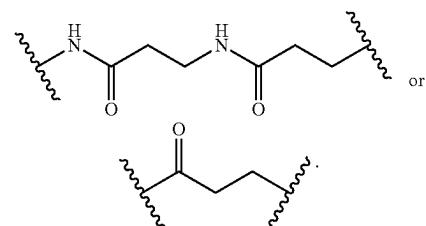
[1018] 200. The ADC of any one of Embodiments 118-191 or 199, wherein A is a 2 to 40 membered heteroalkylene optionally substituted with one R^{b1}.

[1019] 201. The ADC of any one of Embodiments 118-191 or 199, wherein A is a 4 to 12 membered heteroalkylene optionally substituted with one R^{b1}.

[1020] 202. The ADC of any one of Embodiments 118-191 or 199, wherein A is a 2 to 40 membered heteroalkylene.

[1021] 203. The ADC of any one of Embodiments 118-191 or 199, wherein A is a 4 to 12 membered heteroalkylene.

[1022] 204. The ADC of any one of Embodiments 118-191 or 202-203, wherein A is



[1023] 205. The ADC of any one of Embodiments 118-145, wherein subscript a is 0.

[1024] 206. The ADC of any one of Embodiments 118-145, wherein subscript y is 0.

[1025] 207. The ADC of any one of Embodiments 118-145, wherein subscript w is 0.

[1026] 208. The ADC of any one of Embodiments 118-145 or 205-207, wherein the sum of subscript a, subscript y, and subscript w is 0.

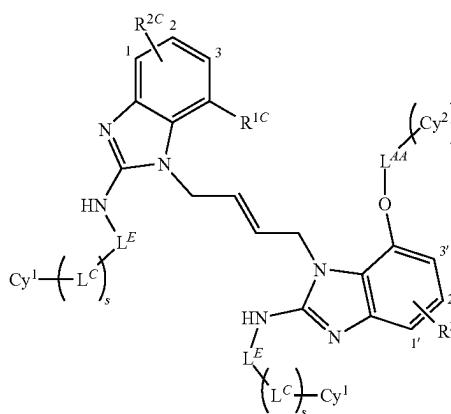
[1027] 209. The ADC of any one of Embodiments 118-208, wherein the linker is a cleavable linker.

[1028] 210. The ADC of any one of Embodiments 118-209, wherein the linker is cleavable by one or more of cathepsin B, C, or D; β-glucuronidase; and β-mannosidase.

[1029] 211. The ADC of Embodiments 118-208, wherein the linker is a non-cleavable linker.

[1030] 212. The ADC of any one of Embodiments 118-211, wherein the antibody is a humanized antibody.

- [1031] 213. The ADC of any one of Embodiments 118-212, wherein the antibody is a monoclonal antibody.
 - [1032] 214. The ADC of any one of Embodiments 118-187, wherein the antibody is fucosylated.
 - [1033] 215. The ADC of any one of Embodiments 118-187, wherein the antibody is afucosylated.
 - [1034] 216. A compound having the structure of Formula (IV):



or a pharmaceutically acceptable salt thereof, wherein:

- [1035] R^{1C} is hydrogen, hydroxyl, C_{1-6} alkoxy, $-(C_{1-6}\text{alkyl})$ C_{1-6} alkoxy, $-(\text{CH}_2)_n-\text{NR}^A\text{R}^B$, or PEG2 to PEG4;

[1036] R^{2C} is $-\text{CO}_2\text{R}^M$, $-(\text{C}=\text{O})\text{NR}^C\text{R}^D$, $-\text{S}(\text{O})$
 $_2\text{NR}^C\text{R}^D$, $-\text{S}(\text{O})_2\text{R}^M$, $-(\text{CH}_2)_q-\text{NR}^E\text{R}^F$, $-(\text{CH}_2)_q-\text{OR}^M$, $-\text{O}(\text{C}=\text{O})-\text{NR}^E\text{R}^F$, or $-\text{NR}^M(\text{C}=\text{O})-\text{NR}^E\text{R}^N$, wherein R^{2C} is attached at any one of positions labeled 1, 2, or 3;

[1037] R^{3C} is $-\text{CO}_2\text{R}^M$, $-(\text{C}=\text{O})\text{NR}^C\text{R}^D$, $-\text{S}(\text{O})$
 $_2\text{NR}^C\text{R}^D$, $-\text{S}(\text{O})_2\text{R}^M$, $-(\text{CH}_2)_q-\text{NR}^E\text{R}^F$, $-(\text{CH}_2)_q-\text{OR}^M$, $-\text{O}(\text{C}=\text{O})-\text{NR}^E\text{R}^F$, or $-\text{NR}^M(\text{C}=\text{O})-\text{NR}^E\text{R}^F$, wherein R^{3C} is attached at any one of positions labeled 1', 2', or 3';

[1038] each R^A , R^B , R^C , R^D , R^E , R^F , and R^M are independently hydrogen or C_{1-6} alkyl;

[1039] each subscript n is independently an integer from 0 to 6;

[1040] each subscript q is independently an integer from 0 to 6;

[1041] L^E is $-(\text{C}=\text{O})-$ or $-\text{S}(\text{O})_2-$;

[1042] L^C is $-(\text{CR}'\text{R}')_{1-3}-$

[1043] each R' and R'' are independently hydrogen or C_{1-3} alkyl;

[1044] subscript s is 0 or 1;

[1045] each Cy^1 is independently a 4-6 membered heterocycle, a 5-6 membered heteroaryl, or a C_{3-6} cycloalkyl, each optionally substituted with one or more R^K ;

[1046] each R^K is independently selected from the group consisting of: C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, halogen, $-\text{OH}$, $=\text{O}$, $-\text{NR}^D\text{R}^{e2}$, $-\text{C}(\text{O})\text{NR}^{d2}\text{R}^{e2}$, $-\text{C}(\text{O})(\text{C}_{1-6}\text{ alkyl})$, and $-\text{C}(\text{O})\text{O}(\text{C}_{1-6}\text{ alkyl})$;

[1047] each R^{d2} and R^{e2} are independently hydrogen or C_{1-3} alkyl;

- [1048] L^{44} is $-(CH_2)_{1-6}-$, $-C(O)(CH_2)_{1-6}-$,
 $-C(O)NR^L(CH_2)_{1-6}-$, $-(CH_2)_{1-6}O-$, $-C(O)(CH_2)_{1-6}O-$, or $-C(O)NR^L(CH_2)_{1-6}O-$;

[1049] R^L is hydrogen or C_{1-3} alkyl;

[1050] Cy^2 is C_{3-6} cycloalkyl, 4-6 membered heterocycle, 5-6 membered heteroaryl, or phenyl, each optionally substituted with one or more RU;

[1051] each R^U is independently selected from the group consisting of $-CO_2R^1$, $-(C=O)NR^{d3}R^{e3}$,

(IV)

- S(O)₂NR^{d3}R^{e3}, —(CH₂)_{q1}—NR^{g1}R^{h1}, —(CH₂)_{q1}—ORⁱ¹, and —(CH₂)₁₋₈i-(OCH₂CH₂)₁₋₈OH;

[1052] each R^{d3}, R^{e3}, R^{g1}, R^{h1}, and R^{j1} are independently hydrogen or C₁₋₆ alkyl;

[1053] subscript q1 is an integer from 0 to 6;

[1054] subscripts t1 and t2 are independently 0 or 1, wherein at least one of t1 and t2 is 1;

[1055] L^D is —(CH₂)₁₋₆—;

[1056] subscript u is 0 or 1;

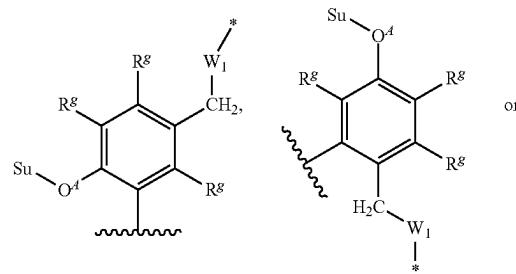
[1057] Z is —N(R^{HH})— or —N⁺(C₁₋₆ alkyl)(R^{HH})—;

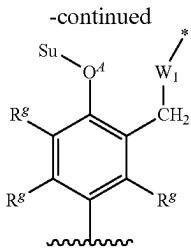
[1058] R^{HH} is hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, —(CH₂)₁₋₃C₃₋₆ cycloalkyl, —(CH₂)₁₋₃C₁₋₃ alkoxy, —(CH₂)₁₋₃ 4-6 membered heterocycle, or —(CH₂)₁₋₃ 5-6 membered heteroaryl;

[1059] Y is a self-immolative moiety, a non-self-immolative releasable moiety, or a non-cleavable moiety;

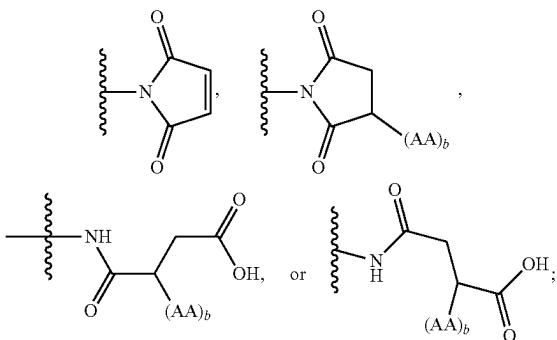
[1060] subscript y is 0 or 1;

[1061] W is a chain of 1-12 amino acids or has the structure:





- [1062] wherein Su is a Sugar moiety;
- [1063] —O⁴— represents a glycosidic bond;
- [1064] each R⁹ is independently hydrogen, halogen, —CN, or —NO₂;
- [1065] W¹ is absent or —O—C(=O)—;
- [1066] ~~~~ represents covalent attachment to L^{BB};
- [1067] * represents covalent attachment to Y, L^D, NR^{III}, or Cy²;
- [1068] subscript w is 0 or 1;
- [1069] L^{BB} is —(CH₂)₁₋₆—, —C(O)(CH₂)₁₋₆—, or —[NHC(O)(CH₂)₁₋₃]—; and
- [1070] M is

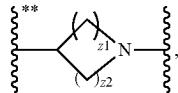


- [1071] each AA is an independently selected amino acid, wherein (AA)_b is connected to the succinimide or hydrolyzed succinimide via a sulfur atom; and
- [1072] each subscript b is independently an integer from 1 to 6.
- [1073] 217. The compound of Embodiment 216, wherein R^{1C} is hydrogen.
- [1074] 218. The compound of Embodiment 216, wherein R^{1C} is hydroxyl.
- [1075] 219. The compound of Embodiment 216, wherein R^{1C} is C₁₋₆ alkoxy.
- [1076] 220. The compound of Embodiment 216, wherein R^{1C} is methoxy.
- [1077] 221. The compound of Embodiment 216, wherein R^{1C} is —(C₁₋₆ alkyl)C₁₋₆ alkoxy.
- [1078] 222. The compound of Embodiment 216, wherein R^{1C} is methoxyethyl.
- [1079] 223. The compound of Embodiment 216, wherein R^{1C} is PEG2 to PEG4.
- [1080] 224. The compound of Embodiment 216, wherein R^{1C} is —(CH₂)_n—NR⁴R^B.
- [1081] 225. The compound of any one of Embodiments 216-224, wherein R^A and R^B are both hydrogen.

- [1082] 226. The compound of any one of Embodiments 216-224, wherein R^A and R^B are independently C₁₋₃ alkyl.
- [1083] 227. The compound of any one of Embodiments 216-224, wherein one of R^A and R^B is hydrogen and the other of R^A and R^B is C₁₋₃ alkyl.
- [1084] 228. The compound of any one of Embodiments 216-227, wherein each subscript n is 0.
- [1085] 229. The compound of any one of Embodiments 216-227, wherein each subscript n is 1.
- [1086] 230. The compound of any one of Embodiments 216-227, wherein each subscript n is 2.
- [1087] 231. The compound of any one of Embodiments 216-227, wherein each subscript n is 3, 4, 5, or 6.
- [1088] 232. The compound of any one of Embodiments 216-231, wherein R^{2C} and R^{3C} are independently —CO₂H, —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F; and R^{2C} and R^{3C} are the same.
- [1089] 233. The compound of any one of Embodiments 216-231, wherein R^{2C} and R^{3C} are independently —CO₂H, —(C=O)_m—NR^CR^D, or —(CH₂)_q—NR^ER^F; and R^{2C} and R^{3C} are different.
- [1090] 234. The compound of any one of Embodiments 216-231, wherein R^{2C} is —(C=O)_m—NR^CR^D.
- [1091] 235. The compound of any one of Embodiments 216-231, wherein R^{3C} is —(C=O)_m—NR^CR^D.
- [1092] 236. The compound of any one of Embodiments 216-235, wherein R^C and R^D are both hydrogen.
- [1093] 237. The compound of any one of Embodiments 216-235, wherein R^C and R^D are each independently C₁₋₃ alkyl.
- [1094] 238. The compound of any one of Embodiments 216-235, wherein one of R^C and R^D is hydrogen and the other of R^C and R^D is C₁₋₃ alkyl.
- [1095] 239. The compound of any one of Embodiments 216-238, wherein each subscript m is 0.
- [1096] 240. The compound of any one of Embodiments 216-238, wherein each subscript m is 1.
- [1097] 241. The compound of any one of Embodiments 216-240, wherein R^{2C} is —(CH₂)_q—NR^ER^F.
- [1098] 242. The compound of any one of Embodiments 216-241, wherein R^{3C} is —(CH₂)_q—NR^ER^F.
- [1099] 243. The compound of any one of Embodiments 216-242, wherein R^E and R^F are both hydrogen.
- [1100] 244. The compound of any one of Embodiments 216-242, wherein R^E and R^F are each independently C₁₋₃ alkyl.
- [1101] 245. The compound of any one of Embodiments 216-242, wherein one of R^E and R^F is hydrogen and the other of R^E and R^F is C₁₋₃ alkyl.
- [1102] 246. The compound of any one of Embodiments 216-245, wherein each subscript q is 0.
- [1103] 247. The compound of any one of Embodiments 216-245, wherein each subscript q is an integer from 1 to 6.
- [1104] 248. The compound of any one of Embodiments 216-247, wherein R^{2C} is —CO₂R^M.
- [1105] 249. The compound of any one of Embodiments 216-248, wherein R^{3C} is —CO₂R^M.
- [1106] 250. The compound of Embodiment 248 or 249, wherein R^M is hydrogen.
- [1107] 251. The compound of Embodiment 248 or 249, wherein R^M is C₁₋₃ alkyl.

- [1108] 252. The compound of any one of Embodiments 216-247, wherein R^{2C} is $-(CH_2)_q-OR^M$.
- [1109] 253. The compound of any one of Embodiments 216-247 and 252, wherein R^{3C} is $-(CH_2)_q-OR^M$.
- [1110] 254. The compound of Embodiment 252 or 253, wherein R^M is hydrogen.
- [1111] 255. The compound of any one of Embodiments 252-254, wherein q is 0.
- [1112] 256. The compound of any one of Embodiments 252-254, wherein q is 1.
- [1113] 257. The compound of any one of Embodiments 216-247, wherein R^{2C} is $-O(C=O)-NR^ER^F$.
- [1114] 258. The compound of any one of Embodiments 216-247 and 257, wherein R^{3C} is $-O(C=O)-NR^ER^F$.
- [1115] 259. The compound of any one of Embodiments 216-258, wherein R^E and R^F are both hydrogen.
- [1116] 260. The compound of any one of Embodiments 216-258, wherein R^E and R^F are each independently C_{1-3} alkyl.
- [1117] 261. The compound of any one of Embodiments 216-258, wherein one of R^E and R^F is hydrogen and the other of R^E and R^F is C_{1-3} alkyl.
- [1118] 262. The compound of any one of Embodiments 216-247, wherein R^{2C} is $-NR^M(C=O)-NR^ER^F$.
- [1119] 263. The compound of any one of Embodiments 216-247 and 262, wherein R^{3C} is $-NR^M(C=O)-NR^ER^F$.
- [1120] 264. The compound of Embodiment 262 or 263, wherein R^E , R^F , and R^M are all hydrogen.
- [1121] 265. The compound of Embodiment 262 or 263, wherein R^E , R^F , and R^M are each independently C_{1-3} alkyl.
- [1122] 266. The compound of Embodiment 262 or 263, wherein one of R^E , R^F , and R^M is C_{1-3} alkyl and the rest of R^E , R^F , and R^M is hydrogen.
- [1123] 267. The compound of any one of Embodiments 216-247, wherein R^{2C} is $-S(O)_2NR^CR^D$.
- [1124] 268. The compound of any one of Embodiments 216-247 and 267, wherein R^{3C} is $-S(O)_2NR^CR^D$.
- [1125] 269. The compound of Embodiment 267 or 268, wherein R^C and R^D are both hydrogen.
- [1126] 270. The compound of Embodiment 267 or 268, wherein R^C and R^D are each independently C_{1-3} alkyl.
- [1127] 271. The compound of Embodiment 267 or 268, wherein one of R^C and R^D is hydrogen and the other of R^C and R^D is C_{1-3} alkyl.
- [1128] 272. The compound of any one of Embodiments 216-247, wherein R^{2C} is $-S(O)_2R^M$.
- [1129] 273. The compound of any one of Embodiments 216-247 and 272, wherein R^{3C} is $-S(O)_2R^M$.
- [1130] 274. The compound of Embodiment 272 or 273, wherein R^M is hydrogen.
- [1131] 275. The compound of Embodiment 272 or 273, wherein R^M is C_{1-3} alkyl.
- [1132] 276. The compound of any one of Embodiments 216-275, wherein R^{2C} is attached at position 1.
- [1133] 277. The compound of any one of Embodiments 216-275, wherein R^{2C} is attached at position 2.
- [1134] 278. The compound of any one of Embodiments 216-275, wherein R^{2C} is attached at position 3.
- [1135] 279. The compound of any one of Embodiments 216-275, wherein R^{3C} is attached at position 1'.
- [1136] 280. The compound of any one of Embodiments 216-275, wherein R^{3C} is attached at position 2'.
- [1137] 281. The compound of any one of Embodiments 216-275, wherein R^{3C} is attached at position 3'.
- [1138] 282. The compound of any one of Embodiments 216-281, wherein L^E is $-(C=O)-$.
- [1139] 283. The compound of any one of Embodiments 216-281, wherein L^E is $-S(O)_2-$.
- [1140] 284. The compound of any one of Embodiments 216-283, wherein each R^I and R^J is hydrogen.
- [1141] 285. The compound of any one of Embodiments 216-283, wherein each R^I and R^J is C_{1-3} alkyl.
- [1142] 286. The compound of any one of Embodiments 216-283, wherein one of R^I and R^J is hydrogen and the other of R^I and R^J is C_{1-3} alkyl.
- [1143] 287. The compound of any one of Embodiments 216-286, wherein L^C is $-(CR^IR^J)-$.
- [1144] 288. The compound of any one of Embodiments 216-287, wherein s is 0.
- [1145] 289. The compound of any one of Embodiments 216-287, wherein s is 1.
- [1146] 290. The compound of any one of Embodiments 216-289, wherein each Cy^1 is independently a 5-6 membered heteroaryl.
- [1147] 291. The compound of any one of Embodiments 216-289, wherein each Cy^1 is pyrazole optionally substituted with one or more R^K .
- [1148] 292. The compound of any one of Embodiments 216-289, wherein each Cy^1 is independently selected from the group consisting of pyrazole, imidazole, furan, thiophene, thiazole, isothiazole, oxazole, isoxazole, pyrrole, pyridazine, pyridine, pyrimidine, and pyrazine, each optionally substituted with one or more R^K .
- [1149] 293. The compound of any one of Embodiments 216-289, wherein each Cy^1 is independently selected from the group consisting of imidazole, furan, thiophene, thiazole, isothiazole, oxazole, isoxazole, pyrrole, pyridazine, pyridine, pyrimidine, and pyrazine, each optionally substituted with one or more R^K .
- [1150] 294. The compound of any one of Embodiments 216-289, wherein each Cy^1 is independently a C_{4-5} cycloalkyl optionally substituted with one or more R^K .
- [1151] 295. The compound of any one of Embodiments 216-294, wherein each R^K is independently selected from the group consisting of C_{1-3} alkyl, C_{1-3} haloalkyl, and halogen.
- [1152] 296. The compound of Embodiment 295, wherein each R^K is independently selected from the group consisting of methyl, ethyl, $-CF_3$, and halogen.
- [1153] 297. The compound of any one of Embodiments 216-296, wherein each Cy^1 is the same.
- [1154] 298. The compound of any one of Embodiments 216-296, wherein each Cy^1 is different.
- [1155] 299. The compound of any one of Embodiments 216-298, wherein L^{AA} is $-(CH_2)_{1-6}-$.
- [1156] 300. The compound of any one of Embodiments 216-298, wherein L^{AA} is $-(CH_2)_{1-3}-$.
- [1157] 301. The compound of any one of Embodiments 216-298, wherein L^{AA} is $-(CH_2)_{1-6}O-$.
- [1158] 302. The compound of any one of Embodiments 216-298, wherein L^{AA} is $-(CH_2)_{1-3}O-$.
- [1159] 303. The compound of any one of Embodiments 216-302, wherein Cy^2 is a 4-6 membered heterocycle.

[1160] 304. The compound of any one of Embodiments 216-302, wherein Cy² has the structure:



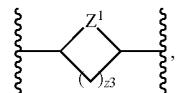
wherein each of subscripts z1 and z2 is independently an integer from 1 to 3 and ** indicates attachment to L^{AA}.

[1161] 305. The compound of Embodiment 304, wherein z1 and z2 are 1.

[1162] 306. The compound of Embodiment 304, wherein z1 and z2 are 2.

[1163] 307. The compound of Embodiment 304, wherein z1 is 1 and z2 is 2.

[1164] 308. The compound of any one of Embodiments 216-302, wherein Cy² has the structure:



wherein

[1165] Z¹ is selected from the group consisting of —O—, —S—, —CR^NR^O—, and —NR^P—; R^N, R^O, and R^P are independently hydrogen or C₁₋₆ alkyl;

[1166] subscript z3 is an integer from 1 to 3; and

[1167] ** indicates attachment to L^{AA}.

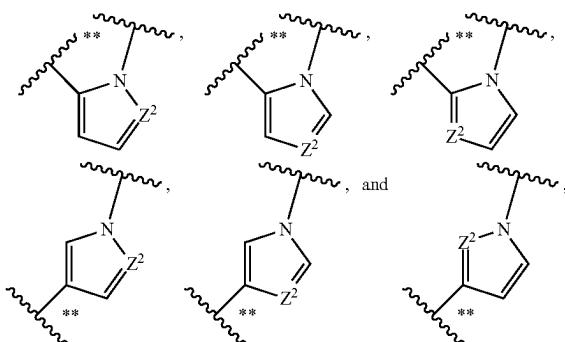
[1168] 309. The compound of Embodiment 308, wherein R^N and R^O are hydrogen.

[1169] 310. The compound of Embodiment 308, wherein R^P is hydrogen.

[1170] 311. The compound of Embodiment 308, wherein R^P is methyl.

[1171] 312. The compound of any one of Embodiments 216-302, wherein Cy² is a 5-6 membered heteroaryl.

[1172] 313. The compound of any one of Embodiments 216-302, wherein Cy² is selected from the group consisting of:



wherein

[1173] Z² is ==CR^N— or ==N—;

[1174] R^N is hydrogen or C₁₋₆ alkyl; and

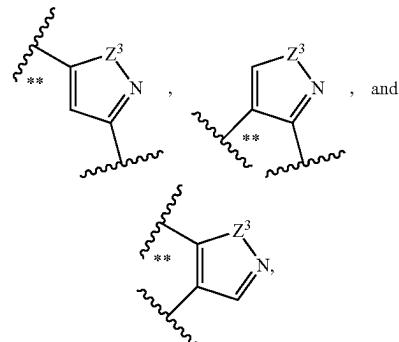
[1175] ** indicates attachment to L^{AA}.

[1176] 314. The compound of Embodiment 313, wherein Z² is ==CR^N—.

[1177] 315. The compound of Embodiment 314, wherein R^N is hydrogen.

[1178] 316. The compound of Embodiment 313, wherein Z² is ==N—.

[1179] 317. The compound of any one of Embodiments 216-302, wherein Cy² is selected from the group consisting of:

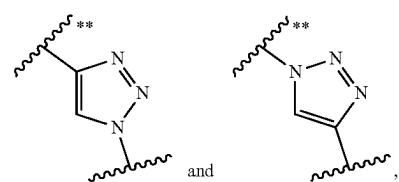


wherein Z³ is —O— or —S— and ** indicates attachment to L^{AA}, L^D, NR^{HH}, Y, W, or L^{BB}.

[1180] 318. The compound of Embodiment 317, wherein ** indicates attachment to L^{AA}.

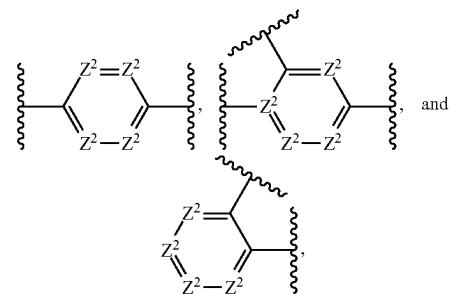
[1181] 319. The compound of Embodiment 317, wherein ** indicates attachment to L^D, NR^{HH}, Y, W, or L^{BB}.

[1182] 320. The compound of any one of Embodiments 216-302, wherein Cy² is selected from the group consisting of:



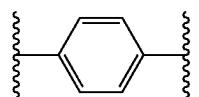
wherein ** indicates attachment to L^{AA}.

[1183] 321. The compound of any one of Embodiments 216-302, wherein Cy² is selected from the group consisting of:

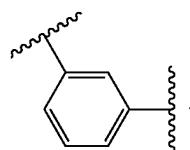


wherein

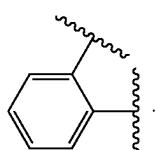
- [1184] each Z^2 is independently $=CR^N-$ or $=N-$;
- and
- [1185] each R^N is hydrogen or C_{1-6} alkyl.
- [1186] 322. The compound of Embodiment 321, wherein at least one Z^2 is $=N-$.
- [1187] 323. The compound of Embodiment 321, wherein one Z^2 is $=N-$ and the remaining Z^2 are $=CR^N-$.
- [1188] 324. The compound of Embodiment 321, wherein two Z^2 are $=N-$ and the remaining Z^2 are $=CR^N-$.
- [1189] 325. The compound of any one of Embodiments 321, 323, and 324, wherein R^N is hydrogen.
- [1190] 326. The compound of any one of Embodiments 216-302, wherein Cy^2 is



- [1191] 327. The compound of any one of Embodiments 216-302, wherein Cy^2 is



- [1192] 328. The compound of any one of Embodiments 216-302, wherein Cy^2 is



- [1193] 329. The compound of any one of Embodiments 216-302, wherein Cy^2 is cyclobutyl.
- [1194] 330. The compound of any one of Embodiments 216-329, wherein each R^{d3} , R^{e3} , R^{g1} , R^{h1} , and R^{j1} are independently hydrogen or $-CH_3$.
- [1195] 331. The compound of any one of Embodiments 216-330, wherein each Ru is independently selected from $-CO_2H$, $-(C=O)NH_2$, $-S(O)_2NH_2$, $-CH_2NH_2$, and $-CH_2OH$.
- [1196] 332. The compound of any one of Embodiments 216-331, wherein t1 is 0 and t2 is 1.
- [1197] 333. The compound of any one of Embodiments 216-331, wherein t1 is 1 and t2 is 0.
- [1198] 334. The compound of any one of Embodiments 216-331, wherein t1 is 1 and t2 is 1.
- [1199] 335. The compound of any one of Embodiments 216-334, wherein u is 1 and L^D is $-(CH_2)_{1-3}-$.
- [1200] 336. The compound of any one of Embodiments 216-334, wherein u is 0.

- [1201] 337. The compound of any one of Embodiments 216-331, wherein t2 is 1 and R^{HH} is hydrogen.

- [1202] 338. The compound of any one of Embodiments 216-331, wherein t2 is 1 and R^{HH} is C_{1-3} alkyl.

- [1203] 339. The compound of any one of Embodiments 216-331, wherein t2 is 1 and R^{HH} is C_{3-4} cycloalkyl.

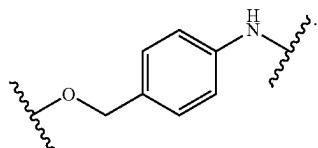
- [1204] 340. The compound of any one of Embodiments 216-331, wherein t2 is 1 and R^{HH} is $-(CH_2) C_{3-4}$ cycloalkyl.

- [1205] 341. The compound of any one of Embodiments 216-331, wherein t2 is 1 and R^{HH} is $-(CH_2) 4-5$ membered heterocycle.

- [1206] 342. The compound of any one of Embodiments 216-331, wherein t2 is 1 and R^{HH} is $-(CH_2) 5$ -membered heteroaryl.

- [1207] 343. The compound of any one of Embodiments 216-331 and 333-342, wherein Z is $-N(R^{HH})-$.

- [1208] 344. The compound of any one of Embodiments 216-343, wherein Y is



- [1209] 345. The compound of any one of Embodiments 216-343, wherein Y is a cyclohexanecarboxyl, undecanoyl, caproyl, hexanoyl, butanoyl or propionyl group.

- [1210] 346. The compound of any one of Embodiments 216-343, wherein Y is PEG4 to PEG12.

- [1211] 347. The compound of any one of Embodiments 216-343, wherein y is 0.

- [1212] 348. The compound of any one of Embodiments 216-346, wherein y is 1.

- [1213] 349. The compound of any one of Embodiments 216-348, wherein W is a chain of 1-12 amino acids.

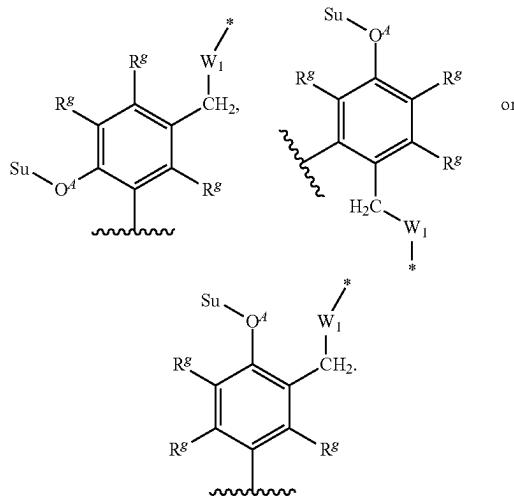
- [1214] 350. The compound of any one of Embodiments 216-348, wherein W is a chain of 1-6 amino acids.

- [1215] 351. The compound of any one of Embodiments 216-348, wherein W is a chain of 1-3 amino acids.

- [1216] 352. The compound of Embodiment 216-351, wherein each amino acid of W is independently selected from the group consisting of alanine, valine, isoleucine, leucine, aspartic acid, glutamic acid, lysine, histidine, arginine, glycine, serine, threonine, phenylalanine, O-methylserine, O-methylethylserine, O-methylglutamic acid, N-methyllysine, O-methyltyrosine, O-methylhistidine, and O-methylthreonine.

- [1217] 353. The compound of any one of Embodiments 216-351, wherein each amino acid in W is independently selected from the group consisting of alanine, glycine, lysine, serine, aspartic acid, aspartate methyl ester, N,N-dimethyl-lysine, phenylalanine, citrulline, valine-alanine, valine-citrulline, phenylalanine-lysine or homoserine methyl ether.

[1218] 354. The compound of any one of Embodiments 216-348, wherein W has the structure:



[1219] 355. The compound of Embodiment 354, wherein W¹ is —O—C(=O)—.

[1220] 356. The compound of Embodiment 354 or 355, wherein one R⁹ is halogen, —CN, or —NO₂, and the remaining R^G are hydrogen.

[1221] 357. The compound of Embodiment 354 or 355, wherein each R⁹ is hydrogen.

[1222] 358. The compound of any one of Embodiments 216-348, wherein w is 0.

[1223] 359. The compound of any one of Embodiments 216-348, wherein w is 1.

[1224] 360. The compound of any one of Embodiments 216-359, wherein L¹¹ is —(CH₂)₁₋₃—.

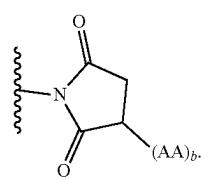
[1225] 361. The compound of any one of Embodiments 216-359, wherein L^{BB} is C(O)(CH₂)₁₋₂—.

[1226] 362. The compound of Embodiment 361, wherein L^{BB} is —C(O)(CH₂)₂—.

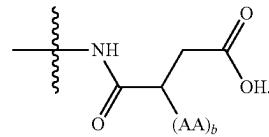
[1227] 363. The compound of any one of Embodiments 216-359, wherein L^{BB} is —[NHC(O)(CH₂)₂]₁₋₂—.

[1228] 364. The compound of Embodiment 363, wherein L^{BB} is [NHC(O)(CH₂)₂]₂.

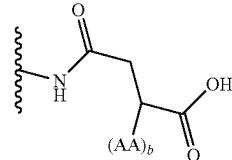
[1229] 365. The compound of any one of Embodiments 216-364, wherein M is



[1230] 366. The compound of any one of Embodiments 216-364, wherein M is



[1231] 367. The compound of any one of Embodiments 216-364, wherein M is



[1232] 368. The compound of any one of Embodiments 216-367, wherein each AA is independently a natural amino acid; wherein (AA)_b is connected to the succinimide or hydrolyzed succinimide via a sulfur atom.

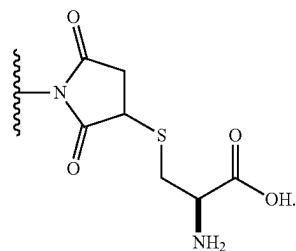
[1233] 369. The compound of any one of Embodiments 216-367, wherein each AA is independently a natural amino acid; wherein (AA)_b is connected to the succinimide or hydrolyzed succinimide via a nitrogen atom.

[1234] 370. The compound of any one of Embodiments 216-369, wherein each subscript b is 1.

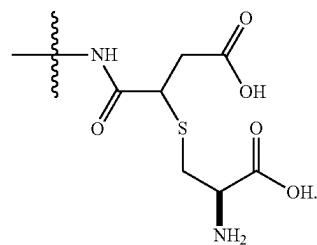
[1235] 371. The compound of any one of Embodiments 216-369, wherein each subscript b is 2.

[1236] 372. The compound of any one of Embodiments 216-369, wherein each subscript b is 3, 4, 5, or 6.

[1237] 373. The compound of any one of Embodiments 216-365, wherein M is

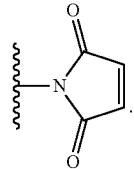
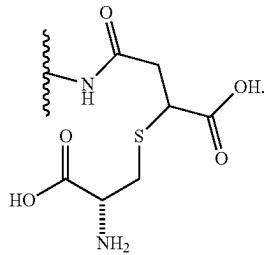


[1238] 374. The compound of any one of Embodiments 216-364, wherein M is

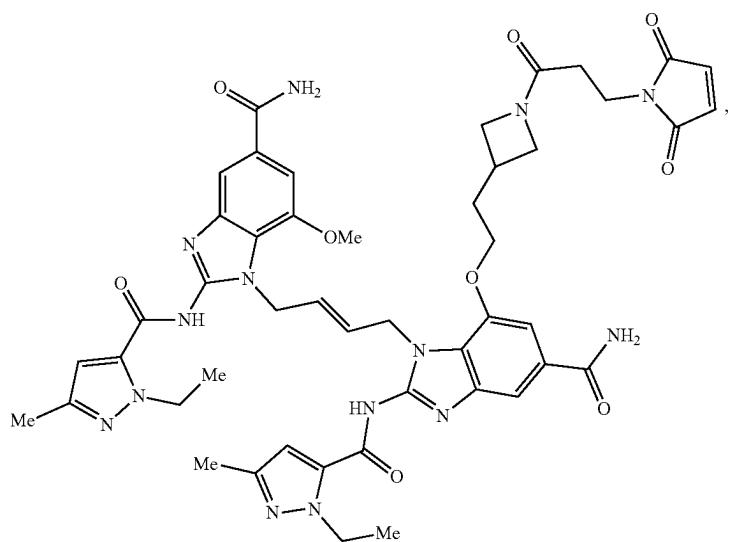
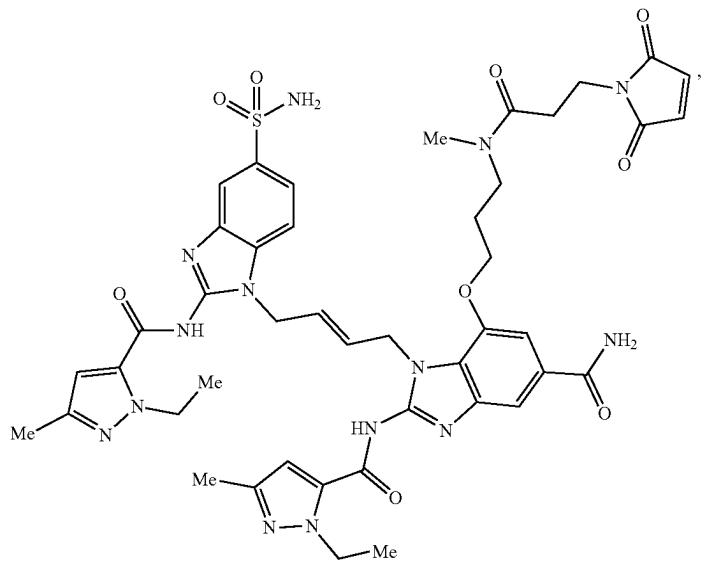


[1239] 375. The compound of any one of Embodiments 216-364, wherein M is

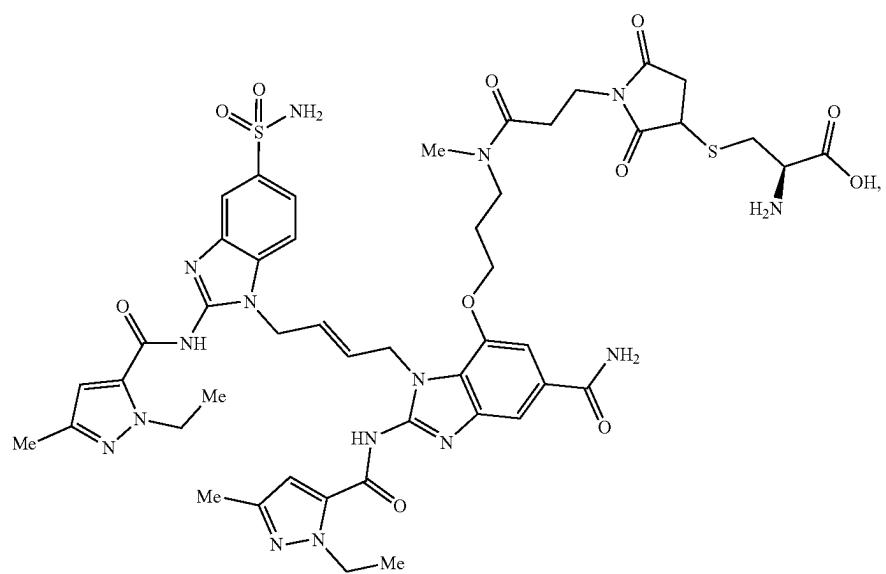
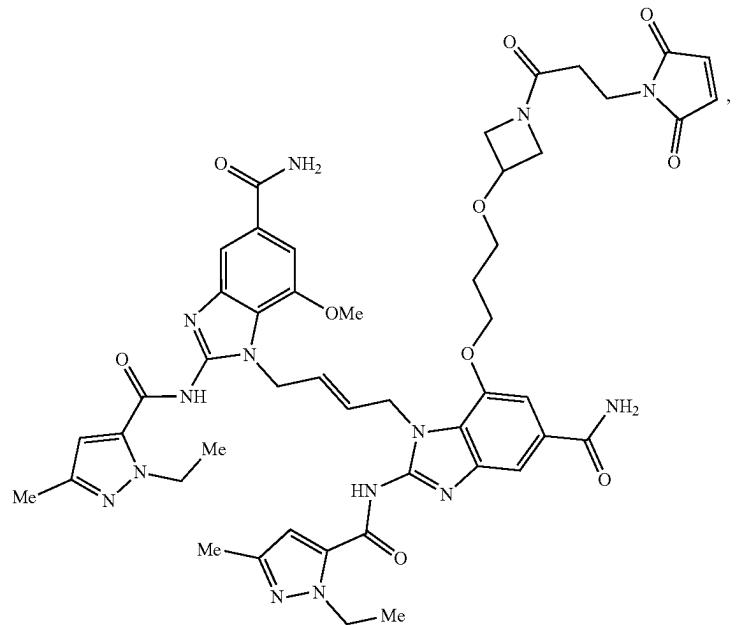
[1240] 376. The compound of any one of Embodiments 216-364, wherein M is



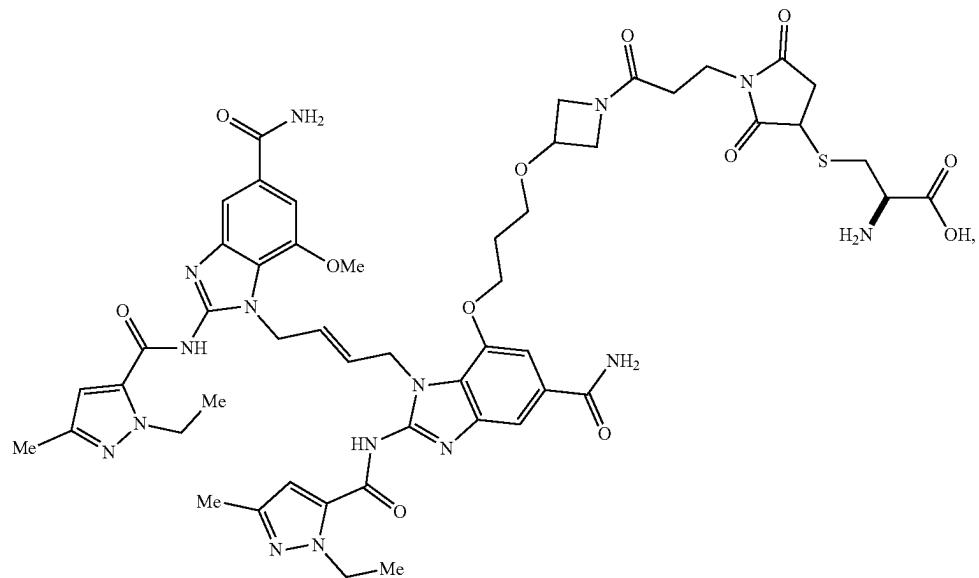
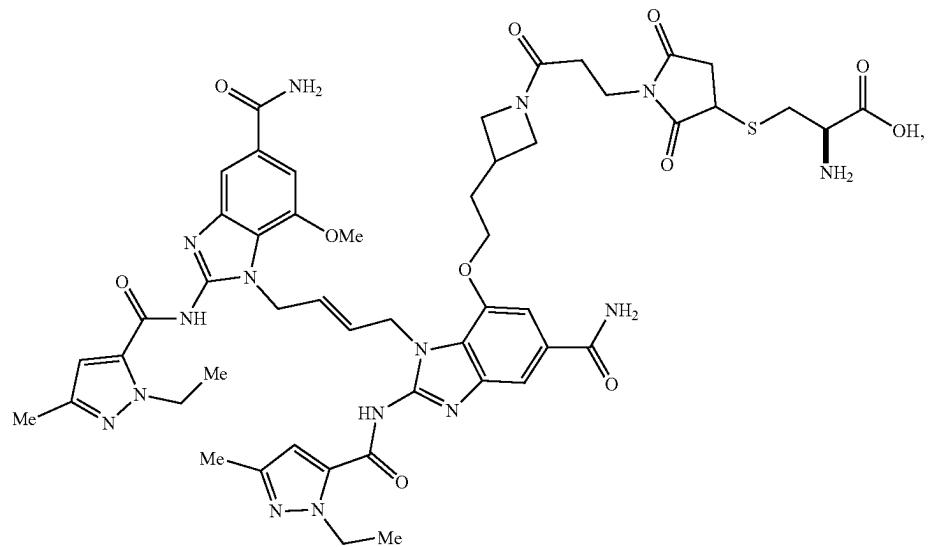
[1241] 377. The compound of Embodiment 216, selected from the group consisting of:



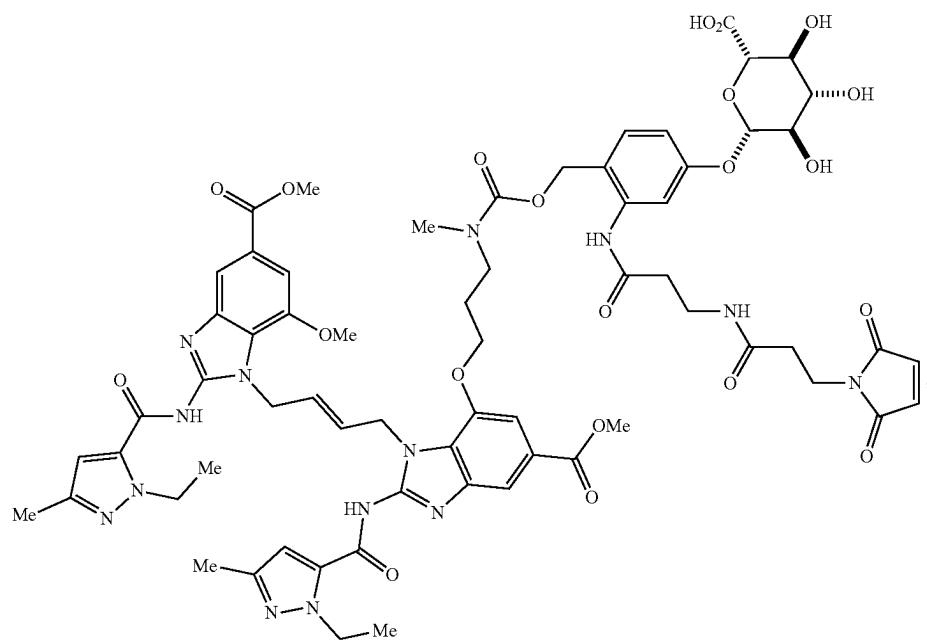
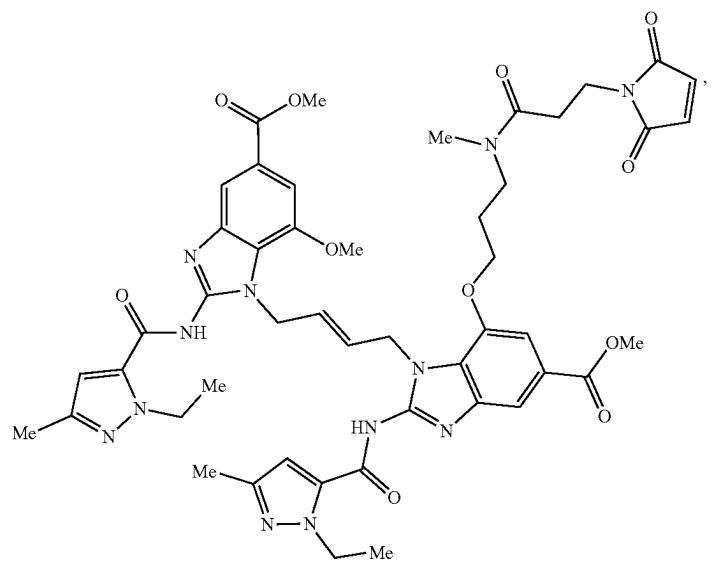
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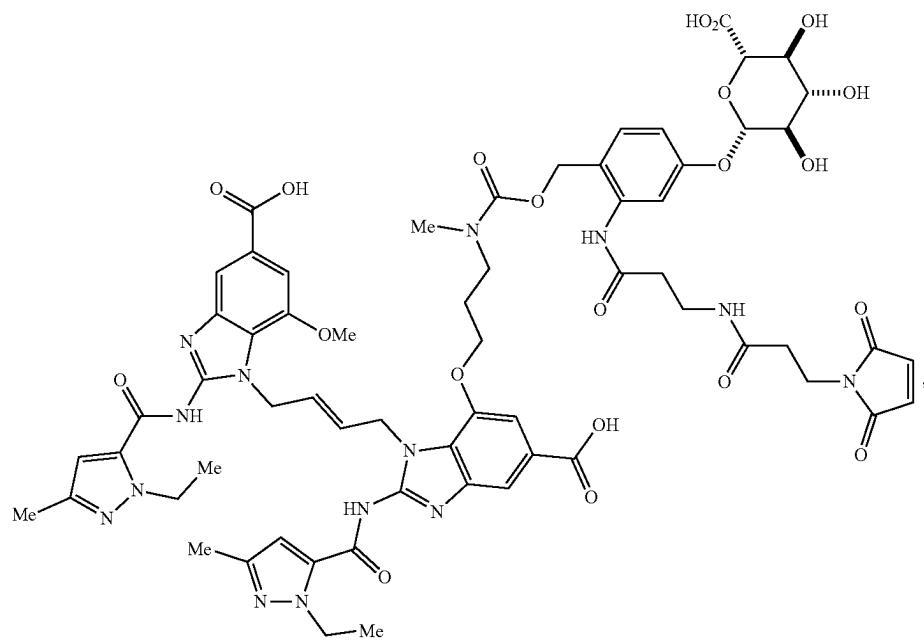
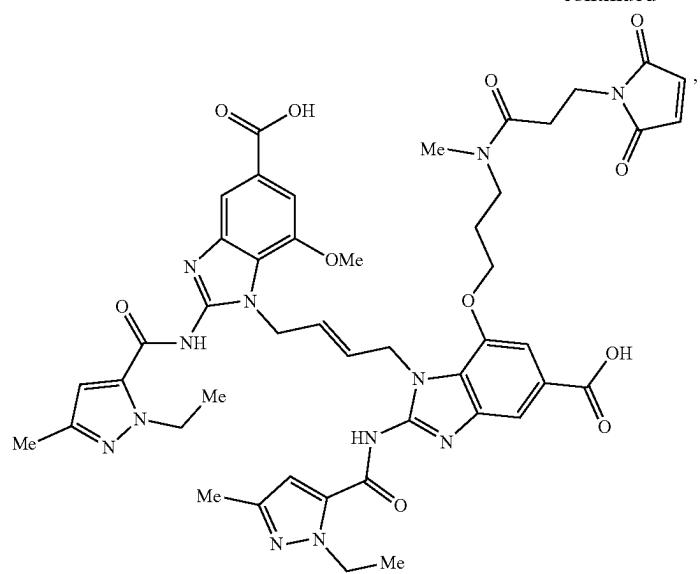
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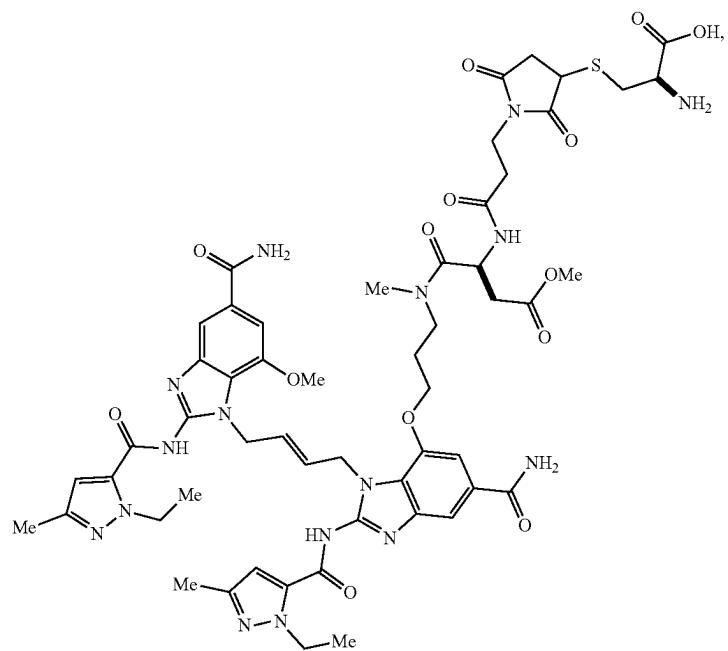
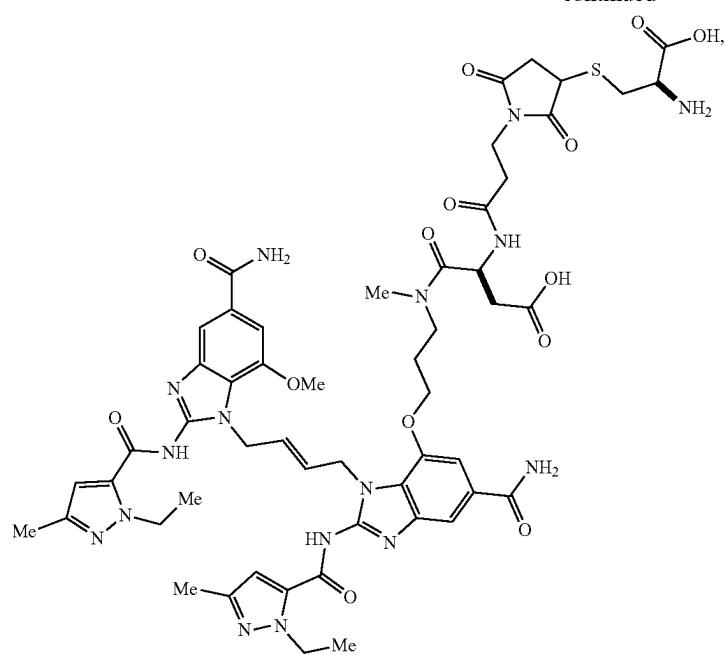
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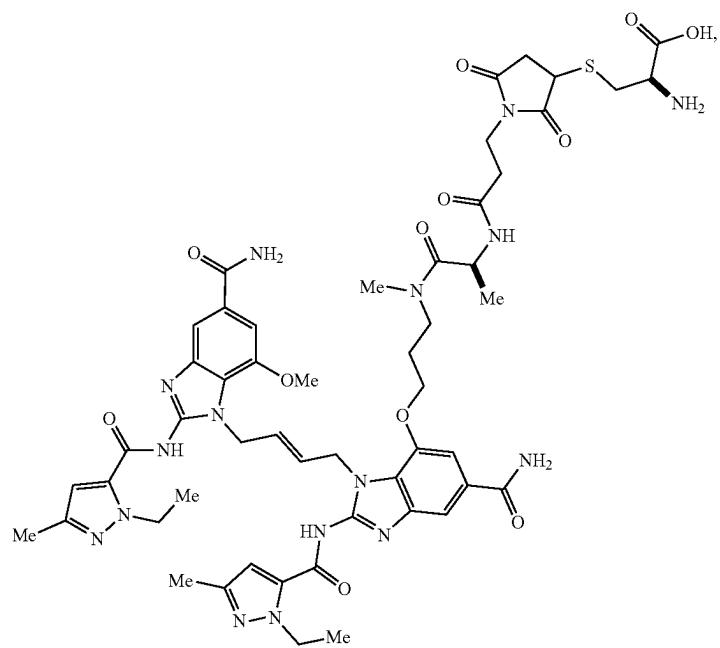
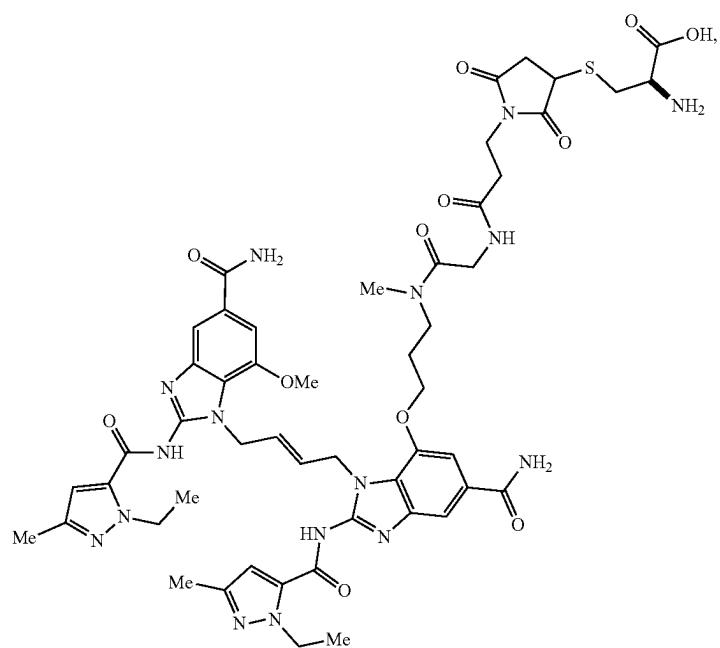
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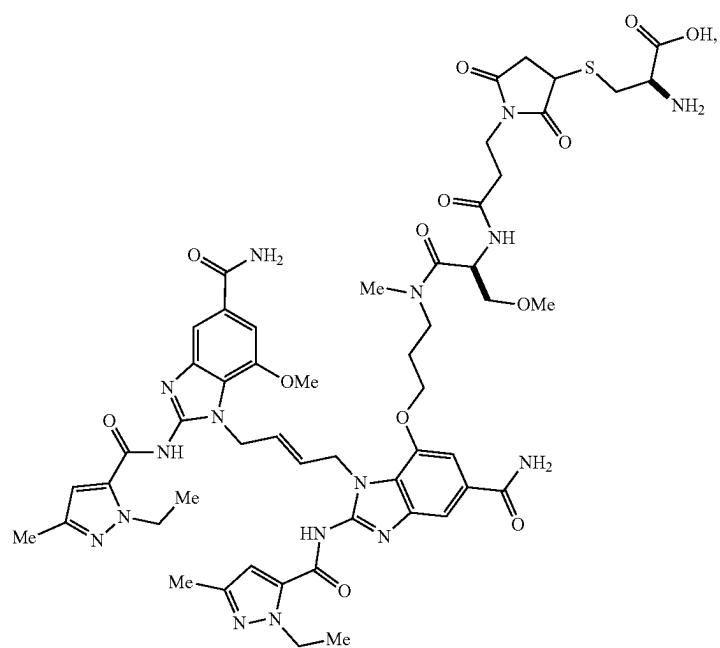
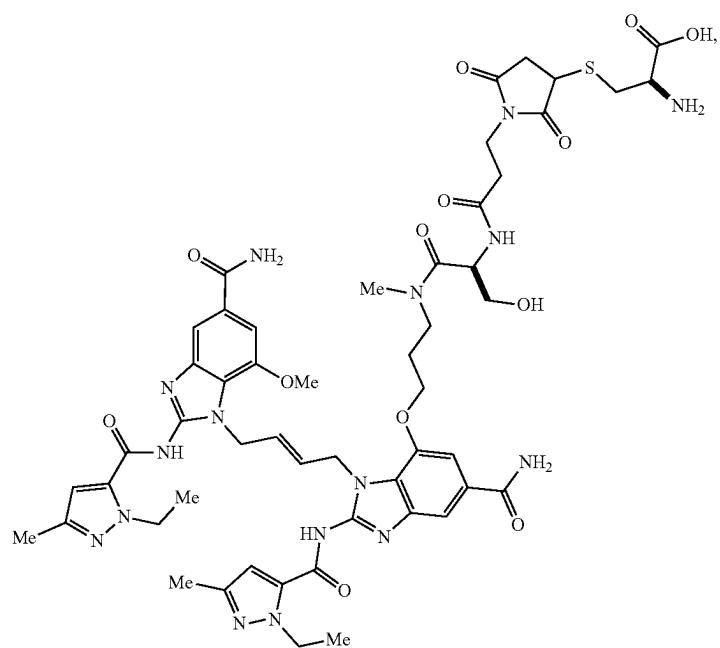
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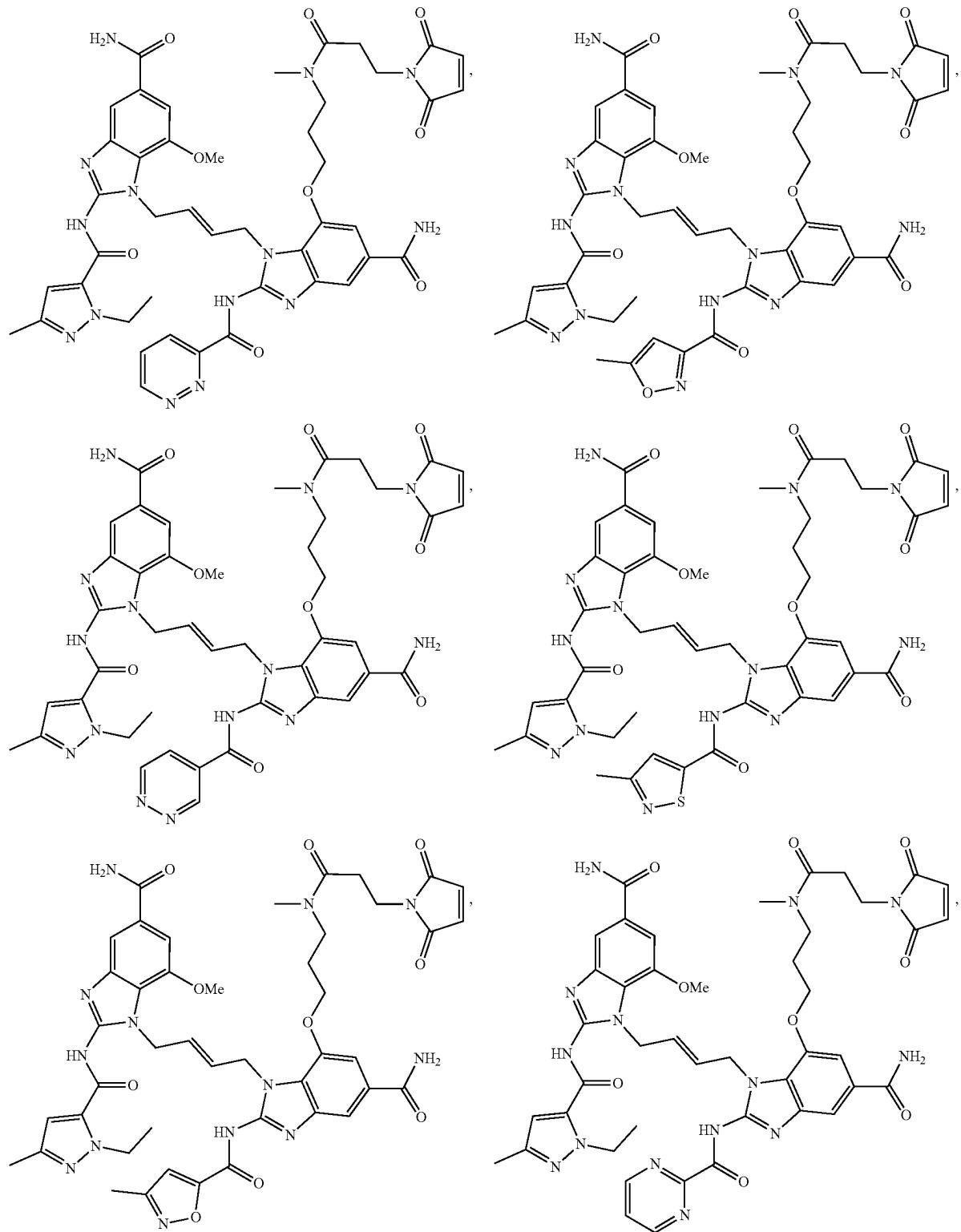
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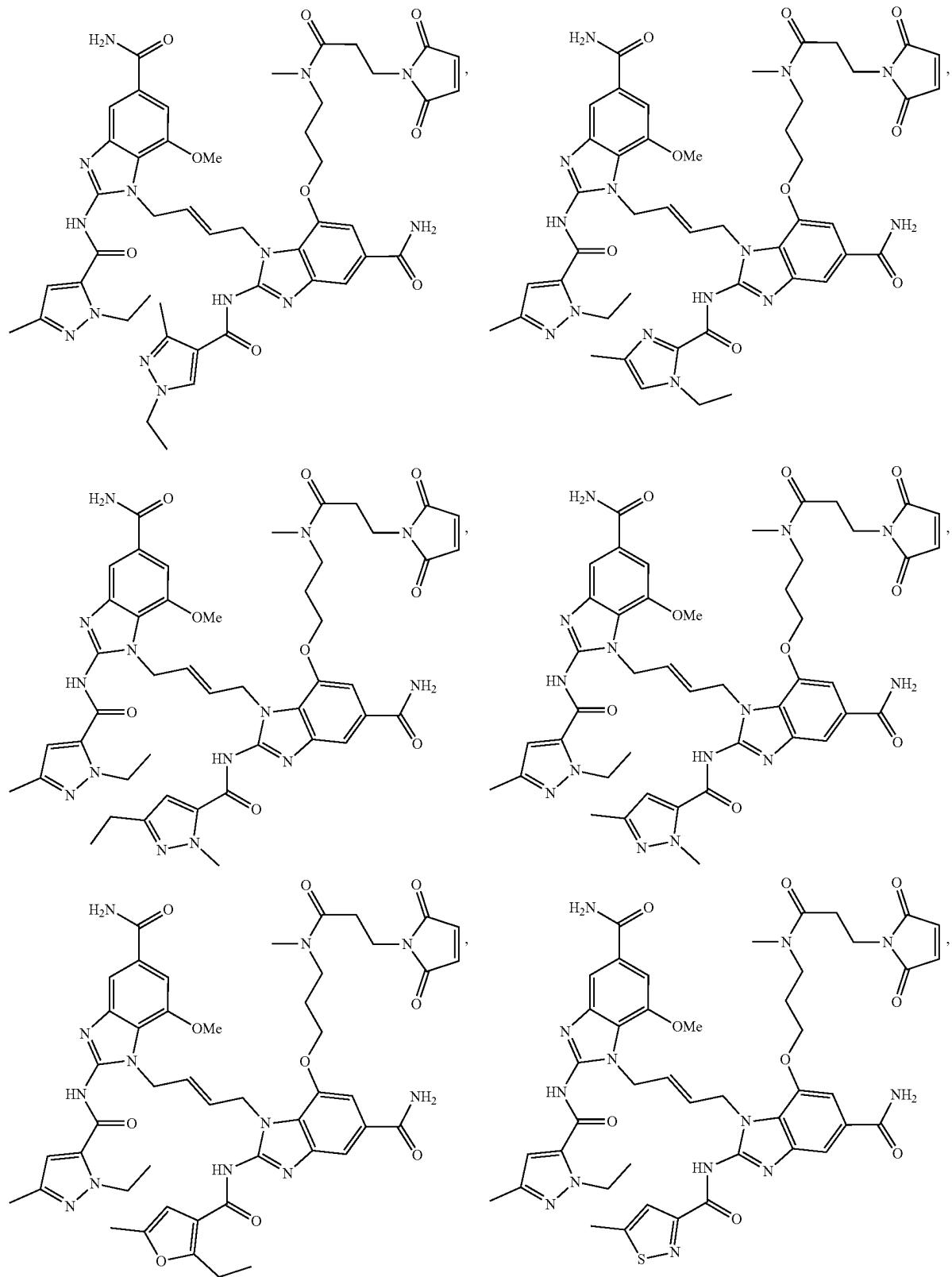
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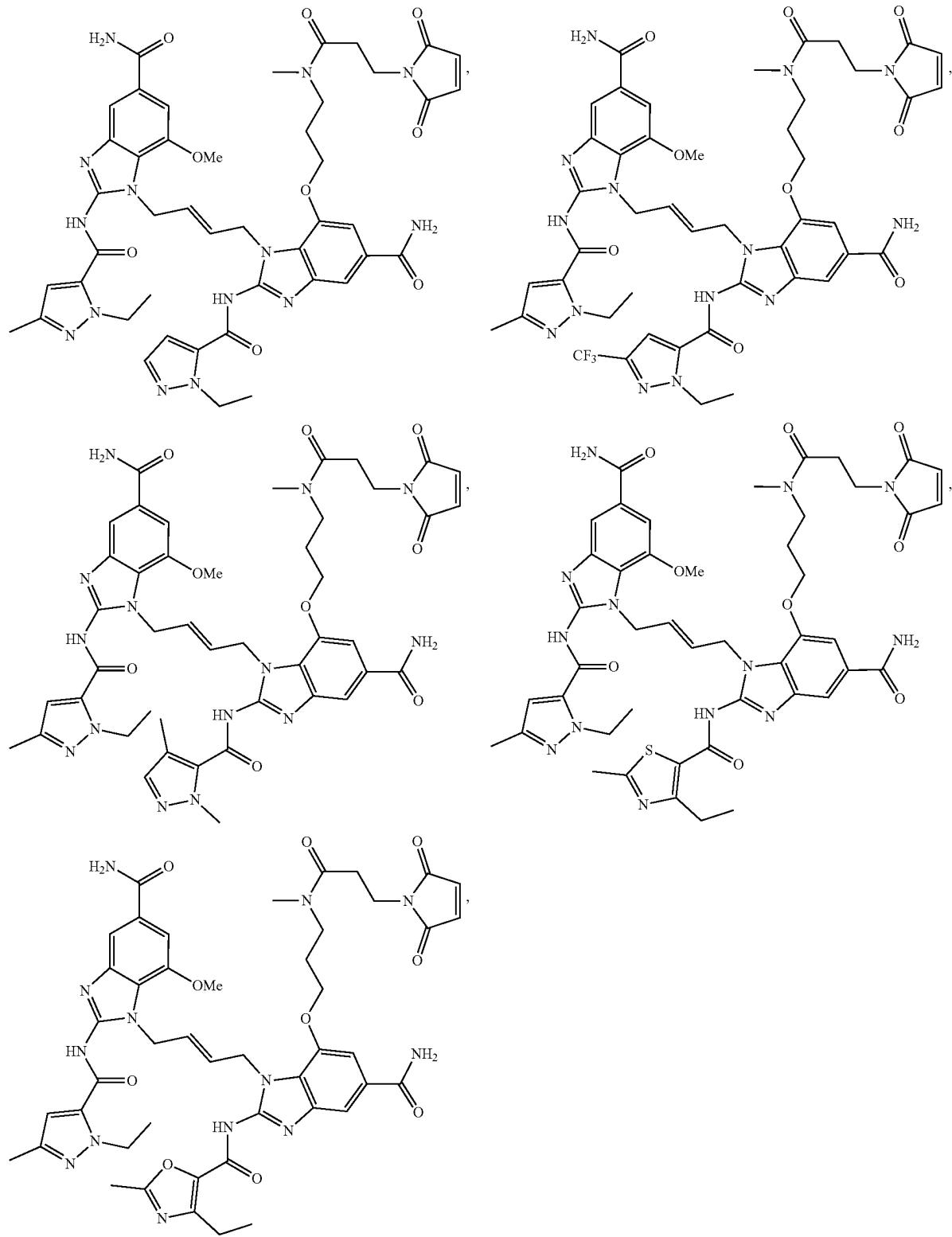
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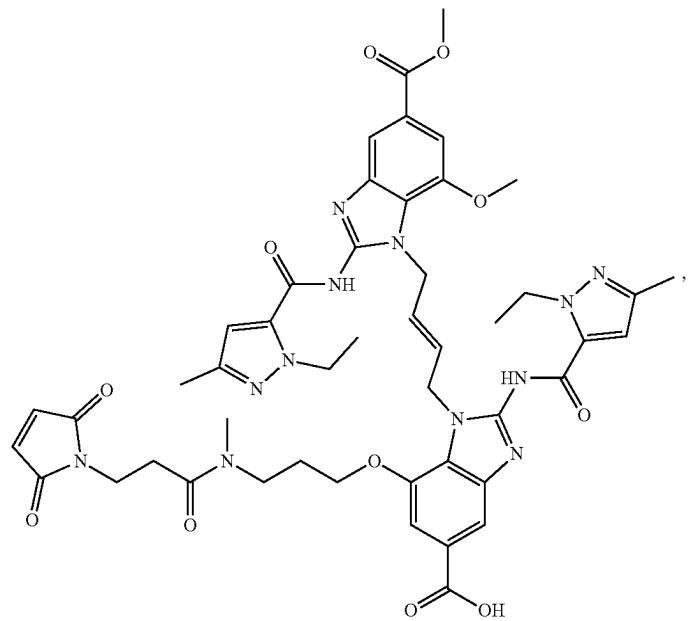
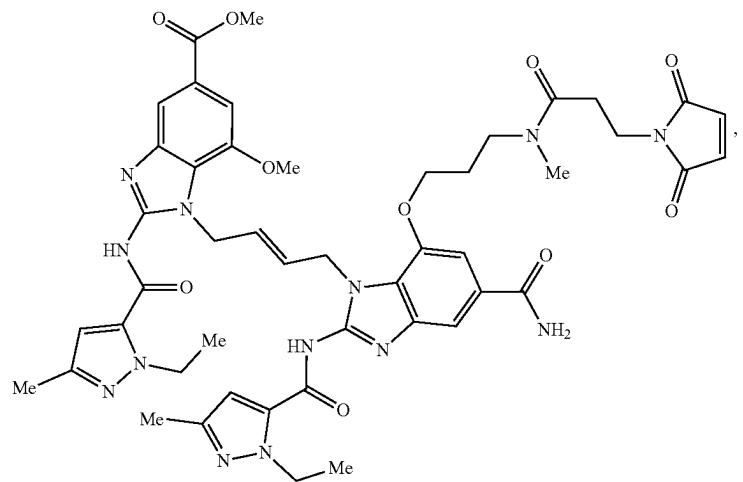
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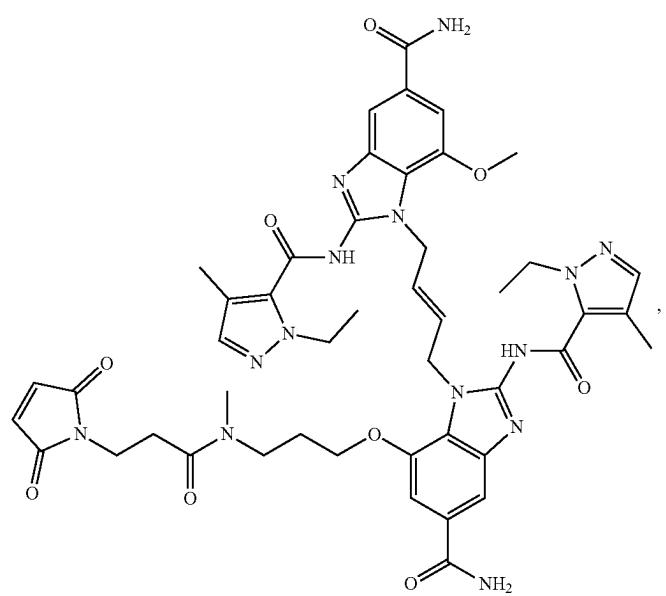
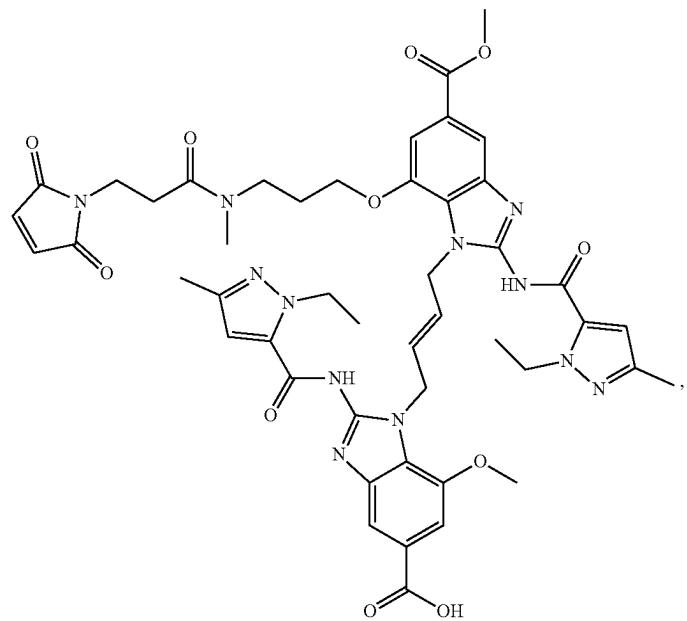
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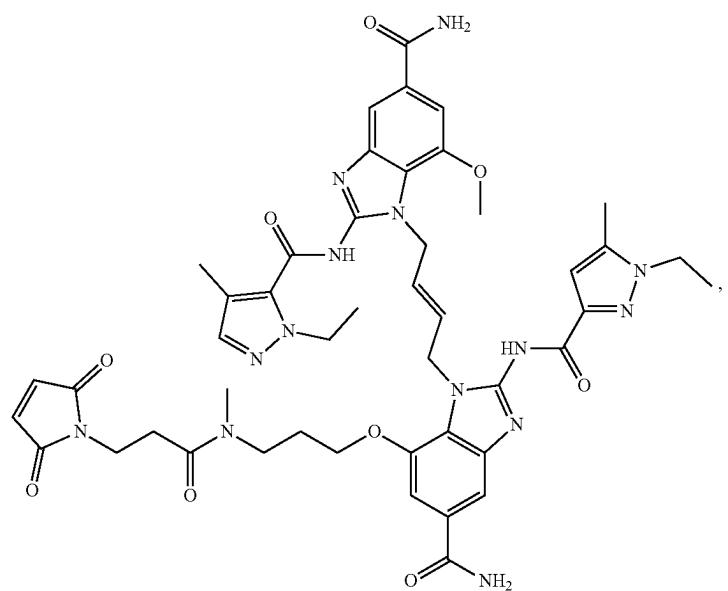
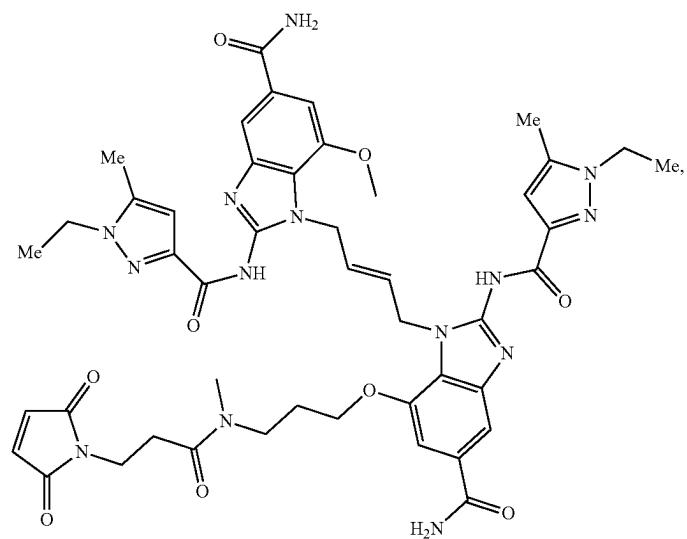
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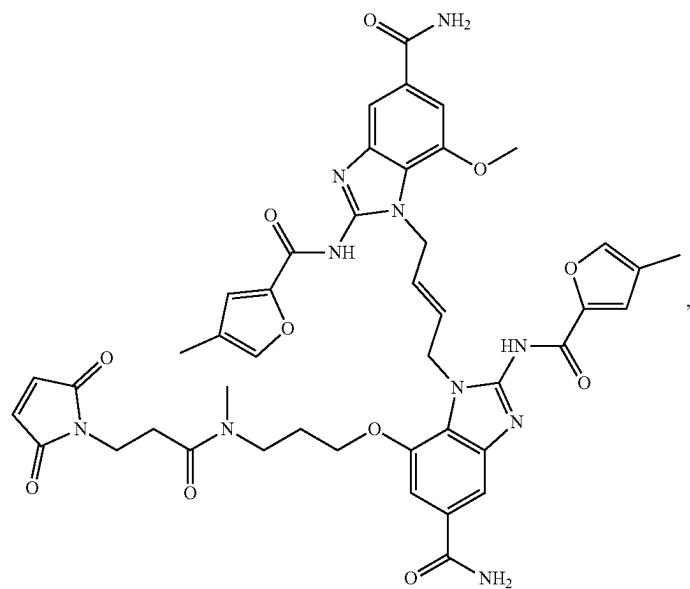
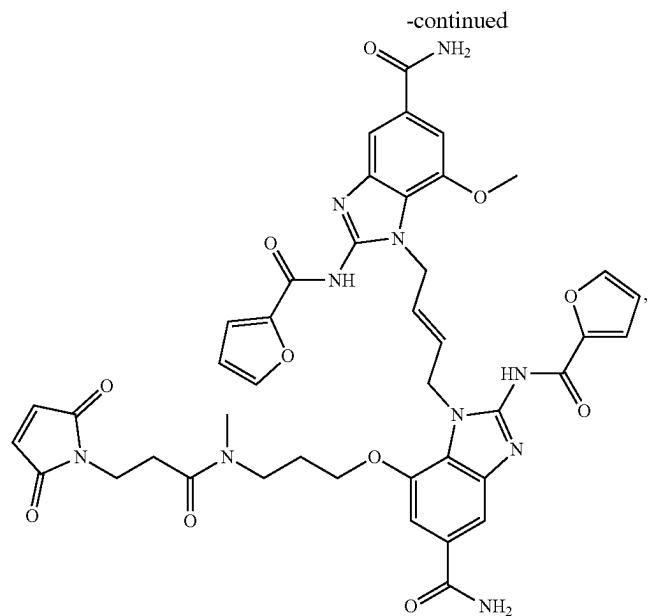
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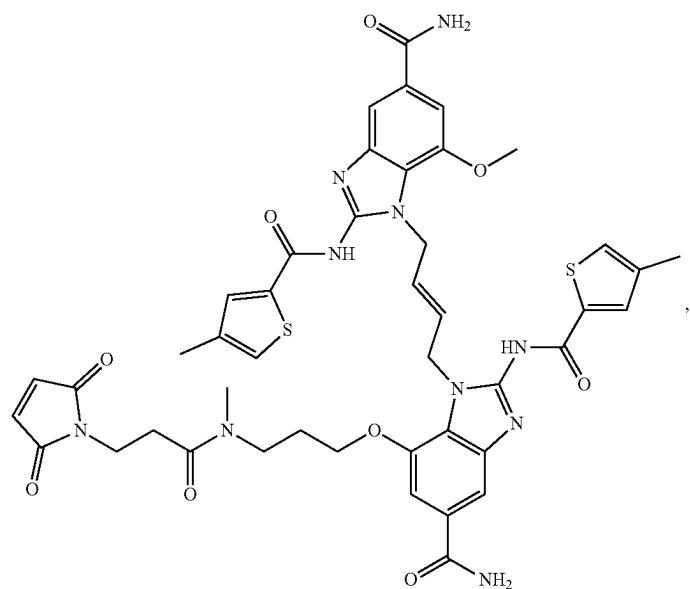
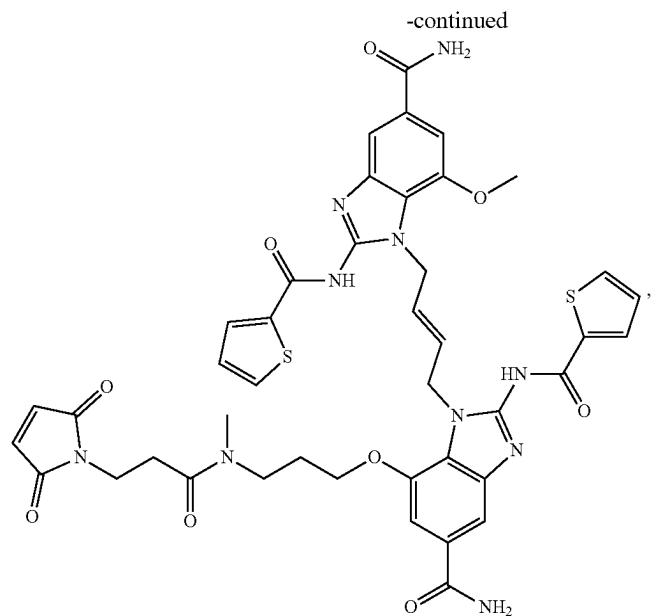
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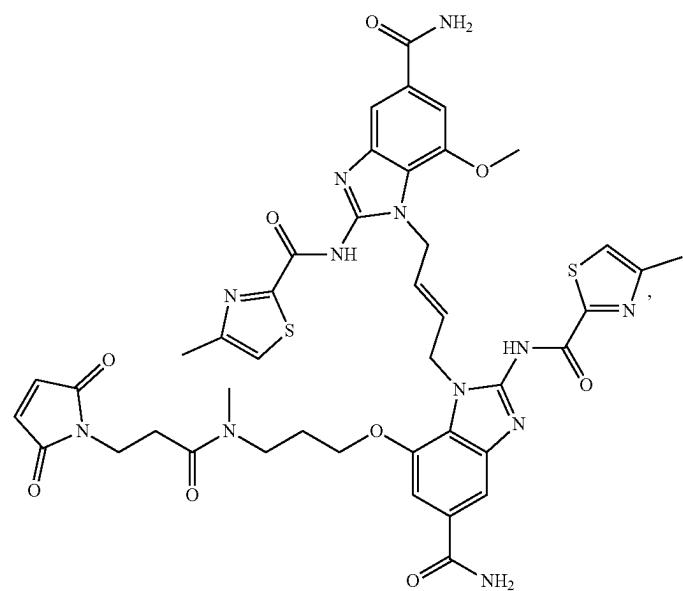
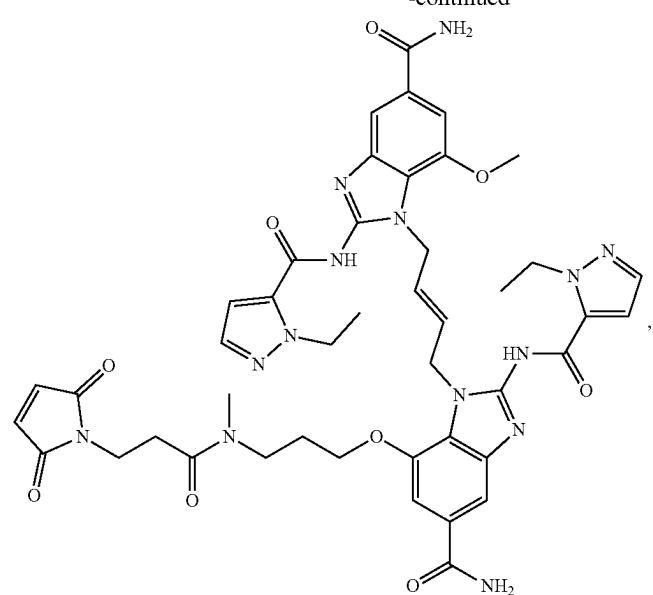
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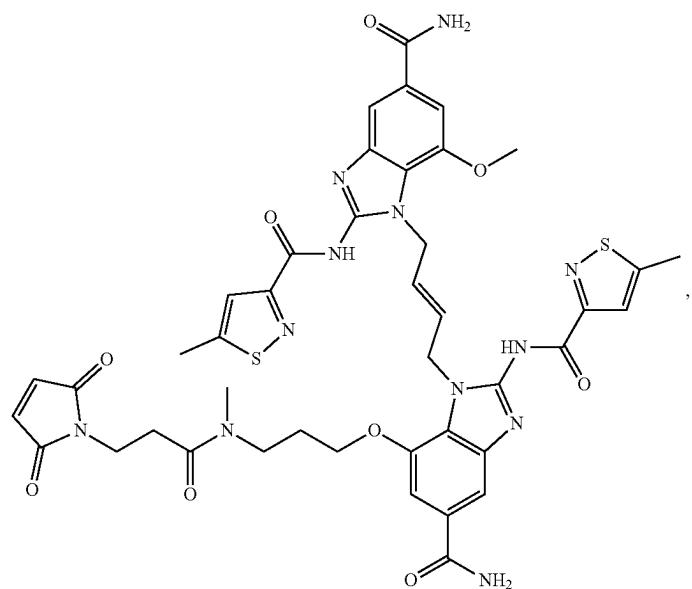
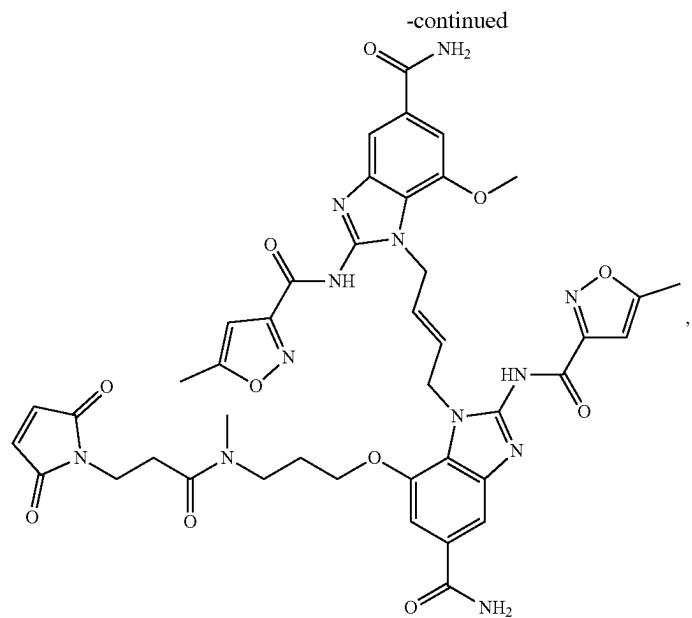
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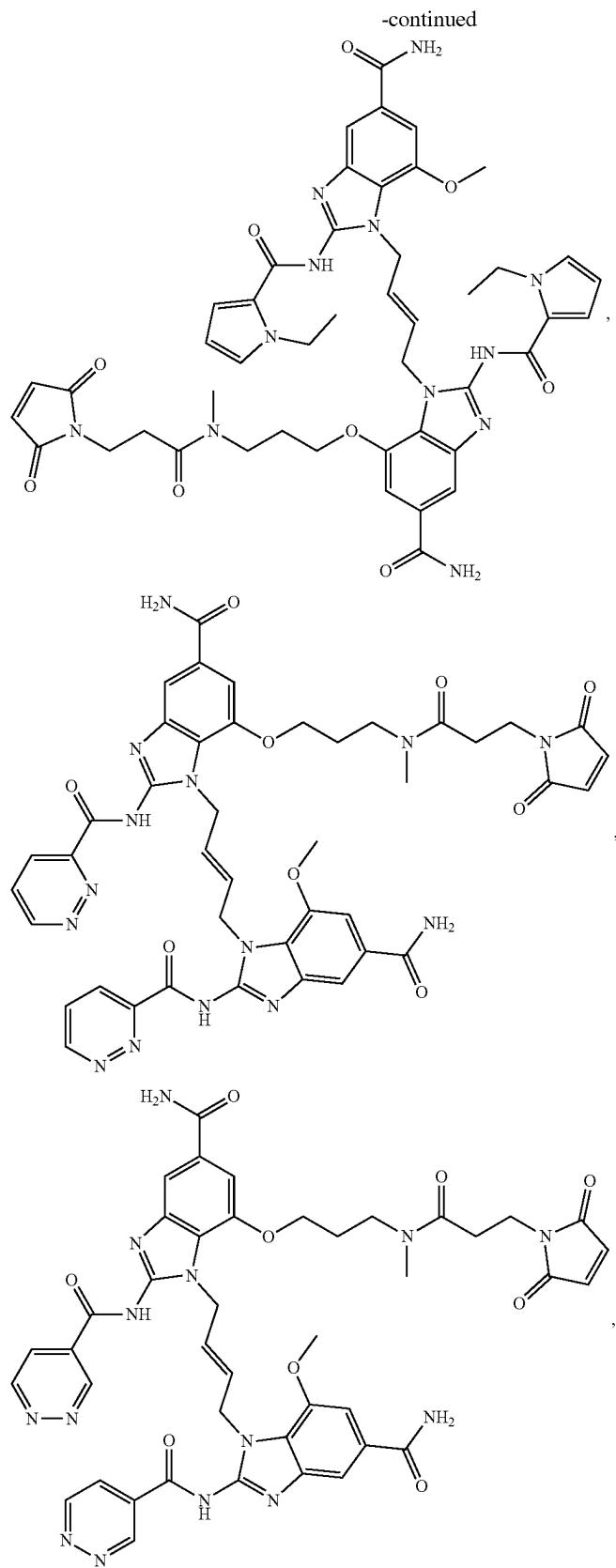


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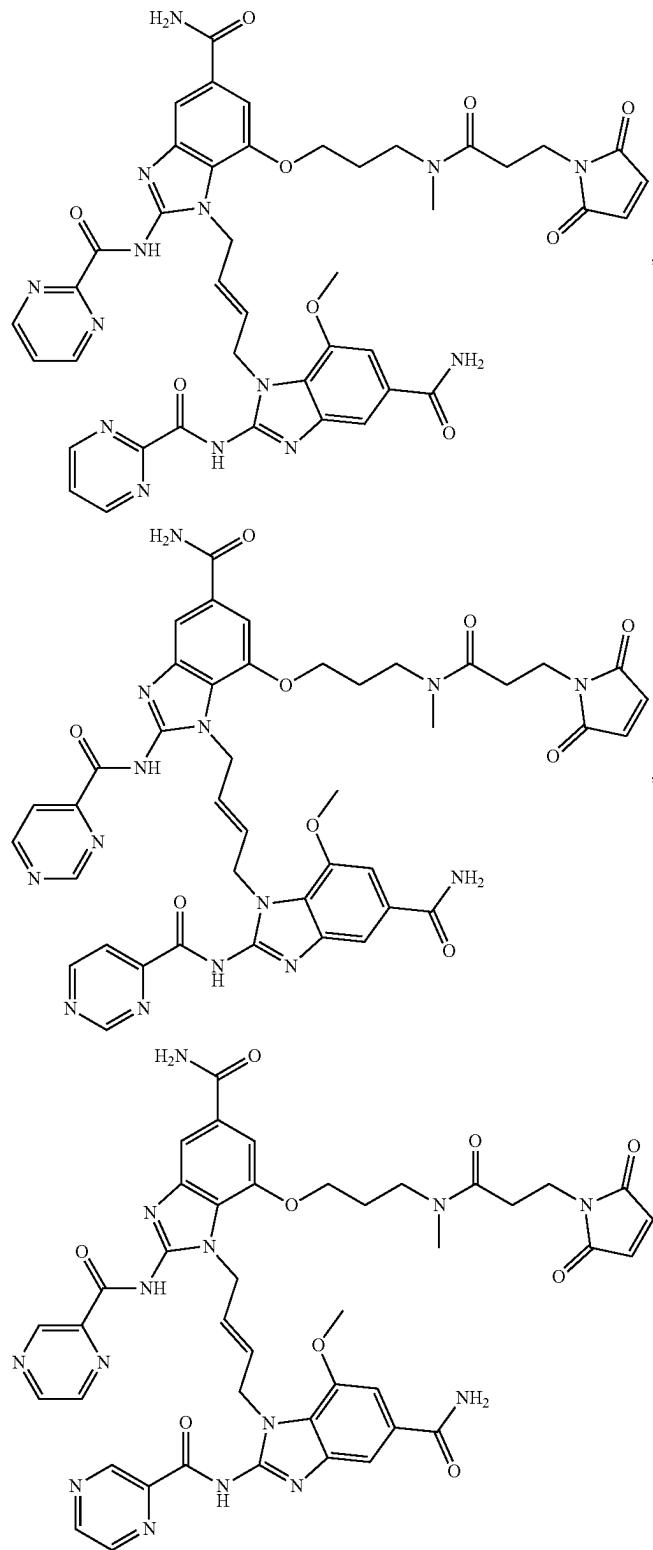


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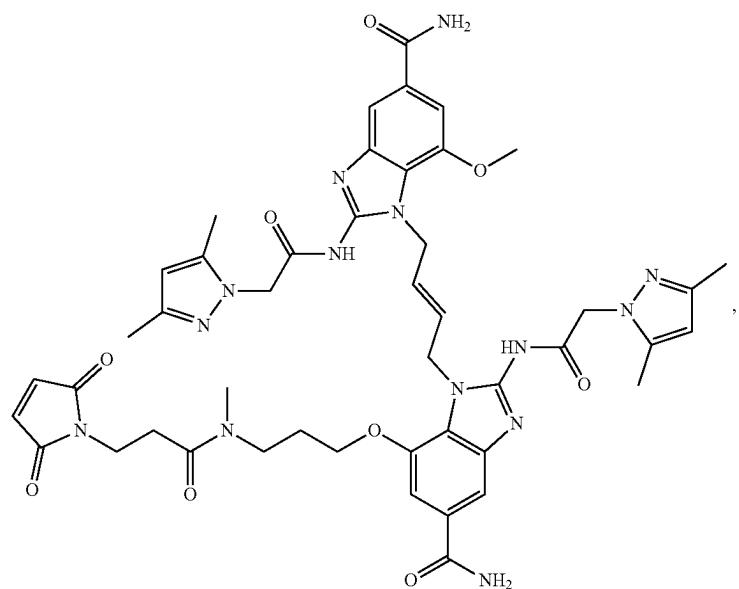
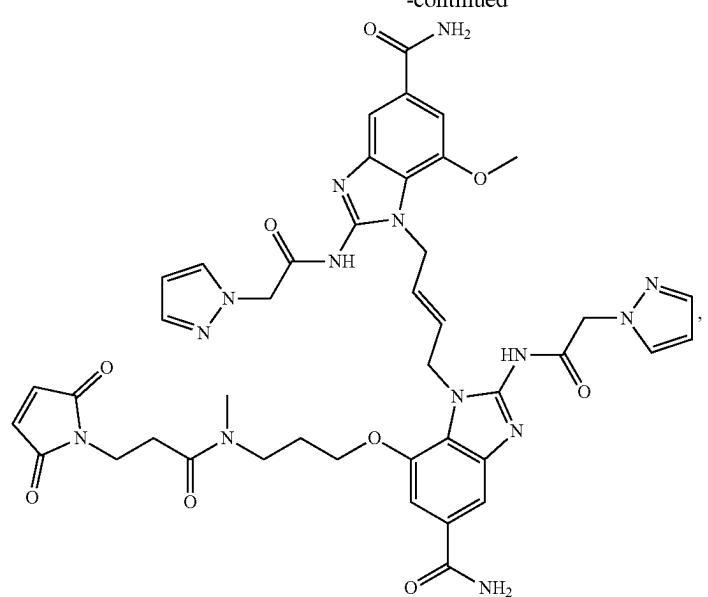




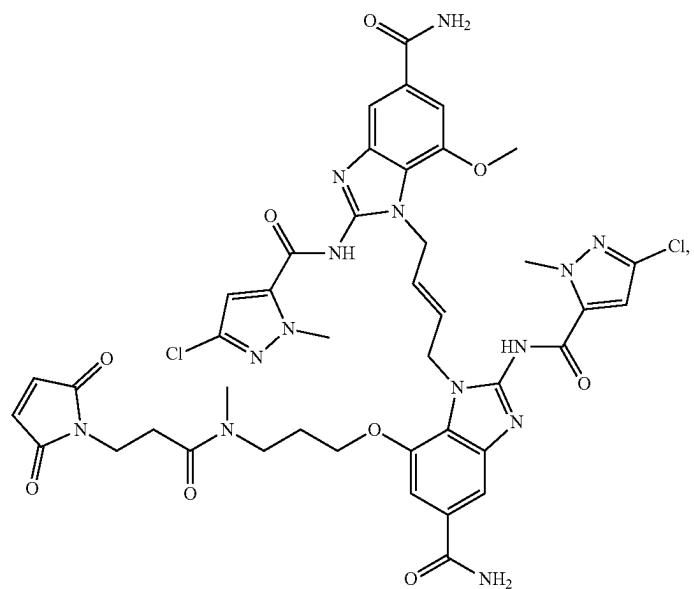
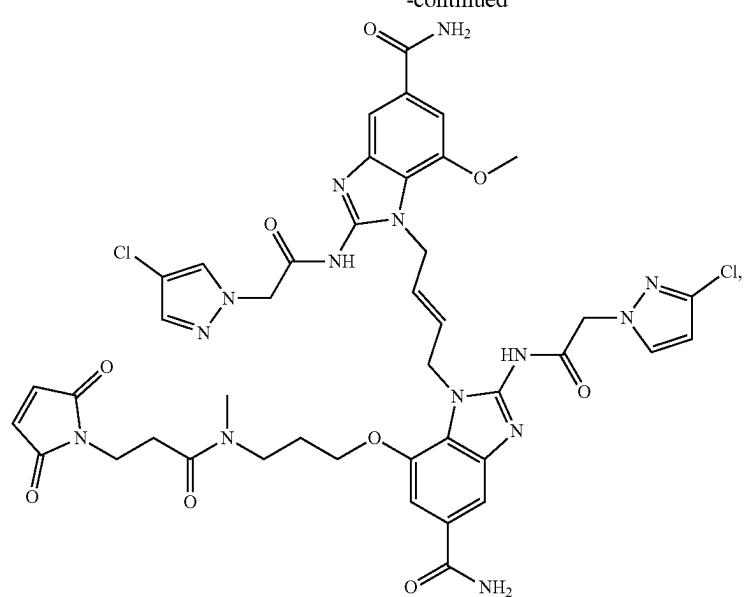
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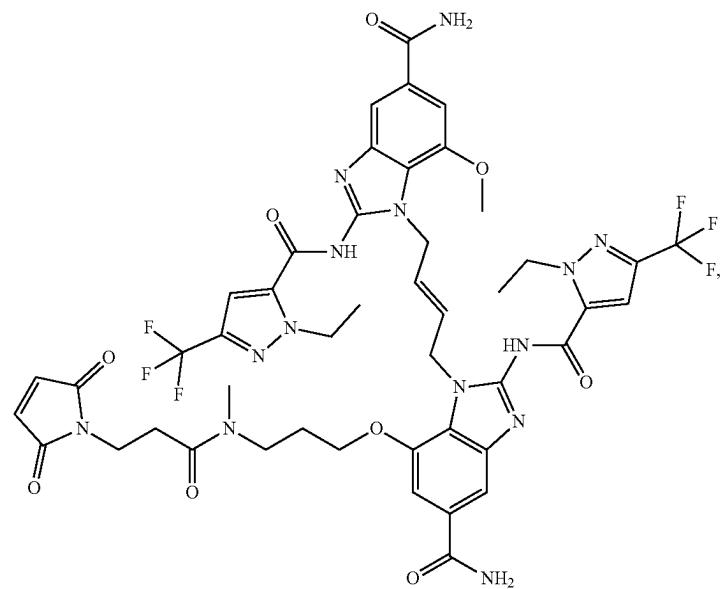
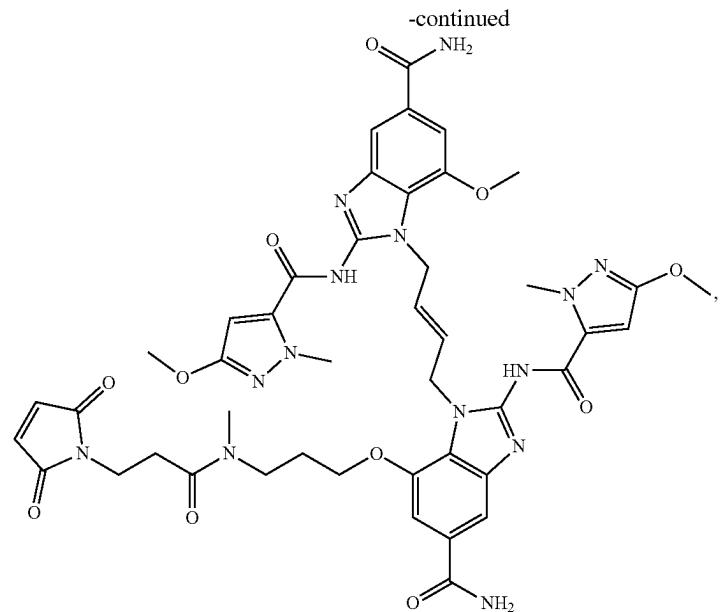
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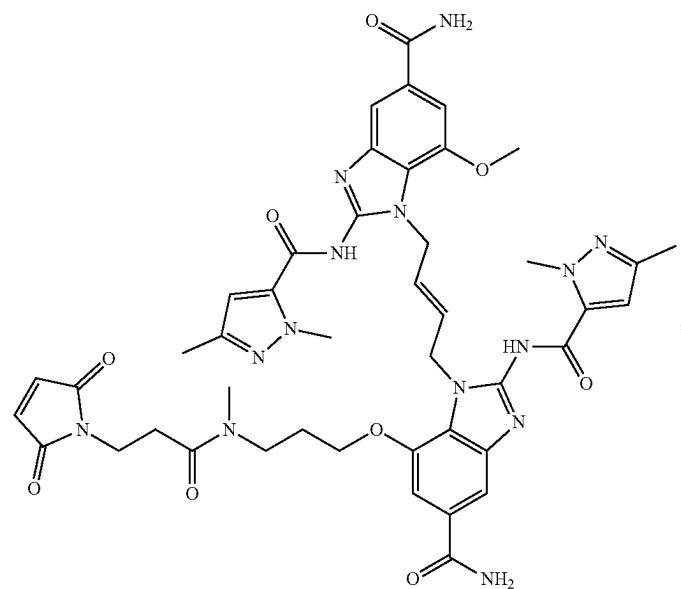
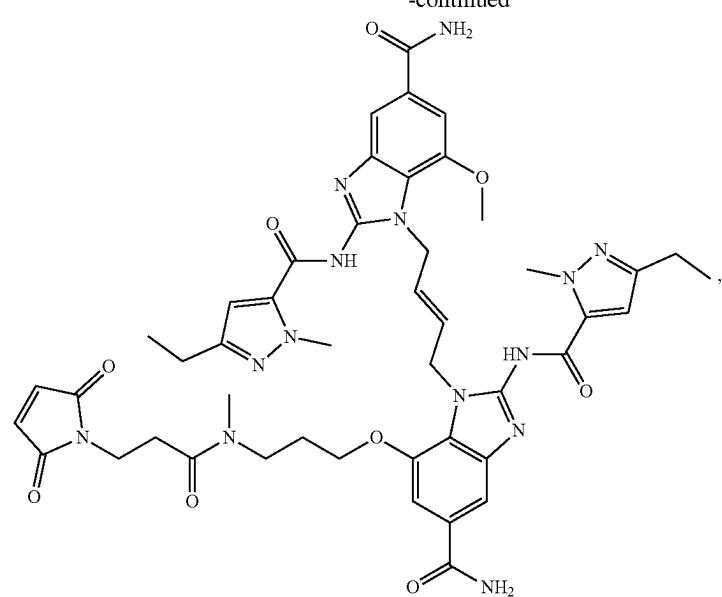
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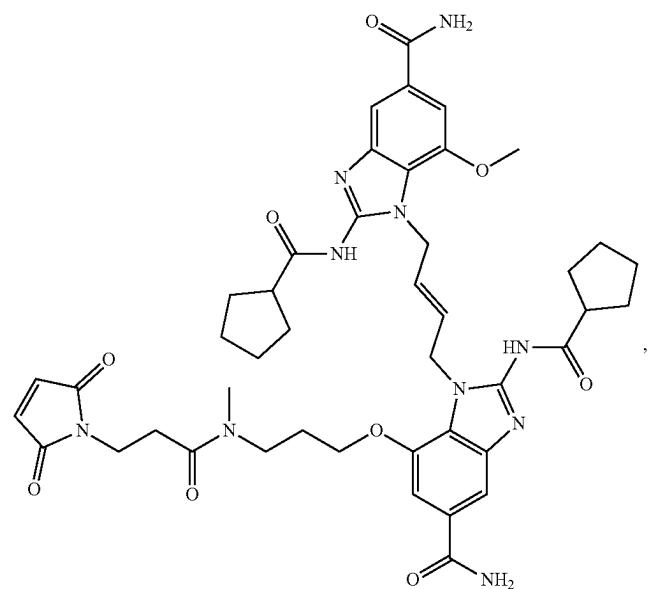
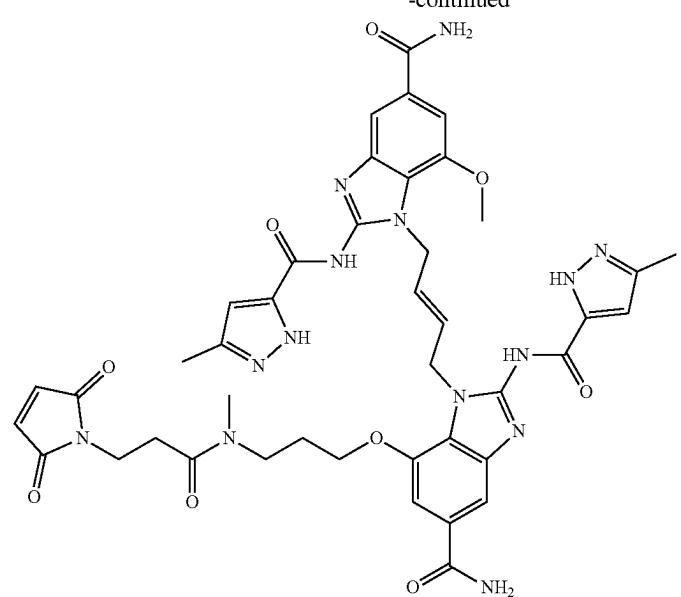
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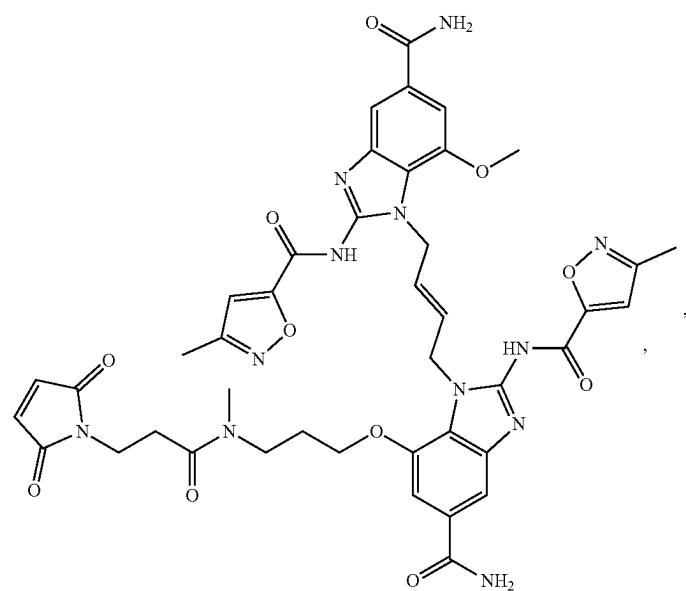
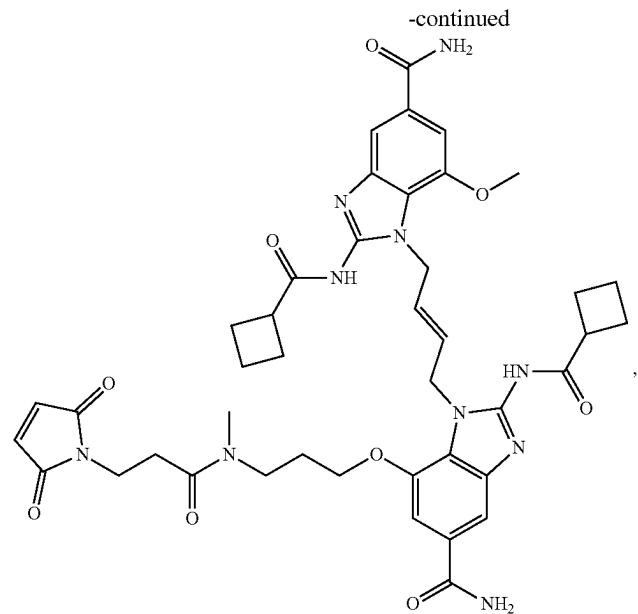
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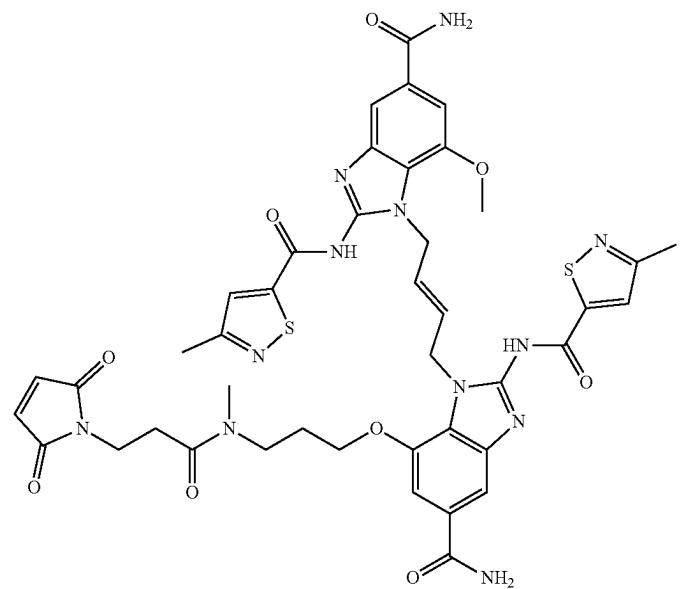
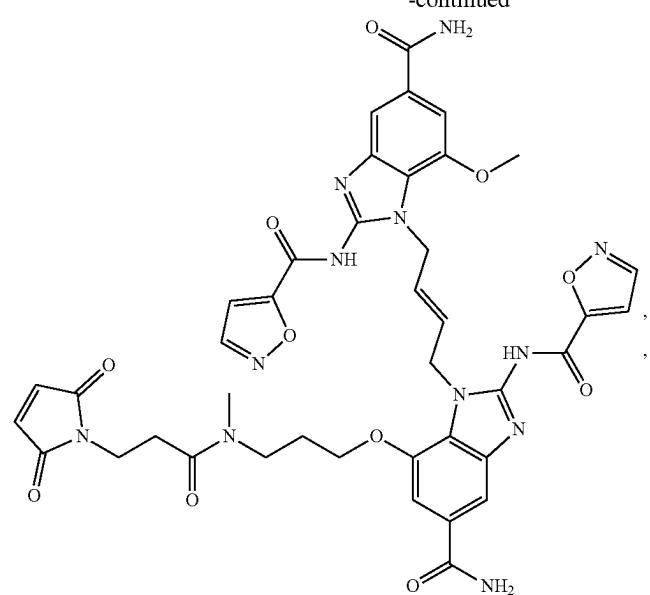
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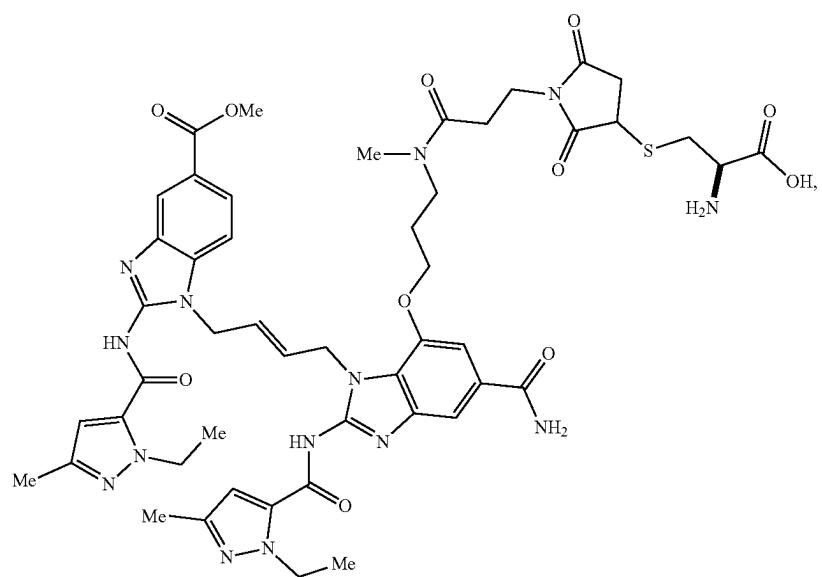
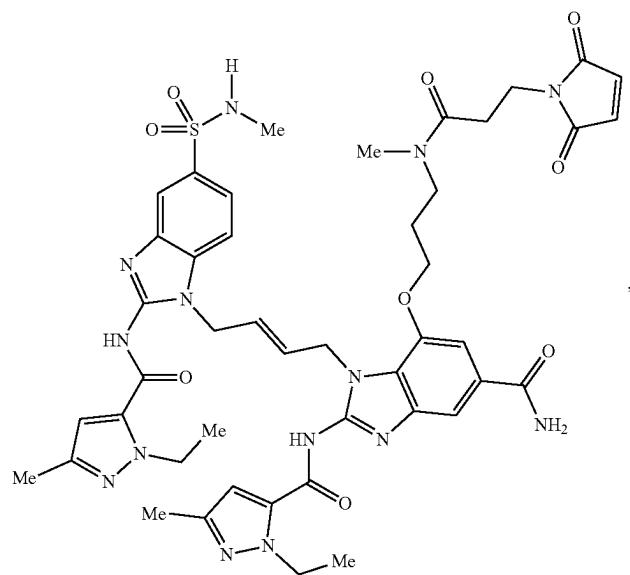
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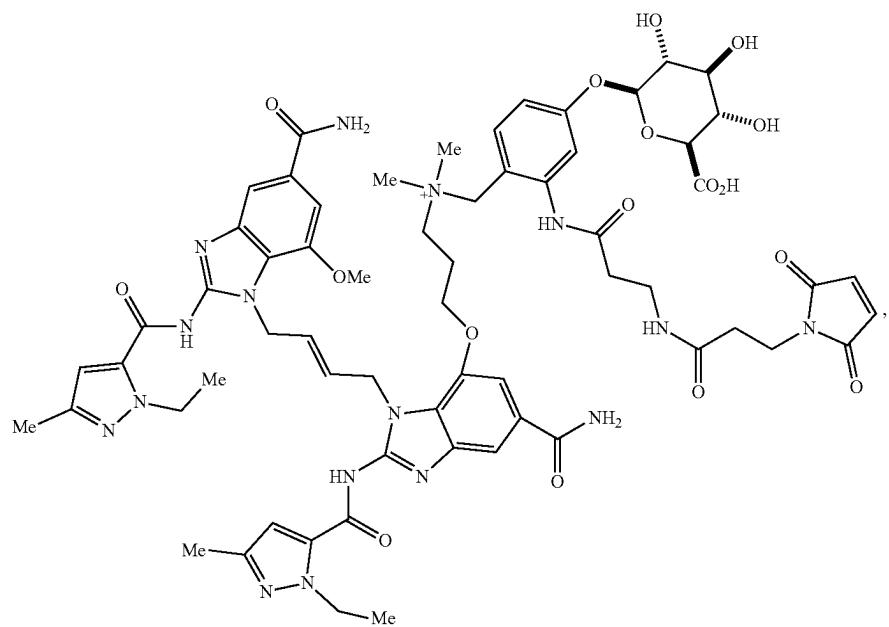
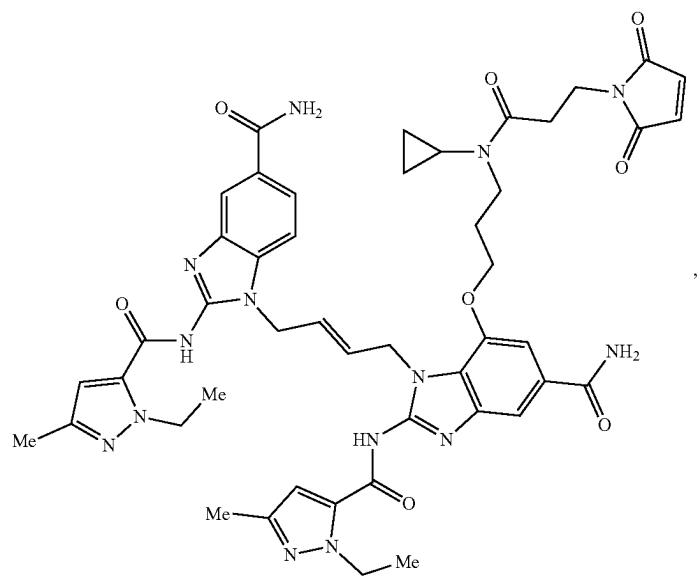
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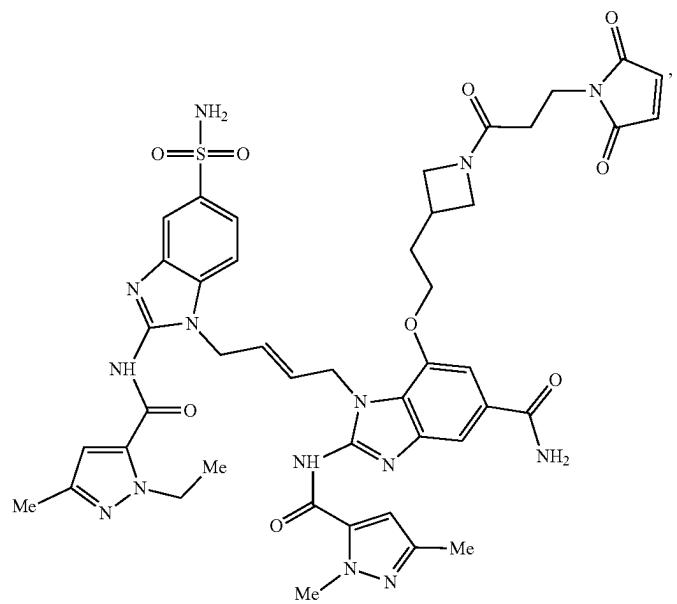
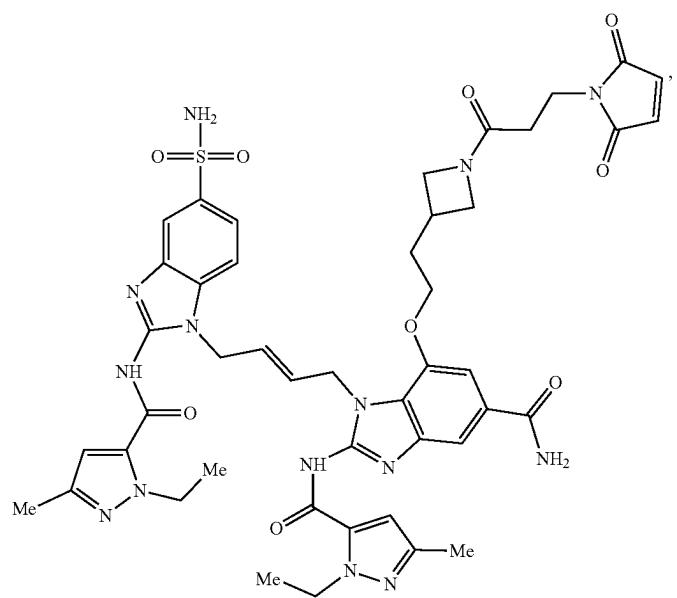


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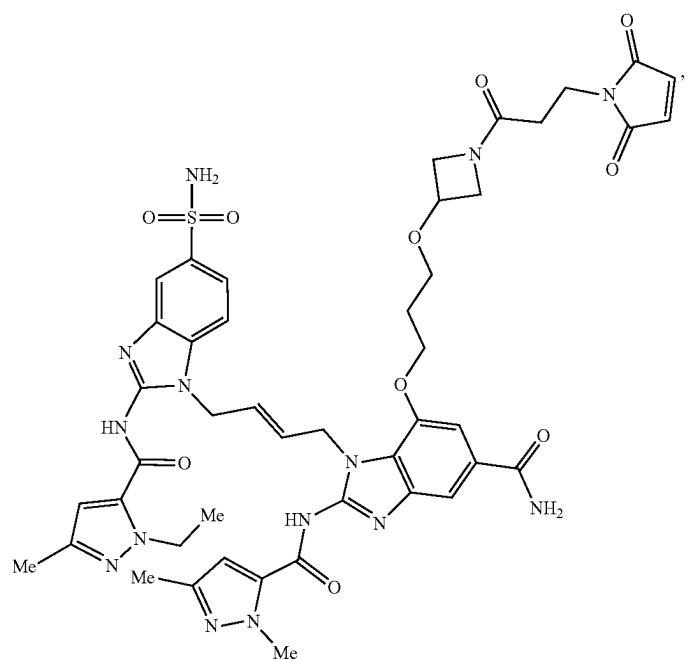
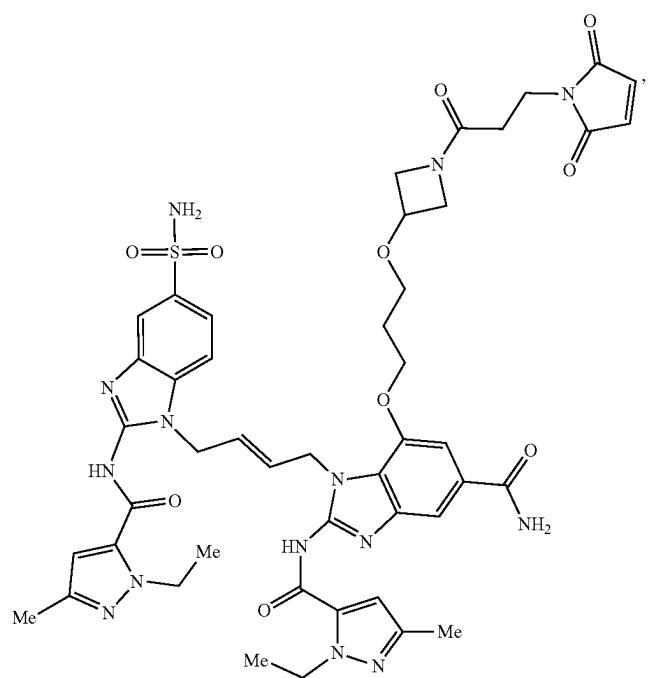


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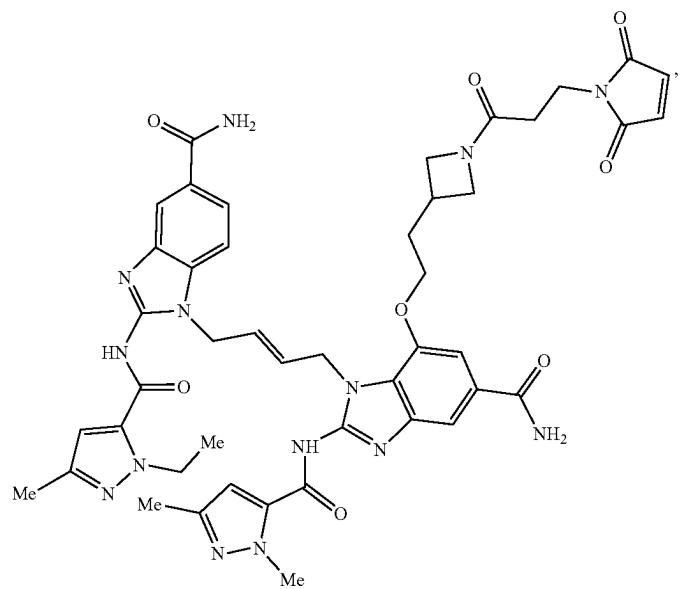
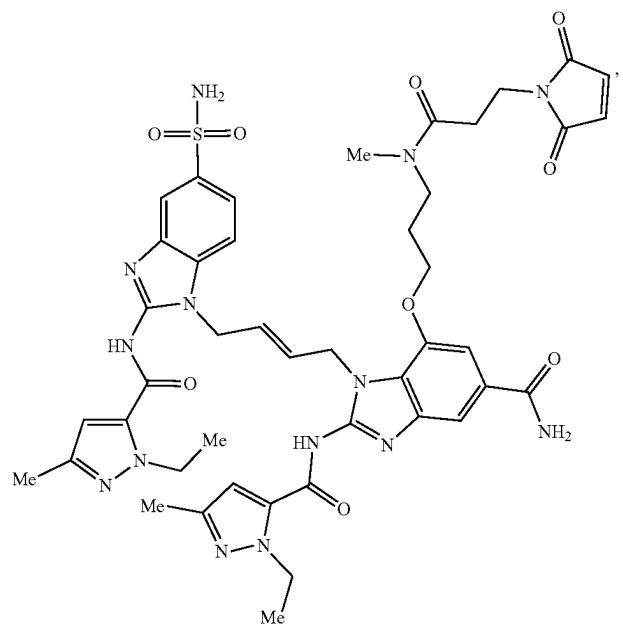




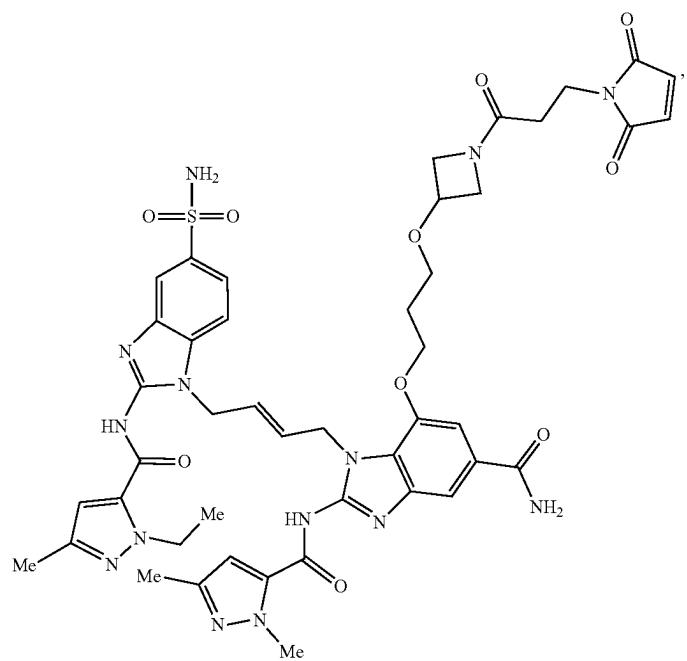
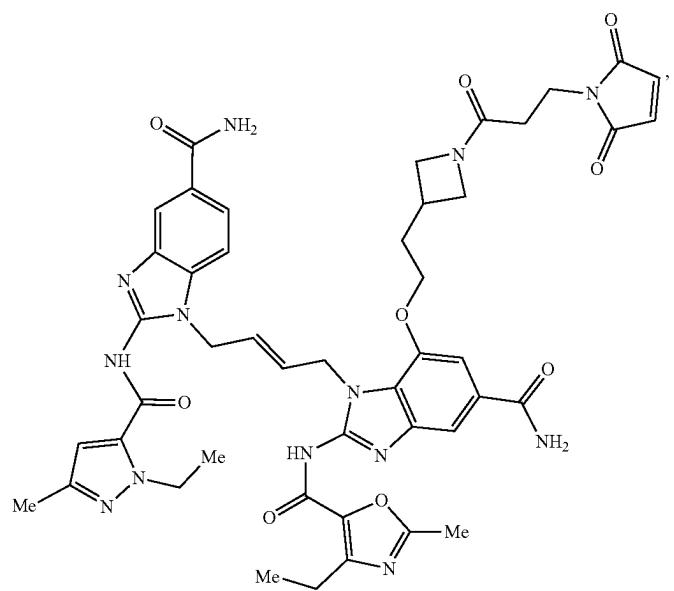
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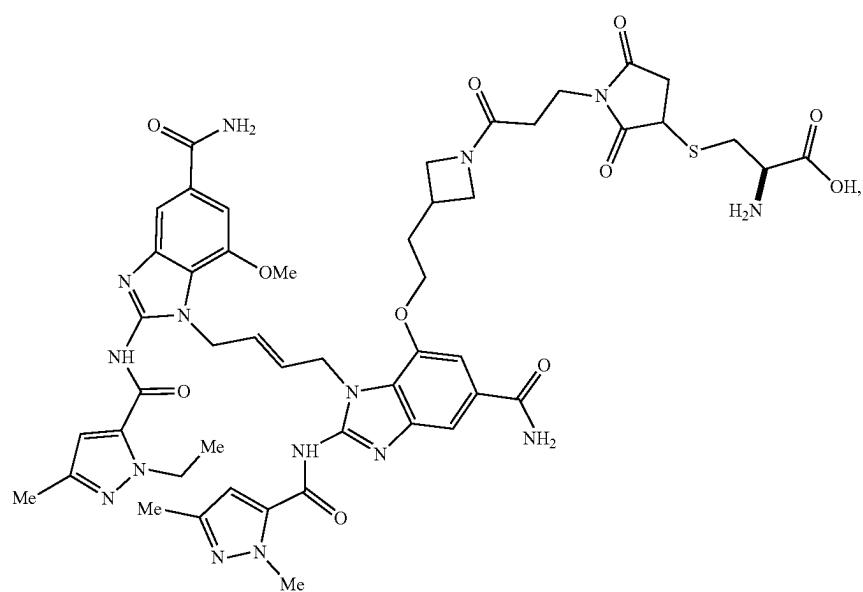
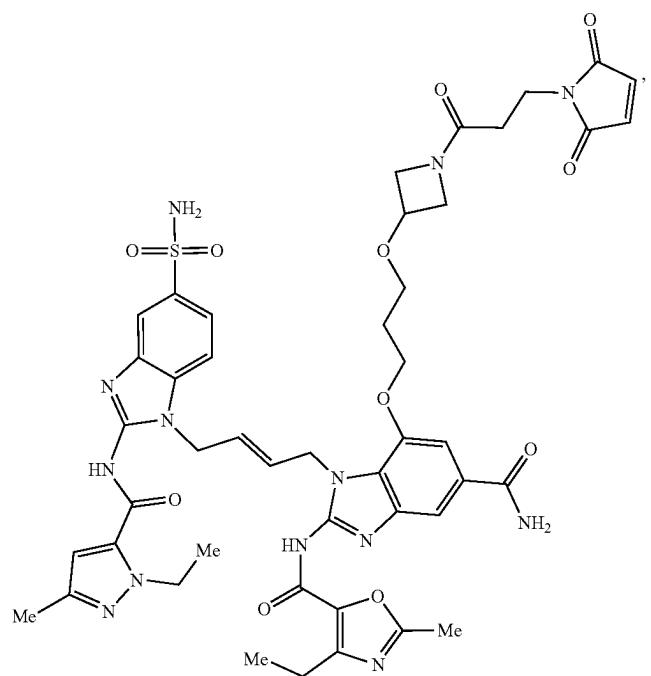
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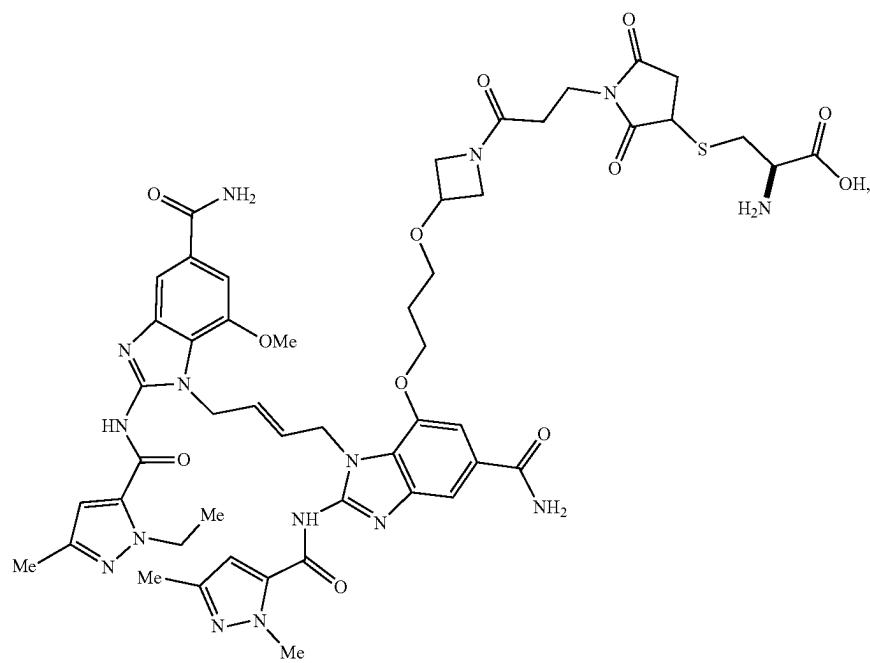
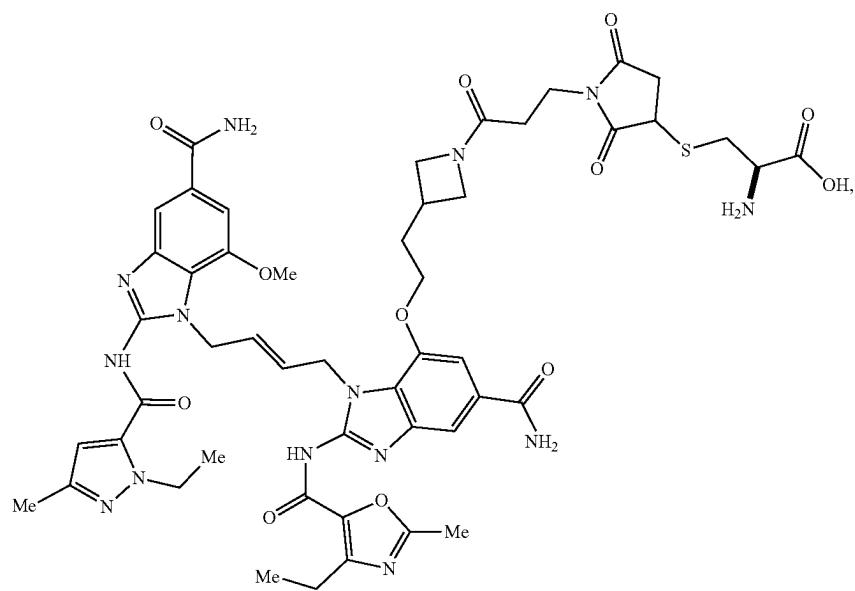
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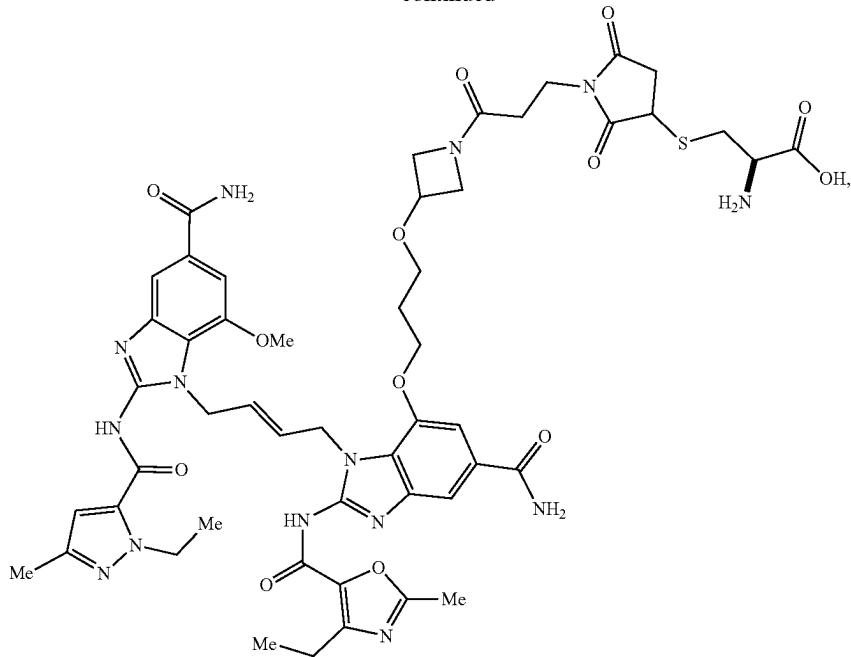
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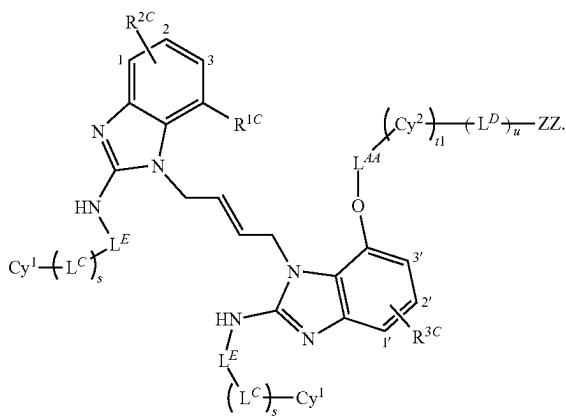
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and pharmaceutically acceptable salts thereof.

[1242] 378. A compound having the structure of Formula (V):

(V)



or a pharmaceutically acceptable salt thereof, wherein:

[1243] R^{1C} is hydrogen, hydroxyl, C₁₋₆ alkoxy, -(C₁₋₆ alkyl), C₁₋₆ alkoxy, -(CH₂)_n-NR^AR^B, or PEG2 to PEG4;

[1244] R^{2C} is -CO₂R^M, -(C=O)NR^CR^D, -S(O)₂NR^CR^D, -S(O)₂R^M, -(CH₂)_q-NR^ER^F, -(CH₂)_q-OR^M, -O(C=O)-NR^ER^F, or -NR^M(C=O)-NR^ER^N, wherein R^{2C} is attached at any one of positions labeled 1, 2, or 3;

[1245] R^{3C} is -CO₂R^M, -(C=O)NR^CR^D, -S(O)₂NR^CR^D, -S(O)₂R^M, -(CH₂)_q-NR^ER^F, -(CH₂)_q-

—OR^M, —O(C=O)—NR^ER^F, or —NR^M(C=O)—NR^ER^F, wherein R^{3C} is attached at any one of positions labeled 1', 2', or 3';

[1246] each R^A, R^B, R^C, R^D, R^E, R^F, and R^M are independently hydrogen or C₁₋₆ alkyl;

[1247] each subscript n is independently an integer from 0 to 6;

[1248] each subscript q is independently an integer from 0 to 6;

[1249] L^E is -(C=O)— or —S(O)₂—;

[1250] L^C is -(CR^IR^J)₁₋₃—

[1251] each R^I and R^J are independently hydrogen or C₁₋₃ alkyl;

[1252] subscript s is 0 or 1;

[1253] each Cy¹ is independently a 4-6 membered heterocycle, a 5-6 membered heteroaryl, or a C₃₋₆ cycloalkyl, each optionally substituted with one or more R^K;

[1254] each R^K is independently selected from the group consisting of: C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, halogen, —OH, =OH, =O, —NR^{d2}R^{e2}, —C(O)NR^{d2}R^{e2}, —C(O)(C₁₋₆ alkyl), and —C(O)(C₁₋₆ alkyl);

[1255] each R^{d2} and R^{e2} are independently hydrogen or C₁₋₃ alkyl;

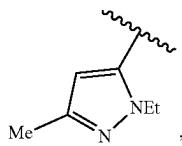
[1256] L^A is -(CH₂)₁₋₆—, —C(O)(CH₂)₁₋₆—, —C(O)NR^L(CH₂)₁₋₆—, —(CH₂)₁₋₆O—, —C(O)(CH₂)₁₋₆O—, or —C(O)NR^L(CH₂)₁₋₆O—;

[1257] R^L is hydrogen or C₁₋₃ alkyl;

[1258] Cy² is C₃₋₆ cycloalkyl, 4-6 membered heterocycle, 5-6 membered heteroaryl, or phenyl, each optionally substituted with one or more RU;

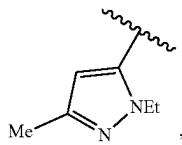
[1259] each R^U is independently selected from the group consisting of —CO₂R^I, —(C=O)NR^{a3}R^{e3}, —S(O)₂NR^{d3}R^{e3}, —(CH₂)_{q1}-NR^{g1}R^{h1}, —(CH₂)_{q1}-OR^I, and —(CH₂)_{q1}-(OCH₂CH₂)₁₋₈OH;

- [1260] each R^{d3} , R^{e3} , R^9 , R^{h1} , and R^{j1} are independently hydrogen or C_{1-6} alkyl;
- [1261] subscript q1 is an integer from 0 to 6;
- [1262] subscript t1 is 0 or 1;
- [1263] L^D is $-(CH_2)_{1-6}-$;
- [1264] subscript u is 0 or 1;
- [1265] when t1 is 0, ZZ is $-NR^Q R^R$, $-N^+(C_{1-6}$ alkyl) $R^Q R^R$, $-C(=O)N^S R^T$, $-C(O)O(C_{1-6}$ alkyl), $-CO_2H$, or an amino acid, or when t1 is 1, ZZ is hydrogen, $-NR^Q R^R$, $-N^+(C_{1-6}$ alkyl) $R^Q R^R$; $-C(=O)N^S R^T$, $-C(O)O(C_{1-6}$ alkyl), $-CO_2H$, or an amino acid;
- [1266] R^Q is hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, $-(CH_2)_{1-3}C_{3-6}$ cycloalkyl, $-(CH_2)_{1-3}C_{1-3}$ alkoxy, $-(CH_2)_{1-3}$ 4-6 membered heterocycle, or $-(CH_2)_{1-3}$ 5-6 membered heteroaryl, provided that
- [1267] if t1 is 0 and both Cy¹ are



then R^Q is C_{2-6} alkyl, C_{3-6} cycloalkyl, $-(CH_2)_{1-3}C_{3-6}$ cycloalkyl, $-(CH_2)_{1-3}C_{1-3}$ alkoxy, $-(CH_2)_{1-3}$ 4-6 membered heterocycle, or $-(CH_2)_{1-3}$ 5-6 membered heteroaryl, and

- [1268] if t1 is 0 and at least one Cy¹ is not



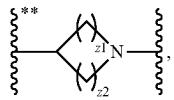
then ZZ is $-NR^Q R^R$, $-N+(C_{1-6}$ alkyl) $R^Q R^R$, or $-C(=O)N^S R^T$, and R^Q is C_{1-6} alkyl, C_{3-6} cycloalkyl, $-(CH_2)_{1-3}C_{3-6}$ cycloalkyl, $-(CH_2)_{1-3}C_{1-3}$ alkoxy, $-(CH_2)_{1-3}$ 4-6 membered heterocycle, or $-(CH_2)_{1-3}$ 5-6 membered heteroaryl;

- [1269] each R^R , R^S , and R^T are independently hydrogen or C_{1-6} alkyl.
- [1270] 379. The compound of Embodiment 378, wherein R^{1C} is hydrogen.
- [1271] 380. The compound of Embodiment 378, wherein R^{1C} is hydroxyl.
- [1272] 381. The compound of Embodiment 378, wherein R^{1C} is C_{1-6} alkoxy.
- [1273] 382. The compound of Embodiment 378, wherein R^{1C} is methoxy.
- [1274] 383. The compound of Embodiment 378, wherein R^{1C} is $-(C_{1-6}$ alkyl) C_{1-6} alkoxy.
- [1275] 384. The compound of Embodiment 378, wherein R^{1C} is methoxyethyl.
- [1276] 385. The compound of Embodiment 378, wherein R^{1C} is PEG2 to PEG4.
- [1277] 386. The compound of Embodiment 378, wherein R^{1C} is $-(CH_2)_n-NR^E R^B$.
- [1278] 387. The compound of any one of Embodiments 378-386, wherein R^A and R^B are both hydrogen.

- [1279] 388. The compound of any one of Embodiments 378-386, wherein R^A and R^B are independently C_{1-3} alkyl.
- [1280] 389. The compound of any one of Embodiments 378-386, wherein one of R^A and R^B is hydrogen and the other of R^A and R^B is C_{1-3} alkyl.
- [1281] 390. The compound of any one of Embodiments 378-389, wherein each subscript n is 0.
- [1282] 391. The compound of any one of Embodiments 378-389, wherein each subscript n is 1.
- [1283] 392. The compound of any one of Embodiments 378-389, wherein each subscript n is 2.
- [1284] 393. The compound of any one of Embodiments 378-389, wherein each subscript n is 3, 4, 5, or 6.
- [1285] 394. The compound of any one of Embodiments 378-393, wherein R^{2C} and R^{3C} are independently $-CO_2H$, $-(C=O)_m-NR^C R^D$, or $-(CH_2)_q-NR^E R^F$; and R^{2C} and R^{3C} are the same.
- [1286] 395. The compound of any one of Embodiments 378-393, wherein R^{2C} and R^{3C} are independently $-CO_2H$, $-(C=O)_m-NR^C R^D$, or $-(CH_2)_q-NR^E R^F$; and R^{2C} and R^{3C} are different.
- [1287] 396. The compound of any one of Embodiments 378-393, wherein R^{2C} is $-(C=O)_m-NR^C R^D$.
- [1288] 397. The compound of any one of Embodiments 378-396, wherein R^{3C} is $-(C=O)_m-NR^C R^D$.
- [1289] 398. The compound of any one of Embodiments 378-397, wherein R^C and R^D are both hydrogen.
- [1290] 399. The compound of any one of Embodiments 378-397, wherein R^C and R^D are each independently C_{1-3} alkyl.
- [1291] 400. The compound of any one of Embodiments 378-397, wherein one of R^C and R^D is hydrogen and the other of R^C and R^D is C_{1-3} alkyl.
- [1292] 401. The compound of Embodiment 396 or 397, wherein each subscript m is 0.
- [1293] 402. The compound of Embodiment 396 or 397, wherein each subscript m is 1.
- [1294] 403. The compound of any one of Embodiments 378-393, wherein R^{2C} is $-(CH_2)_q-NR^E R^F$.
- [1295] 404. The compound of any one of Embodiments 378-393 and 403, wherein R^{3C} is $-(CH_2)_q-NR^E R^F$.
- [1296] 405. The compound of any one of Embodiments 378-404, wherein R^E and R^F are both hydrogen.
- [1297] 406. The compound of any one of Embodiments 378-404, wherein R^E and R^F are each independently C_{1-3} alkyl.
- [1298] 407. The compound of any one of Embodiments 378-404, wherein one of R^E and R^F is hydrogen and the other of R^E and R^F is C_{1-3} alkyl.
- [1299] 408. The compound of any one of Embodiments 378-407, wherein each subscript q is 0.
- [1300] 409. The compound of any one of Embodiments 378-407, wherein each subscript q is an integer from 1 to 6.
- [1301] 410. The compound of any one of Embodiments 378-393, wherein R^{2C} is $-CO_2 R^M$.
- [1302] 411. The compound of any one of Embodiments 378-393 and 410, wherein R^{3C} is $-CO_2 R^M$.
- [1303] 412. The compound of Embodiment 410 or 411, wherein R^M is hydrogen.
- [1304] 413. The compound of Embodiment 410 or 411, wherein R^M is C_{1-3} alkyl.

- [1305] 414. The compound of any one of Embodiments 378-393, wherein R^{2C} is $-(CH_2)_q-OR^M$.
- [1306] 415. The compound of any one of Embodiments 378-393 and 414, wherein R^{3C} is $-(CH_2)_q-OR^M$.
- [1307] 416. The compound of Embodiment 414 or 415, wherein R^M is hydrogen.
- [1308] 417. The compound of any one of Embodiments 414-415, wherein q is 0.
- [1309] 418. The compound of any one of Embodiments 414-415, wherein q is 1.
- [1310] 419. The compound of any one of Embodiments 378-393, wherein R^{2C} is $-O(C=O)-NR^ER^F$.
- [1311] 420. The compound of any one of Embodiments 378-393 and 419, wherein R^{3C} is $-O(C=O)-NR^ER^F$.
- [1312] 421. The compound of Embodiment 419 or 420, wherein R^E and R^F are both hydrogen.
- [1313] 422. The compound of Embodiment 419 or 420, wherein R^E and R^F are each independently C_{1-3} alkyl.
- [1314] 423. The compound of Embodiment 419 or 420, wherein one of R^E and R^F is hydrogen and the other of R^E and R^F is C_{1-3} alkyl.
- [1315] 424. The compound of any one of Embodiments 378-393, wherein R^{2C} is $-NR^M(C=O)-NR^ER^F$.
- [1316] 425. The compound of any one of Embodiments 378-393 and 424, wherein R^{3C} is $-NR^M(C=O)-NR^ER^F$.
- [1317] 426. The compound of Embodiment 424 or 425, wherein R^E , R^F , and R^M are all hydrogen.
- [1318] 427. The compound of Embodiment 424 or 425, wherein R^E , R^F , and R^M are each independently C_{1-3} alkyl.
- [1319] 428. The compound of Embodiment 424 or 425, wherein one of R^E , R^F , and R^M is C_{1-3} alkyl and the rest of R^E , R^F , and R^M is hydrogen.
- [1320] 429. The compound of any one of Embodiments 378-393, wherein R^{2C} is $-S(O)_2NR^DR^D$.
- [1321] 430. The compound of any one of Embodiments 378-393 and 429, wherein R^{3C} is $-S(O)_2NR^CR^D$.
- [1322] 431. The compound of Embodiment 429 or 430, wherein R^C and R^D are both hydrogen.
- [1323] 432. The compound of Embodiment 429 or 430, wherein R^C and R^D are each independently C_{1-3} alkyl.
- [1324] 433. The compound of Embodiment 429 or 430, wherein one of R^C and R^D is hydrogen and the other of R^C and R^D is C_{1-3} alkyl.
- [1325] 434. The compound of any one of Embodiments 378-393, wherein R^{2C} is $-S(O)_2R^M$.
- [1326] 435. The compound of any one of Embodiments 378-393 and 434, wherein R^{3C} is $-S(O)_2R^M$.
- [1327] 436. The compound of Embodiment 434 or 435, wherein R^M is hydrogen.
- [1328] 437. The compound of Embodiment 434 or 435, wherein R^M is C_{1-3} alkyl.
- [1329] 438. The compound of any one of Embodiments 378-437, wherein R^{2C} is attached at position 1.
- [1330] 439. The compound of any one of Embodiments 378-437, wherein R^{2C} is attached at position 2.
- [1331] 440. The compound of any one of Embodiments 378-437, wherein R^{2C} is attached at position 3.
- [1332] 441. The compound of any one of Embodiments 378-437, wherein R^{3C} is attached at position 1'.
- [1333] 442. The compound of any one of Embodiments 378-437, wherein R^{3C} is attached at position 2'.
- [1334] 443. The compound of any one of Embodiments 378-437, wherein R^{3C} is attached at position 3'.
- [1335] 444. The compound of any one of Embodiments 378-443, wherein L^E is $-(C=O)-$.
- [1336] 445. The compound of any one of Embodiments 378-443, wherein L^E is $-S(O)_2-$.
- [1337] 446. The compound of any one of Embodiments 378-445, wherein each R^I and R^J is hydrogen.
- [1338] 447. The compound of any one of Embodiments 378-445, wherein each R^I and R^J is C_{1-3} alkyl.
- [1339] 448. The compound of any one of Embodiments 378-445, wherein one of R^I and R^J is hydrogen and the other of R^I and R^J is C_{1-3} alkyl.
- [1340] 449. The compound of any one of Embodiments 378-448, wherein L^C is $-(CR^IR^J)-$.
- [1341] 450. The compound of any one of Embodiments 378-449, wherein s is 0.
- [1342] 451. The compound of any one of Embodiments 378-449, wherein s is 1.
- [1343] 452. The compound of any one of Embodiments 378-451, wherein each Cy^1 is independently a 5-6 membered heteroaryl.
- [1344] 453. The compound of any one of Embodiments 378-451, wherein each Cy^1 is pyrazole optionally substituted with one or more R^K .
- [1345] 454. The compound of any one of Embodiments 378-451, wherein each Cy^1 is independently selected from the group consisting of pyrazole, imidazole, furan, thiophene, thiazole, isothiazole, oxazole, isoxazole, pyrrole, pyridazine, pyridine, pyrimidine, and pyrazine, each optionally substituted with one or more R^K .
- [1346] 455. The compound of any one of Embodiments 378-451, wherein each Cy^1 is independently selected from the group consisting of imidazole, furan, thiophene, thiazole, isothiazole, oxazole, isoxazole, pyrrole, pyridazine, pyridine, pyrimidine, and pyrazine, each optionally substituted with one or more R^K .
- [1347] 456. The compound of any one of Embodiments 378-451, wherein each Cy^1 is independently a C_{4-5} cycloalkyl optionally substituted with one or more R^K .
- [1348] 457. The compound of any one of Embodiments 378-456, wherein each R^K is independently selected from the group consisting of C_{1-3} alkyl, C_{1-3} haloalkyl, and halogen.
- [1349] 458. The compound of Embodiment 457, wherein each R^K is independently selected from the group consisting of methyl, ethyl, $-CF_3$, and halogen.
- [1350] 459. The compound of any one of Embodiments 378-451, wherein each Cy^1 is the same.
- [1351] 460. The compound of any one of Embodiments 378-451, wherein each Cy^1 is different.
- [1352] 461. The compound of any one of Embodiments 378-460, wherein L^{AA} is $-(CH_2)_{1-6}-$.
- [1353] 462. The compound of any one of Embodiments 378-460, wherein L^{AA} is $-(CH_2)_{1-3}-$.
- [1354] 463. The compound of any one of Embodiments 378-460, wherein L^{AA} is $-(CH_2)_{1-6}O-$.
- [1355] 464. The compound of any one of Embodiments 378-460, wherein L^{AA} is $-(CH_2)_{1-3}O-$.
- [1356] 465. The compound of any one of Embodiments 378-464, wherein Cy^2 is a 4-6 membered heterocycle.

[1357] 466. The compound of any one of Embodiments 378-464, wherein Cy² has the structure:



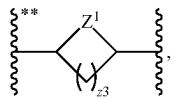
wherein each of subscripts z1 and z2 is independently an integer from 1 to 3 and ** indicates attachment to L^{A4}

[1358] 467. The compound of Embodiment 466, wherein z1 and z2 are 1.

[1359] 468. The compound of Embodiment 466, wherein z1 and z2 are 2.

[1360] 469. The compound of Embodiment 466, wherein z1 is 1 and z2 is 2.

[1361] 470. The compound of any one of Embodiments 378-464, wherein Cy² has the structure:



wherein

[1362] Z¹ is selected from the group consisting of —O—, —S—, —CR^NR^O—, and —NR^P—;

[1363] R^N, R^O, and R^P are independently hydrogen or C₁₋₆ alkyl; subscript z3 is an integer from 1 to 3; and

[1364] ** indicates attachment to L^{A4}

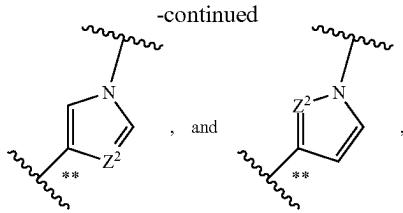
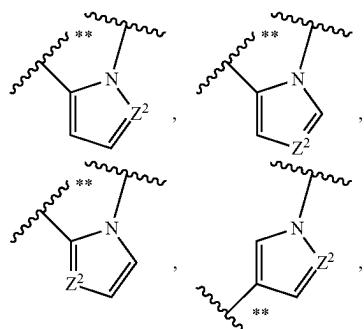
[1365] 471. The compound of Embodiment 470, wherein R^N and R^O are hydrogen.

[1366] 472. The compound of Embodiment 470, wherein R^P is hydrogen.

[1367] 473. The compound of Embodiment 470, wherein R^P is methyl.

[1368] 474. The compound of any one of Embodiments 378-464, wherein Cy² is a 5-6 membered heteroaryl.

[1369] 475. The compound of any one of Embodiments 378-464, wherein Cy² is selected from the group consisting of:



wherein

[1370] Z² is =CR^N— or =N—;

[1371] R^N is hydrogen or C₁₋₆ alkyl; and

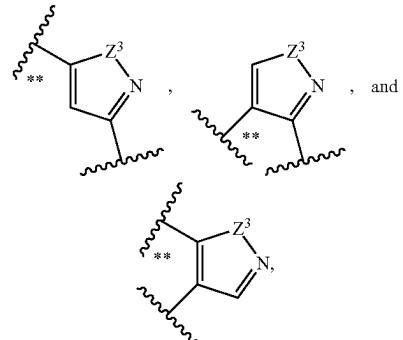
[1372] ** indicates attachment to L^{A4}.

[1373] 476. The compound of Embodiment 475, wherein Z² is =CR^N—.

[1374] 477. The compound of Embodiment 476, wherein R^N is hydrogen.

[1375] 478. The compound of Embodiment 475, wherein Z² is =N—.

[1376] 479. The compound of any one of Embodiments 378-464, wherein Cy² is selected from the group consisting of:

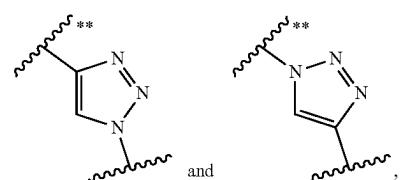


wherein Z³ is —O— or —S— and ** indicates attachment to L^{A4}, L^D, NR^{HH}, Y, W, or L^{BB}.

[1377] 480. The compound of Embodiment 479, wherein ** indicates attachment to L^{A4}

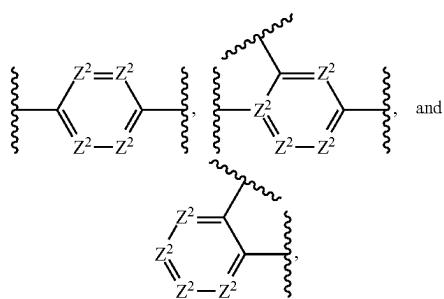
[1378] 481. The compound of Embodiment 479, wherein ** indicates attachment to L^D, NR^{HH}, Y, W, or L^{BB}.

[1379] 482. The compound of any one of Embodiments 378-464, wherein Cy² is selected from the group consisting of:



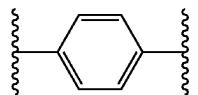
wherein ** indicates attachment to L^{A4}.

[1380] 483. The compound of any one of Embodiments 378-464, wherein Cy² is selected from the group consisting of:

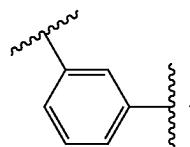


wherein

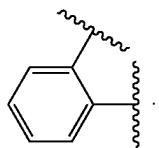
- [1381] each Z^2 is independently $=CR^N-$ or $=N-$; and
- [1382] each R^N is independently hydrogen or C_{1-6} alkyl.
- [1383] 484. The compound of Embodiment 483, wherein at least one Z^2 is $=N-$.
- [1384] 485. The compound of Embodiment 483, wherein one Z^2 is $=N-$ and the remaining Z^2 are $=CR^N-$.
- [1385] 486. The compound of Embodiment 483, wherein two Z^2 are $=N-$ and the remaining Z^2 are $=CR^N-$.
- [1386] 487. The compound of any one of Embodiments 483, 485, and 486, wherein R^N and R^O are hydrogen.
- [1387] 488. The compound of any one of Embodiments 378-464, wherein Cy^2 is



- [1388] 489. The compound of any one of Embodiments 378-464, wherein Cy^2 is



- [1389] 490. The compound of any one of Embodiments 378-464, wherein Cy^2 is



- [1390] 491. The compound of any one of Embodiments 378-464, wherein Cy^2 is cyclobutyl.
- [1391] 492. The compound of any one of Embodiments 378-491, wherein each R^{d3} , R^{e3} , R^9 , R^{h1} , and R^{j1} are independently hydrogen or $-CH_3$.

[1392] 493. The compound of any one of Embodiments 378-492, wherein each R_u is independently selected from $-CO_2H$, $-(C=O)NH_2$, $-S(O)_2NH_2$, $-CH_2NH_2$, and $-CH_2OH$.

[1393] 494. The compound of any one of Embodiments 378-493, wherein t_1 is 0.

[1394] 495. The compound of any one of Embodiments 378-493, wherein t_1 is 1.

[1395] 496. The compound of any one of Embodiments 378-495, wherein u is 1 and L^D is $-(CH_2)_{1-3}$.

[1396] 497. The compound of any one of Embodiments 378-495, wherein u is 0.

[1397] 498. The compound of any one of Embodiments 378-497, wherein ZZ is $-NR^O R^R$.

[1398] 499. The compound of Embodiment 498, wherein R^Q is C_{1-6} alkyl,

[1399] 500. The compound of Embodiment 498, wherein R^Q is C_{3-6} cycloalkyl.

[1400] 501. The compound of Embodiment 500, wherein R^Q is cyclopropyl.

[1401] 502. The compound of Embodiment 498, wherein R^Q is $-(CH_2)_{1-3} C_{3-6}$ cycloalkyl.

[1402] 503. The compound of any one of Embodiments 498-501, wherein R^R is hydrogen.

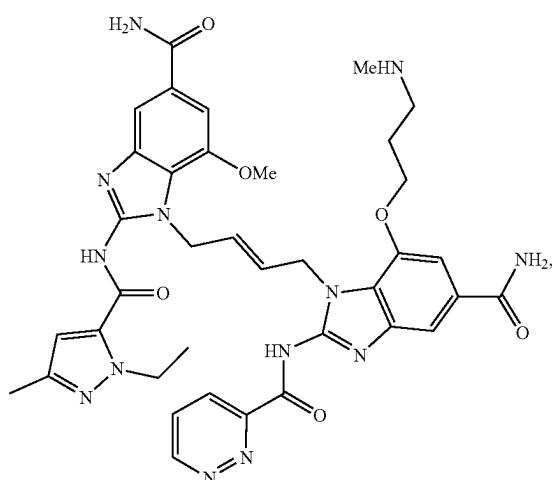
[1403] 504. The compound of any one of Embodiments 378-497, wherein ZZ is $-C(=O)N^SR^T$.

[1404] 505. The compound of any one of Embodiments 378-497, wherein ZZ is $-C(O)O(t\text{-butyl})$.

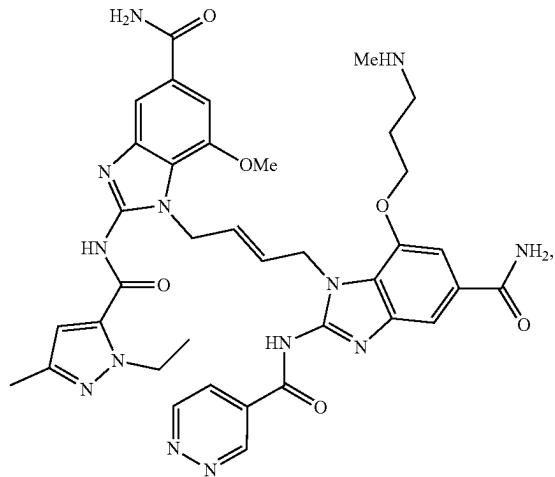
[1405] 506. The compound of any one of Embodiments 378-497, wherein ZZ is $-CO_2H$.

[1406] 507. The compound of any one of Embodiments 378-497, wherein ZZ is an amino acid selected from the group consisting of alanine, valine, isoleucine, leucine, aspartic acid, glutamic acid, lysine, histidine, arginine, glycine, serine, threonine, phenylalanine, O-methylserine, O-methyllaspartic acid, O-methylglutamic acid, N-methyllysine, O-methyltyrosine, O-methylhistidine, and O-methylthreonine.

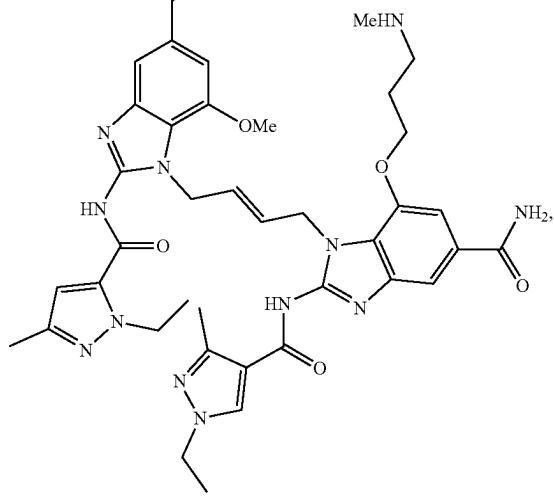
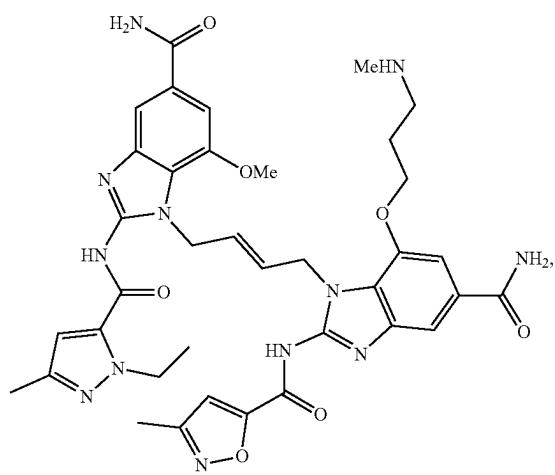
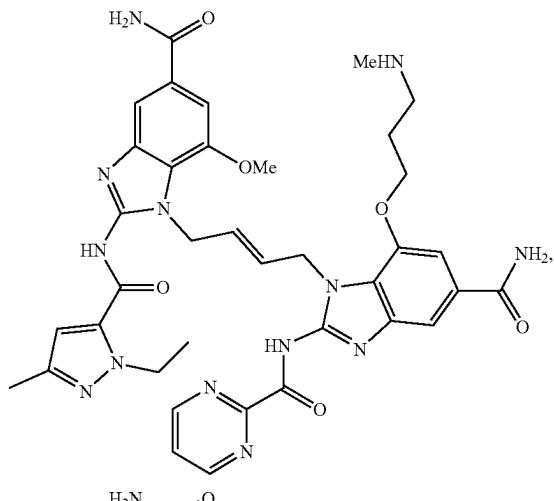
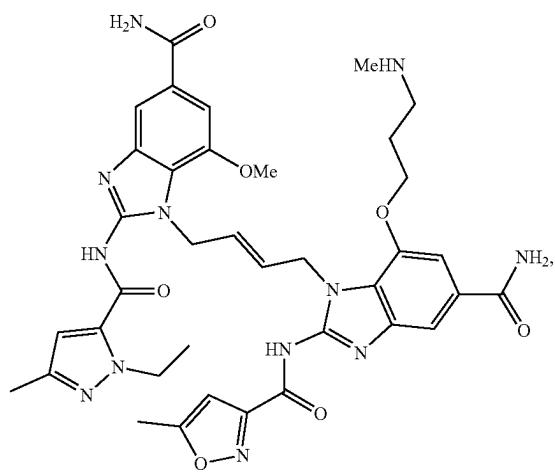
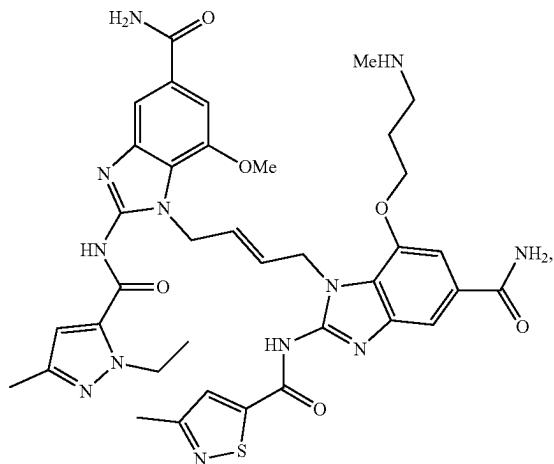
[1407] 508. The compound of Embodiment 378, selected from the group consisting of:



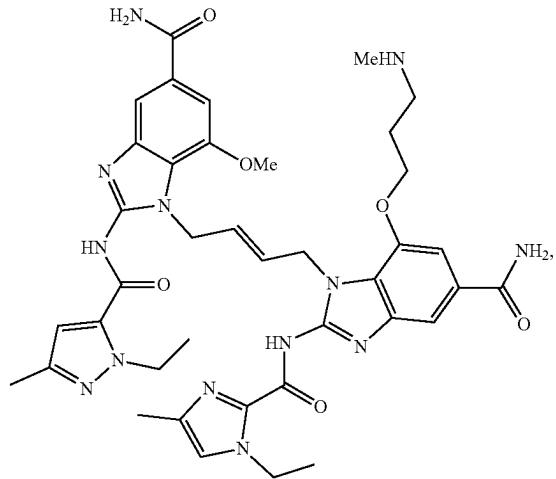
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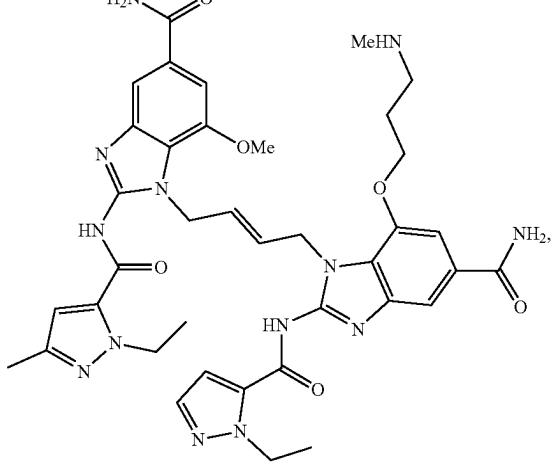
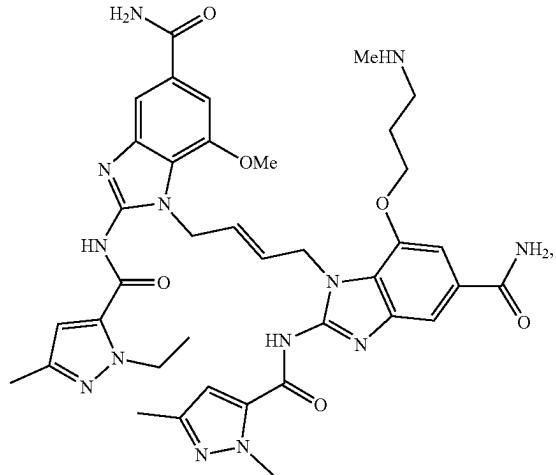
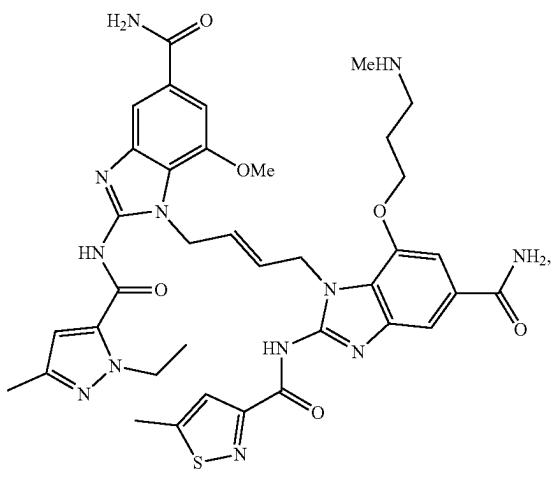
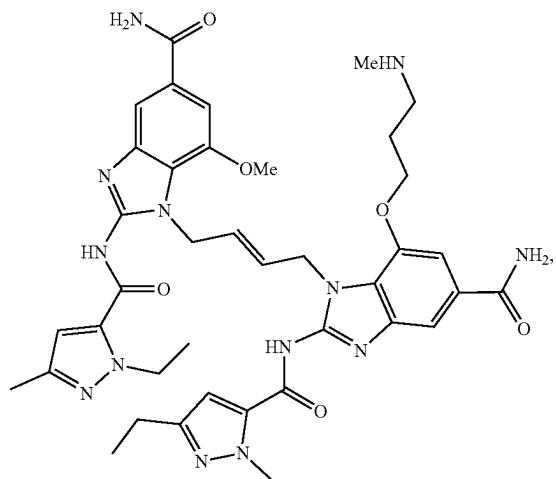
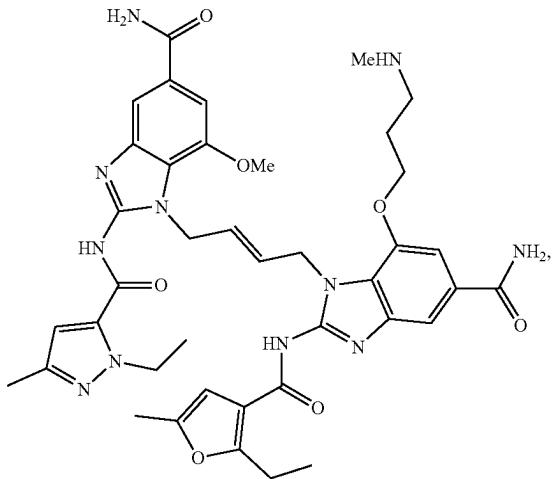
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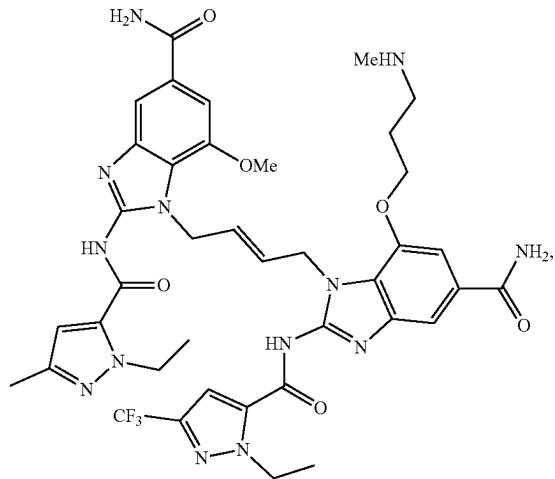
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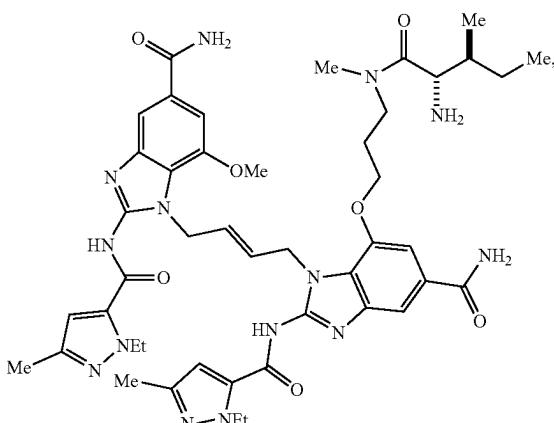
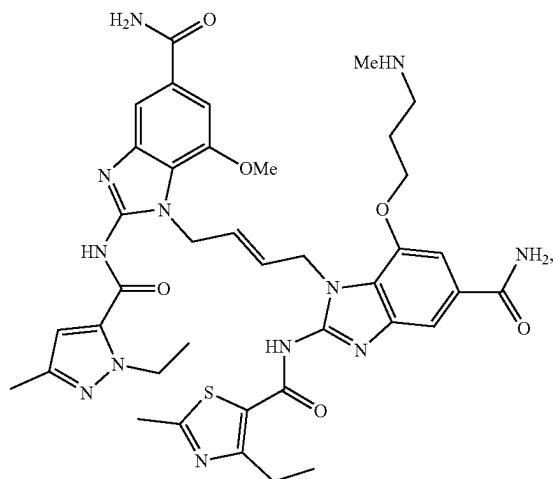
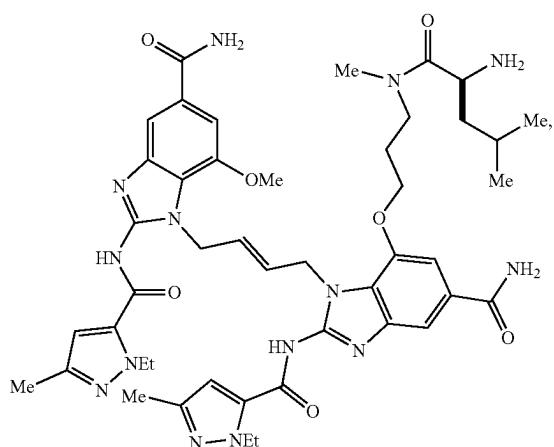
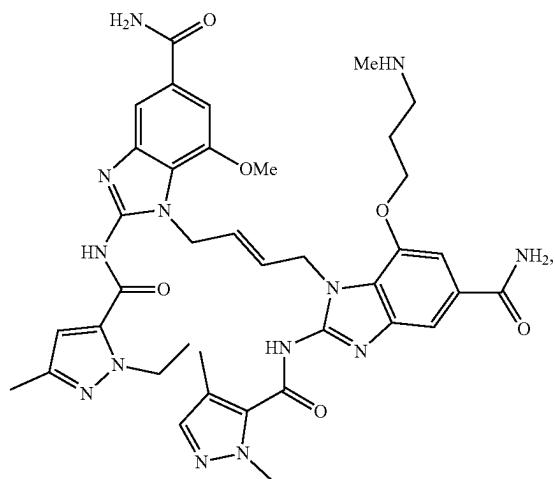
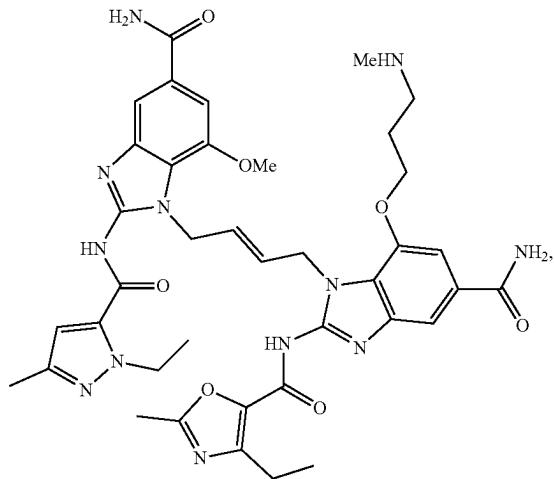
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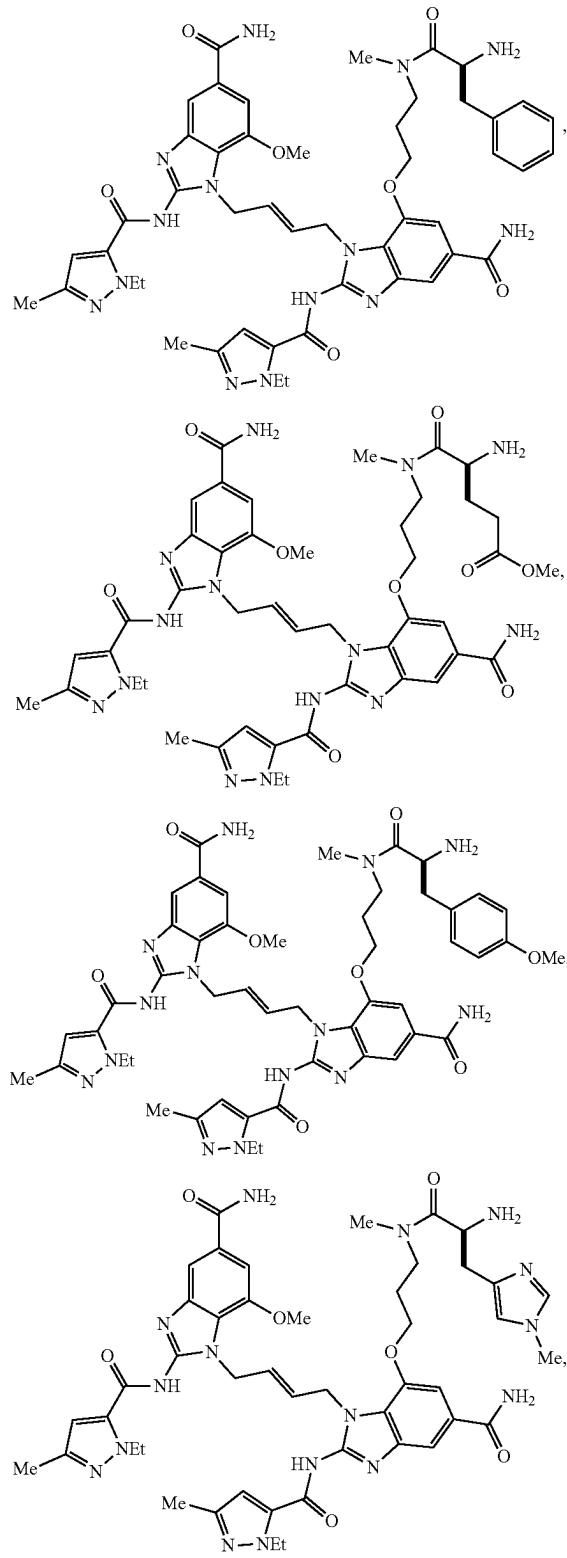
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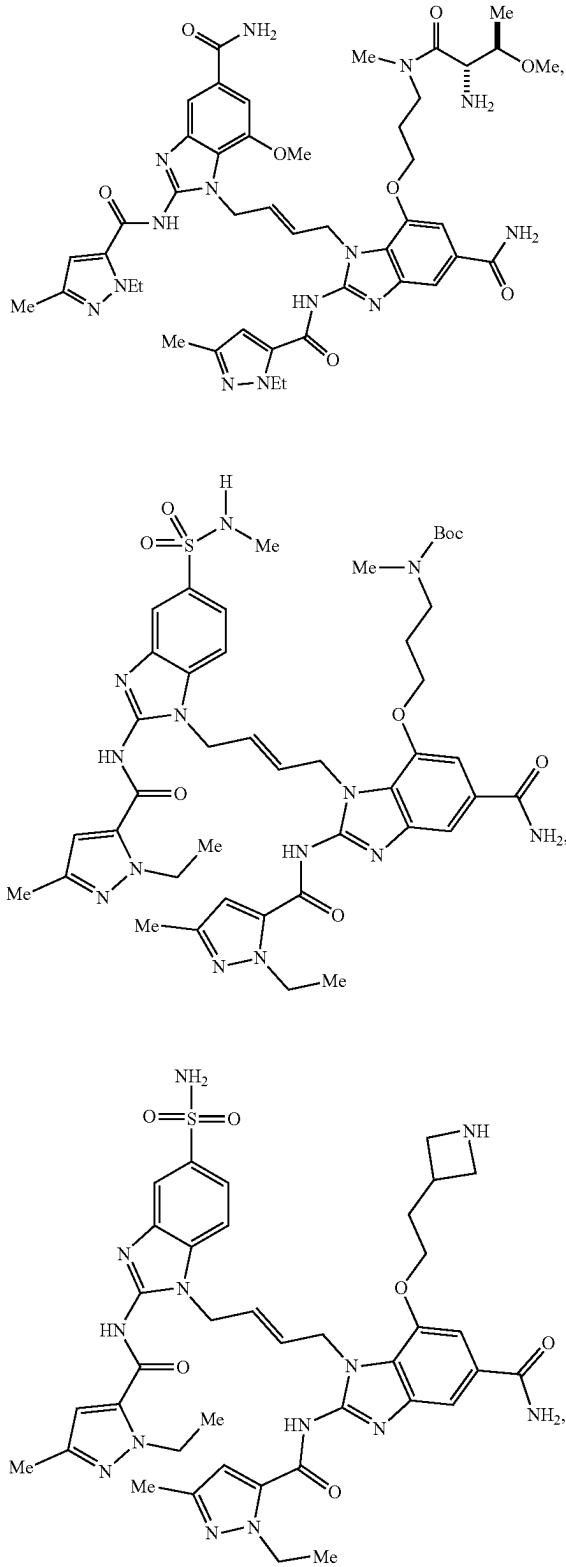
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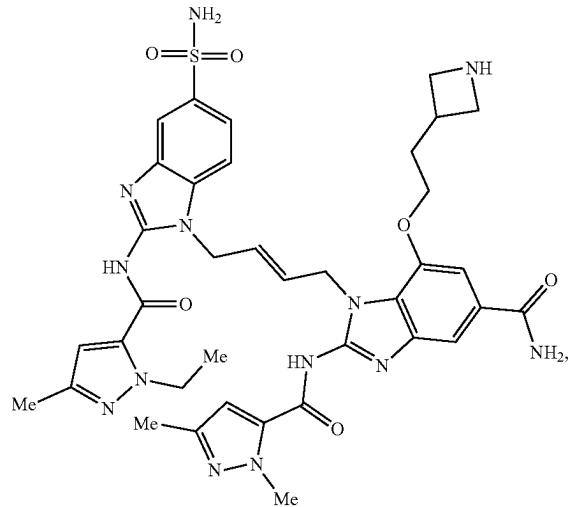
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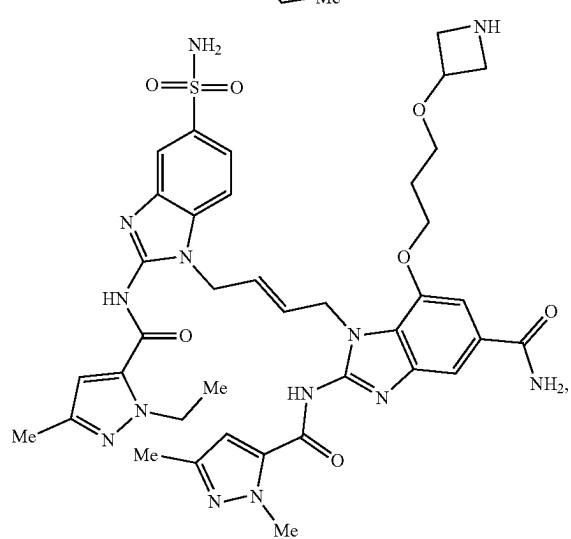
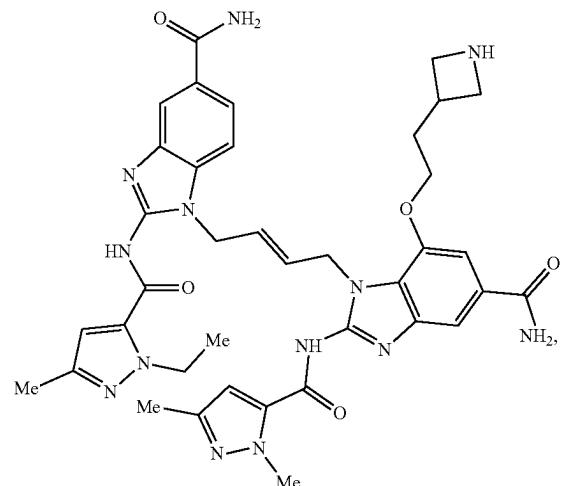
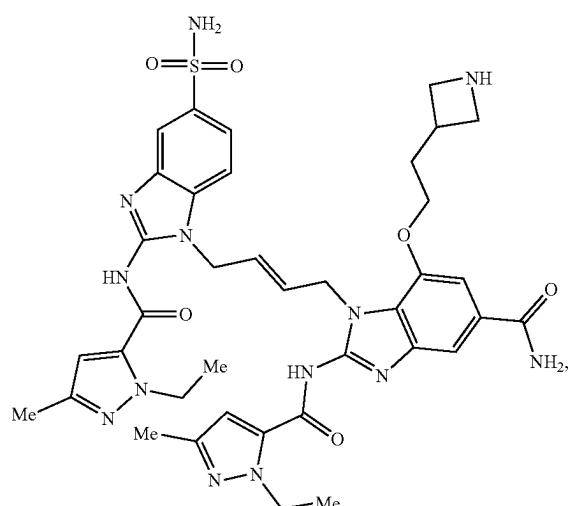
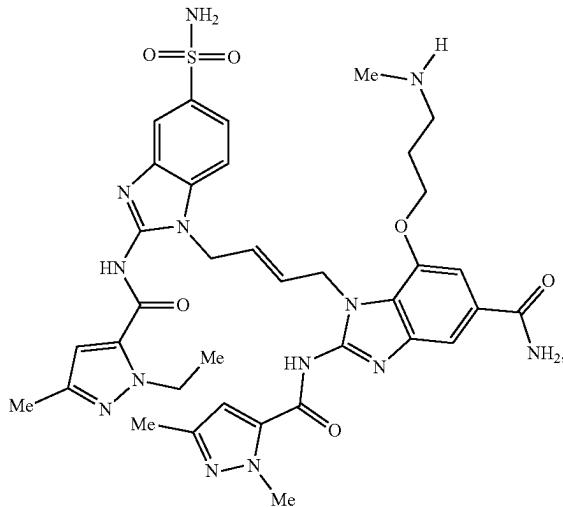
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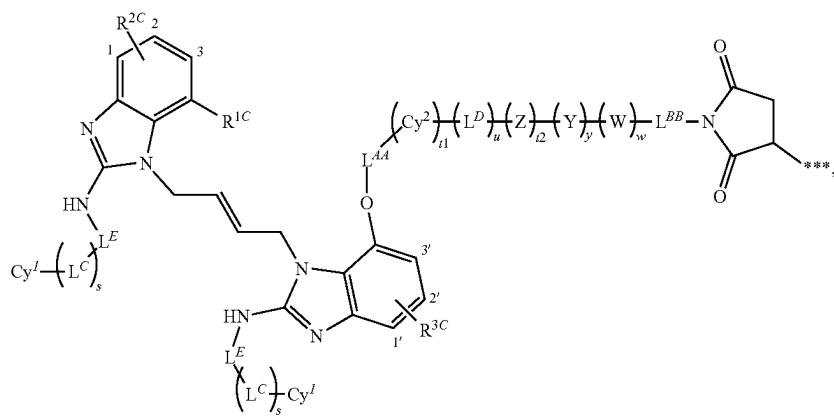
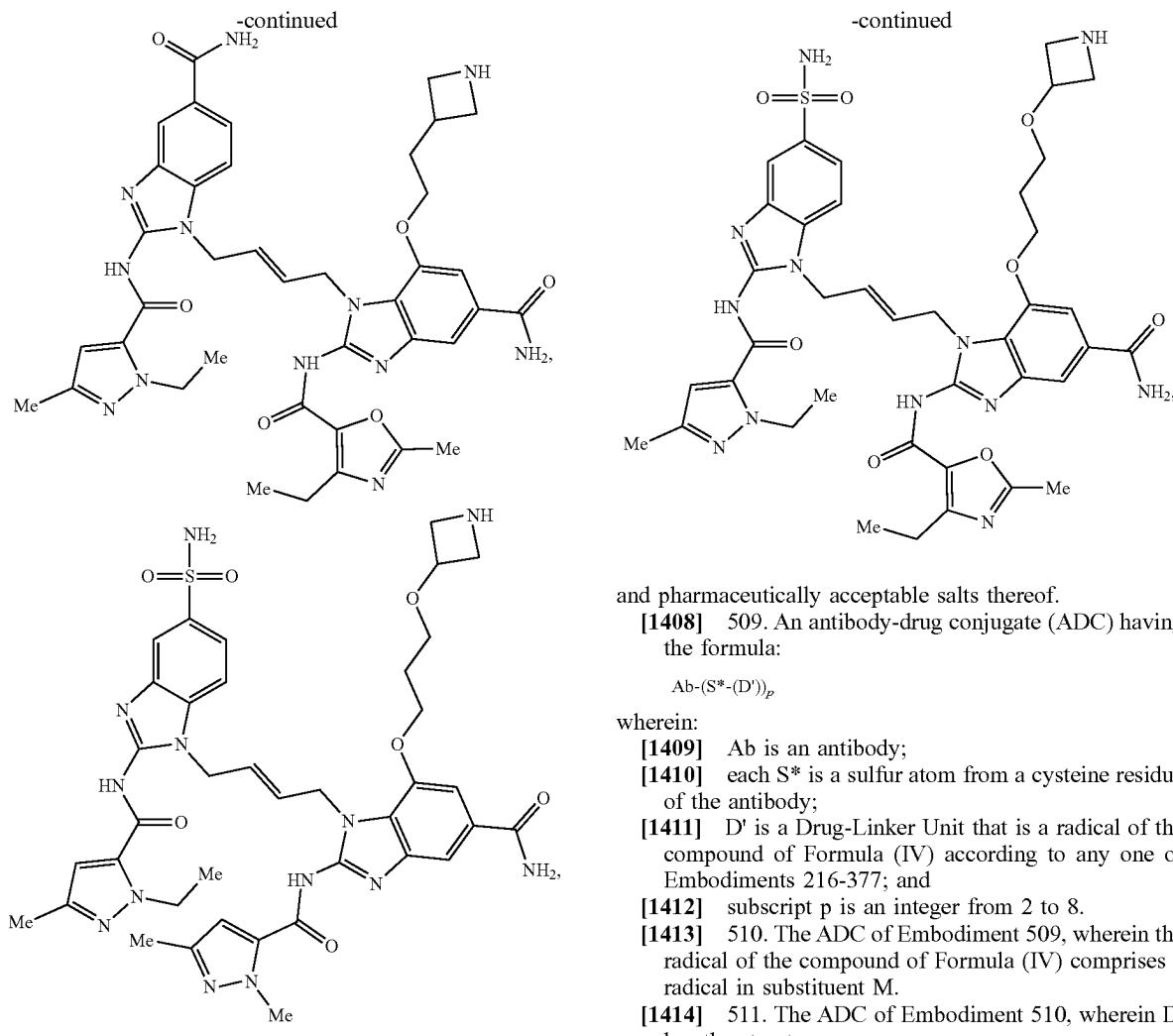


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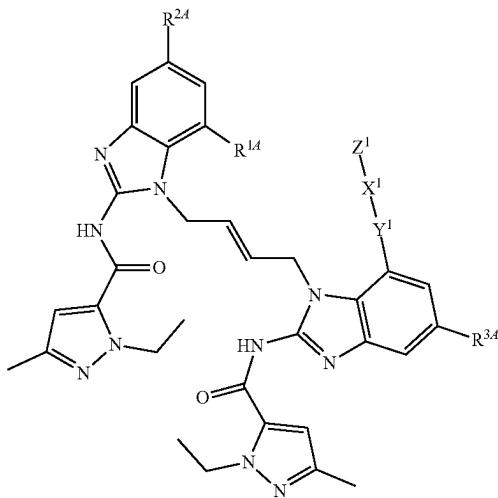




where *** indicates attachment to S*.

- [1415] 512. The ADC of any one of Embodiments 509 to 511, wherein the antibody is a humanized antibody.
- [1416] 513. The ADC of Embodiment 509 or 511, wherein the antibody is a monoclonal antibody.
- [1417] 514. The ADC of Embodiment 509 or 511, wherein the antibody is fucosylated.
- [1418] 515. The ADC of Embodiment 509 or 511, wherein the antibody is afucosylated.
- [1419] 516. A composition comprising a distribution of the ADCs of any one of Embodiments 118-215 and 509-515.
- [1420] 517. The composition of Embodiment 516, further comprising and at least one pharmaceutically acceptable carrier.
- [1421] 518. A method of treating cancer in a subject in need thereof, comprising administering a therapeutically effective amount of the composition of Embodiment 516 or 517, to the subject.
- [1422] 519. A method of treating cancer in a subject in need thereof, comprising administering a therapeutically effective amount of the ADC of any one of Embodiments 118-215 and 509-515, to the subject.
- [1423] 520. A method of inducing an anti-tumor immune response in a subject in need thereof, comprising administering a therapeutically effective amount of the composition of Embodiment 516 or 517, to the subject.
- [1424] 521. A method of inducing an anti-tumor immune response in a subject in need thereof, comprising administering a therapeutically effective amount of the ADC of any one of Embodiments 118-215 and 509-515, to the subject.
- [1425] 522. A compound of Formula (III):

(III)



or a pharmaceutically acceptable salt thereof, wherein:

- [1426] R¹⁴ is hydrogen, hydroxyl, C₁₋₆ alkoxy, -(C₁₋₆ alkyl)C₁₋₆ alkoxy, -(CH₂)_{nn}-NR^{AA}R^{BB};
- [1427] R²⁴ and R³⁴ are independently -CO₂H, -(C=O)_m-NR^{CC}R^{DD}, or -(CH₂)_q-NR^{EE}R^{FF};
- [1428] each subscript nn is independently an integer from 0 to 6;
- [1429] each subscript mm is independently 0 or 1;

- [1430] each subscript qq is an integer from 0 to 6;
- [1431] Y¹ is -CH₂-, -O-, -S-, -NH-, or -N(CH₃)-;
- [1432] X¹ is a C₂₋₆ alkylene;
- [1433] Z¹ is -NR^{EE}R^{FF}, -C(=O)NR^{GG}R^{HH}, or -CO₂H;
- [1434] each R^{AA}, R^{BB}, R^{CC}, and R^{DD}, R^{EE}1, and R^{FF}1 are independently hydrogen or C₁₋₃ alkyl; and
- [1435] each R^{EE}, R^{FF}, R^{GG}, and R^{HH} are independently hydrogen or C₁₋₆ alkyl.
- [1436] 523. The compound of Embodiment 522, wherein R¹⁴ is hydrogen.
- [1437] 524. The compound of Embodiment 522, wherein R¹⁴ is hydroxyl.
- [1438] 525. The compound of Embodiment 522, wherein R¹⁴ is C₁₋₆ alkoxy.
- [1439] 526. The compound of Embodiment 522 or 525, wherein R¹ is methoxy.
- [1440] 527. The compound of Embodiment 522, wherein R¹⁴ is -(C₁₋₆ alkyl)C₁₋₆ alkoxy.
- [1441] 528. The compound of Embodiment 522 or 527, wherein R¹⁴ is methoxyethyl.
- [1442] 529. The compound of Embodiment 522, wherein R¹ is -(CH₂)_{nn}-NR^{AA}R^{BB}.
- [1443] 530. The compound of Embodiment 522 or 529, wherein R^{AA} and R^{BB} are both hydrogen.
- [1444] 531. The compound of Embodiment 522 or 529, wherein R^{AA} and R^{BB} are independently C₁₋₃ alkyl.
- [1445] 532. The compound of Embodiment 522 or 529, wherein one of R^{AA} and R^{BB} is hydrogen and the other of R^{AA} and R^{BB} is C₁₋₃ alkyl.
- [1446] 533. The compound of any one of Embodiments 522 or 529-532, wherein each subscript nn is 0.
- [1447] 534. The compound of any one of Embodiments 522 or 529-532, wherein each subscript nn is 1.
- [1448] 535. The compound of any one of Embodiments 522 or 529-532, wherein each subscript nn is 2.
- [1449] 536. The compound of any one of Embodiments 522 or 529-532, wherein each subscript nn is 3, 4, 5, or 6.
- [1450] 537. The compound of any one of Embodiments 522-536, wherein R²⁴ and R³⁴ are independently -CO₂H, -(C=O)_{mm}-NR^{CC}R^{DD}, or -(CH₂)_q-NR^{EE}R^{FF}; and R²⁴ and R³⁴ are the same.
- [1451] 538. The compound of any one of Embodiments 522-536, wherein R²⁴ and R³⁴ are independently -CO₂H, -(C=O)_{mm}-NR^{CC}R^{DD}, or -(CH₂)_q-NR^{EE}R^{FF}; and R²⁴ and R³⁴ are different.
- [1452] 539. The compound of any one of Embodiments 522-538, wherein R²⁴ is -(C=O)_{mm}-NR^{CC}R^{DD}.
- [1453] 540. The compound of any one of Embodiments 522-538, wherein R³⁴ is -(C=O)_{mm}-NR^{CC}R^{DD}.
- [1454] 541. The compound of any one of Embodiments 522-537 or 539-540, wherein each R^{CC} and each R^{DD} is hydrogen.
- [1455] 542. The compound of any one of Embodiments 522-537 or 539-540, wherein each R^{CC} and each R^{DD} is independently C₁₋₃ alkyl.
- [1456] 543. The compound of any one of Embodiments 522-536 or 538-540, wherein one of each R^{CC} and R^{DD} is hydrogen and the other of each R^{CC} and R^{DD} is C₁₋₃ alkyl.
- [1457] 544. The compound of any one of Embodiments 522-543, wherein each subscript mm is 0.

- [1458] 545. The compound of any one of Embodiments 522-543, wherein each subscript mm is 1.
- [1459] 546. The compound of any one of Embodiments 522-538, wherein R^{2A} is —(CH₂)_q—NR^{EE1}R^{FF1}.
- [1460] 547. The compound of any one of Embodiments 522-538, wherein R^{3A} is —(CH₂)_q—NR^{EE1}R^{FF1}.
- [1461] 548. The compound of any one of Embodiments 522-538 or 546-547, wherein each R^{EE1} and each R^{FF1} is hydrogen.
- [1462] 549. The compound of any one of Embodiments 522-538 or 546-547, wherein each R^{EE1} and each R^{FF1} is independently C₁₋₃ alkyl.
- [1463] 550. The compound of any one of Embodiments 522-538 or 546-547, wherein one of each R^{EE1} and each R^{FF1} is hydrogen and the other of each R^{EE1} and each R^{FF1} is C₁₋₃ alkyl.
- [1464] 551. The compound of any one of Embodiments 522-538 or 546-547, wherein each subscript qq is 0.
- [1465] 552. The compound of any one of Embodiments 522-538 or 546-550, wherein each subscript qq is an integer from 1 to 6.
- [1466] 553. The compound of any one of Embodiments 522-538, wherein R^{3A} is —CO₂H.
- [1467] 554. The compound of any one of Embodiments 522-538, wherein R^{2A} is —CO₂H.
- [1468] 555. The compound of any one of Embodiments 522-554, wherein Y¹ is —CH₂—.
- [1469] 556. The compound of any one of Embodiments 522-554, wherein Y¹ is —O—.
- [1470] 557. The compound of any one of Embodiments 522-554, wherein Y¹ is —S—.
- [1471] 558. The compound of any one of Embodiments 522-554, wherein Y¹ is —NH—.
- [1472] 559. The compound of any one of Embodiments 522-558, wherein X¹ is a C₂₋₅ alkylene.
- [1473] 560. The compound of any one of Embodiments 522-559, wherein X¹ is a C₂₋₄ alkylene.
- [1474] 561. The compound of any one of Embodiments 522-560, wherein X¹ is ethylene or n-propylene.
- [1475] 562. The compound of any one of Embodiments 522-561, wherein Z¹ is —NR^{E1}R^{F1}.
- [1476] 563. The compound of any one of Embodiments 522-562, wherein R^{EE} and R^{FF} are both hydrogen.
- [1477] 564. The compound of any one of Embodiments 522-562, wherein R^{EE} and R^{FF} are independently C₁₋₆ alkyl.
- [1478] 565. The compound of any one of Embodiments 522-562, wherein one of R^{EE} and R^{FF} is hydrogen and the other of R^{EE} and R^{FF} is C₁₋₆ alkyl.
- [1479] 566. The compound of Embodiment 564 or 565, wherein the C₁₋₆ alkyl is a C₁₋₃ alkyl.
- [1480] 567. The compound of Embodiment 566, wherein the C₁₋₃ alkyl is methyl.
- [1481] 568. The compound of any one of Embodiments 522-561, wherein Z¹ is —C(=O)NR^{GG}R^{HH}.
- [1482] 569. The compound of any one of Embodiments 522-561 or 568, wherein R^{GG} and R^{HH} are both hydrogen.
- [1483] 570. The compound of any one of Embodiments 522-561 or 568, wherein R^{GG} and R^{HH} are independently C₁₋₆ alkyl.
- [1484] 571. The compound of any one of Embodiments 522-561 or 568, wherein one of R^{GG} and R^{HH} is hydrogen and the other of R^{GG} and R^{HH} is C₁₋₆ alkyl.
- [1485] 572. The compound of Embodiment 570 or 571, wherein the C₁₋₆ alkyl is a C₁₋₃ alkyl.
- [1486] 573. The compound of Embodiment 569, wherein the C₁₋₃ alkyl is methyl.
- [1487] 574. The compound of any one of Embodiments 522-561, wherein Z¹ is —CO₂H.
- [1488] 575. The compound of Embodiment 522, wherein R^{1A} is methoxy and R^{2A} and R^{3A} are both —C(=O)NH₂.
- [1489] 576. The compound of Embodiment 522 or 575, wherein Y¹ is —O— and X¹ is a C₃ alkylene.
- [1490] 577. The compound of any one of Embodiments 522 or 575-576, wherein X¹ is n-propylene.
- [1491] 578. The compound of any one of Embodiments 522 or 575-577, wherein Z¹ is —NR^{EE}R^{FF}.
- [1492] 579. The compound of any one of Embodiments 522 or 575-578, wherein R^{EE} is hydrogen and R^{FF} is methyl.

EXAMPLES

General Methods:

[1493] All commercially available anhydrous solvents were used without further purification. All commercially available reagents were used without further purification unless otherwise noted. Analytical thin layer chromatography (TLC) was performed on silica gel 60 F254 aluminum sheets or glass plates (EMD Chemicals, Gibbstown, NJ). Flash column chromatography was performed on a Biotage Isolera One™ flash purification system 20 or Biotage Selekt™ flash purification system (Charlotte, NC). UPLC-MS analysis was performed on one of four systems. UPLC-MS system 1: Waters single quad detector mass spectrometer interfaced to a Waters Acquity UPLC system equipped with a Waters Acquity UPLC BEH C18 2.1×50 mm, 1.7 µm, reversed-phase column. UPLC-MS system 2: Waters Xevo G2 TOF mass spectrometer interfaced to a Waters Acquity H-class Ultra Performance LC equipped with a C8 Phenomenex Synergi 2.0×150 mm, 4 µm, 80 Å reversed-phase column with a Waters 2996 Photodiode Array Detector. UPLC-MS system 3 (C18): Shimadzu LC-20 AD & MS 2020 interfaced with a diode array detector (DAD) and positive ESI mass spectrometer equipped with either a Luna-C18 2.0×30 mm, 3 µm particle size reversed-phase column maintained at 40° C. or a Kinetex-C18 2.1×30 mm, 5 µm reversed-phase column maintained at 40° C. UPLC-MS system 4 (C18): Agilent 1200 series LC system interfaced a diode array detector (DAD) and Agilent 6110B positive ESI quadrupole mass spectrometer equipped with a Kinetex-C18 2.1×50 mm, 5 m reversed-phase column maintained at 40° C.

[1494] Compounds were eluted using one of Methods A-E, as described herein.

[1495] Method A—a linear gradient of 5-95% acetonitrile in water (1 mL/min) over 1.0 min, followed by isocratic flow of 95% acetonitrile to 1.80 min (1.0 mL/min) and column equilibration back to 5% acetonitrile to 2.20 min (1.2 mL/min). The water contained 0.037% TFA (v/v) and the

acetonitrile contained 0.018% TFA (v/v). The column used was a Phenomenex Luna C18 2.0×30 mm, 3 m reversed-phase column.

[1496] Method B—a linear gradient of 5-95% acetonitrile in water (1 mL/min) over 1.0 min, followed by isocratic flow of 95% acetonitrile to 1.80 min (1.0 mL/min) and column equilibration back to 5% acetonitrile to 2.20 min (1.2 mL/min). The water contained 0.05% TFA (v/v) and the acetonitrile contained 0.05% TFA (v/v). The column used was a Phenomenex Kinetex C18 2.1×300 mm, 5 m reversed-phase column.

[1497] Method C—isocratic flow of 5% acetonitrile in water for 0.4 min, followed by a linear gradient of 5-95% acetonitrile in water to 3.0 min, followed by isocratic flow for 95% acetonitrile to 4.0 min and column equilibration back to 5% acetonitrile to 4.5 min. The flow rate was 1.0 mL/min and the water contained 0.05% TFA (v/v) and the acetonitrile contained 0.05% TFA (v/v). The column used was a Phenomenex Kinetex C18 2.1×30 mm, 5 m reversed-phase column.

[1498] Method D—a linear gradient of 3-60% acetonitrile over 1.7 min, then 60-95% acetonitrile to 2.0 min, followed by isocratic flow of 95% acetonitrile to 2.5 min followed by column equilibration back to 3% acetonitrile. The flow rate was 0.6 mL/min and the water contained 0.1% (v/v) formic acid and the acetonitrile contained 0.1% (v/v) formic acid. The column used was either a Waters Acquity UPLC BEH C18 2.1×50 mm, 1.7 μm, reversed-phase column or a C8 Phenomenex Syngi 2.0×150 mm, 4 μm, reversed-phase column.

[1499] Method E—a linear gradient of 3-95% acetonitrile over 1.5 min, followed by isocratic elution of 95% acetonitrile to 2.4 min, followed by equilibration back to 3% acetonitrile. The flow rate was 0.6 mL/min and the water contained 0.1% (v/v) formic acid and the acetonitrile contained 0.1% (v/v) formic acid. The column used was either a Waters Acquity UPLC BEH C18 2.1×50 mm, 1.7 μm, reversed-phase column or a C8 Phenomenex Syngi 2.0×150 mm, 4 m, reversed-phase column.

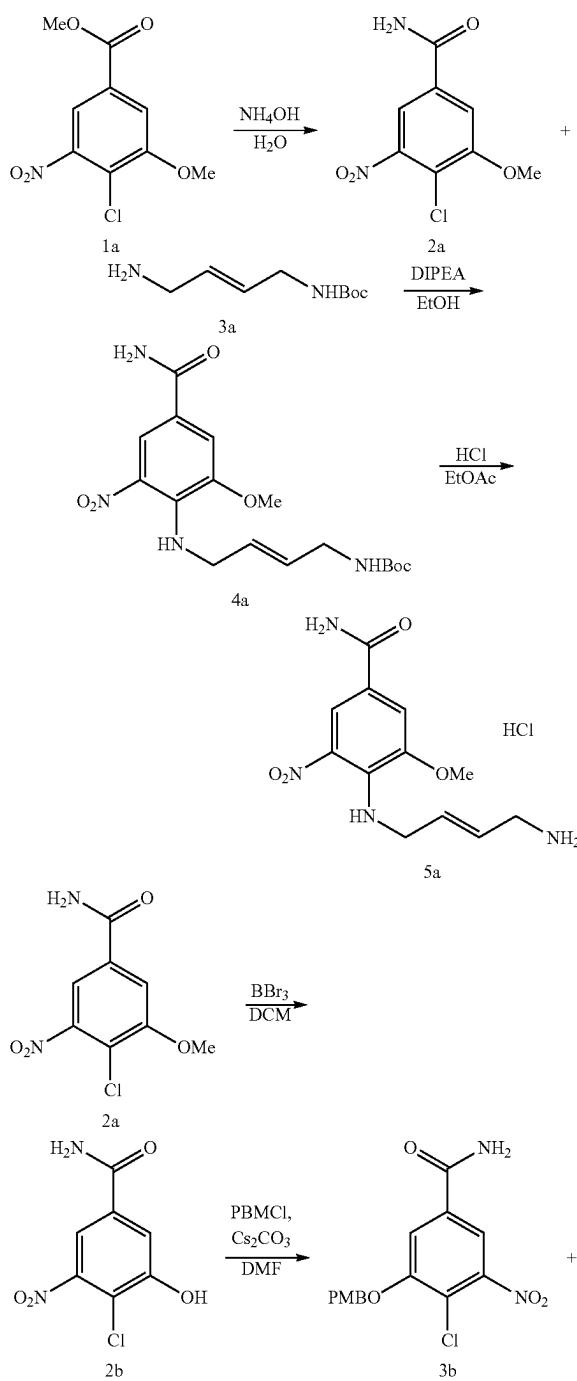
[1500] Unless otherwise specified, preparatory HPLC (PrepHPLC) was performed on one of two instruments using the procedures listed herein: (Method F) a Shimadzu LC-8A preparative HPLC with a Phenomenex Luna C-18 250×50 mm, 10 m using water/acetonitrile mobile phase with 0.09% (v/v) TFA at a flow rate of 80 mL/min or on a Teledyne ISCO ACCQPrep HP150 equipped with one of three Phenomenex preparatory HPLC columns: (i) (Method G) 10×250 mm Syngi C12, 4 μm, Max-RP 80 Å LC Column, (ii) (Method H) 21.2×250 mm Syngi C12, 4 μm, Max-RP 80 Å LC Column or (iii) (Method I) 30×250 mm Syngi C12, 4 μm, Max-RP 80 Å LC Column using acetonitrile/water mobile phases containing either 0.05% (v/v) trifluoroacetic acid or 0.1% (v/v) formic acid as additives.

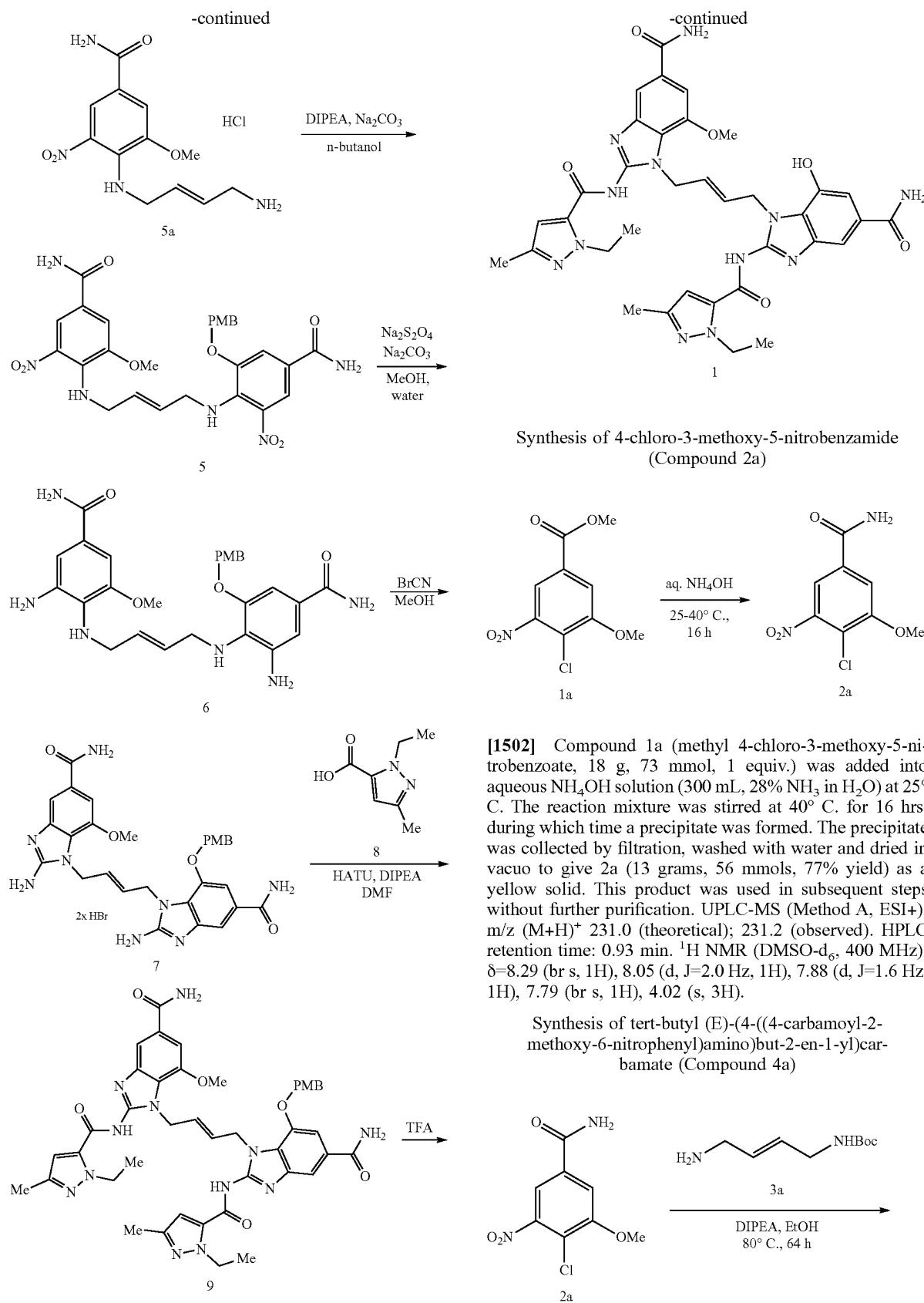
[1501] NMR spectra were recorded on one of three instruments: Bruker Avance III HD (400 MHz), Varian 400-MR (400 MHz) or Bruker Avance NEO (400 MHz).

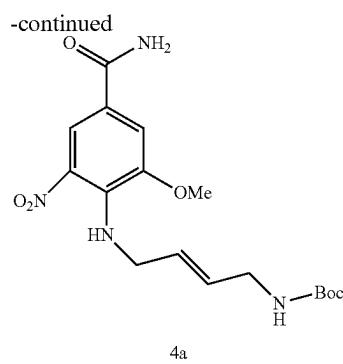
Example 1

Synthetic Procedures for Sting Agonists and Linkers

Synthesis of (E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-hydroxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxamide (Compound 1)

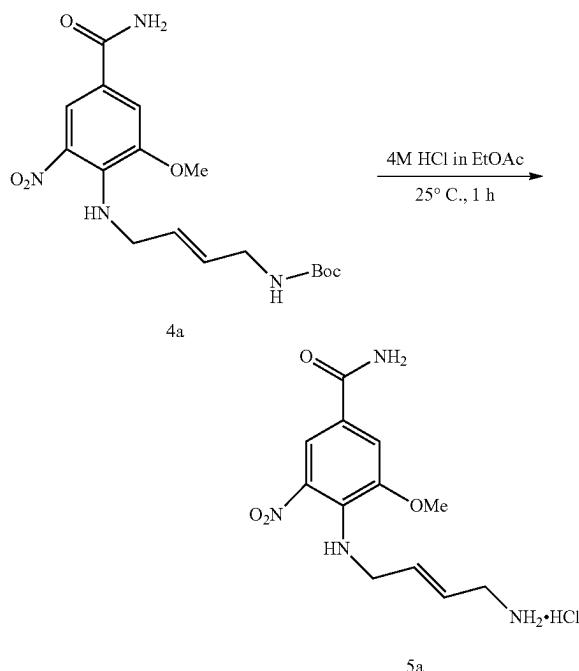






[1503] To a solution of 2a (10 g, 43.4 mmol, 1 equiv.) in ethanol (EtOH, 200 mL) was added 3a (tert-butyl (E)-(4-aminobut-2-en-1-yl)carbamate, 9.69 g, 52.0 mmol, 1.2 equiv.) and N,N-diisopropylethylamine (DIPEA, 16.8 g, 130 mmol, 3 equiv.) at 25° C. The reaction mixture was stirred at 80° C. for 64 hours which point the precipitate was collected by filtration, washed with ethanol, and dried under high vacuum to give 4a (8 grams, 21 mmols, 48% yield) as a red solid. This product was used in subsequent steps without further purification. ¹H NMR (DMSO-d₆, 400 MHz): δ=8.18 (s, 1H), 8.01 (br s, 1H), 7.74 (br t, J=5.6 Hz, 1H), 7.55 (s, 1H), 7.31 (br s, 1H), 6.92 (br s, 1H), 5.53 (br s, 2H), 4.08 (br s, 2H), 3.87 (s, 311), 3.47 (br s, 2H), 1.35 (s, 911).

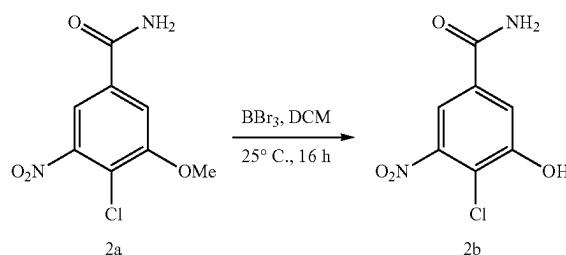
Synthesis of Compound 5a



[1504] Compound 4a (8 g, 21.0 mmol, 1 equiv.) was added into a 4M solution of HCl in ethyl acetate (200 mL, 800 mmol HCl) at 25° C. The reaction mixture was stirred at 25° C. for 1 h. The precipitate was collected by filtration, washed with EtOAc and dried under high vacuum to give 5a as HCl

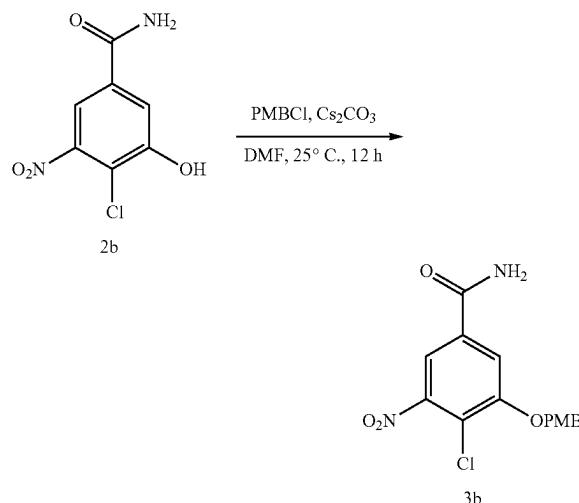
salt (7.2 g, quantitative yield) as a red solid. This product was used in subsequent steps without further purification. ¹H NMR (DMSO-d₆, 400 MHz): δ=8.21 (d, J=1.6 Hz, 1H), 8.02 (br s, 4H), 7.59 (d, J=2.0 Hz, 1H), 7.34 (br s, 1H), 5.87 (td, J=5.6, 15.6 Hz, 1H), 5.67-5.56 (m, 1H), 4.17 (br d, J=5.6 Hz, 2H), 3.89 (s, 3H), 3.39 (br t, J=5.6 Hz, 2H).

Synthesis of Compound 2b



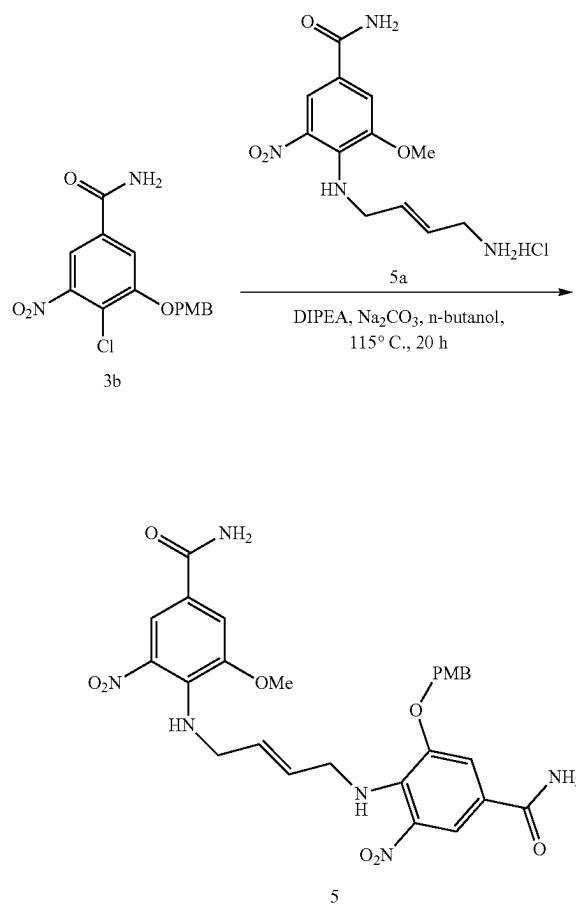
[1505] To a solution of compound 2a (4-chloro-3-methoxy-5-nitrobenzamide, 16 g, 69.4 mmol, 1 equiv.) in dichloromethane (DCM, 500 mL) was added a solution of boron tribromide (BBr₃, 1 M in DCM, 275 mL, 4 equiv.) dropwise at 20° C. under nitrogen. The reaction mixture was stirred at 20° C. for 16 h, upon which LC-MS analysis (Method B) showed the reaction was complete. The reaction mixture was poured into ice water (2 L) and stirred vigorously for 20 min. The resulting suspension was filtered and the filtrate was extracted with ethyl acetate (2×300 mL), dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo to give a crude product. The crude product (9 g) was dissolved in DMF (30 mL) and purified by reversed-phase flash chromatography on a Biotope Isolera One (330 gram Agela C18 column (20-35 µm particle size), utilizing water/acetonitrile with 0.09% (v/v) TFA eluting with a gradient of 20-40% acetonitrile over 20 min followed by 40-45% acetonitrile at 35 min to give 2b (6 grams, 27.7 mmols, 40% yield) as an off-white solid. LCMS (Method B, ESI+): m/z [M+H]⁺ 217.0 (theoretical); 217.2 (observed). HPLC retention time: 0.84 min.

Synthesis of Compound 3b



[1506] To a solution of 2b (4.5 g, 20.8 mmol, 1 equiv.) in dimethylformamide (DMF, 20 mL) was added 1-(chloromethyl)-4-methoxybenzene (PMBCl, 3.42 g, 21.8 mmol, 1.05 equiv.) and cesium carbonate (Cs_2CO_3 , 7.45 g, 22.9 mmol, 1.1 equiv.), the reaction mixture was stirred at 25° C. for 12 h, upon which LC-MS analysis (Method B) showed the reaction was complete. The reaction mixture was poured into ice water, and the precipitate was filtered and dried to give 3b (6.4 grams, 19.0 mmols, 91% yield) as a light yellow solid. This product was used in subsequent steps without further purification. LC-MS (Method B, EST+): m/z [M+H]⁺: 337.1 (theoretical); 337.2 (observed). HPLC Retention Time: 1.11 min.

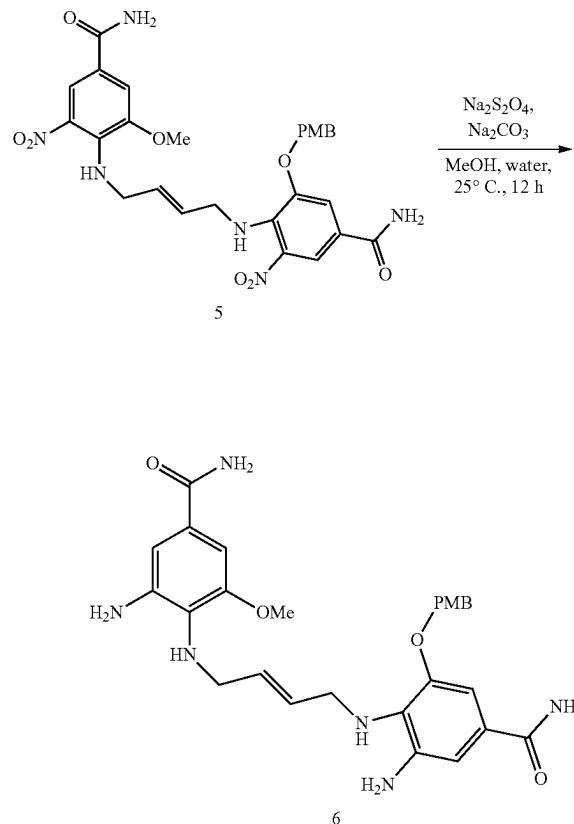
Synthesis of Compound 5



[1507] A solution of 5a (762 mg, 2.16 mmol, 1.2 equiv.) in *n*-butanol (10 mL) was added to a vial, followed by the addition of DIPEA (1.11 g, 8.62 mmol, 4.8 equiv.) and sodium bicarbonate (457 mg, 4.31 mmol, 2 equiv.). The vial was scaled and the reaction mixture was stirred at 20° C. for 10 min. This was followed by the addition of 3b (600 mg, 1.78 mmol, 2.4 equiv.), and the reaction mixture was stirred at 115° C. for 20 hours upon which time UPLC-MS analysis (Method B) showed the reaction was complete. Four additional vials were set up as described above. All five reaction mixtures were combined at the end of the reaction. The resulting combined reaction mixture was cooled to 20° C.

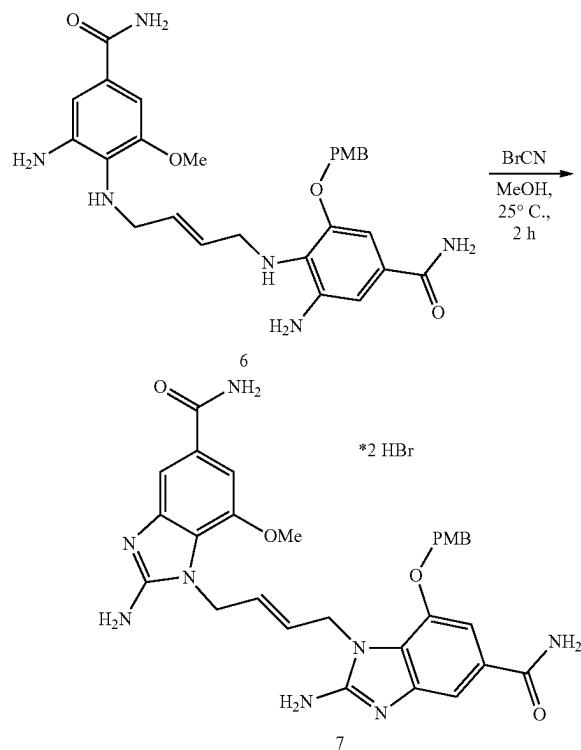
and diluted with MeCN (180 mL). The solid material in the reaction mixture was filtered and rinsed with MeCN (80 mL) to give a dark red solid. The solid was then washed with water and dried under high vacuum to give 5 (2.7 grams, 4.65 mmols, 52% yield) as a brick-red solid. This product was used in subsequent steps without further purification. ^1H NMR (400 MHz, DMSO- d_6): δ =8.17 (dd, J =1.9, 7.8 Hz, 2H), 8.08-7.96 (m, 2H), 7.77-7.63 (m, 3H), 7.51 (d, J =1.8 Hz, 1H), 7.37 (d, J =8.6 Hz, 2H), 7.33 (br s, 2H), 6.92 (d, J =8.6 Hz, 2H), 5.57-5.42 (m, 2H), 5.04 (s, 2H), 4.01 (q, J =5.8 Hz, 2H), 3.79 (s, 3H), 3.74 (s, 3H).

Synthesis of Compound 6



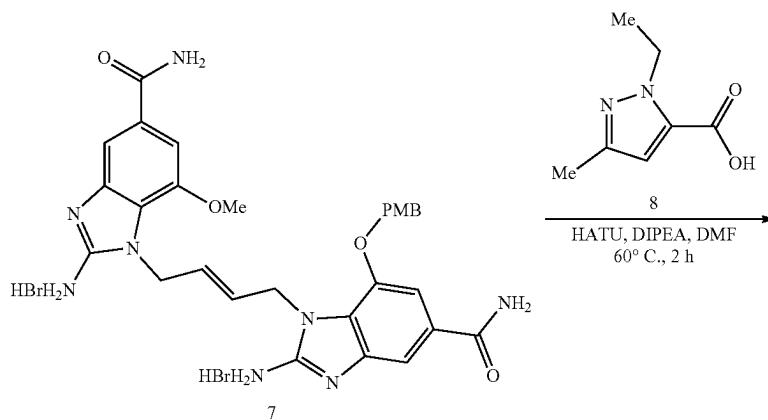
[1508] To a solution of 5 (2 g, 3.45 mmol, 1 equiv.) in a 1:1 (v/v) mixture of methanol and water (160 mL) was added Na_2CO_3 (10.95 g, 103 mmol, 30 equiv.) and sodium dithionite ($\text{Na}_2\text{S}_2\text{O}_4$, 8.40 g, 48.2 mmol, 14 equiv.). The resulting red reaction mixture was stirred at 25° C. for 12 h, upon which the red mixture turned into a pale yellow color, and UPLC-MS analysis (Method B) showed the reaction was complete. The reaction mixture was filtered, and the filtrate was concentrated and diluted with water. The mixture was extracted with *EtOAc* and the organic layer was concentrated to give 6 (1.0 grams, 1.81 mmols, 52% yield) as an off-white solid. This product was used in subsequent steps without further purification. ^1H NMR (400 MHz, DMSO- d_6): δ =7.61 (br s, 2H), 7.37 (d, J =8.6 Hz, 2H), 6.97 (br s, 2H), 6.94 (s, 1H), 6.93-6.90 (m, 2H), 6.86 (s, 2H), 6.77 (d, J =1.8 Hz, 1H), 5.71-5.53 (m, 2H), 4.98 (s, 2H), 4.65 (br d, J =12.6 Hz, 4H), 3.74 (s, 3H), 3.71 (s, 3H), 3.49 (br s, 4H).

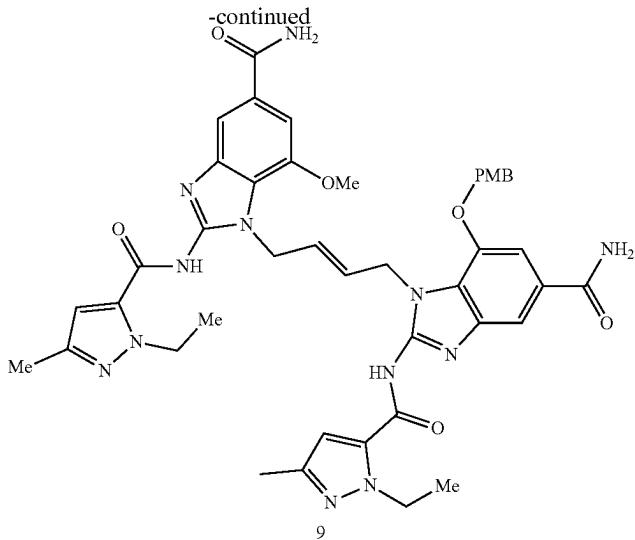
Synthesis of Compound 7



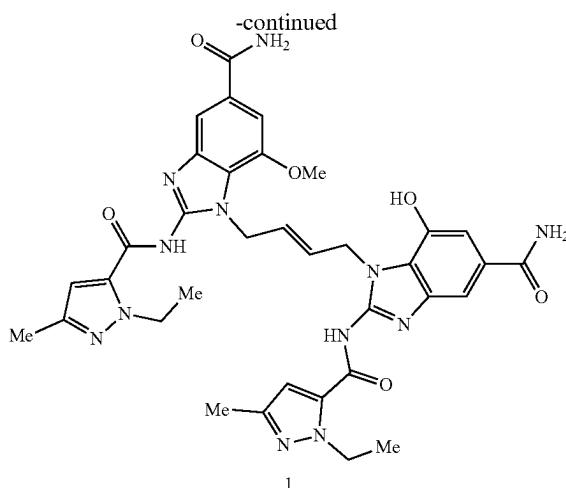
[1509] To a solution of 6 (1.4 g, 2.69 mmol, 1 equiv.) in methanol (20 mL) was added cyanogen bromide (BrCN, 1.71 g, 16.1 mmol, 6 equiv.). The reaction mixture was stirred at 25° C. for 2 h, during which time a precipitate was observed. LC-MS analysis (Method C) showed the reaction was complete. The solid was collected by filtration, washed with ethanol and petroleum ether to give 7 (1.2 g, 1.64 mmols, 61% yield) as a light yellow solid. This product was used in subsequent steps without further purification. LC-MS (Method C, ESI+): m/z [M+H]⁺ 571.2 (theoretical); 571 (observed). HPLC retention time: 1.634 min. ¹H NMR (400 MHz, DMSO-d₆): δ=12.94 (br s, 2H), 8.63 (br d, J=12.8 Hz, 4H), 8.08 (br s, 2H), 7.62-7.52 (m, 3H), 7.47 (br s, 2H), 7.38 (s, 1H), 7.24 (d, J=8.6 Hz, 2H), 6.84 (d, J=8.6 Hz, 2H), 5.81-5.69 (m, 1H), 5.57 (td, J=5.4, 15.5 Hz, 1H), 5.07 (s, 2H), 4.80 (br t, J=6.6 Hz, 4H), 3.74 (s, 3H), 3.69 (s, 3H).

Synthesis of Compound 9

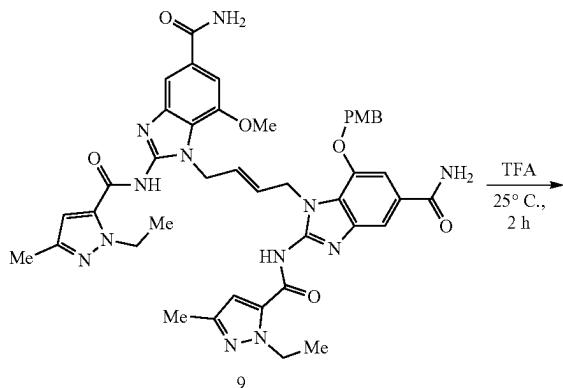




[1510] To a solution of compound 8 (1-ethyl-3-methyl-1H-pyrazole-5-carboxylic acid, 331 mg, 2.15 mmol, 2.1 equiv.) in dimethylformamide (DMF, 3 mL) was added 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (HATU, 973 mg, 2.56 mmol, 2.5 equiv.) and the reaction mixture was stirred at 60° C. for 10 min. A solution of DIPEA (596 mg, 4.61 mmol, 4.5 equiv.) and 7 (750 mg, 1.02 mmol, 1 equiv.) in DMF (1 mL) was then added to the reaction mixture, which was stirred at 60° C. for 2 h, upon which LC-MS analysis (Method B,) showed the reaction was complete. The reaction mixture was poured into ice water, the solid was collected by filtration and dried to give a crude product. The crude product was used in the next step without further purification. LC-MS (Method B, ESI+): m/z [M+H]⁺ 843.4 (theoretical); 843.4 (observed). HPLC Retention Time: 1.062 min.



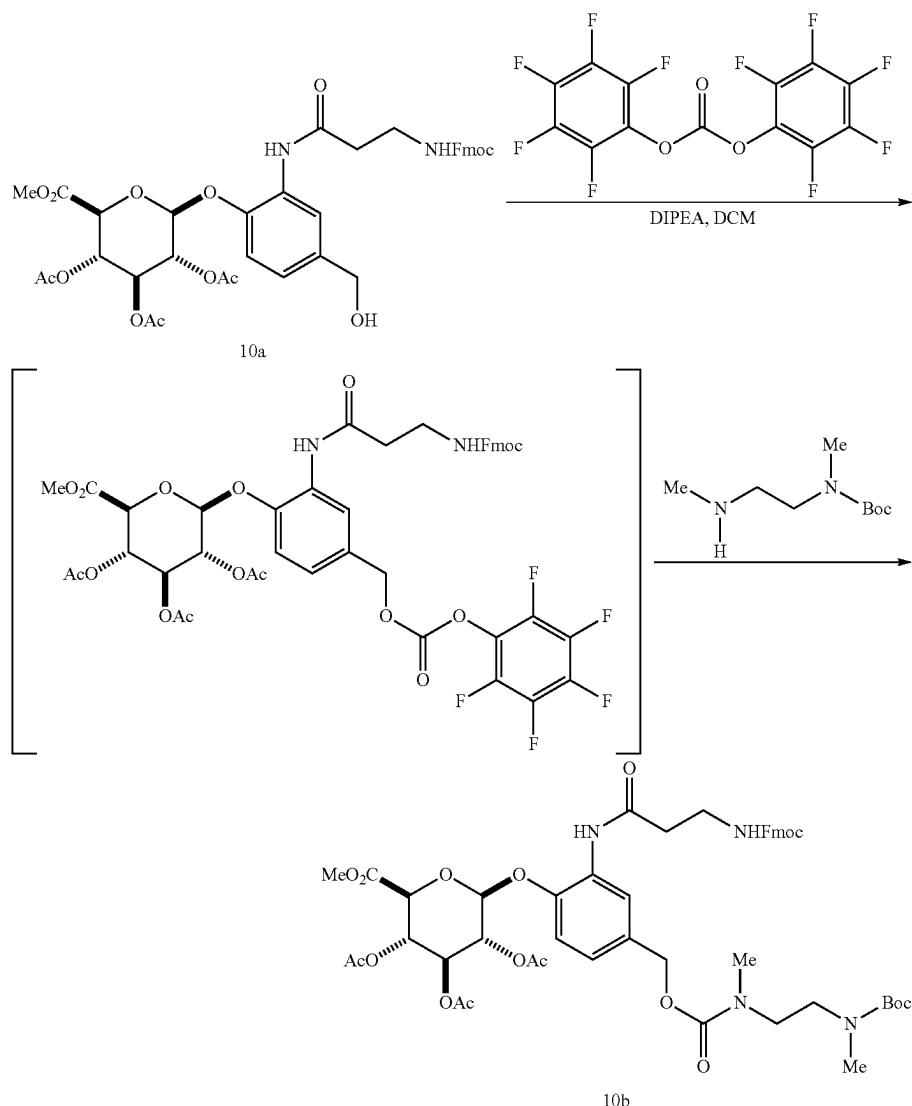
Synthesis of Compound 1



[1511] Compound 9 (700 mg, 0.83 mmol) was added to a glass vial containing trifluoroacetic acid (TFA, 3 mL), and the resulting mixture was stirred at 25° C. for 2 h, upon which LC-MS analysis showed the reaction was complete. The TFA was removed in vacuo and the residue was dissolved in DMSO and acetonitrile and purified by preparatory HPLC (Method F,) to give 1 (40 mg, 0.055 mmols, 7% yield over 2 steps) as an off-white solid. LCMS (Method B, ESI+): m/z [M+H]⁺ 723.3 (theoretical); 723.1 (observed); [M+H]⁺, HPLC retention time: 2.04 min. ¹H NMR (400 MHz, DMSO-d₆): δ=13.00-12.51 (m, 2H), 10.41 (s, 1H), 7.96 (br s, 1H), 7.81 (br s, 1H), 7.63 (s, 1H), 7.43 (s, 1H), 7.37-7.28 (m, 2H), 7.22 (br s, 1H), 7.14-7.07 (m, 1H), 6.51 (br d, J=11.0 Hz, 2H), 5.97-5.75 (m, 2H), 4.91 (br dd, J=3.5, 16.3 Hz, 4H), 4.51 (br d, J=3.3 Hz, 4H), 3.77 (s, 3H), 2.10 (d, J=6.0 Hz, 6H), 1.25 (dt, J=3.6, 6.9 Hz, 6H).

Synthesis of (2S,3S,4S,5R,6S)-6-(4-(((2-((5-carbamoyl-1-((E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)carbonyl)(methyl)amino)ethyl)(methyl carbamoyl)oxy)methyl)-3-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanamido)propanamido phenoxy)-3,4,5-trihydroxytetrahydro-2H-pyran-2-carboxylic acid (Compound 11)

Synthesis of Compound 10b

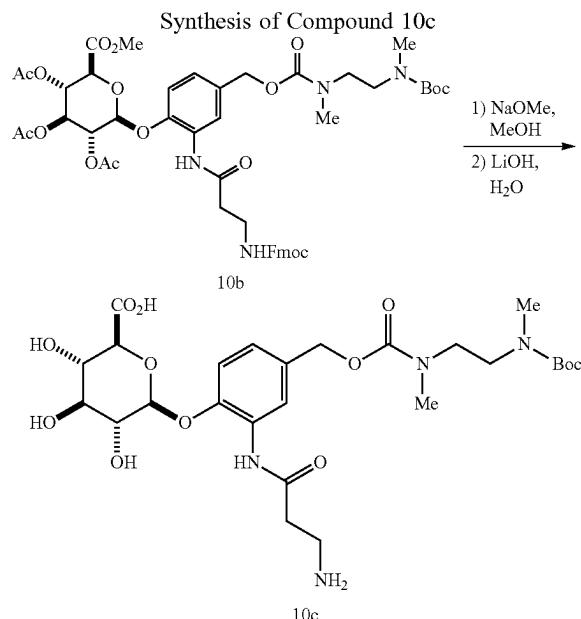


[1512] Compound 10a was prepared as previously reported (*ACS Med. Chem. Lett.* 2010, 1, 6, 277-280).

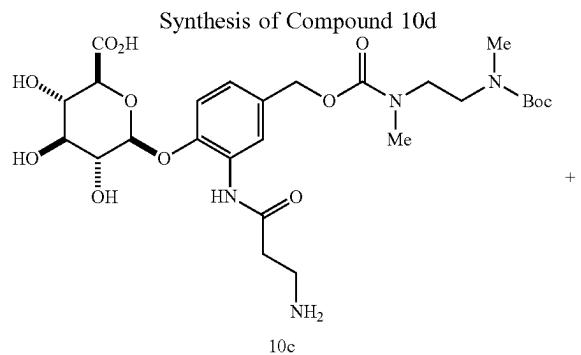
[1513] An oven-dried 4 mL glass vial was charged with 10a (150 mg, 0.20 mmol, 1 equiv.) and pentafluorophenyl carbonate (88 mg, 0.22 mmol, 1.1 equiv.), DMF (1 mL) and DIPEA (0.15 mL, 0.86 mmol, 4.3 equiv.). The reaction mixture was stirred at room temperature for 30 minutes upon which a light pink homogenous solution was observed.

Tert-butyl methyl(2-(methylamino)ethyl)carbamate (50 uL, 0.27 mmol, 1.3 equiv.) was added to the solution, which resulted in the reaction mixture turning to a light yellow color. The reaction mixture was stirred at room temperature overnight. The reaction mixture was diluted with water (50 mL), transferred to a separatory funnel and extracted with EtOAc (3×50 mL). The organic layers were collected and combined, washed with 1M HCl, dried with MgSO₄, filtered

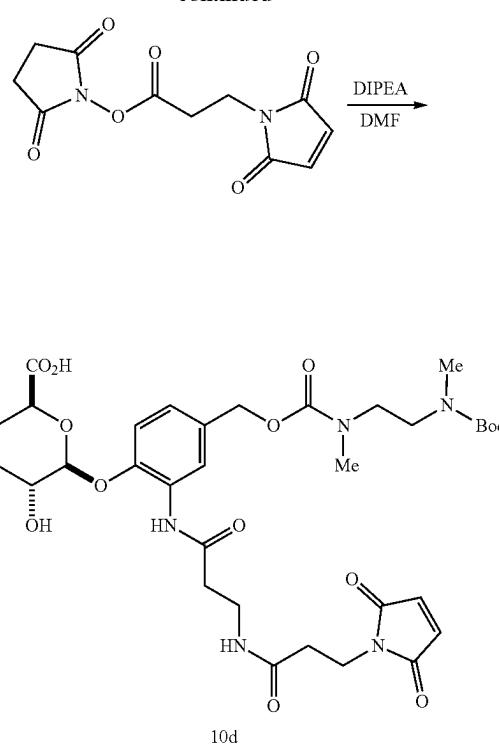
and the solvent removed in vacuo. The resulting solid was purified by flash column chromatography (25 g SiO₂ column, eluting with 0-25% MeOH in DCM) to yield 10b as a light yellow solid (70.4 mg, 0.073 mmol, 36% yield). UPLC-MS (Method E, EST+) m/z [(M-Boc)+2H]⁺: 863.33 (theoretical); 863.14 (observed). HPLC retention time: 1.54 min.



[1514] Compound 10b (70.4 mg, 0.073 mmol, 1 equiv.) was transferred as a solution in MeOH to an oven-dried 4 mL glass vial equipped with a magnetic stir bar. The MeOH was removed under vacuum and the vial back-filled with argon. To the vial, under Ar, was added MeOH (0.5 mL) and the resulting solution was cooled to 0° C. and sodium methoxide (0.5 M solution in MeOH, 150 μ L, 0.075 mmol, 1 equiv.) was added. The reaction was monitored by LC-MS (Method D) and upon complete removal of all three acetate groups, lithium hydroxide (1M in water, 0.225 mL, 0.225 mmol, 3 equiv.) was added and the reaction mixture was stirred at room temperature for 30 min. DMSO (0.5 mL) and glacial acetic acid (50 μ L) were added to the reaction mixture, yielding a homogenous solution. The crude product was purified by preparatory HPLC (Method H, 5-40% MeCN in water with 0.05% TFA as mobile phase additive) to give 10c as a white solid (16.8 mg, 0.028 mmol, 38% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺ 601.26 (theoretical); 601.15 (observed). HPLC retention time: 1.09 min.

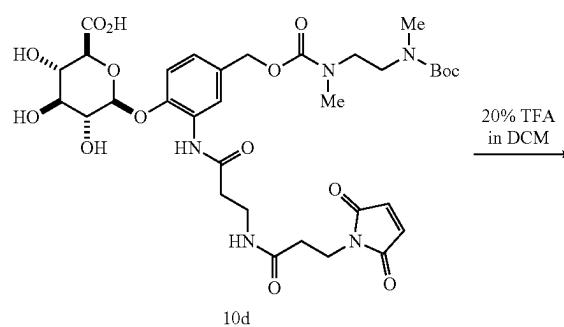


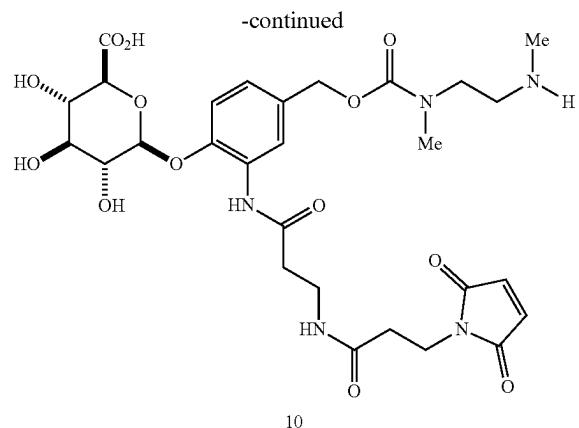
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[1515] Compound 10c (16.8 mg, 0.028 mmol, 1 equiv.) was added to an oven-dried 4 mL glass vial equipped with a magnetic stir bar as a solution in MeOH. The MeOH was removed under vacuum and the vial filled with argon. To the vial was added 3-(maleimido)propionic acid N-hydroxysuccinimide ester (MP-OSu, 16 mg, 0.06 mmol, 2 equiv.) followed by DMF (0.5 mL) and DIPEA (50 μ L, 0.28 mmol, 10 equiv.). After 15 minutes, DMSO (0.5 mL) and glacial acetic acid (100 μ L) were added and the crude product purified by preparatory HPLC (Method H, 10-60% MeCN in water with 0.05% TFA as mobile phase additive) to give 10d as a white solid (15 mg, 0.020 mmol, 71% yield). UPLC-MS (Method A, ESI+): m/z [M+H]⁺: 752.29 (theoretical); 752.26 (observed). HPLC retention time: 1.27 min.

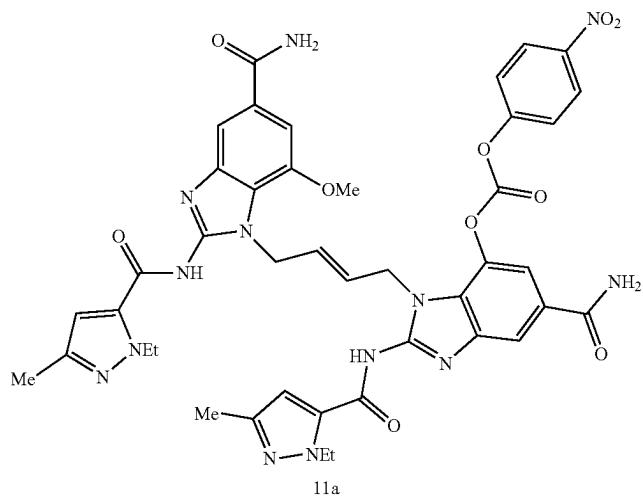
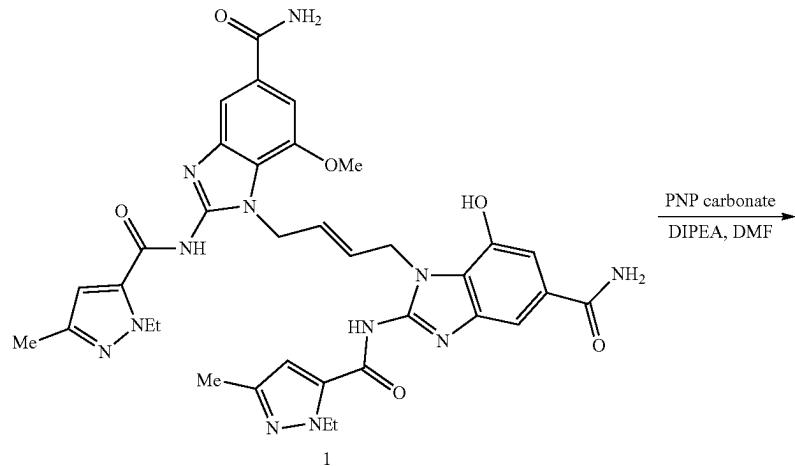
Synthesis of Compound 10



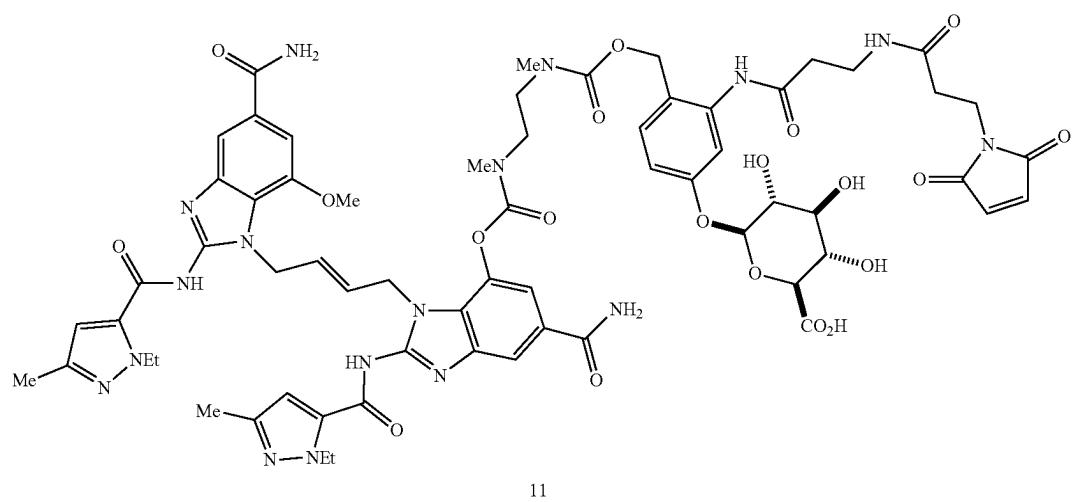
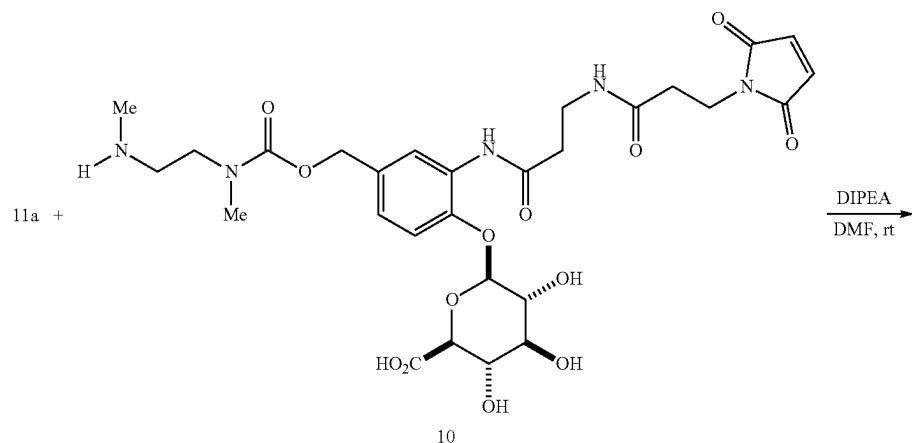


[1516] Compound 10d (15 mg, 0.020 mmols, 1 equiv.) was dissolved in 20% (v/v) TFA in DCM (1 mL) and transferred to a 4 mL glass vial equipped with a magnetic stir bar. The vial was left uncapped and the reaction progress was monitored by LC-MS. After 2 h, the solvent was removed in vacuo to give 10 as a white solid (13 mg, 0.02 mmol, quantitative yield) which was used in subsequent steps without any further purification. UPLC-MS (Method D, ESI+): m/z [M+H]+: 652.24 (theoretical); 652.45 (observed). HPLC retention time: 0.69 min.

Synthesis of Compound 11



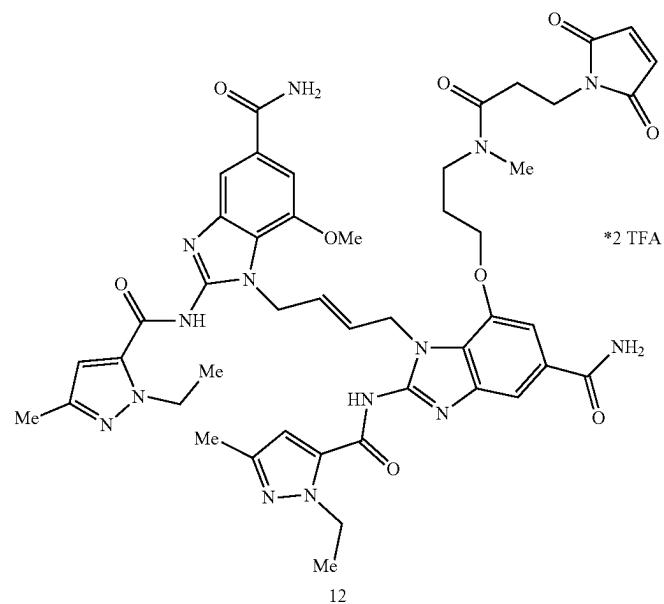
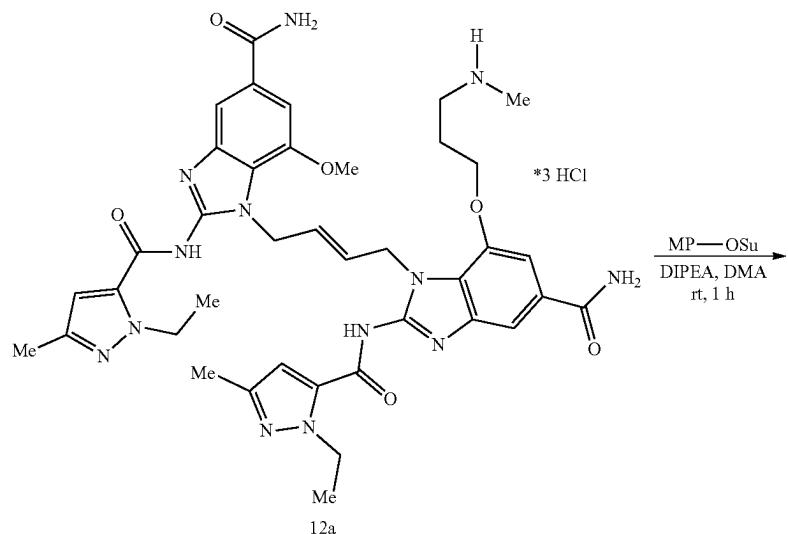
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[1517] To an oven-dried 4 mL glass vial was added Compound 1 (9.5 mg, 0.010 mmol, 1 equiv.) followed by DMF (0.5 mL), p-nitrophenyl carbonate (9.0 mg, 0.030 mmol, 3 equiv.) and DIPEA (20 μ L, 0.115 mmol, 11.5 equiv.). The reaction mixture was stirred at room temperature for 1 hour at which point full conversion to 11a was confirmed by UPLC-MS analysis (Method D). Compound 10 (20 mg, 0.031 mmol, 3.1 equiv.) was added in a single portion to the reaction mixture which was stirred at room temperature for 2 h. Glacial acetic acid (20 μ L) was added

and the crude product purified by preparatory HPLC (Method H, 0-45% MeCN in water with 0.05% TFA as mobile phase additive). The fractions containing 11 were combined and the solvent was removed via lyophilization to give 11 (6.31 mg, 0.0039 mmol, 39% yield). Compound 1 was also recovered (2.81 mg, 0.0030 mmol, 30% recovery) as a white fluffy solid. UPLC-MS (Method D, ESI+): m/z $[\text{M}+\text{H}]^+$: 1400.52 (theoretical); 1400.25 (observed) & $[\text{M}+2\text{H}]^{2+}$: 701.43 (observed). HPLC retention time: 1.28 min.

Synthesis of (E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(3-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-N-methylpropanamido)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazole-5-carboxamide (Compound 12)



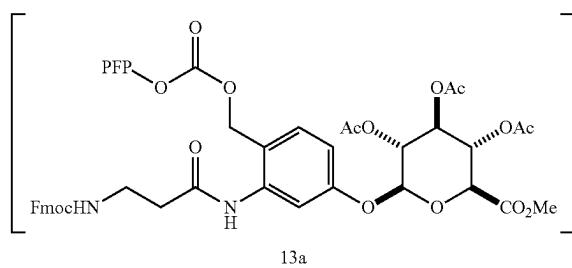
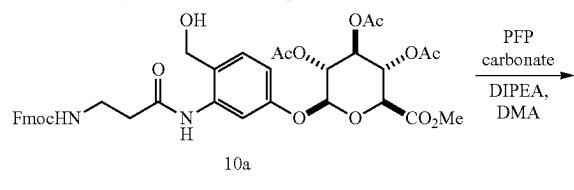
[1518] Compound 12a was prepared as previously reported (WO2017/175147, example 40, page 292).

[1519] To a solution of 12a (28.7 mg, 0.032 mmol, 1.0 equiv.) in DMA (635 μ L) was added MP-OSu (15.9 mg, 0.0596 mmol, 1.9 equiv.), and DIPEA (35 μ L, 0.199 mmol, 6.2 equiv.). The reaction mixture was stirred for 1 h at room temperature. Upon completion, the solution was concen-

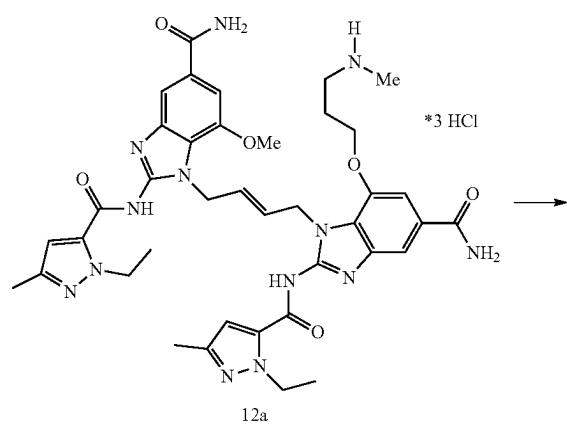
trated under reduced pressure and the crude product was purified by preparatory HPLC (Method G, 20-50-95% MeCN in water with 0.1% formic acid as mobile phase additive) to yield 12 (46% yield, 17.8 mg, 0.0152 mmol). UPLC-MS (Method D, ESI+): m/z [M+H]⁺ 945.40 (theoretical); 945.72 (observed). HPLC retention time: 1.79 min.

Synthesis of (2S,3S,4S,5R,6S)-6-(4-(((3-((5-carbamoyl-1-((E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)propyl)(methyl)carbamoyl)oxy)methyl)-3-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanamido)propanamido)phenoxy)-3,4,5-trihydroxytetrahydro-2H-pyran-2-carboxylic acid (Compound 13)

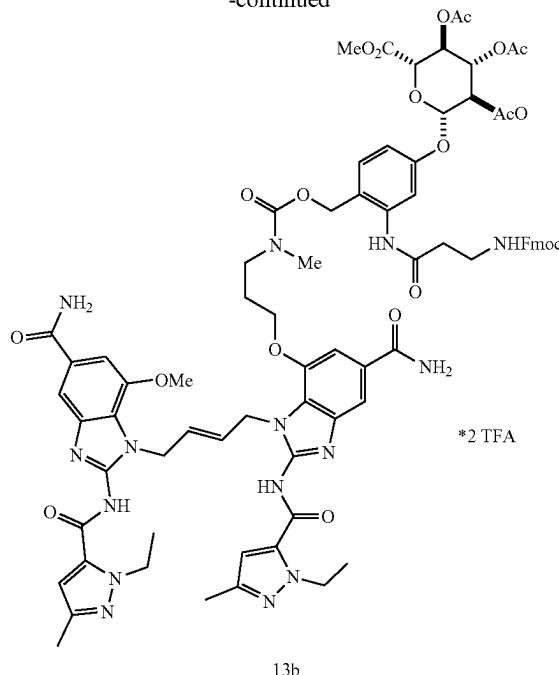
Synthesis of Compounds 13a and 13b



13a +

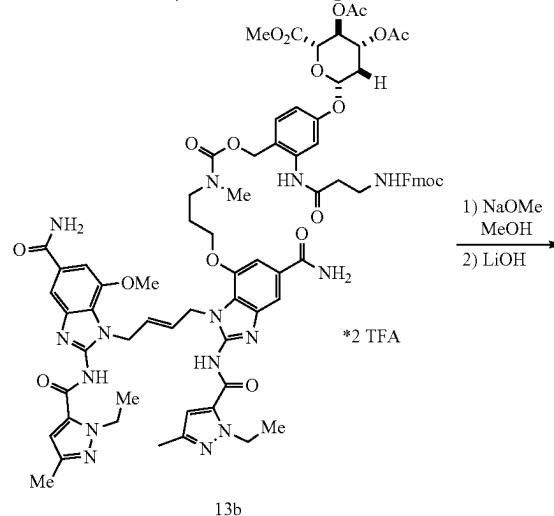


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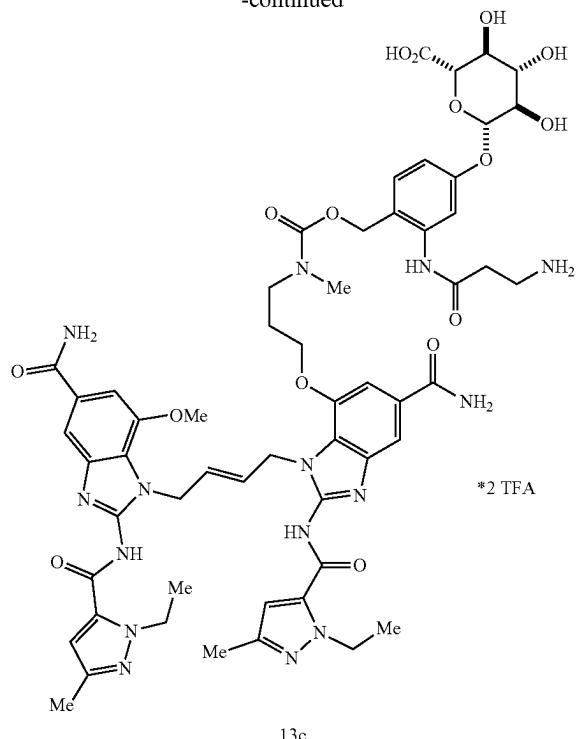


[1520] Compound 10a (13 mg, 0.017 mmol) was dissolved in DMA (87 μ L). To this solution was added pentfluorophenyl carbonate (13.7 mg, 0.035 mmol), and DIPEA (14 μ L, 0.078 mmol). The mixture was stirred for 30 min at room temperature. Upon full conversion to intermediate 13a, this solution was transferred to a second vial containing 12a (10.6 mg, 0.012 mmol). The reaction mixture was stirred for 18 h at room temperature. The reaction was then diluted with water and extracted three times with EtOAc (20 mL \times 3). The combined organic layers were then washed with 1M HCl. The organic layers were combined, dried with $MgSO_4$, filtered, and concentrated in vacuo. The product was purified by preparatory HPLC (Method H, 5-50-95% MeCN in water using 0.05% TFA as mobile phase additive) to yield compound 13b as a trifluoroacetate salt (10.0 mg, 0.0056 mmol, 48% yield). UPLC-MS (Method D, ESI+): m/z [M+H] $^{+}$ 1568.60 (theoretical); 1568.95 (observed). HPLC retention time: 1.70 min.

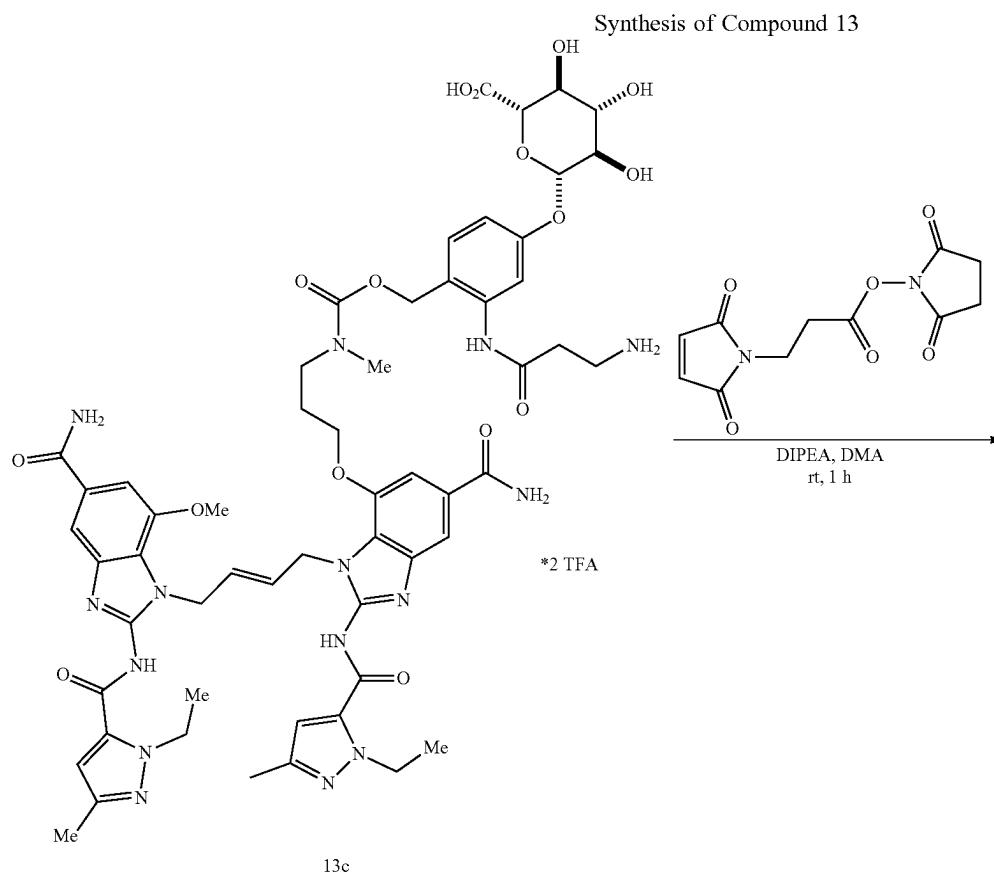
Synthesis of Compound 13c



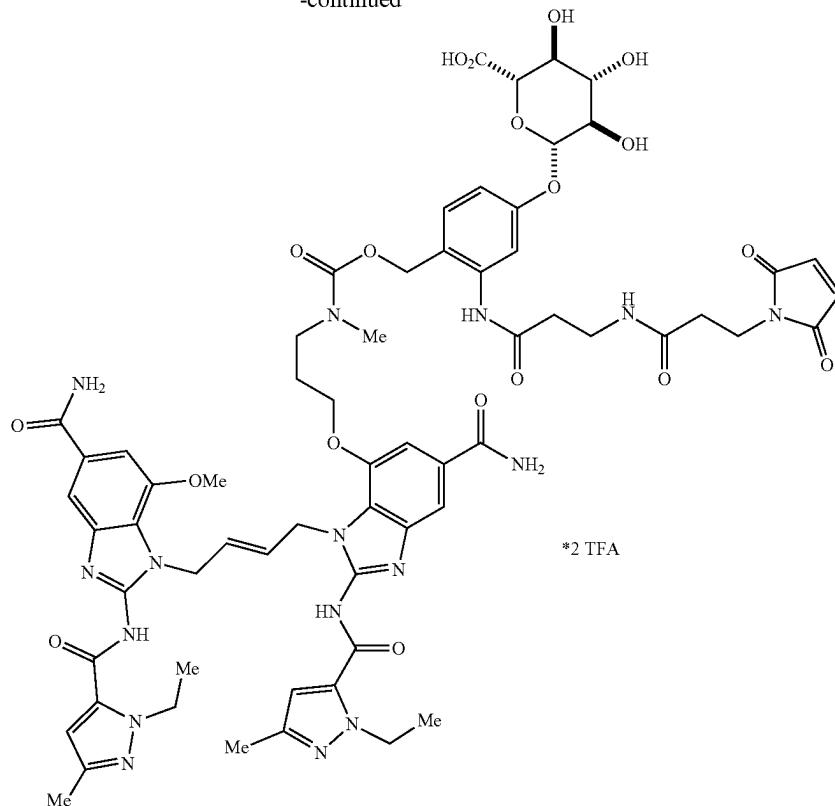
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[1521] To a dry, well purged glass vial was added compound 13b (10.0 mg, 0.0056 mmol) in anhydrous methanol (40 μ L). The solution was cooled in an ice bath, and NaOMe (0.5 M in MeOH, 11.13 μ L) was added. After about 1 h, 1 M aqueous LiOH (17 μ L, 0.017 mmols, 3 equiv.) solution was added. Significant white precipitate formed upon the addition of the LiOH solution. After 1 hr, glacial acetic acid (12 μ L) was added, and the solvents were removed in vacuo. The crude product was purified by preparatory HPLC (Method G, 20-60-95% MeCN in water, with 0.05% TFA as mobile phase additive) to yield compound 13c as trifluoroacetate salt (4.13 mg, 0.0029 mmol, 52% yield). UPLC-MS (Method D, ESI+): m/z [M+H] $^{+}$ =1206.49 (theoretical); 1206.50 (observed). HPLC retention time: 1.45 min.



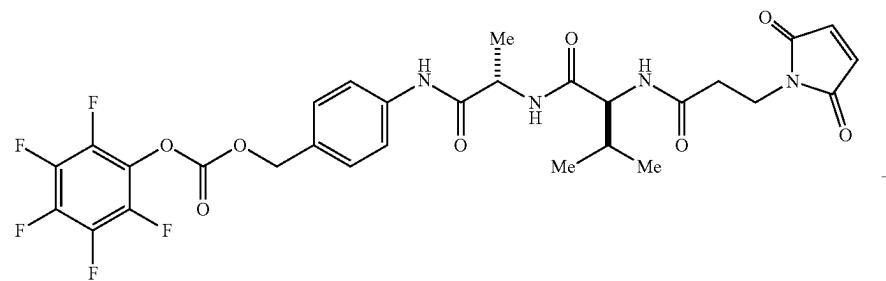
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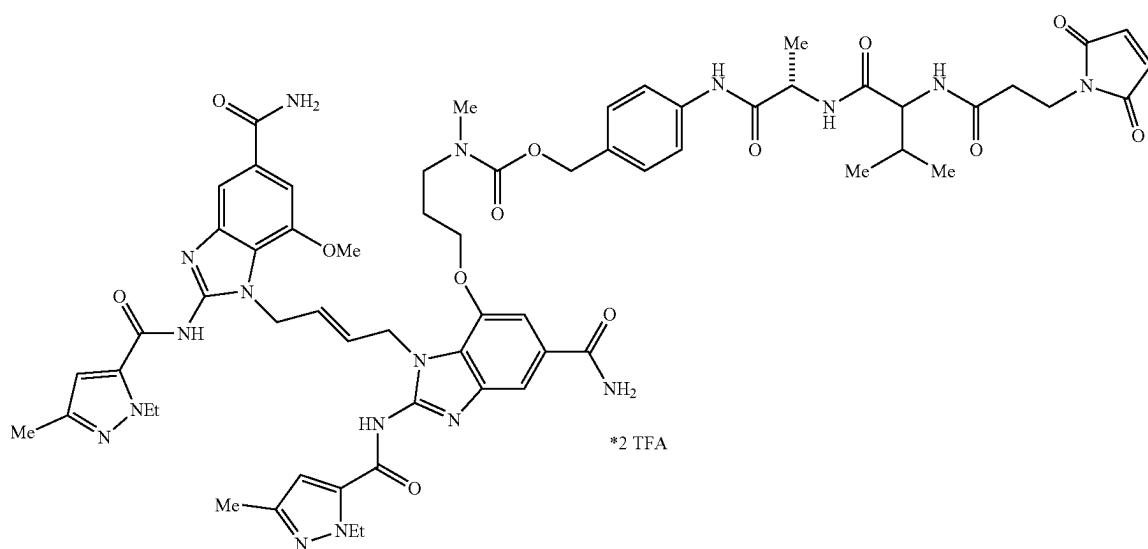
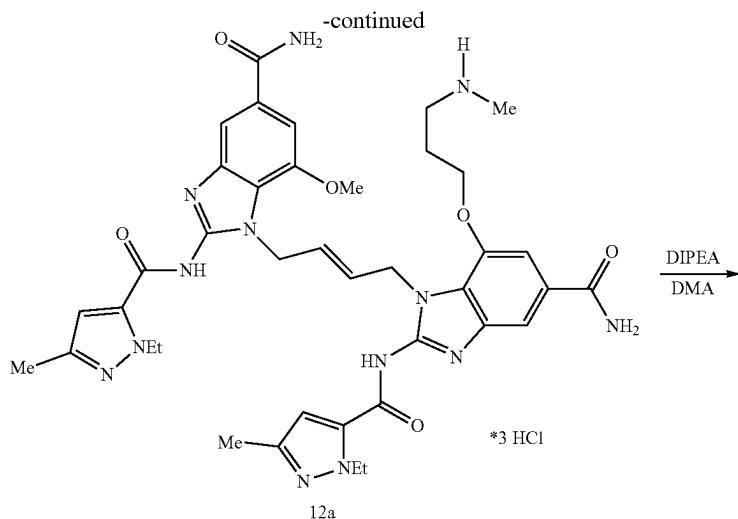
13

[1522] Compound 13c (4.13 mg, 0.00342 mmol, 1.0 equiv.) was dissolved in DMA (68 L) in a glass vial under argon. MP-OSu (1.82 mg, 0.00685 mmol, 2 equiv.) and DIPEA (3.0 μ L, 0.0171 mmol, 5 equiv.) were added and the reaction mixture was stirred for 1 h at RT. Glacial acetic acid (3.0 μ L) was added, and the crude product purified by preparatory HPLC (Method G, 10-60-95% MeCN in water using 0.1% formic acid as mobile phase additive) to yield 13 as trifluoroacetate salt (5.43 mg, 0.0034 mmol, 93% yield). UPLC-MS (Method E, ESI+): m/z [M+H]⁺=1357.52 (theoretical); 1357.82 (observed). HPLC retention time: 1.54 min.

Synthesis of 4-((S)-2-((S)-2-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanamido)-3-methylbutanamido)propanamido)benzyl (3-((5-carbamoyl-1-((E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)propyl)(methyl)carbamate (Compound 14)



14a

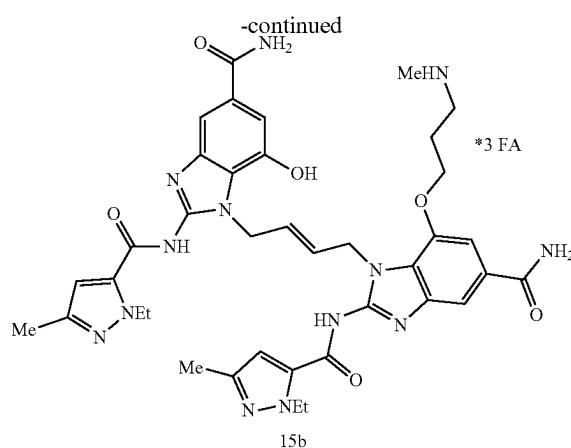
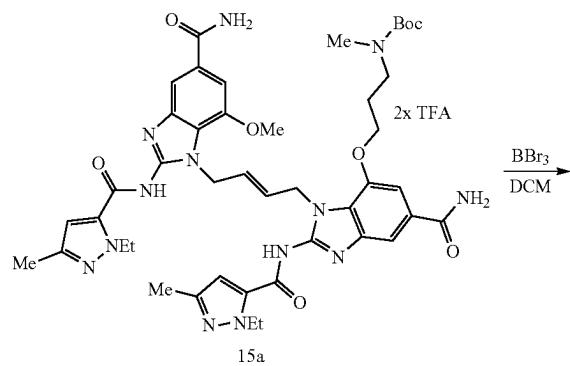


[1523] To a dry glass vial charged with compound 12a (2.6 mg, 0.0033 mmol) was added DMA (66 μ L) followed by MP-Val-Ala-PAB-Ofpf (14a, 3.2 mg, 0.049 mmol, 15 equiv.) and DIPEA (2.8 μ L, 0.016 mmol, 4.9 equiv.). The reaction mixture was stirred for 30 minutes at RT and then glacial acetic acid (2.85 μ L) was added, and the crude product purified by preparatory HPLC (Method G, 30-60

95% MeCN in water, with 0.1% formic acid as mobile phase additive), to yield compound 14 as trifluoroacetate salt (4.0 mg, 0.0027 mmol, 82% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1264.56 (theoretical); 1264.85 (observed). HPLC retention time: 1.75 min.

Synthesis of (E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-hydroxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(3-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-N-methylpropanamido)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazole-5-carboxamide (Compound 15)

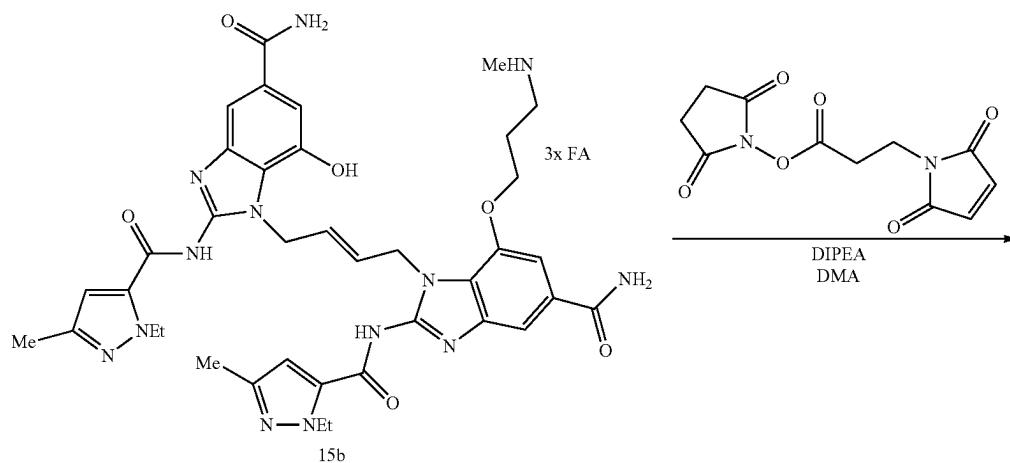
Synthesis of Compound 15b



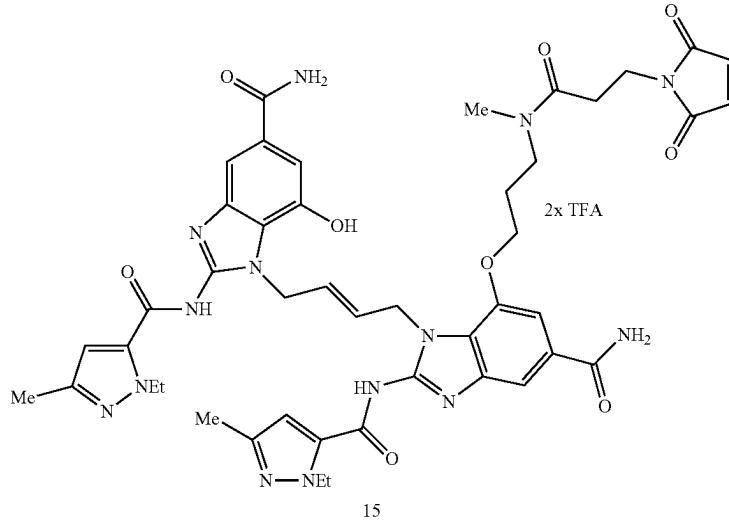
[1524] Compound 15a was prepared as previously reported (WO2017/175147, page 292)

[1525] To a dry glass vial containing compound 15a (31.4 mg, 0.0280 mmol) in DCM (280 μL) was added boron tribromide (BBr_3 , 1M in DCM, 168 μL , 0.168 mmol, 6 equiv.) dropwise. The reaction mixture was stirred at 40° C. for 18 h. The reaction mixture was cooled to RT and cold water (170 μL) was slowly added. The resulting mixture was concentrated in vacuo and purified by preparatory HPLC (20-50-95%, 0.1% formic acid in acetonitrile, Method G). Fractions containing the desired product were combined and solvent removed via lyophilization to yield compound 15b as the formate salt (17% yield, 4.36 mg, 0.0047 mmol). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=780.36 (theoretical); 780.38 (observed). HPLC retention time: 1.33 min.

Synthesis of Compound 15



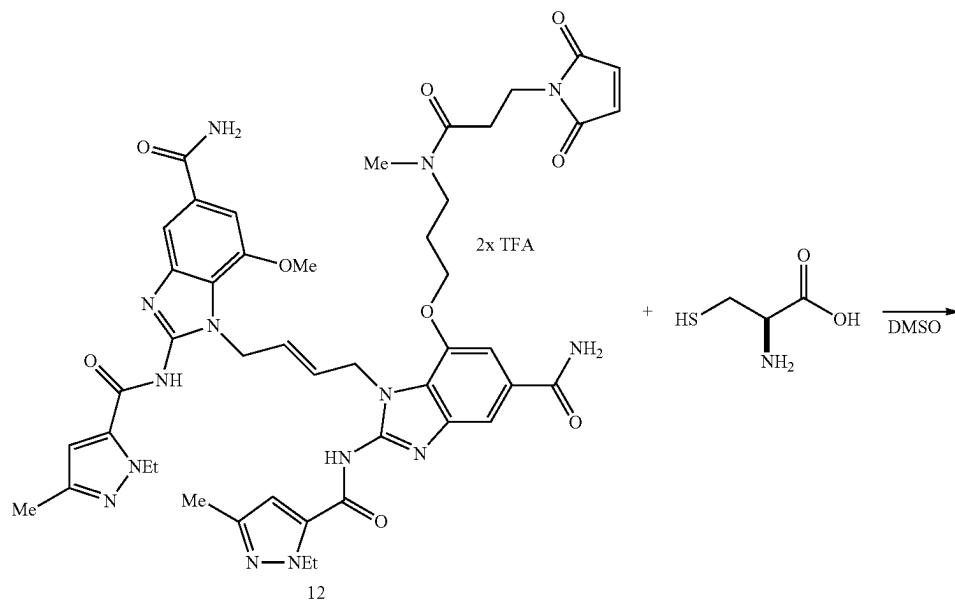
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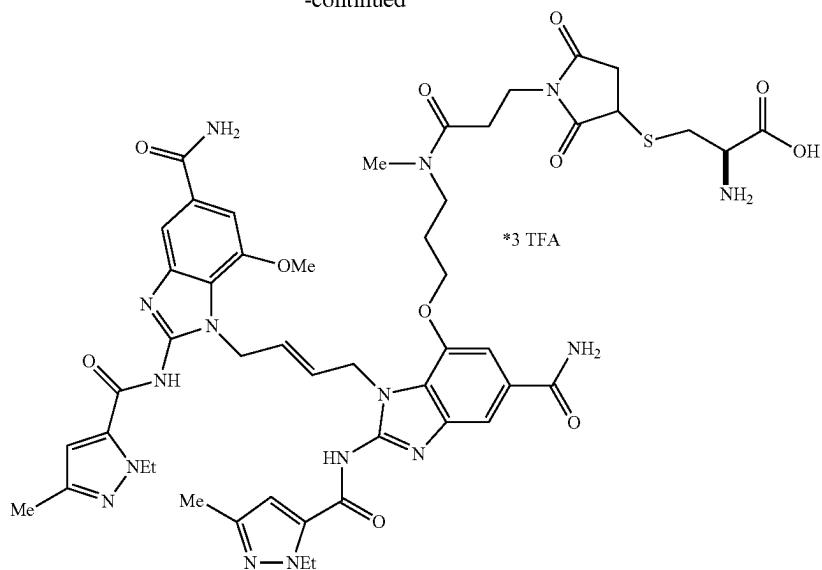
[1526] To a dry 4 mL vial containing 2,5-dioxopyrrolidin-1-yl 3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoate (MP-OSu, 1.7 mg, 0.0063 mmol) was added compound 15b (3.9 mg, 0.0042 mmol) as a solution in DMA (423 μ L). To the mixture was added DIPEA (3.7 μ L, 0.0211 mmol, 5 equiv.) and the reaction mixture was stirred for 30 min at RT, after which glacial acetic acid (3.68 μ L) was added, and the product was purified via preparatory HPLC (10-40-95%, 0.05% TFA in acetonitrile, Method G). Fractions containing the desired product were combined and solvents removed via lyophilization to yield compound 15 as trifluoroacetate

salt (20% yield, 1.0 mg, 0.0009 mmol). UPLC-MS (Method D, ESI+): m/z [M+H] $^{+}$ =931.39 (theoretical); 931.41 (observed). HPLC retention time: 1.62 min.

Synthesis of S-(1-(3-((3-((5-carbamoyl-1-(E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)propyl) (methyl)amino)-3-oxopropyl)-2,5-dioxopyrrolidin-3-yl-L-cysteine (Compound 16)



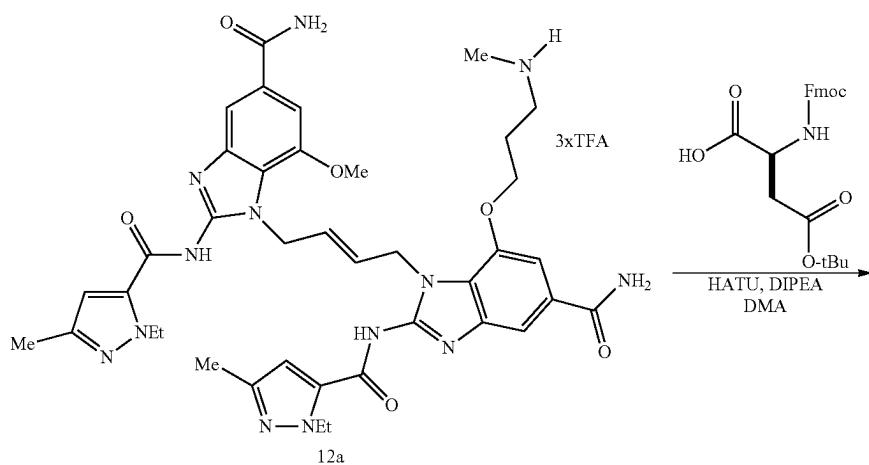
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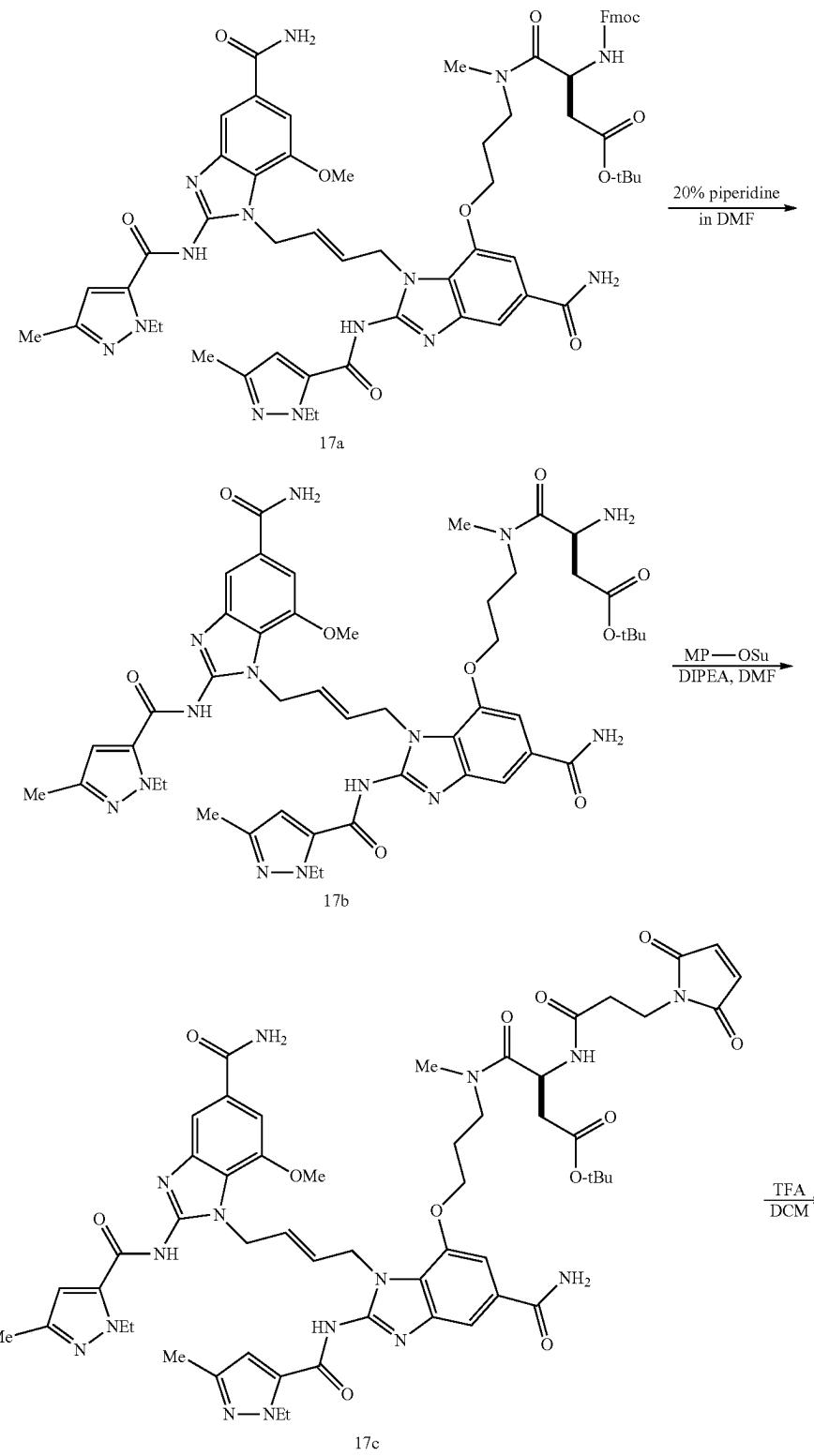
[1527] Compound 12 (1.5 mg, 0.0015 mmol, 1 equiv.) was dissolved in DMSO (50 μ L). L-cysteine (1 M, 2.2 μ L, 0.0022 mmols, 1.5 equiv.) was added as a solution in water. The reaction mixture was stirred at 30° C. for 30 min, and subsequently purified directly via preparatory HPLC (30-70-95%, 0.05% TFA in acetonitrile, Method G). Fractions containing the desired product were combined and frozen. The solvents were removed via lyophilization to yield compound 16 as the trifluoroacetate salt (49% yield, 1.03 mg, 0.0007 mmol). UPLC-MS (Method E, ESI+): m/z

$[M+H]^+$ 1066.42 (theoretical); 1066.44 (observed). HPLC retention time: 1.65 min.

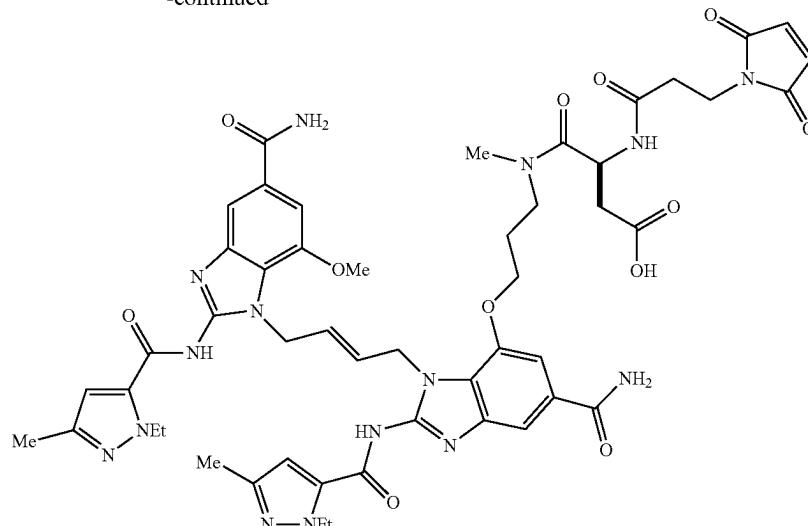
Synthesis of (S,E)-4-((3-((5-carbamoyl-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)propyl)(methyl)amino)-3-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanamido)-4-oxobutanoic acid
(Compound)



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17

Synthesis of Compound 17a

[1528] An oven dried 4 mL vial equipped with a stir bar was charged with compound 12a (10 mg, 0.011 mmol, 1.0 equiv.), Fmoc-aspartate 4-tert-butyl ester (9.1 mg, 0.022 mmol, 2.0 equiv.) and HATU (8.4 mg, 0.022 mmol, 2.0 equiv.), followed by DMF (0.5 mL) and DIPEA (9.6 uL, 0.055 mmol, 5.0 equiv.). The reaction mixture was stirred at room temperature overnight and full conversion to the amide was observed. Solvent was removed in vacuo, and the resulting crude oil was dissolved in DCM and the desired product isolated by flash chromatography (10 g SiO₂, 0-40% MeOH in DCM) to give 17a (12 mg, 0.0104 mmol, 94% yield) as a light brown solid. The isolated material still contained some impurities, but was used in subsequent steps without further purification. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1187.54 (theoretical); 1187.53 (observed). HPLC retention time: 2.40 min.

Synthesis of Compound 17b

[1529] An oven dried 4 mL vial equipped with a stir bar was charged with 17a (12 mg, 0.0104 mmol, 1.0 equiv.) and 20% piperidine in DMF (1 mL). The reaction mixture was stirred for 1 hour, solvent removed in vacuo and product purified by prepHPLC (Method G, 5-95% acetonitrile in water) to yield 17b (9.3 mg, 0.0096 mmol, 93% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=965.47 (theoretical); 965.48 (observed). HPLC retention time: 1.68 min.

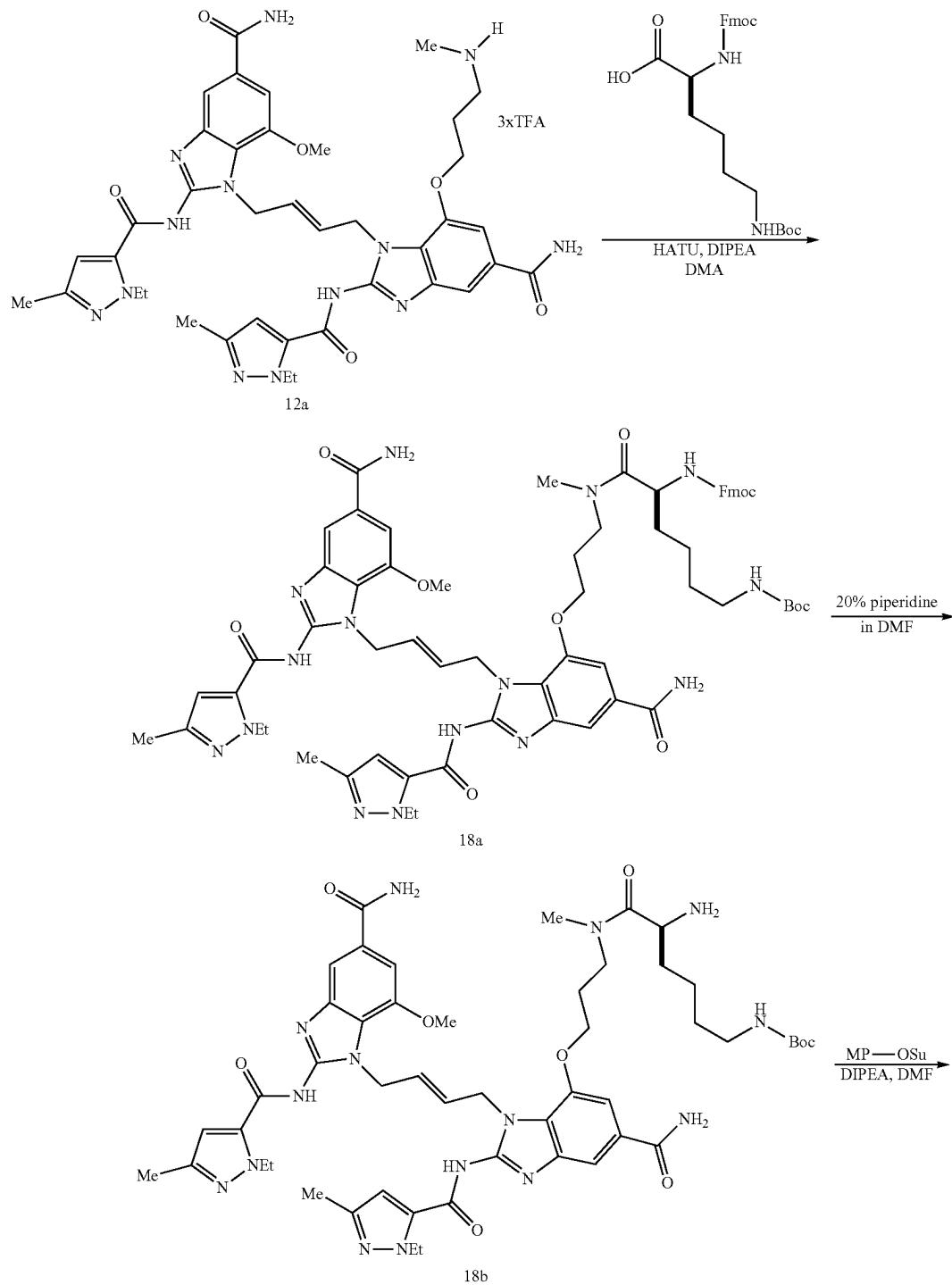
Synthesis of Compound 17c

[1530] A stock solution of MP-OSu and DIPEA was prepared by dissolving 7.7 mg of MP-OSu and 10 μ L of DIPEA in 1.0 mL of DMF. An oven dried 4 mL vial equipped with a stir bar was charged with 17b (9.3 mg, 0.0096 mmol, 1.0 equiv.) and 0.5 mL of the stock solution containing MP-OSu (3.8 mg, 0.014 mmol, 1.5 equiv.) and DIPEA (0.029 mmol, 3 equiv.) was added to the vial. The reaction mixture was stirred at room temperature for 2 hours and solvent removed in vacuo to yield crude 17c, which was used in the next step without any further purification. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1116.50 (theoretical); 1116.80 (observed). HPLC retention time: 1.51 min.

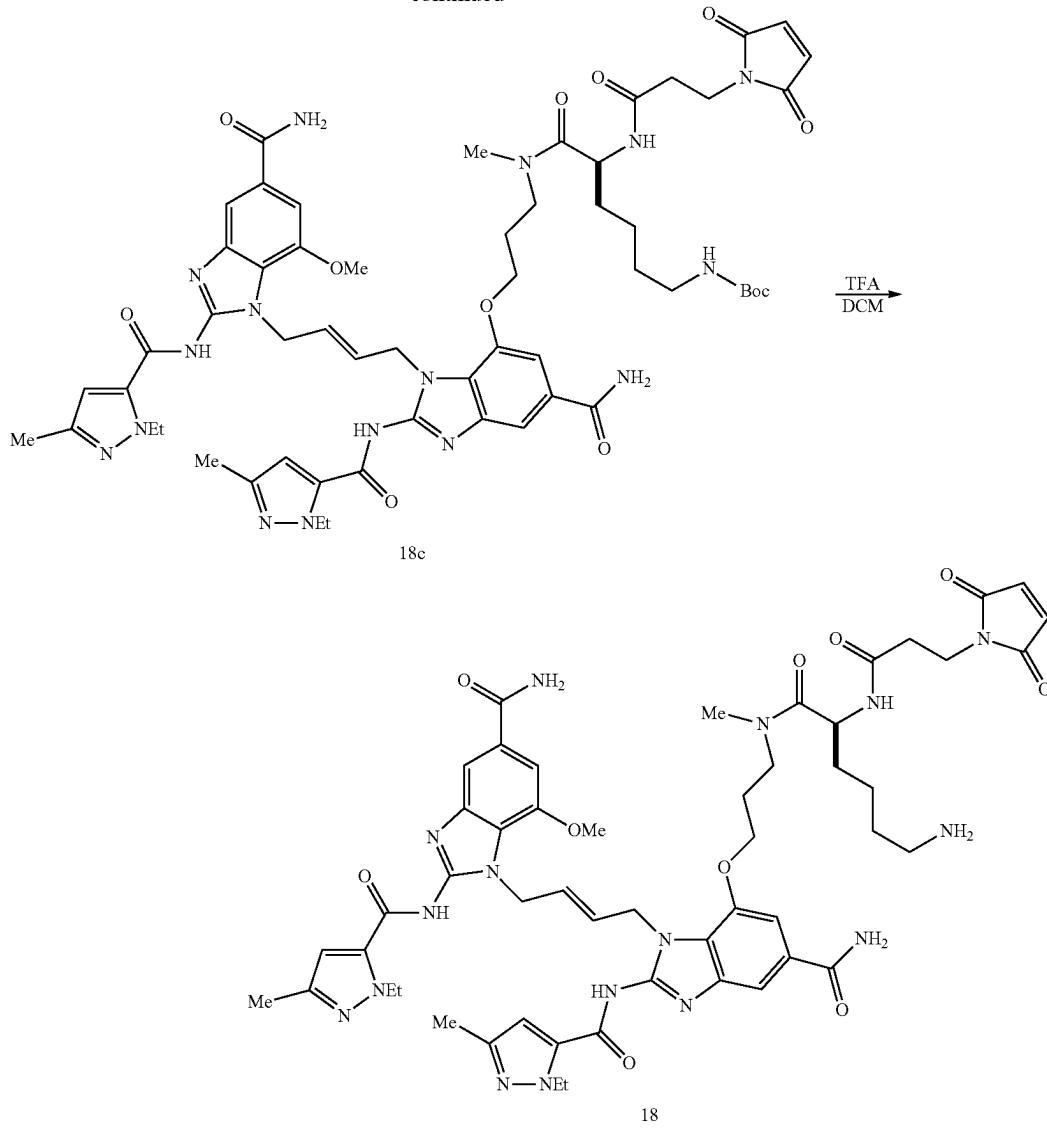
Synthesis of Compound 17

[1531] A 4 mL vial was charged with compound 17c (10.7 mg, 0.0096 mmol, 1 equiv.) dissolved in 20% (v/v) TFA in DCM (1 mL) and the reaction mixture was stirred at room temperature for 3 hours. Solvent was subsequently removed in vacuo, and the crude product was dissolved in DMSO (0.75 mL) and purified by prepHPLC (Method G, 5-50% MeCN in water) to give Compound 17 (5.4 mg, 0.0051 mmol, 53% yield) as a white solid. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1060.44 (theoretical); 1061.12 (observed). HPLC retention time: 1.28 min.

Synthesis of (S,E)-7-(3-(6-amino-2-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanamido)-N-methylhexanamido)propoxy)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazole-5-carboxamide (Compound 18)



-continued



Synthesis of Compound 18a

[1532] An oven dried 4 mL vial equipped with a stir bar was charged with HATU (7.8 mg, 0.021 mmol, 2.0 equiv.) and Fmoc-lysine N-epsilon-Boc (9.6 mg, 0.021 mmol, 2.0 equiv.); to which was added a solution of compound 12a (9.3 mg, 0.0103 mmol, 1.0 equiv.) and DIPEA (9 μ L, 0.051 mmol, 5 equiv.) in DMF (0.5 mL). The vial was capped and sealed with parafilm and the mixture was stirred at RT overnight. Full conversion was observed by UPLC-MS (Method D). Solvent was removed in vacuo and product was purified by flash chromatography (10 g SiO_2 , 0-40% MeOH in DCM) to give 18a (12 mg, 0.0097 mmol, 95%) as a tan solid. UPLC-MS (Method D, ESI+): m/z [M+H] $^{+}$ =1244.60 (theoretical); 1244.61 (observed). HPLC retention time: 2.40 min.

Synthesis of Compound 18b

[1533] An oven-dried 4 mL vial equipped with a stir bar was charged with 18a (12 mg, 0.0096 mmol) and 20% (v/v)

piperidine in DMF (1 mL) was added to the reaction. The reaction mixture was stirred until full conversion was observed by UPLC-MS (Method D), which took approximately 1 hour. Solvent was removed in vacuo and product was purified by preparatory HPLC (Method G, 5-95% MeCN in water with 0.1% (v/v) formic acid). The HPLC solvents were removed in vacuo to give 18b (4.2 mg, 0.0041 mmol, 36%) as an off-white solid. UPLC-MS (Method D, ESI+): m/z [M+H] $^{+}$ =1022.53 (theoretical); 1022.80 (observed). HPLC retention time: 1.30 min.

Synthesis of Compound 18c

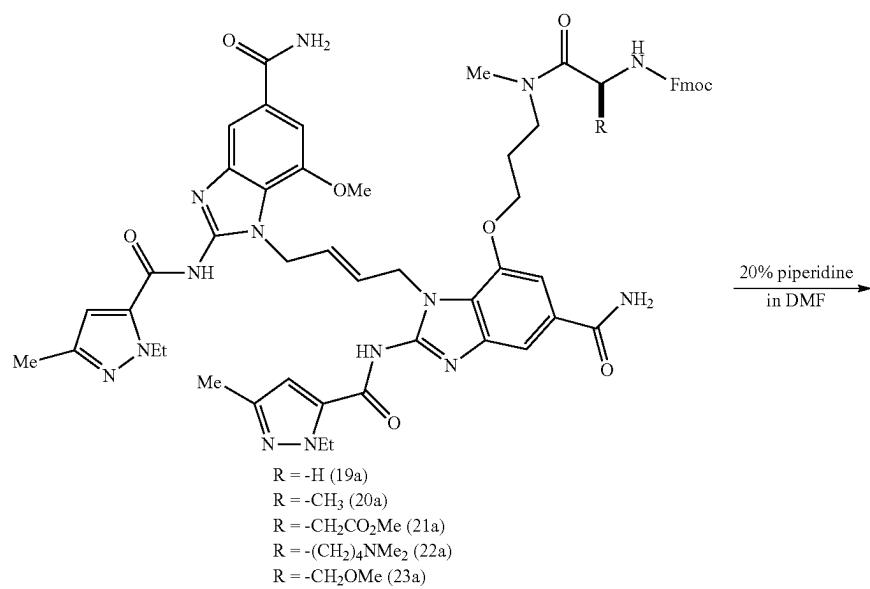
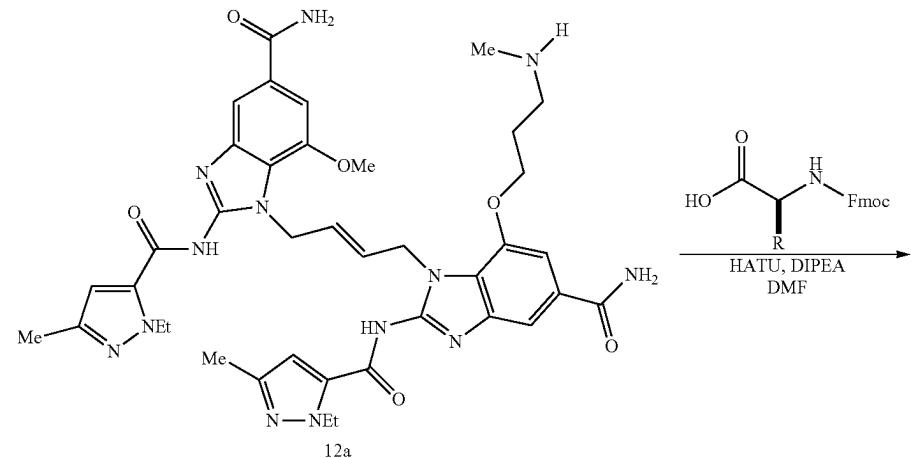
[1534] An oven-dried 4 mL vial equipped with a stir bar was charged with 18b (4.2 mg, 0.0034 mmol, 1 equiv.), followed by MP-OSu (1.8 mg, 0.0068 mmol, 2.0 equiv.), DIPEA (5.9 μ L, 0.034 mmol, 10 equiv.) and DMF (0.8 mL). The reaction mixture was stirred at room temperature for 3 hours at which point UPLC-MS (Method D) analysis

showed full conversion. Solvent was removed in vacuo to yield the crude product 18c, which was used in the next step without purification. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1173.56 (theoretical); 1173.94 (observed). HPLC retention time: 1.54 min.

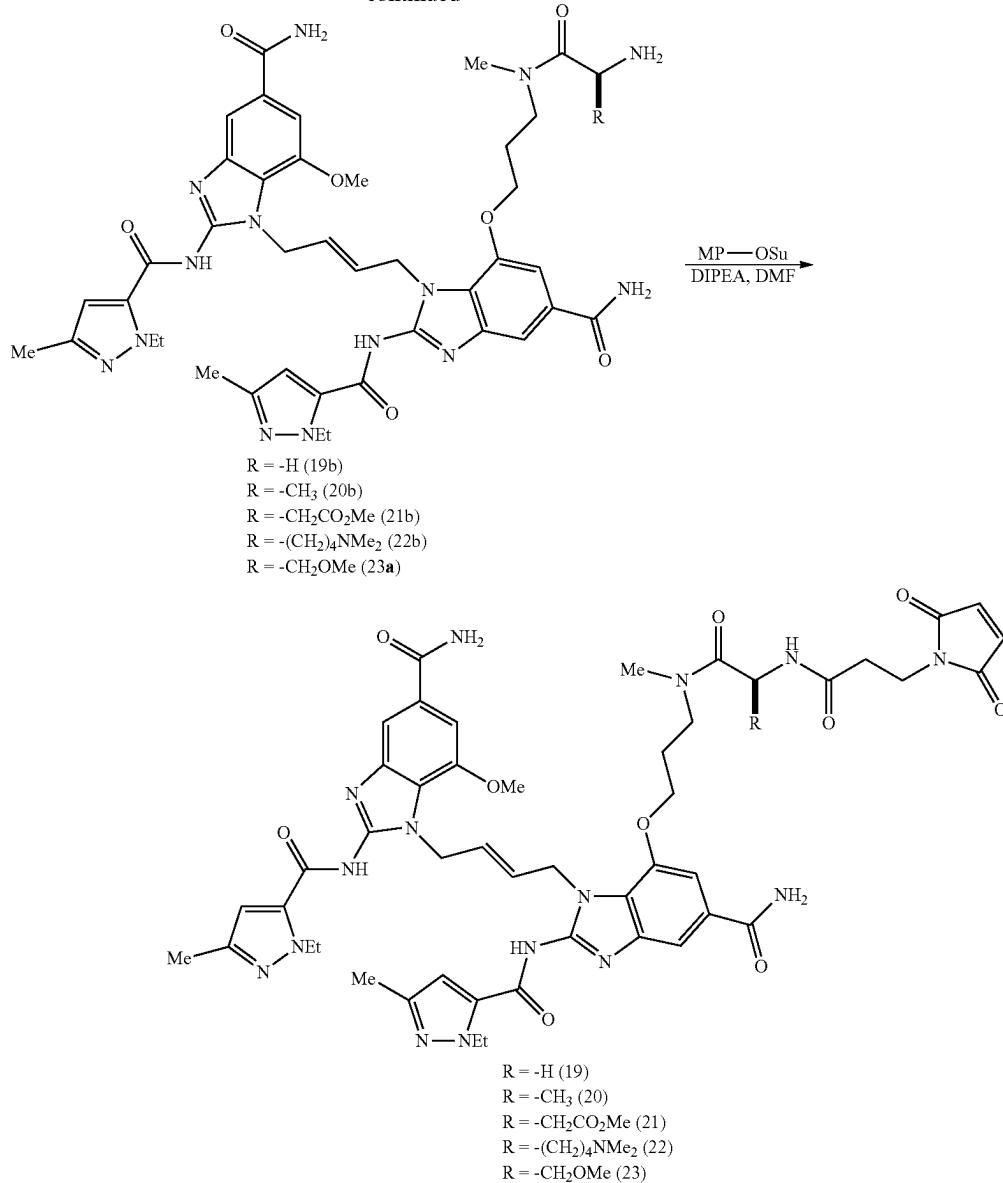
Synthesis of Compound 18

[1535] An oven-dried 4 mL vial containing a stir bar was charged with crude 18c from the previous step (0.0034

mmol.) and 20% (v/v) TFA in DCM (1 mL) was added. The reaction mixture was stirred for one hour and the product was subsequently purified by preparatory HPLC (Method G, 5-50% MeCN in water with 0.1% (v/v) formic acid). The HPLC solvents were removed in vacuo to give 18c (4.2 mg, 0.0035 mmol, 56% yield over 2 steps) as a white solid. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1073.51 (theoretical); 1073.73 (observed). HPLC retention time: 1.15 min.



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General Methods for HATU Coupling, Fmoc Deprotection, and MP Coupling

[1536] HATU coupling (Method 1): An oven-dried 4 mL vial equipped with a stir bar was charged with compound 12a (1.0 equiv.), HATU (2.0 equiv.), DIPEA (5 equiv.) and DMF (20 mM in 12a) and the reaction mixture was stirred at room temperature overnight. The solvent was removed in vacuo and product purified via chromatography.

[1537] Fmoc deprotection (Method 2): An oven-dried 4 mL vial equipped with a stir bar was charged with the HATU coupled product from above, which was dissolved in 20% (v/v) piperidine in DMF (1 mL). The reaction mixture was stirred at room temperature for 1 hour, solvent removed in vacuo, and product purified via chromatography.

[1538] MP coupling (Method 3): An oven-dried 4 mL vial equipped with a stir bar was charged with the product from the previous reaction, to which was added MP-OSu (2

equiv.) and DIPEA (10 equiv.) and DMF (10 mM in Fmoc-deprotected amine starting material). The reaction mixture was stirred at room temperature for 3 hours, solvent removed in vacuo and product purified by preparatory HPLC.

[1539] Compound 19a was prepared according to General Method 1 (8.0 mg, 0.0075 mol, 85% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1073.47 (theoretical); 1074.03 (observed). HPLC retention time: 1.76 min.

[1540] Compound 19b was prepared according to General Method 2 (6.1 mg, 0.0072 mol, 95% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=851.41 (theoretical); 851.69 (observed). HPLC retention time: 1.15 min.

[1541] Compound 19 was prepared according to General Method 3 (4.3 mg, 0.0043 mol, 60% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1002.43 (theoretical); 1002.72 (observed). HPLC retention time: 1.31 min.

[1542] Compound 20a was prepared according to General Method 1 (8.7 mg, 0.0080 mol, 91% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1087.49 (theoretical); 1087.90 (observed). HPLC retention time: 1.75 min.

[1543] Compound 20b was prepared according to General Method 2 (5.6 mg, 0.0065 mol, 81% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=865.42 (theoretical); 865.66 (observed). HPLC retention time: 1.12 min.

[1544] Compound 20 was prepared according to General Method 3 (3.4 mg, 0.0034 mol, 52% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1016.45 (theoretical); 1017.08 (observed). HPLC retention time: 1.33 min.

[1545] Compound 21a was prepared according to General Method 1 (14 mg, 0.0119 mmol). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1145.50 (theoretical); 1145.42 (observed). HPLC retention time: 1.74 min.

[1546] Compound 21b was prepared according to General Method 2 (7.2 mg, 0.0078 mol, 76% yield over 2 steps). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=923.43 (theoretical); 923.67 (observed). HPLC retention time: 1.13 min.

[1547] Compound 21 was prepared according to General Method 3 (1.5 mg, 0.0014 mols, 22% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1074.45 (theoretical); 1074.90 (observed). HPLC retention time: 1.36 min.

[1548] Compound 22a was prepared according to General Method 1 (7.6 mg, 0.0065 mols, 63% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1172.58 (theoretical); 1172.59 (observed). HPLC retention time: 1.84 min.

[1549] Compound 22b was prepared according to General Method 2 (6.1 mg, 0.0064 mmols, 57% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=950.51 (theoretical); 950.83 (observed). HPLC retention time: 0.99 min.

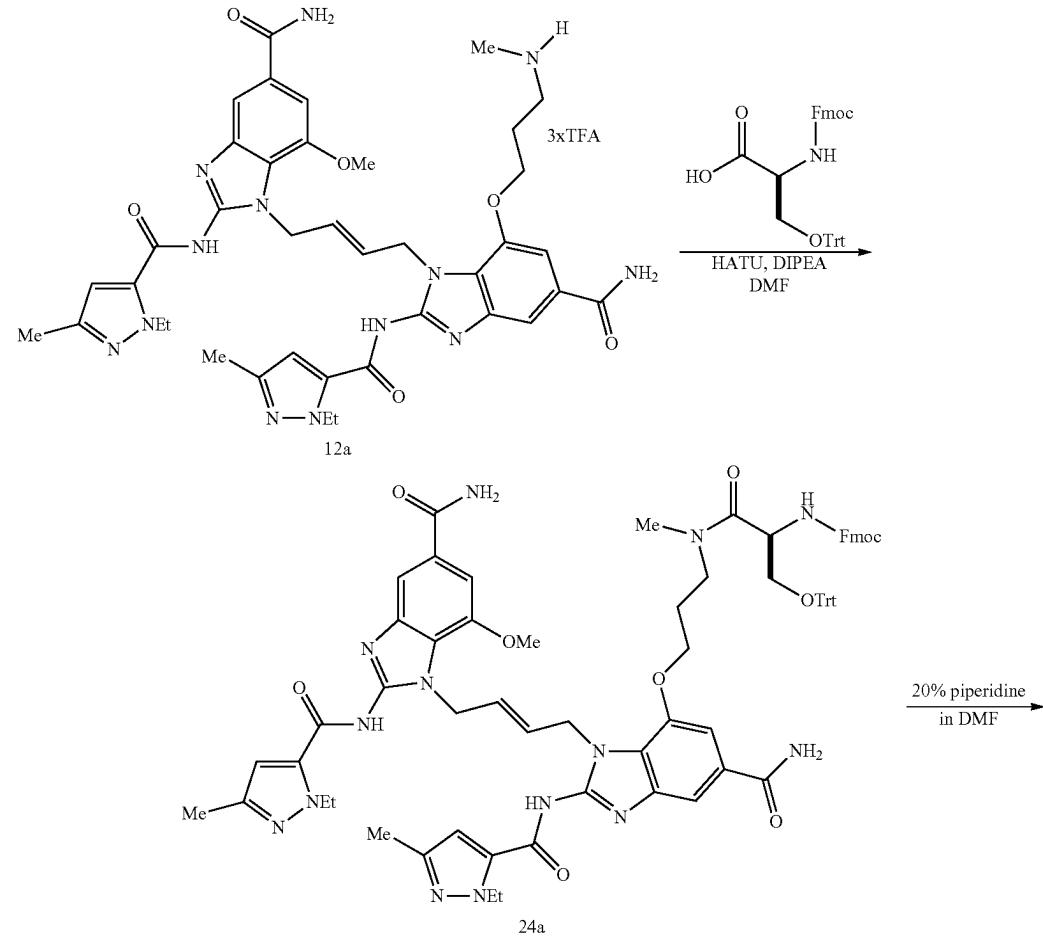
[1550] Compound 22 was prepared according to General Method 1 (2.6 mg, 0.0023 mols, 37% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1101.54 (theoretical); 1101.96 (observed). HPLC retention time: 1.18 min.

[1551] Compound 23a was prepared according to General Method 1 (12 mg, 0.0105 mmol). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1117.50 (theoretical); 1117.77 (observed). HPLC retention time: 1.75 min.

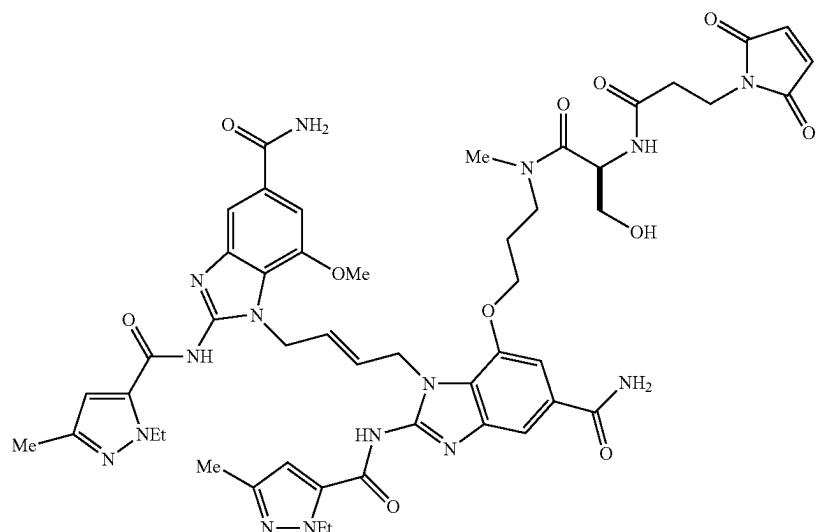
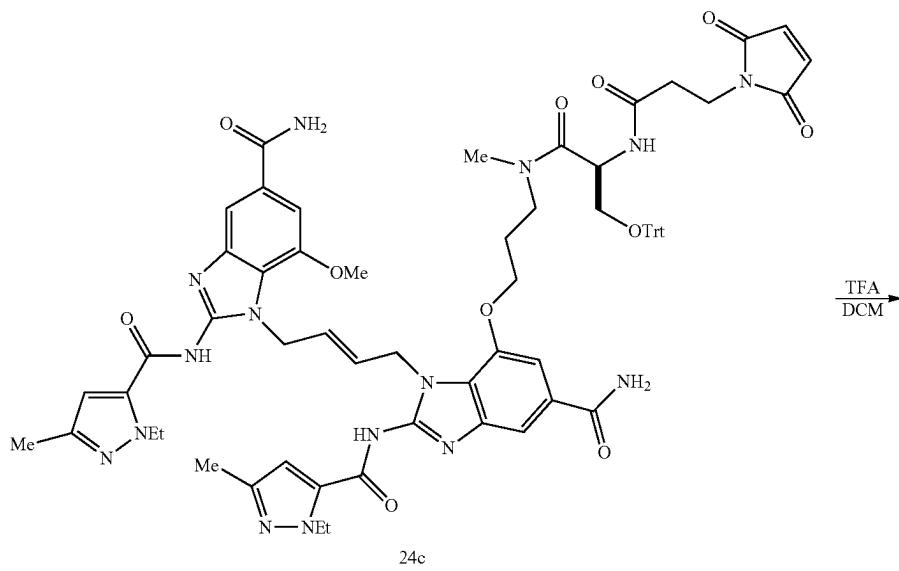
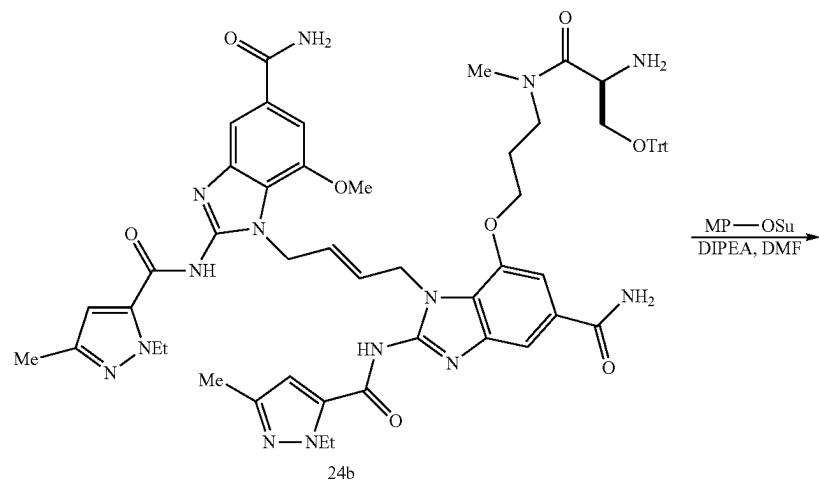
[1552] Compound 23b was prepared according to General Method 2 (7.2 mg, 0.00804 mmol, 91% over 2 steps). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=895.43 (theoretical); 895.73 (observed). HPLC retention time: 1.12 min.

[1553] Compound 23 was prepared according to General Method 3 (8.4 mg, 0.0047, 58% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=1046.46 (theoretical); 1047.06 (observed). HPLC retention time: 1.36 min.

Synthesis of (S,E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(3-(2-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanamido)-3-hydroxy-N-methylpropanamido)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazole-5-carboxamide
(Compound 0 NH₂ 0



-continued



Synthesis of Compound 24a

[1554] An oven dried 4 mL vial equipped with a stir bar was charged with HATU (6.7 mg, 0.018 mmol, 2.0 equiv.) and 2-(9H-fluoren-9-ylmethoxycarbonylamino)-3-methoxy-propanoic acid (6.0 mg, 0.018 mmol, 2.0 equiv.), and a solution of compound 12a (8 mg, 0.0088 mmols, 1.0 equiv.) and DIPEA (8 μ L, 0.044 mmols, 5 equiv.) in DMF (0.5 mL) was added to the vial. The vial was capped and sealed with parafilm and the reaction mixture was stirred at room temperature overnight, upon which full conversion was observed by UPLC-MS (Method D). Solvent was removed in vacuo and product purified by flash chromatography (10 g SiO₂, 0-40% MeOH in DCM) to give 24a (15 mg), which was used in the next reaction without further purification. UPLC-MS (Method D, ESI+): m/z [M+H]⁺ = 1345.59 (theoretical); 1346.12 (observed). HPLC retention time: 2.23 min.

Synthesis of Compound 24b

[1555] An oven-dried 4 mL vial equipped with a stir bar was charged with 24a (15 mg, 0.011 mmol) and 20% (v/v) piperidine in DMF (1 mL) was added to it. The reaction mixture was stirred until full conversion was observed by UPLC-MS (Method D), which took approximately 1 hour. Solvent was removed in vacuo and the crude product was purified by preparatory HPLC (Method G, 5-95% MeCN in water with 0.1% (v/v) formic acid); the HPLC solvents were removed in vacuo to give 24b (8.4 mg, 0.0075 mmol, 94% over 2 steps) as an off-white solid. UPLC-MS (Method D, ESI+): m/z [M+H]⁺ = 1123.53 (theoretical); 1123.98 (observed). HPLC retention time: 1.47 min.

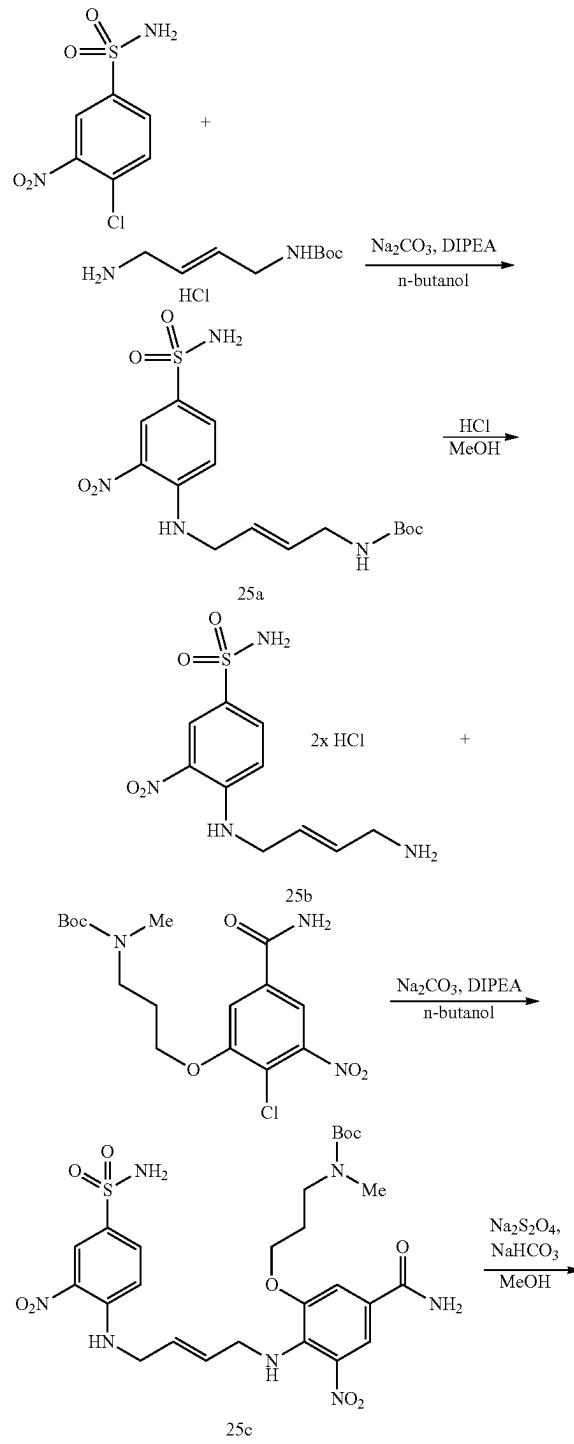
Synthesis of Compound 24c

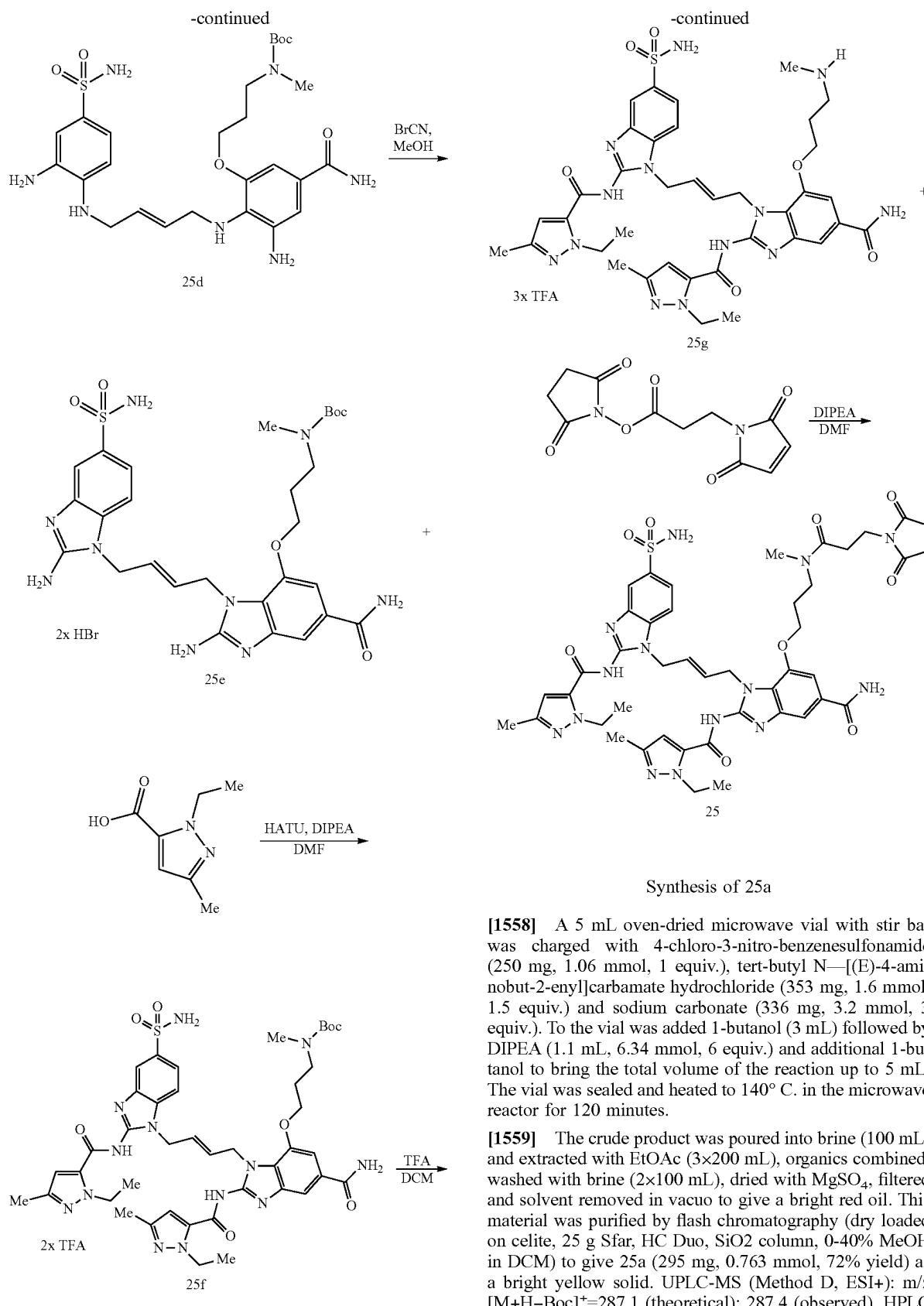
[1556] An oven-dried 4 mL vial equipped with a stir bar was charged with 24b (8.4 mg, 0.0075 mmol, 1 equiv.), followed by MP-OSu (3.0 mg, 0.011 mmol, 1.5 equiv.), DIPEA (3.9 μ L, 0.022 mmol, 3 equiv.) and DMF (0.5 mL). The reaction mixture was stirred at room temperature for 3 hours at which point UPLC-MS (Method D) analysis showed full conversion. Solvent was removed in vacuo and the resulting crude product was used in the next step without purification. UPLC-MS (Method D, ESI+): m/z [M+H]⁺ = 1274.55 (theoretical); 1275.21 (observed). HPLC retention time: 1.89 min.

Synthesis of Compound 24

[1557] An oven-dried 4 mL vial containing a stir bar was charged with crude 24c (0.0075 mmol,) and 20% (v/v) TFA in DCM (1 mL) was added to the vial. The reaction mixture was stirred for 20 minutes, and solvent removed in vacuo. The resulting crude product was dissolved in DMSO (0.5 mL) and purified by preparatory HPLC (Method G, 5-50% MeCN in water with 0.1% (v/v) formic acid) and solvent removed in vacuo to give 24 (4.0 mg, 0.0031 mmol, 42% yield over 2 steps) as a white solid. UPLC-MS (Method D, ESI+): m/z [M+H]⁺ = 1032.44 (theoretical); 1033.09 (observed). HPLC retention time: 1.28 min.

Synthesis of (E)-7-(3-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-N-methylpropanamido)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzod[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzod[d]imidazole-5-carboxamide
(Compound 25)





[1558] A 5 mL oven-dried microwave vial with stir bar was charged with 4-chloro-3-nitro-benzenesulfonamide (250 mg, 1.06 mmol, 1 equiv.), tert-butyl N-[*(E*)-4-amino-but-2-enyl]carbamate hydrochloride (353 mg, 1.6 mmol, 1.5 equiv.) and sodium carbonate (336 mg, 3.2 mmol, 3 equiv.). To the vial was added 1-butanol (3 mL) followed by DIPEA (1.1 mL, 6.34 mmol, 6 equiv.) and additional 1-butanol to bring the total volume of the reaction up to 5 mL. The vial was sealed and heated to 140° C. in the microwave reactor for 120 minutes.

[1559] The crude product was poured into brine (100 mL) and extracted with EtOAc (3×200 mL), organics combined, washed with brine (2×100 mL), dried with MgSO₄, filtered and solvent removed in vacuo to give a bright red oil. This material was purified by flash chromatography (dry loaded on celite, 25 g Sfar, HC Duo, SiO₂ column, 0-40% MeOH in DCM) to give 25a (295 mg, 0.763 mmol, 72% yield) as a bright yellow solid. UPLC-MS (Method D, ESI+): m/z [M+H-Boc]⁺=287.1 (theoretical); 287.4 (observed). HPLC retention time: 1.53 min.

Synthesis of 25b

[1560] A 20 mL vial was charged with 25a (295 mg, 0.763 mmol, 1 equiv.) which was dissolved in methanol (7.5 mL) and 4M HCl in 1,4-dioxane (40 eq. 7.5 mL, 30.0 mmol). The solution was stirred at 40° C. for 30 minutes and solvent removed in vacuo to give 25b as the 2×HCl salt (274 mg, 0.764 mmol, quantitative yield) as a bright red solid. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=287.1 (theoretical); 287.6 (observed). HPLC retention time: 0.52 min.

Synthesis of 25c

[1561] An oven dried 5 mL microwave vial with stir bar was charged with 25b (135 mg, 0.376 mmol, 1 equiv.), tert-butyl N-[3-(5-carbamoyl-2-chloro-3-nitro-phenoxy)propyl]carbamate (211 mg, 0.564 mmol, 1.5 equiv., prepared as described below) and sodium carbonate (119 mg, 1.13 mmol, 3 equiv.) which was followed by addition of n-butanol (3.75 mL) and DIPEA (0.39 mL, 2.25 mmol, 6 equiv.). The vial was sealed and heated to 140° C. for 3 hours in a microwave reactor to give a bright red heterogeneous mixture. This solution was filtered over celite washing with 1:1 DCM:MeOH (100 mL), solvent removed in vacuo and crude product was loaded onto celite and purified by flash chromatography (25 g SiO₂ column, 0-40% MeOH in DCM) to give 25c (245 mg, 0.384 mmol) as a mixture of product and starting material (3:2). Product mixture was used in the next step without any further purification. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=638.2 (theoretical); 638.5 (observed). HPLC retention time: 1.75 min.

Synthesis of 25d

[1562] A 20 mL vial with stirbar was charged with 25c (245 mg, 0.384 mmol, 1 equiv.) and sodium bicarbonate (580 mg, 6.90 mmol, 18 equiv.) and methanol (4 mL) was added. To the vial was then added sodium hydrosulfite (1.20 g, 6.90 mmol, 18 equiv. in 4 mL water) and the vial was heated to 50° C. for 60 minutes. The reaction was cooled to room temperature, filtered over celite washing with MeOH (50 mL) and DCM (50 mL) and the crude product loaded onto celite. The product was purified by flash chromatography (25 g Sfar HC Duo, SiO₂ column, 0-40% 10:1 MeOH:NH₄OH in DCM) to give 25d (89 mg, 0.154 mmol, 41% yield over 2 steps) as a mixture of inseparable rotational conformers. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=578.3 (theoretical); 578.5 (observed). HPLC retention time: 0.98 & 1.18 min.

Synthesis of 25e

[1563] Two identical reactions were setup side by side. An oven dried 4 mL vial with stir bar was charged with 25d (45 mg, 0.156 mmol, 1 equiv.), dissolved in methanol (1 mL) and cyanogen bromide (200 uL, 1.20 mmol, 8 equiv.) was added. Reaction was stirred overnight, and solvent removed in vacuo and two reactions combined to give 25e as the 2×HBr salt (120 mg, 0.15 mmol, 97% yield) as a light gray solid. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=628.3 (theoretical); 628.4 (observed). HPLC retention time: 0.79 min.

Synthesis of 25f

[1564] An oven dried 4 mL vial with stir bar was charged with 25e (120 mg, 0.152 mmol, 1 equiv.), 2-ethyl-5-methyl-

pyrazole-3-carboxylic acid (94 mg, 0.61 mmol, 4.0 equiv.) and HATU (231 mg, 0.61 mmol, 4 equiv.). The solids were dissolved in DMF (1 mL) and DIPEA (0.22 mL, 1.2 mmol, 8 equiv.) was added. The reaction was stirred at room temperature overnight, acetic acid was added (100 uL) and product purified by prepHPLC (Method T, 5-95% MeCN in water with 0.05% TFA) and solvent removed in vacuo to give 25f (107 mg, 0.12 mmol, 78% yield) as an off-white solid. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=900.4 (theoretical); 900.6 (observed). HPLC retention time: 1.69 min.

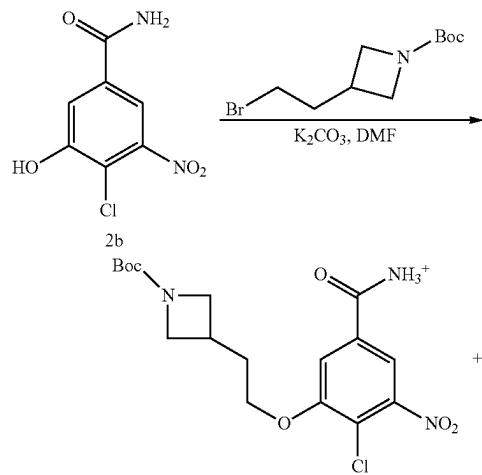
Synthesis of 252

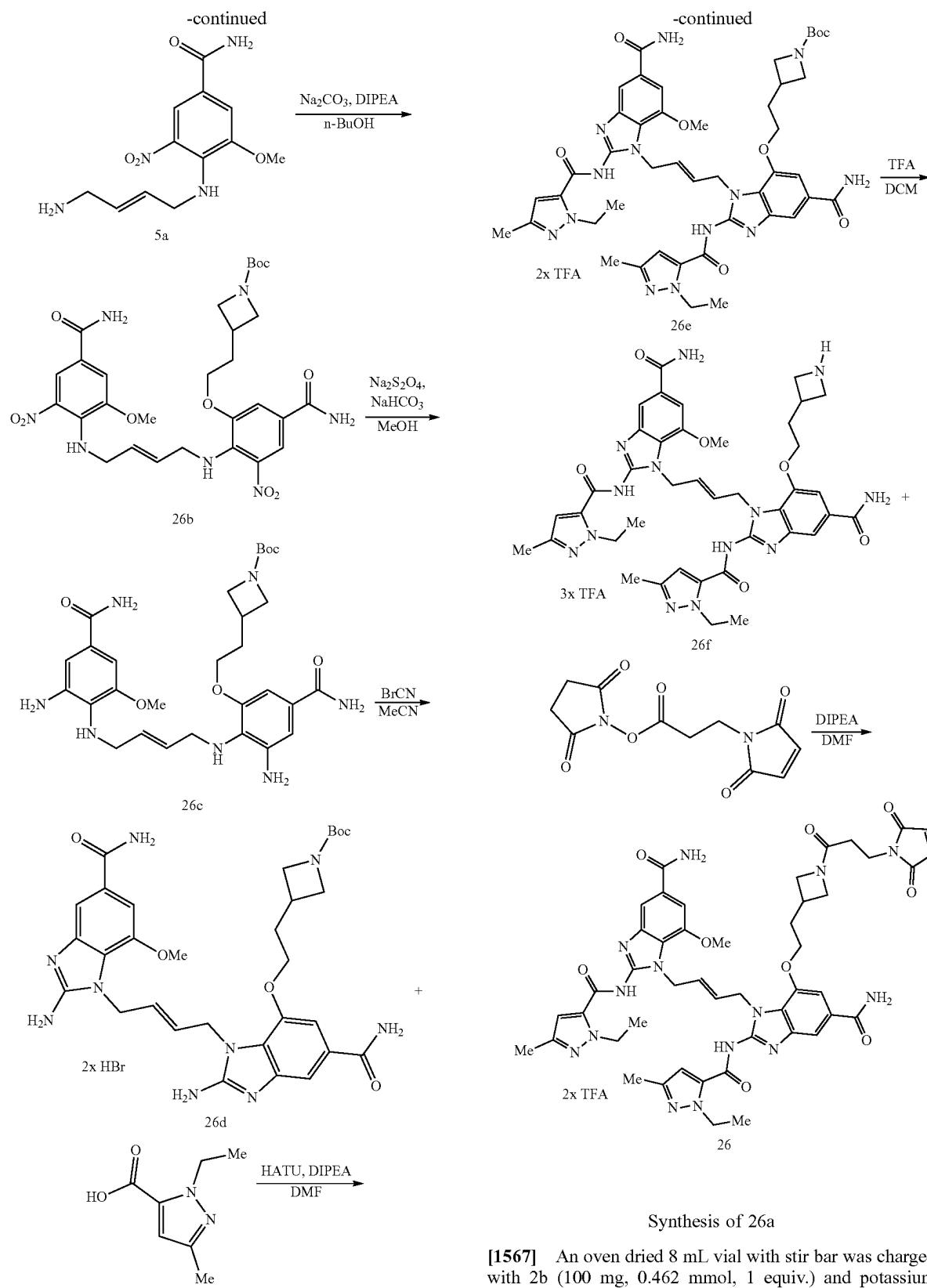
[1565] Compound 25f (107 mg, 0.12 mmol, 1 equiv.) was added to a 20 mL vial with stir bar and dissolved in 20% TFA in DCM (5 mL). Reaction was stirred at room temperature for 20 minutes and then solvent removed in vacuo to give 25 g as the 3×TFA salt and an off-white solid (70 mg, 0.0615 mmol, 52% yield). A sample of analytical purity was obtained by prepHPLC purification (Method G, 5-95% MeCN in water with 0.05% TFA). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=800.3 (theoretical); 800.6 (observed). HPLC retention time: 1.12 min.

Synthesis of 25

[1566] An oven dried 4 mL vial with stir bar was charged with 25g (12 mg, 0.011 mmol, 1 equiv.) which was dissolved in DMF (1 mL) and then both DIPEA (15 uL, 0.087 mmol, 8 equiv.) and MP-OSu (4.3 mg, 0.0163 mmol, 1.5 equiv.) were added to the reaction. The solution was stirred at room temperature for 30 minutes, quenched with 20% TFA in DCM (100 uL) and purified by prepHPLC (Method G, 5-95% MeCN in water with 0.05% TFA) to 25 as the 2×TFA salt (5.7 mg, 0.0048 mmol, 45% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=951.4 (theoretical); 951.2 (observed). HPLC retention time: 2.18 min.

Synthesis of (E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(2-(1-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)azetidin-3-yl)ethoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazole-5-carboxamide (Compound 26)





Synthesis of 26a

[1567] An oven dried 8 mL vial with stir bar was charged with 2b (100 mg, 0.462 mmol, 1 equiv.) and potassium carbonate (191 mg, 1.39 mmol, 3 equiv.) followed by addition of tert-butyl 3-(2-bromoethyl)azetidine-1-carboxylate (152 mg, 0.577 mmol, 1.25 equiv.). The starting mate-

rials were dissolved in DMF (3 mL), vial sealed with parafilm and stirred at 70° C. for 24 hours. The crude material was poured into a separatory funnel containing saturated ammonium chloride (100 mL) and EtOAc (100 mL each), shaken, layers separated, and aqueous layer extracted with EtOAc (2×100 mL). The combined organic fractions were washed with brine (2×50 mL), dried with MgSO₄, filtered and solvent removed in vacuo to give crude product as a light-yellow solid. The crude product was purified by flash chromatography (25 g Sfar HC Duo SiO₂ column, 0-20% MeOH in DCM) to give 26a as a yellow solid (86 mg, 0.215 mmol, 47% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=400.1 (theoretical); 400.5 (observed). HPLC retention time: 1.79 min.

Synthesis of 26b

[1568] An oven-dried 2 mL microwave vial was charged with 25a (35 mg, 0.0875 mmol, 1 equiv.), 5a (62 mg, 0.175 mmol, 2 equiv.) and sodium carbonate (28 mg, 0.263 mmol, 3 equiv.) and to this vial was added n-butanol (1 mL) and DIPEA (0.1 mL, 0.5 mmol, 6 equiv.). The vial was sealed and heated to 140° C. for 3 hours in a microwave reactor. The reaction was then filtered over celite washing with 1:1 MeOH:DCM (100 mL), solvent removed in vacuo and crude material loaded onto celite. The product was purified by flash chromatography (25 g Sfar HC Duo SiO₂ column, 0-20% MeOH in DCM) to give 25b as a bright red solid (38 mg, 0.0592 mmol, 68% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=644.3 (theoretical); 644.6 (observed). HPLC retention time: 1.72 min.

Synthesis of 26c

[1569] An oven-dried 4 mL vial was charged with 25b (38 mg, 0.0592 mmol, 1 equiv.) which was dissolved in methanol (1 mL) and sodium bicarbonate (90 mg, 1.1 mmol, 18 equiv.) was added followed by sodium hydrosulfite (186 mg, 1.07 mmol, 18 equiv.) as a solution in water (1 mL). The reaction was heated to 50° C. for 1 hour and filtered over celite washing with 1:1 DCM:MeOH (50 mL). The crude product was loaded onto celite and purified by flash chromatography (25 g Sfar HC Duo, SiO₂ column, 0-40% 10:1 MeOH:NH₄OH in DCM) to give 25c (10 mg, 0.017 mmol, 29% yield) as a light yellow solid. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=584.3 (theoretical); 584.6 (observed). HPLC retention time: 1.18 min.

Synthesis of 26d

[1570] An oven dried 4 mL vial with stir bar was charged with 25c (10 mg, 0.017 mmol, 10 equiv.) which was dissolved in methanol (0.5 mL) and cyanogen bromide (0.050 mL, 0.150 mmol, 3M in DCM, 8.7 equiv.) was added. The reaction was stirred for 18 hours and solvent removed in vacuo to give the 25d as a light grey solid and the 2×HBr salt (13 mg, 0.0165 mmol, 95% yield) which was used without any further purification. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=634.3 (theoretical); 634.6 (observed). HPLC retention time: 0.98 min.

Synthesis of 26e

[1571] An oven dried 4 mL vial with stir bar was charged with 25d (13 mg, 0.0165 mmol, 1 equiv.), HATU (25 mg, 0.066 mmol, 4 equiv.) and 2-ethyl-5-methyl-pyrazole-3-carboxylic acid (10 mg, 0.066 mmol, 4 equiv.) which were

dissolved in DMF (0.5 mL) and then DIPEA (0.050 mL, 0.20 mmol, 17 equiv.) was added. The reaction was stirred at room temperature for 24 hours. The reaction was quenched with acetic acid (100 uL) and product purified by via prepHPLC (Method H, 5-95% MeCN in water with 0.05% TFA) to give 25e as the 2×TFA salt (14 mg, 0.016 mmol, 95% yield) as a light tan solid. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=906.4 (theoretical); 906.3 (observed). HPLC retention time: 2.44 min.

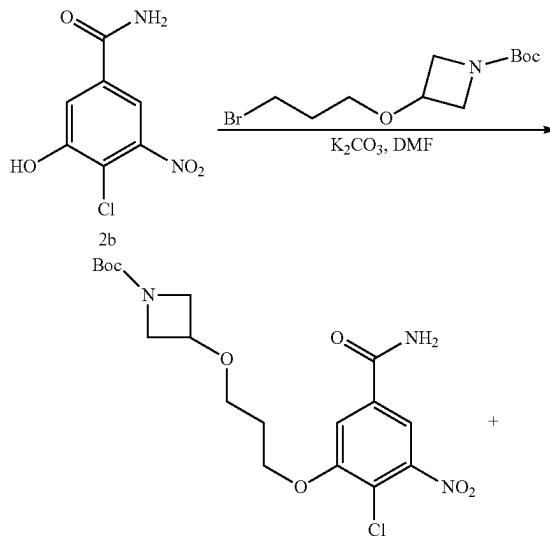
Synthesis of 26f

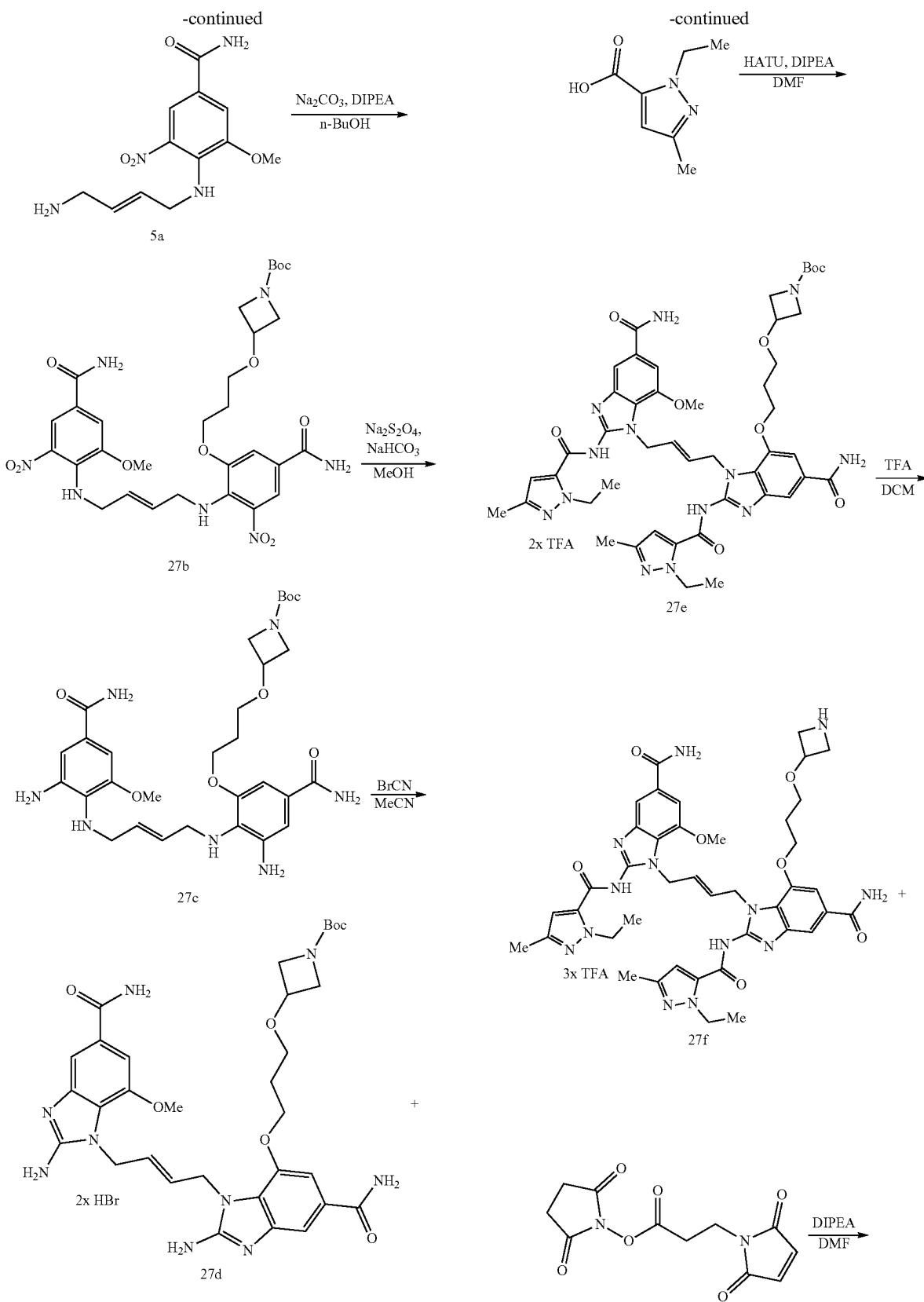
[1572] An oven dried 4 mL vial with stir bar was charged with 25e (14 mg, 0.016 mmol, 1 equiv.) which was dissolved in 20% TFA in DCM (1 mL) and stirred at room temperature for 15 minutes. Solvent was removed in vacuo to give 25f as the 3×TFA salt (15 mg, 0.013 mmol, 82% yield) as a white solid and the product used without any further purification. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=806.4 (theoretical); 806.6 (observed). HPLC retention time: 1.25 min.

Synthesis of 26

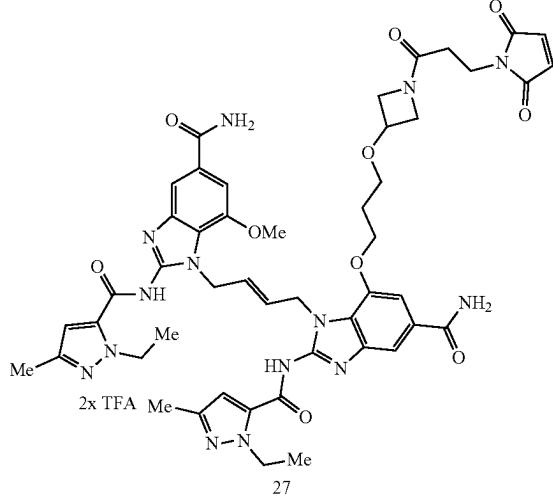
[1573] An oven dried 4 mL vial with stir bar was charged with 25f (5.7 mg, 0.0050 mmol, 1 equiv.) in DMSO (0.5 mL) and MP-OSu (2.0 mg, 0.00750 mmol, 1.5 equiv.) and DIPEA (5 uL, 0.030 mmol, 6 equiv.) was added. The reaction was stirred at room temperature for 1 hour. The reaction was quenched added 20% TFA in DCM (100 uL) and product purified by prepHPLC (Method G, 5-95% MeCN in water with 0.05% TFA) to give 25 as the 2×TFA salt (3.8 mg, 0.00321 mmol, 64% yield) as a white solid. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=957.4 (theoretical); 957.3 (observed). HPLC retention time: 2.19 min.

Synthesis of (E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzod[d]imidazol-1-yl)but-2-en-1-yl)-7-(3-((1-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrrol-1-yl)propanoyl)azetidin-3-yl)oxy)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzod[d]imidazole-5-carboxamide (Compound 27)





-continued



Synthesis of 27a

[1574] An oven dried 8 mL vial with stir bar was charged with 2b as the TFA salt (150 mg, 0.454 mmol, 1 equiv.), tert-butyl 3-(3-bromopropoxy)azetidine-1-carboxylate (133 mg, 0.454 mmol, 1 equiv.) and potassium carbonate (141 mg, 1.02 mmol, 2.3 equiv.) which were dissolved in DMF (4.5 mL) and heated to 55° C. for 24 hours. The reaction was poured into a separatory funnel containing sat. NaHCO₃ (100 mL) and EtOAc (100 mL), shaken, layers separated, and aqueous layer extracted with EtOAc (3×50 mL). The organic fractions were combined and further washed with sat. NaHCO₃ (3×50 mL) and brine (2×50 mL). They were then dried with MgSO₄, filtered and solvent removed in vacuo to 27a (194 mg, 0.353 mmol, 78% yield) as a light yellow solid in a 4:1 ratio of starting material to product and used without further purification. MS (Method D, ESI+): m/z [M+H]⁺=430.1 (theoretical); 430.6 (observed). HPLC retention time: 1.82 min.

Synthesis of 27b

[1575] An oven-dried 5 mL microwave vial was charged with Sodium carbonate (144 mg, 1.36 mmol, 3.00 eq), 5a as the 2×HCl salt (240 mg, 0.678 mmol, 1.50 eq) and 27a (194 mg, 0.452 mmol, 1 equiv.) and then 1-butanol (4 mL) and DIPEA (0.5 mL, 2.7 mmol, 6 equiv.) were added. The vial was sealed and heated to 140° C. for 3 hours in a microwave reactor. The reaction was cooled to room temperature and solution was filtered over celite washing with 1:1 MeOH: DCM (100 mL). The crude product was loaded onto celite and purified by flash chromatography (25 g Sfar HC Duo, SiO₂ column, 0-20% MeOH in DCM) to give 27b (95 mg, 0.141 mmol, 31% yield) as a bright red solid. MS (Method D, ESI+): m/z [M+H]⁺=674.3 (theoretical); 674.6 (observed). HPLC retention time: 1.73 min.

Synthesis of 27c

[1576] A 20 mL vial was charged 27b (95 mg, 0.141 mmol, 1 equiv.) and sodium bicarbonate (442 mg, 5.3 mmol, 37 equiv.) and starting material dissolved in methanol (4 mL). To the vial was added sodium hydrosulfite (442 mg,

2.54 mmol, 18 equiv.) as solution in water (4 mL) and reaction was heated, open to the atmosphere, to 50° C. for 1 hour. The solution went from bright red to light yellow over the course of an hour. The reaction was filtered, filter cake washed with 1:1 MeOH:DCM (3×50 mL), solvent removed in vacuo, crude product redissolved in 1:1 MeOH: DCM (100 mL) and filtered over celite. The crude product was loaded onto celite and purified by flash chromatography (25 g Sfar HC Duo, SiO₂ column, 0-40% 10:1 MeOH: NH₄OH in DCM) to give 27c (42 mg, 0.0689 mmol, 49% yield) as an off-white solid. UPLC-MS (Method D, ESI+): m/z [M+H]⁺=614.3 (theoretical); 614.5 (observed). HPLC retention time: 0.78 min.

Synthesis of 27d

[1577] An oven-dried 4 mL vial was charged with 27c (42 mg, 0.0689 mmol, 1 equiv.) which was dissolved in methanol (1.3 mL) and then cyanogen bromide (3M in DCM, 0.14 mL, 0.414 mmol, 6 equiv.) was added. The vial was stirred at room temperature for 24 hours and solvent removed in vacuo to give 27d as the 2×HBr salt (57 mg, 0.0694 mmol, quantitative yield) as an off-white solid. MS (Method D, ESI+): m/z [M+H]⁺=664.3 (theoretical); 664.7 (observed). HPLC retention time: 0.95 min.

Synthesis of 27e

[1578] An oven dried 4 mL vial with stir bar was charged with 27d (57 mg, 0.0694 mmol, 1 equiv.), 2-ethyl-5-methyl-pyrazole-3-carboxylic acid (43 mg, 0.278 mmol, 4 equiv.) and HATU (106 mg, 0.278 mmol, 4 equiv.) which were dissolved in DMF (1 mL) and then DIPEA (0.097 mL, 0.555 mmol, 8 equiv.) was added. The reaction was stirred at room temperature for 24 hours, quenched with 20% TFA in MeCN (200 uL) and product purified by prepHPLC (Method 1, 5-95% MeCN in water with 0.05% TFA), solvent removed via lyophilization to give 27e as the 2×TFA salt (35 mg, 0.0302 mmol, 43% yield) as a tan solid. A sample of analytical purity was prepared via a second prepHPLC purification (Method G, 5-60% MeCN in water with 0.05% TFA). MS (Method D, ESI+): m/z [M+H]⁺=936.4 (theoretical); 936.3 (observed). HPLC retention time: 2.37 min.

Synthesis of 27f

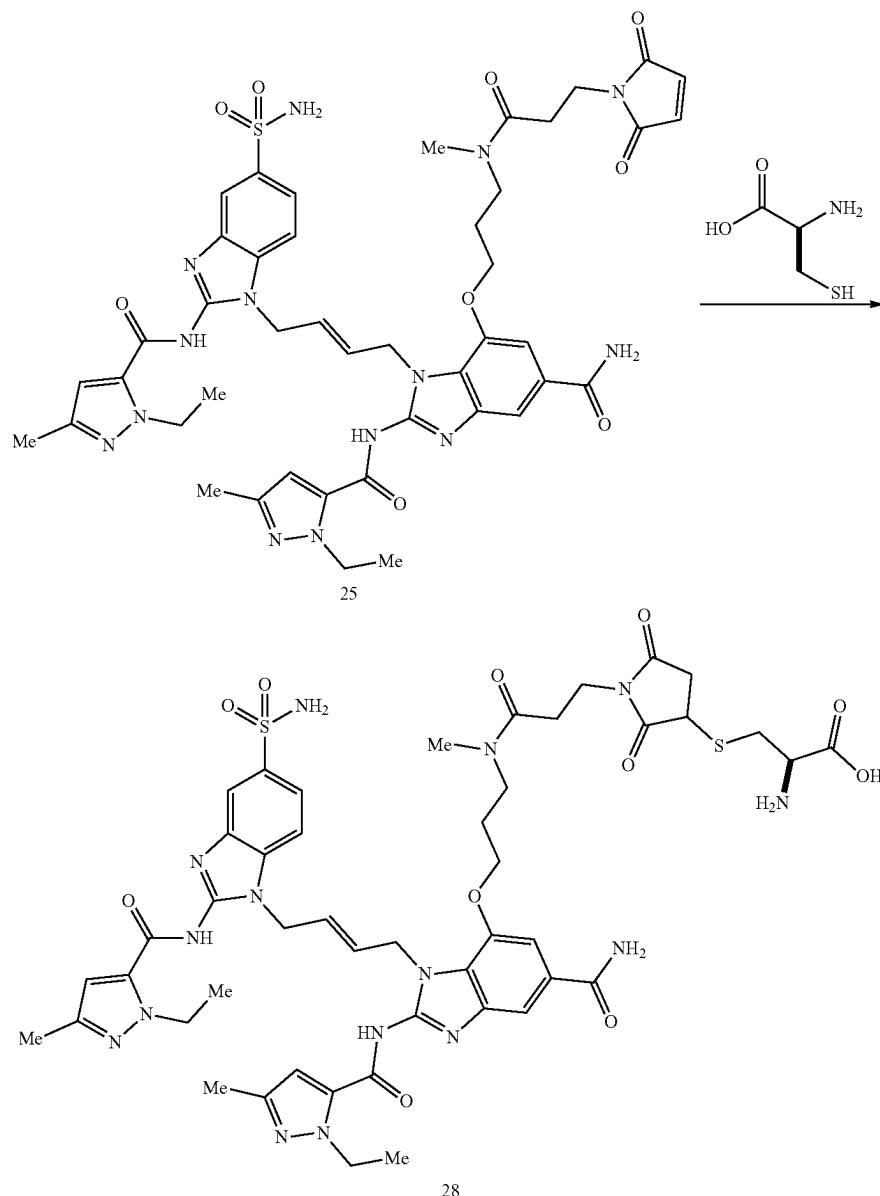
[1579] A 20 mL vial was charged with 27e (31 mg, 0.0266 mmol, 1 equiv.) which was dissolved in 20% TFA in DCM (2 mL) and stirred at room temperature for 15 minutes. Solvent was removed in vacuo and crude product purified by prepHPLC (Method H, 5-95% MeCN in water with 0.05% TFA) to give 27f as the 3×TFA salt (7.2 mg, 0.0061 mmol, 23% yield) as a white solid. MS (Method D, ESI+): m/z [M+H]⁺=836.4 (theoretical); 836.3 (observed). HPLC retention time: 2.02 min.

Synthesis of 27

[1580] An oven-dried 4 mL vial was charged with 27f (10 mM in DMSO, 0.50 mL, 0.0050 mmol, 1 equiv.) and then MP-OSu (2.0 mg, 0.0075 mmol, 1.5 equiv.) and DIPEA (20 uL, 0.12 mmol, 23 equiv.) was added. The reaction was stirred at room temperature for 90 minutes, quenched with 20% TFA in MeCN (100 uL) and crude product was purified by prepHPLC (Method G, 5-95% MeCN in water with 0.05% TFA) to 27 as the 3×TFA salt (3.6 mg, 0.0029 mmol,

58% yield) as a white solid. MS (Method D, ESI+): m/z [M+H]⁺=987.4 (theoretical); 987.2 (observed). HPLC retention time: 2.23 min.

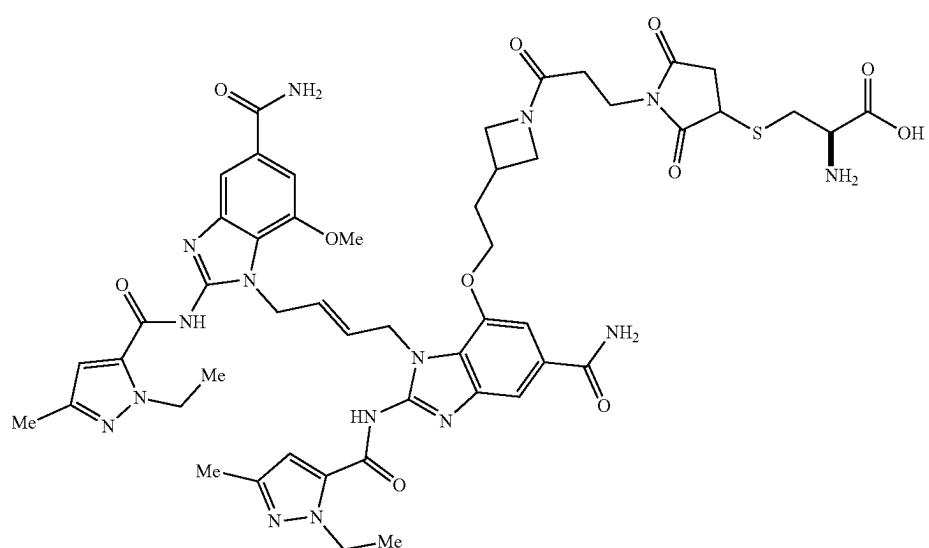
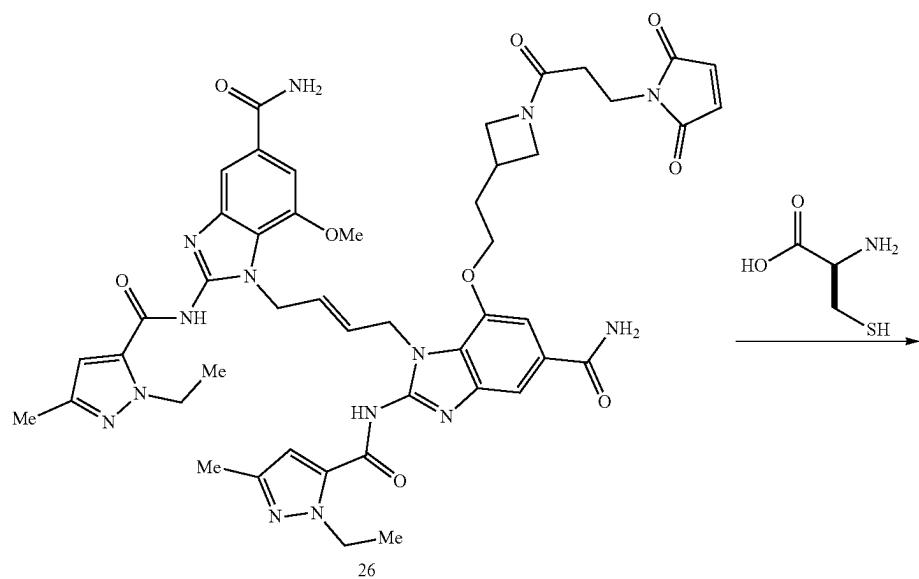
Synthesis of S-(1-((3-((3-((5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-((E)-4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazol-7-yl)oxy)propyl)(methyl)amino)-3-oxopropyl)-2,5-dioxopyrrolidin-3-yl)-L-cysteine (Compound 28)



[1581] A 1.7 mL eppendorf tube was charged with 25 (10 mM in DMSO, 100 μ L, 0.00100 mmol, 1 equiv.) and L-cysteine (15 mM in 4:1 DMSO:water, 150 μ L, 0.00300 mmol, 3 equiv.) was added. The reaction was heated to 37° C. for 90 minutes and the crude product was then purified by

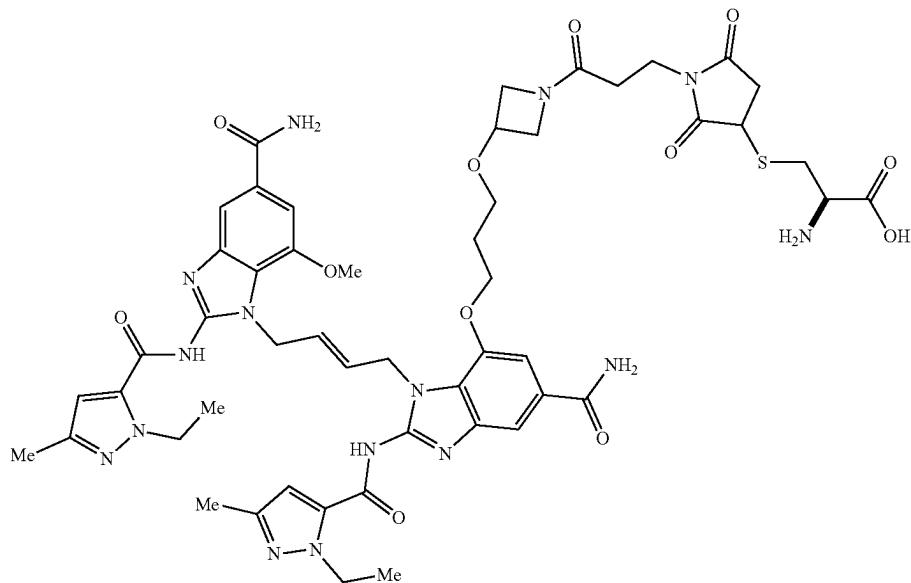
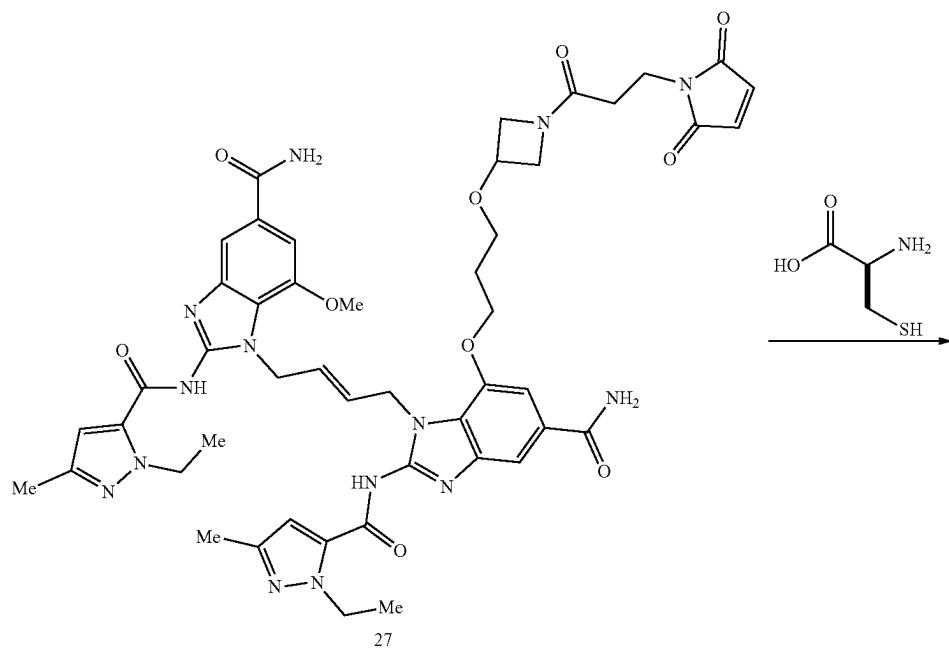
prepHPLC (Method G, 5-95% MeCN in water with 0.05% TFA) to give 28 as the 2xTFA salt (1.1 mg, 0.000861 mmol, 86% yield) as a white solid. MS (Method D, ESI+): m/z [M+H]⁺=1072.4 (theoretical); 1072.2 (observed). HPLC retention time: 1.98 min.

Synthesis of S-(1-(3-(2-((5-carbamoyl-1-((E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)ethyl)azetidin-1-yl)-3-oxopropyl)-2,5-dioxopyrrolidin-3-yl)-L-cysteine (Compound 29)



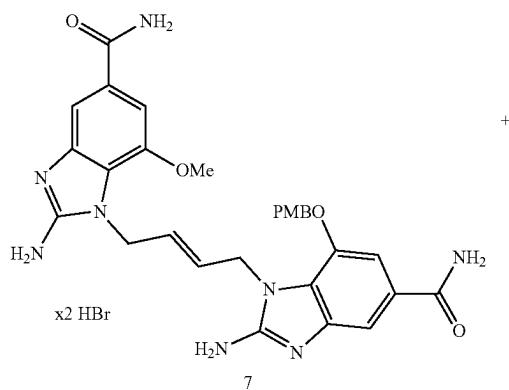
[1582] A 1.7 mL eppendorf tube was charged with 26 (10 mM in DMSO, 100 μ L, 0.00100 mmol, 1 equiv.) and L-cysteine (15 mM in 4:1 DMSO:water, 150 μ L, 0.00300 mmol, 3 equiv.) was added. The reaction was heated to 37° C. for 2 hours and the crude product was then purified by prepHPLC (Method G, 5-95% MeCN in water with 0.05% TFA) to give 29 as the 2 \times TFA salt (0.91 mg, 0.000697 mmol, 70% yield) as a white solid. MS (Method D, ESI+): m/z [M+H] $^{+}$ =1078.4 (theoretical); 1078.3 (observed). HPLC retention time: 2.03 min.

S-(1-(3-(3-((5-carbamoyl-1-((E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)propoxy)azetidin-1-yl)-3-oxopropyl)-2,5-dioxopyrrolidin-3-yl)-L-cysteine (Compound 30)



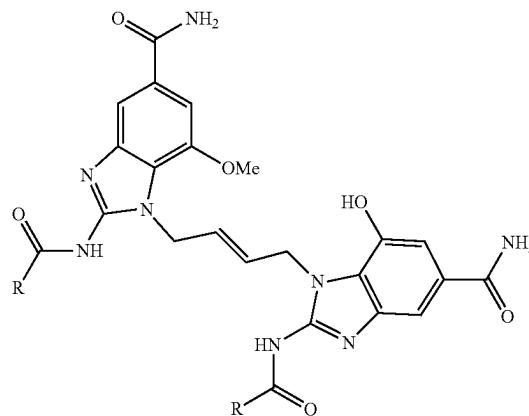
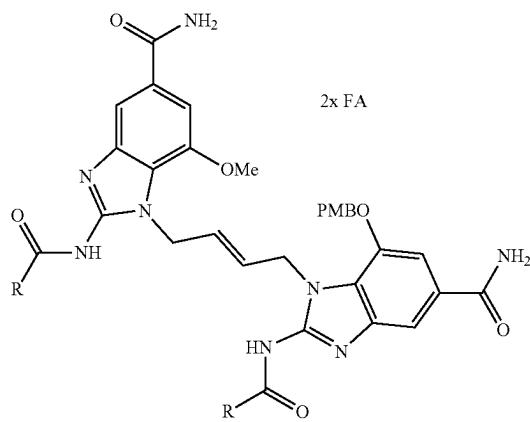
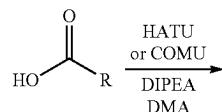
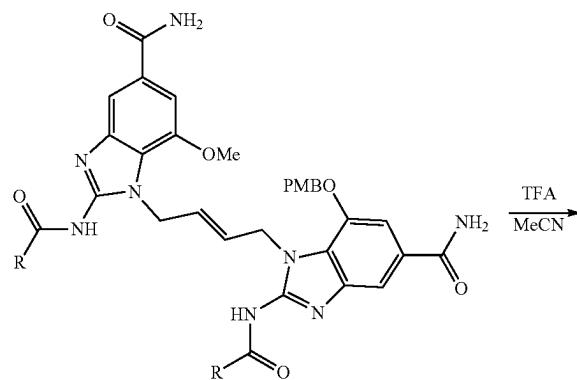
[1583] A 1.7 mL eppendorf tube was charged with 27 (10 mM in DMSO, 100 μ L, 0.00100 mmol, 1 equiv.) and L-cysteine (100 mM in DMSO, 30 μ L, 0.00300 mmol, 3 equiv.) and the solution incubated at 37° C. for 30 minutes. The crude product was purified by prepHPLC (Method G, 5-95% MeCN in water with 0.05%) to give 30 as the 2xTFA salt (1.2 mg, 0.000913 mmol, 61% yield) as a white solid. MS (Method D, ESI+): m/z [M+H]⁺=1108.4 (theoretical); 1108.5 (observed). HPLC retention time: 2.08 min.

Library Synthesis of Amide Analogs. Scheme and General Methods. Compounds 31-60.



was heated to 70° C. for 18 hr. At which point, acetic acid (4.3 μ L) was added, and resulting products were purified by prepHPLC (20-50-95% MeCN in water with 0.1% FA). All molecules were characterized using LC-MS Method D with ESI+ ionization.

[1585] COMU Couplings (General Method 4B) To a solution of carboxylic acid (4 equiv.) in DMA (400 μ L) was added COMU (7 mg, 0.016 mmol, 4 equiv.) and DIPEA (4.3 μ L, 0.025 mmol, 6 equiv.). The mixture was stirred at room temperature for 30 min and then compound 7 (3 mg, 0.0041 mmol, 1 equiv.) was added to the mixture, and the solution was heated to 40° C. for 18 hr. At which point, acetic acid was added (4.3 μ L), and the resulting products were purified by prepHPLC (20-50-95% MeCN in water with 0.1% FA).



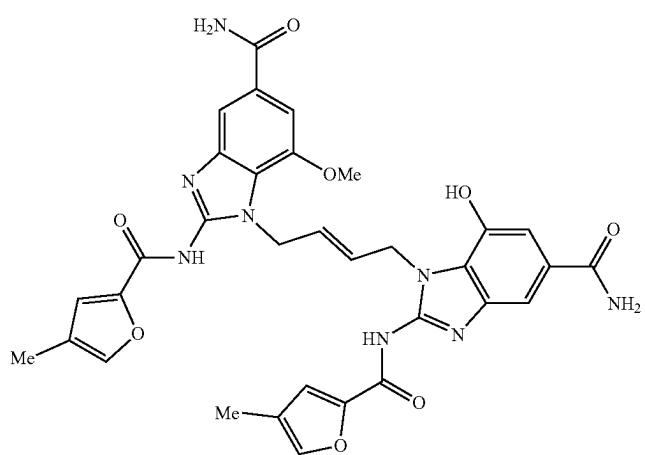
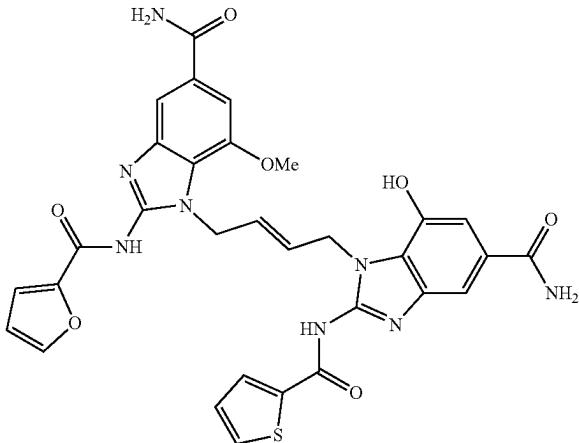
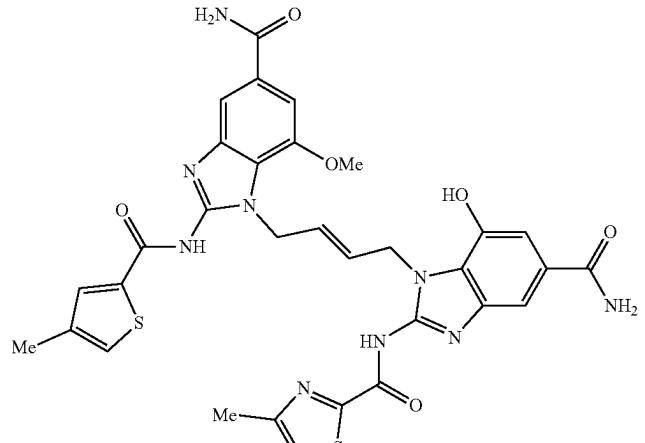
[1584] HATU Couplings (General Method 4A) To a solution of carboxylic acid (4 equiv.) in DMA (400 μ L) was added HATU (6.2 mg, 0.016 mmol, 4 equiv.) and DIPEA (4.3 μ L, 0.025 mmol, 6 equiv.). The mixture was stirred at room temperature for 30 minutes and then compound 7 (3 mg, 0.0041 mmol, 1 equiv.) was added to the mixture, and

[1586] PMB deprotection (General Method 5) The resulting amide from the previous step was dissolved in 50% TFA in MeCN (0.01 M) and stirred at 30° C. for 30 min. Upon completion, the mixture was concentrated, and the product purified by prep-HPLC (20-50-95% water/acetonitrile 0.1% TFA).

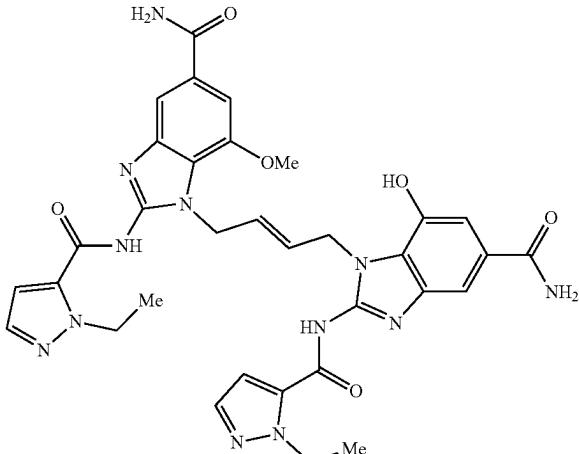
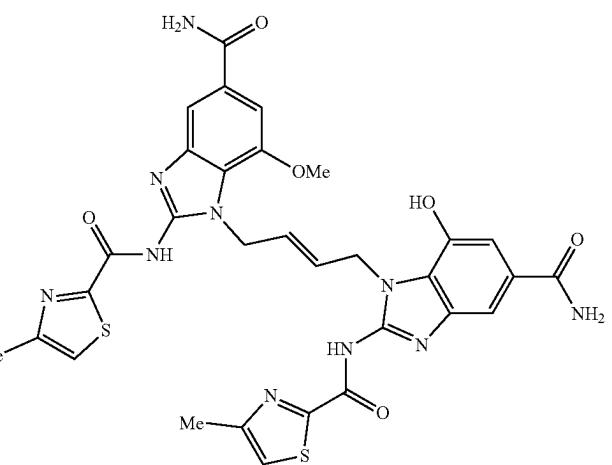
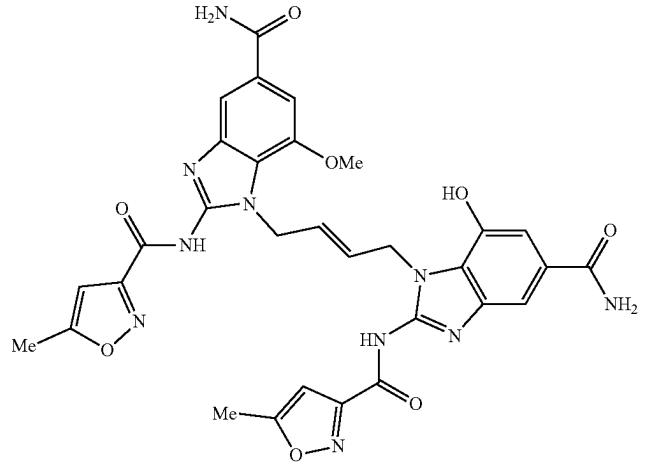
[1587] Examples below were prepared using the general methods specified above.

Cmpd.	Structure	Method	Yield (over PMB LC-MS 2 steps)	Phenol LC-MS data	Phenol LC-MS data
31		HATU - Method 4a	45% 1.74 mg 0.00183 mmol	RT: 1.49 Theoretical: 843.4 Observed: 843.5	RT: 1.25 Theoretical: 723.3 Observed: 723.5
32		HATU - Method 4a	58% 2.25 mg 0.00237 mmol	RT: 1.67 Theoretical: 843.4 Observed: 843.5	RT: 1.42 Theoretical: 723.3 Observed: 723.5
33		HATU - Method 4a	56% 2.00 mg 0.00231 mmol	RT: 1.78 Theoretical: 759.2 Observed: 759.4	RT: 1.60 Theoretical: 639.2 Observed: 639.3

-continued

Cmpd.	Structure	Method	Yield (over PMB LC-MS		Phenol LC-MS data
			2 steps)	data	
34		HATU - Method 4a	61% 2.24 mg 0.00251 mmol	RT: 1.92 Theoretical: 787.3 Observed: 787.4	RT: 1.74 Theoretical: 667.2 Observed: 667.4
35		HATU - Method 4a	59% 2.19 mg 0.00244 mmol	RT: 2.00 Theoretical: 791.2 Observed: 791.3	RT: 1.85 Theoretical: 671.1 Observed: 671.3
36		HATU - Method 4a	40% 1.52 mg 0.00164 mmol	RT: 2.14 Theoretical: 819.2 Observed: 819.4	RT: 2.01 Theoretical: 699.2 Observed: 699.3

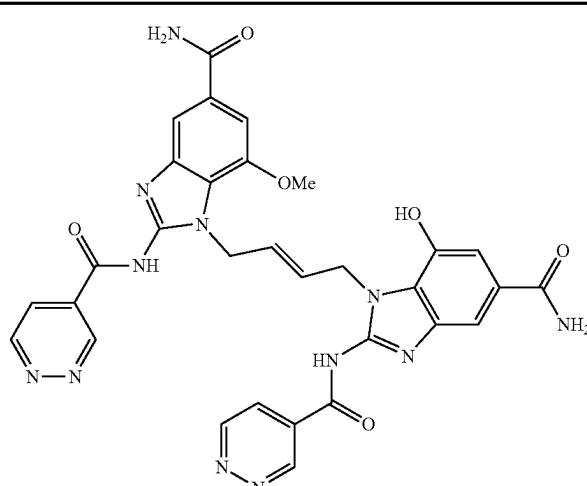
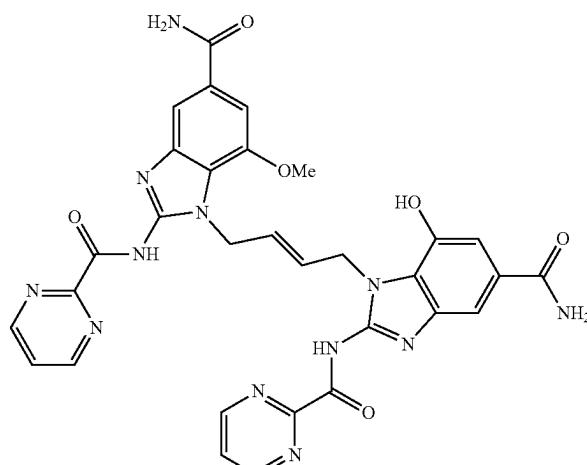
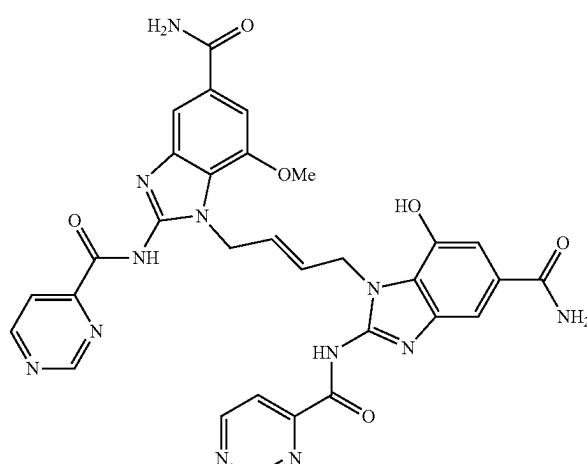
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Cmpd.	Structure	Method	Yield (over PMB LC-MS		Phenol LC-MS data
			2 steps)	data	
37		COMU - Method 4b	35% 1.32 mg 0.00143 mmol	RT: 2.02 Theoretical: 815.3 Observed: 815.5	RT: 1.63 Theoretical: 695.3 Observed: 695.4
38		COMU - Method 4b	39% 1.47 mg 0.00158 mmol	RT: 2.02 Theoretical: 821.2 Observed: 821.4	RT: 1.63 Theoretical: 701.2 Observed: 701.3
39		COMU - Method 4b	57% 2.08 mg 0.00232 mmol	RT: 1.86 Theoretical: 789.3 Observed: 789.5	RT: 1.65 Theoretical: 669.2 Observed: 669.4

-continued

Cmpd.	Structure	Method	Yield (over PMB LC-MS		Phenol LC-MS data
			2 steps)	data	
40		COMU - Method 4b	36% 1.37 mg 0.00148 mmol	RT: 2.00 Theoretical: 821.2 Observed: 821.4	RT: 1.61 Theoretical: 701.2 Observed: 701.3
41		HATU - Method 4a	66% 2.50 mg 0.00272 mmol	RT: 2.24 Theoretical: 813.3 Observed: 813.5	RT: 1.84 Theoretical: 693.3 Observed: 693.5
42		COMU - Method 4b	45% 1.64 mg 0.00184 mmol	RT: 1.59 Theoretical: 783.3 Observed: 783.4	RT: 1.31 Theoretical: 663.2 Observed: 663.4

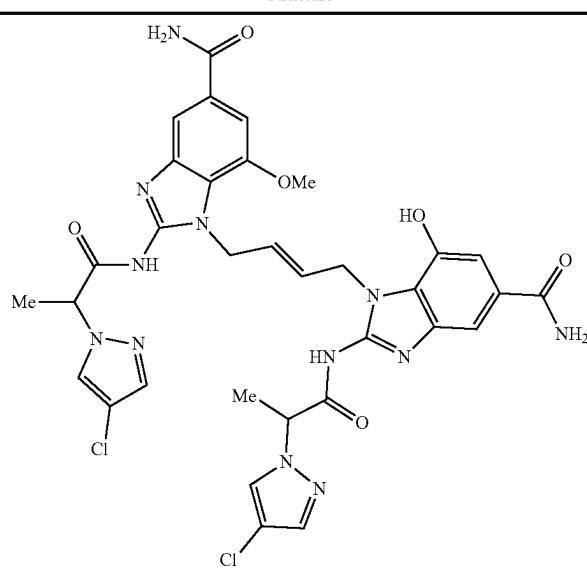
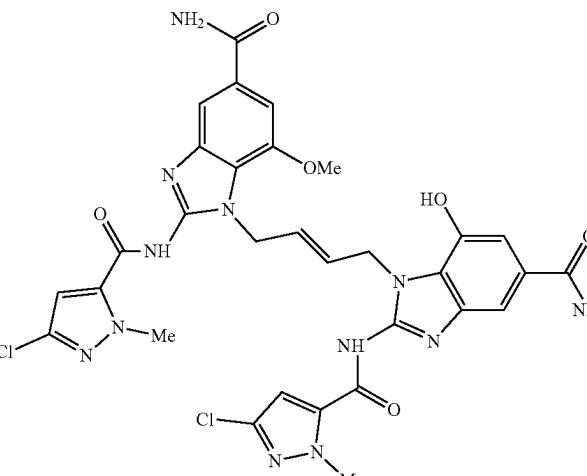
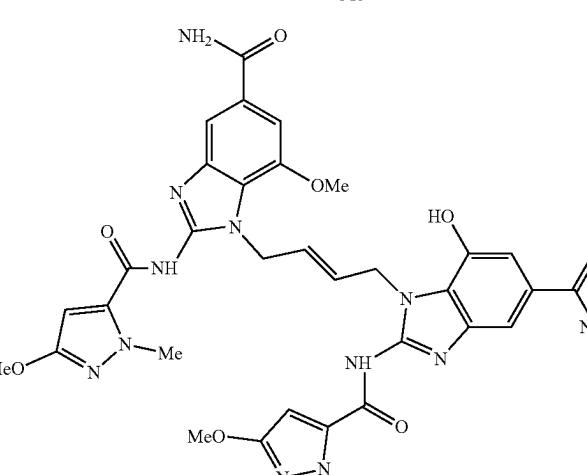
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Cmpd.	Structure	Method	Yield (over PMB LC-MS		Phenol LC-MS data
			2 steps)	data	
43		COMU - Method 4b	29% 1.07 mg 0.00120 mmol	RT: 1.63 Theoretical: 783.3 Observed: 783.4	RT: 1.36 Theoretical: 663.2 Observed: 663.4
44		COMU - Method 4b	55% 2.00 mg 0.00225 mmol	RT: 1.47 Theoretical: 783.3 Observed: 783.4	RT: 1.19 Theoretical: 663.2 Observed: 663.4
45		COMU - Method 4b	37% 1.36 mg 0.00153 mg	RT: 1.61 Theoretical: 783.3 Observed: 783.4	RT: 1.34 Theoretical: 663.2 Observed: 663.4

-continued

Cmpd.	Structure	Method	Yield (over PMB LC-MS		Phenol LC-MS data
			2 steps)	data	
46		COMU - Method 4b	63% 2.30 mg 0.00258 mmol	RT: 1.62 Theoretical: 783.3 Observed: 783.4	RT: 1.34 Theoretical: 663.2 Observed: 663.4
47		COMU - Method 4b	46% 1.67 mg 0.00187 mmol	RT: 1.74 Theoretical: 787.3 Observed: 787.5	RT: 1.46 Theoretical: 667.2 Observed: 667.4
48		COMU - Method 4b	60% 2.35 mg 0.00247 mmol	RT: 1.79 Theoretical: 843.4 Observed: 843.5	RT: 1.52 Theoretical: 723.3 Observed: 723.5

-continued

Cmpd.	Structure	Method	Yield (over PMB 2 steps)	PMB LC-MS data	Phenol LC-MS data
49		COMU - Method 4b	60% 2.42 mg 0.00244 mmol	RT: 2.18 Theoretical: 883.3 Observed: 883.5	RT: 1.90 Theoretical: 763.2 Observed: 763.4
50		COMU - Method 4b	55% 2.17 mg 0.00225 mmol	RT: 2.17 Theoretical: 855.2 Observed: 855.4	RT: 1.59 Theoretical: 735.2 Observed: 735.3
51		COMU - Method 4b	71% 2.76 mg 0.00289 mmol	RT: 1.89 Theoretical: 847.3 Observed: 847.5	RT: 1.31 Theoretical: 727.3 Observed: 727.6

-continued

Cmpd.	Structure	Method	Yield (over PMB LC-MS		Phenol LC-MS data
			2 steps)	data	
52		COMU - Method 4b	51% 2.23 mg 0.00211 mmol	RT: 2.50 Theoretical: 951.3 Observed: 951.6	RT: 1.99 Theoretical: 831.3 Observed: 831.6
53		COMU - Method 4b	51% 2.00 mg 0.00210 mmol	RT: 2.01 Theoretical: 843.4 Observed: 843.5	RT: 1.44 Theoretical: 723.3 Observed: 723.6
54		COMU - Method 4b	52% 1.97 mg 0.00214 mmol	RT: 1.86 Theoretical: 815.3 Observed: 615.5	RT: 1.28 Theoretical: 695.3 Observed: 695.5

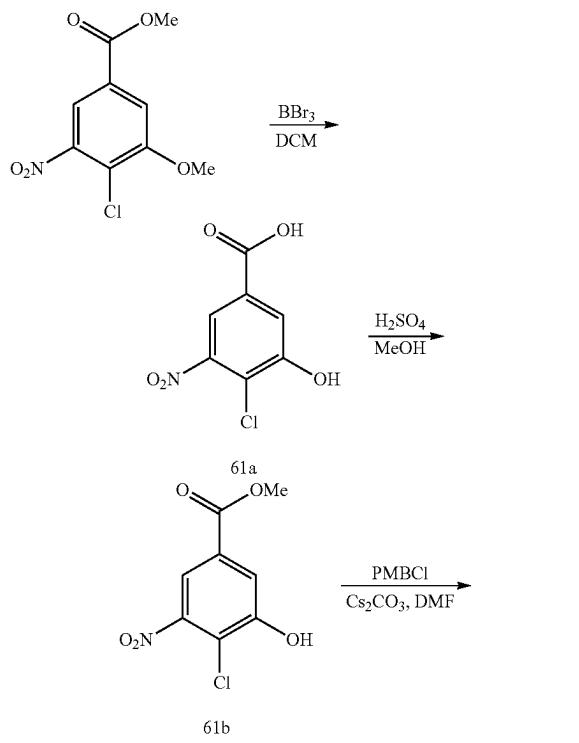
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Cmpd.	Structure	Method	Yield (over PMB LC-MS		Phenol LC-MS data
			2 steps)	data	
55		HATU - Method 4a	56% 2.04 mg 0.00228 mmol	RT: 1.88 Theoretical: 1027.4 Observed: 1028.0	RT: 1.35 Theoretical: 667.2 Observed: 667.8
56		COMU - Method 4b	63% 2.24 mg 0.00257 mmol	RT: 1.78 Theoretical: 763.4 Observed: 763.5	RT: 1.11 Theoretical: 643.3 Observed: 643.9
57		HATU - Method 4a	60% 2.08 mg 0.00247 mmol	RT: 1.31 Theoretical: 735.3 Observed: 735.7	RT: 0.99 Theoretical: 615.3 Observed: 615.6

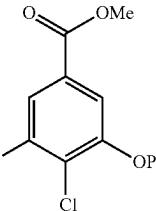
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Cmpd.	Structure	Method	Yield (over PMB LC-MS		Phenol LC-MS data
			2 steps)	data	
58		HATU - Method 4a	55% 2.02 mg 0.00225 mmol	RT: 1.88 Theoretical: 789.3 Observed: 789.4	RT: 1.60 Theoretical: 669.2 Observed: 669.3
59		HATU - Method 4a	56% 2.00 mg 0.00230 mmol	RT: 1.81 Theoretical: 761.2 Observed: 761.4	RT: 1.56 Theoretical: 641.2 Observed: 641.3
60		HATU - Method 4a	48% 1.82 mg 0.00196 mmol	RT: 1.98 Theoretical: 821.2 Observed: 821.4	RT: 1.68 Theoretical: 701.2 Observed: 701.4

Synthesis of methyl 4-chloro-3-((4-methoxybenzyl)oxy)-5-nitrobenzoate (Compound 61)



61b



Compound 61

Synthesis of 61a

[1588] To a solution of methyl 4-chloro-3-methoxy-5-nitrobenzoate (15 g, 61 mmol, 1 equiv.) in DC (60 mL) at 0° C. under nitrogen was added BBr₃ (1 M in DCM, 153 mL, 153 mmols, 2.5 equiv.) dropwise over 20 min. The reaction mixture was stirred at 0° C. for 30 min and then allowed to warm to 25° C. and stirred for a further 12 h. The reaction mixture was cooled to 0° C., quenched with methanol, and concentrated in vacuo to give 61a (12.3 g, 56.5 mmols, 93% yield) as dark brown oil. LC-MS (Method C, ESI+): m/z [M+H]⁺=218.0 (theoretical); 217.9 (observed). HPLC retention time: 0.21 min.

Synthesis of 61b

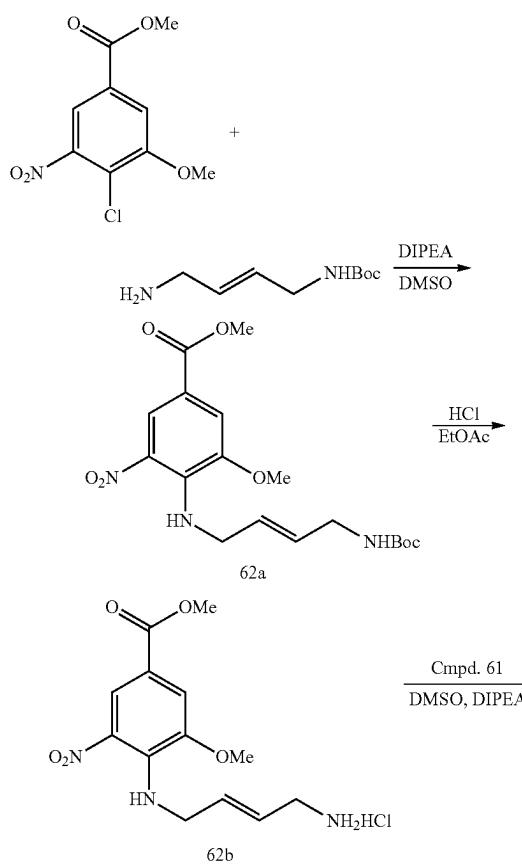
[1589] To a solution of 61a (26.6 g, 122 mmol, 1 equiv.) in methanol (800 mL), was added concentrated H₂SO₄ (600 mg, 6.11 mmol, 0.05 equiv.), the mixture was stirred at 60° C. for 12 h. LCMS analysis (Method C) showed the reaction was completed. The mixture was cooled to room temperature and concentrated in vacuo. The crude residue was

diluted with water (50 mL) and saturated NaHCO₃ (50 mL) was carefully added to achieve a pH>7. The resultant solid was collected by filtration, washed with water (25 mL) and dried under vacuum to give 61b (25 g, 88% yield) as a brown solid. LC-MS (Method C, EST+): m/z [M+H]⁺=232.0 (theoretical); 231.9 (observed). HPLC retention time: 0.92 min.

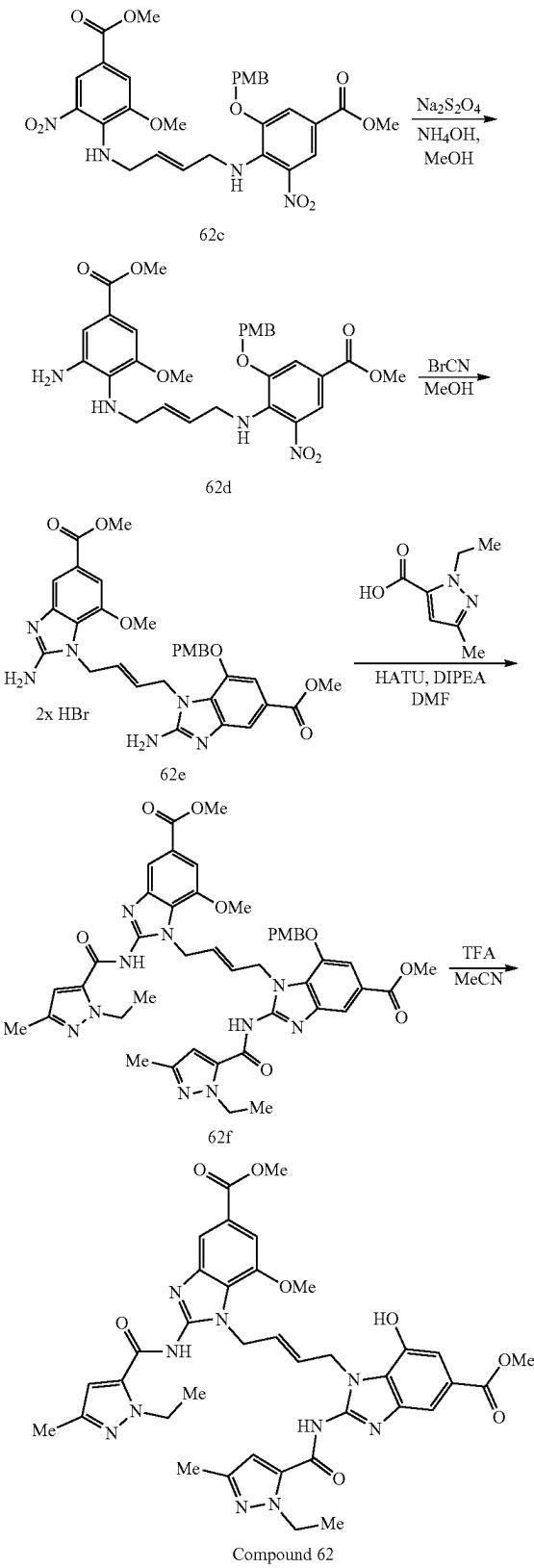
Synthesis of 61

[1590] To a solution of 61b (18 g, 78 mmol, 1 equiv.) in DMF (200 mL) was added Cs₂CO₃ (27.9 g, 86 mmol, 1.1 equiv.) and 1-(chloromethyl)-4-methoxybenzene (12.8 g, 82 mmol, 1.05 equiv.) and the mixture was stirred at 25° C. for 16 h. LCMS analysis (Method C) showed the reaction was completed. The reaction was poured into water, filtered and dried under high vacuum to give 61 (22.3 g, 82% yield) as a light-yellow solid. ¹H NMR (400 MHz, DMSO-d₆): δ=8.11 (d, J=1.4 Hz, 1H), 7.97 (d, J=1.4 Hz, 1H), 7.43 (d, J=8.5 Hz, 2H), 6.99 (d, J=8.5 Hz, 2H), 5.33 (s, 2H), 3.92 (s, 3H), 3.77 (s, 3H).

Synthesis of methyl (E)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-hydroxy-5-(methoxycarbonyl)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-methoxy-1H-benzo[d]imidazole-5-carboxylate (Compound 62)



-continued

**Synthesis of 62a**

[1591] To a solution of tert-butyl (E)-(4-aminobut-2-en-1-yl)carbamate (12.5 g, 67.2 mmol, 1.1 equiv.) in DMSO (150 mL) was added methyl 4-chloro-3-methoxy-5-nitrobenzoate (15 g, 61.1 mmol, 1 equiv.) and DIPEA (39.5 g, 305 mmol, 5 equiv.) the mixture was stirred at 100° C. for 12 h. The mixture was poured into water, extracted with EtOAc and concentrated in vacuo to give 62a (16.4 g, 41.4 mmols, 68% yield) as a dark red solid. LC-MS (Method C, ESI+): m/z [M-tBu]⁺=340.1 (theoretical); 340.1 (observed). HPLC retention time: 1.08 min.

Synthesis of 62b

[1592] 62a (21 g, 53.1 mmol, 1 equiv.) was added to a solution of HCl in ethyl acetate (4 M, 350 mL, 1400 mmols, 26 equiv.) and the mixture was stirred at 25° C. for 2 h. The mixture was concentrated in vacuo and crude solid washed with EtOAc to give 62b as the HCl salt (14.5 g, 43.7 mmols, 82% yield) as a dark red solid. ¹H NMR (400 MHz, DMSO-d₆): δ=8.19 (d, J=1.8 Hz, 1H), 8.12 (br s, 1H), 8.01 (br s, 3H), 7.46 (d, J=1.6 Hz, 1H), 5.87 (td, J=5.8, 15.5 Hz, 1H), 5.71-5.55 (m, 1H), 4.21 (br s, 2H), 3.90 (s, 3H), 3.84 (s, 3H), 3.42-3.35 (m, 2H).

Synthesis of 62c

[1593] To a solution of 61 (4.5 g, 12.8 mmol) in DMSO (70 mL) was added 62b (4.67 g, 14.1 mmol, HCl salt) and DIPEA (8.3 g, 64 mmol, 5 equiv.) and the reaction was stirred at 80° C. for 10 h. The mixture was poured into ice water, extracted with EtOAc and concentrated in vacuo. The residue was recrystallized (ethyl acetate, 20V, reflux) to give 62c (6.4 g, 10.5 mmols, 82% yield) as a dark red solid. MS (Method C, ESI+): m/z [M+H]⁺=611.2 (theoretical); 611.2 (observed). HPLC retention time: 1.34 min. ¹H NMR (400 MHz, DMSO-d₆): δ=8.06 (dd, J=1.5, 9.5 Hz, 2H), 7.96 (br d, J=2.9 Hz, 2H), 7.44 (s, 1H), 7.36 (d, J=8.5 Hz, 2H), 7.30 (s, 1H), 6.94 (d, J=8.5 Hz, 2H), 5.53-5.29 (m, 2H), 5.00 (s, 2H), 4.03 (br t, J=5.4 Hz, 4H), 3.84 (s, 6H), 3.76 (d, J=3.5 Hz, 6H).

Synthesis of 62d

[1594] To a solution of 62c (6.0 g, 9.83 mmol, 1 equiv.) in MeOH (300 mL) was added NH₄OH (60 mL, 28% NH₃ in H₂O) and Na₂S₂O₄ (20.5 g, 118 mmol, 12 equiv.). The mixture was stirred at 25° C. for 16 h and went from bright red to a light yellow/nearly colorless heterogenous mixture. The mixture was filtered, concentrated to remove MeOH and the remaining aqueous solution was extracted with EtOAc. The organic phases were combined, dried with Na₂SO₄ and concentrated in vacuo to give 62d (4.0 g, 7.25 mmols, 74% yield) as an off white solid. MS (Method B, ESI+): m/z [M+H]⁺=551.25 (theoretical); 551.2 (observed). HPLC retention time: 1.29 min.

Synthesis of 62e

[1595] To a solution of 62d (4.0 g, 7.25 mmol, 1 equiv.) in MeOH (200 mL) was added BrCN (4.62 g, 43.6 mmol, 6 equiv.). The mixture was stirred at 25° C. for 2 h at which point LC-MS analysis (Method C) showed full conversion. The reaction mixture was concentrated in vacuo and the crude product washed with ethanol and petroleum ether to give 62e as the 2×HBr salt (2.6 g, 3.53 mmols 49% yield)

as an off white solid. MS (Method C, ESI+): m/z [M+H]⁺ = 601.2 (theoretical); 601.3 (observed). HPLC retention time: 2.73 min. ¹H NMR (400 MHz, DMSO-d₆): δ=12.87 (br s, 1H), 8.72 (br d, J=17.0 Hz, 4H), 7.59 (s, 2H), 7.42 (s, 1H), 7.26-7.16 (m, 3H), 6.82 (d, J=8.6 Hz, 2H), 5.70 (br d, J=15.7 Hz, 1H), 5.57-5.48 (m, 1H), 5.00 (s, 2H), 4.83-4.73 (m, 4H), 3.88 (s, 6H), 3.71 (s, 3H), 3.65 (s, 3H).

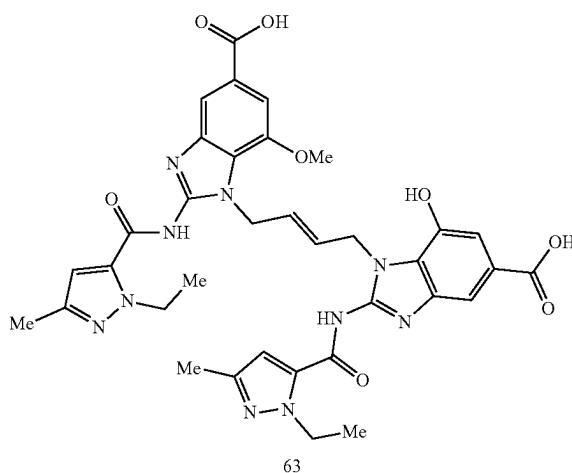
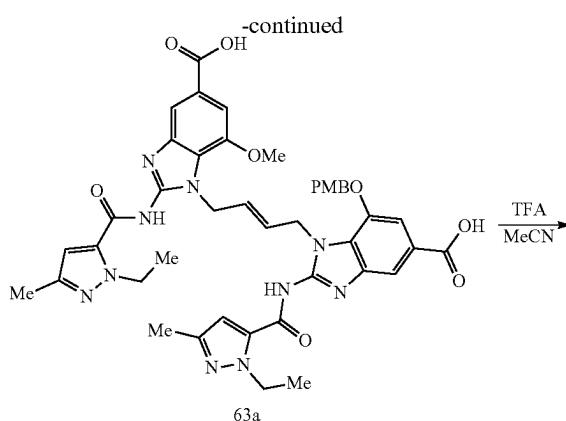
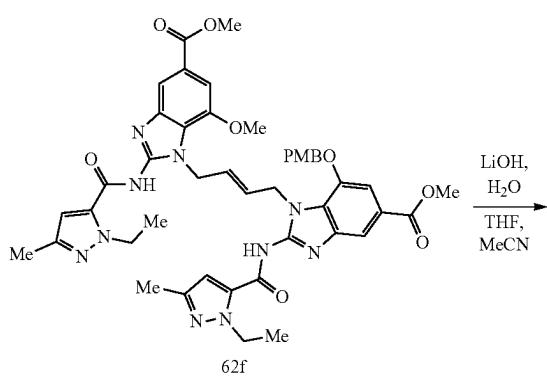
Synthesis of 62f

[1596] To a solution of 1-ethyl-3-methyl-1H-pyrazole-5-carboxylic acid (3.15 g, 20.5 mmol, 2.6 equiv.) in DMF (30 mL) was added HATU (8.38 g, 22.0 mmol, 2.8 equiv.) and the solution was stirred at 60° C. for 10 min. A second solution containing DIPEA (5.09 g, 39 mmol, 5 equiv.) and 62e (6.0 g, 7.87 mmol, 1 equiv. 2×HBr salt) in DMF, 30 mL) was prepared and added to the activated acid. The reaction was then stirred at 60° C. for 2 h. The solution was poured into water, filtered and triturated with acetonitrile to give 62f (2.54 g, 2.91 mmols, 37% yield) as an off-white solid. MS (Method C, ESI+): m/z [M+H]⁺=873.4 (theoretical); 873.4 (observed). HPLC retention time: 3.44 min. ¹H NMR (400 MHz, DMSO-d₆) δ=12.88 (br s, 2H), 7.74 (br s, 2H), 7.22 (br s, 1H), 7.16-6.97 (m, 3H), 6.66 (br d, J=7.9 Hz, 2H), 6.57-6.36 (m, 2H), 5.87-5.37 (m, 2H), 4.78 (br s, 6H), 4.51 (br dd, J=7.0, 17.3 Hz, 4H), 3.85 (s, 6H), 3.59 (s, 3H), 3.52 (br s, 3H), 2.10 (br d, J=11.1 Hz, 6H), 1.26 (td, J=6.8, 18.8 Hz, 6H).

Synthesis of 62

[1597] An oven-dried 4 mL vial with stir bar was charged with 62f (9 mg, 0.010 mmols, 1 equiv.) which was dissolved in 1:1 MeCN:TFA (1 mL) and stirred for 1 hour at room temperature. Solvent was removed in vacuo and product dried on high-vac overnight to give 62 (7.5 mg, 0.0099 mmols, quant. yield) as a tan solid. MS (Method D, ESI+): m/z [M+H]⁺=753.3 (theoretical); 753.7 (observed). HPLC retention time: 1.99 min.

Synthesis of (E)-1-(4-(5-carboxy-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-hydroxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxylic acid
(Compound 63)



Synthesis of 63a

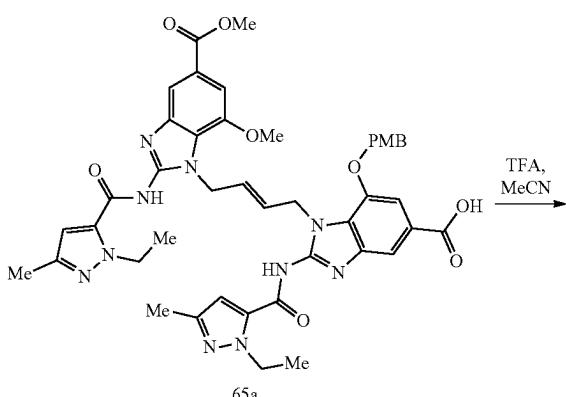
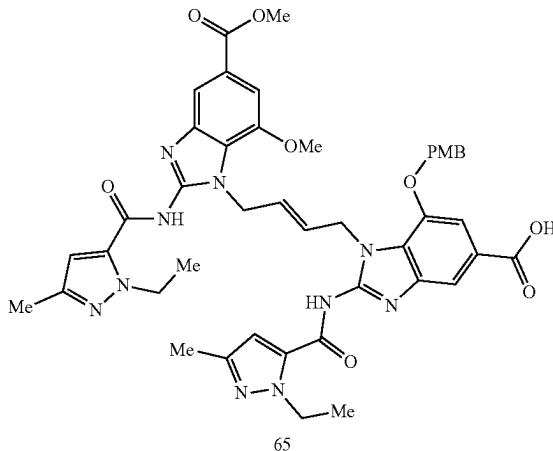
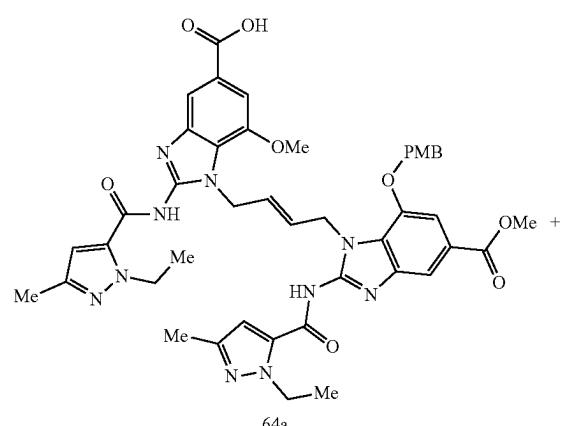
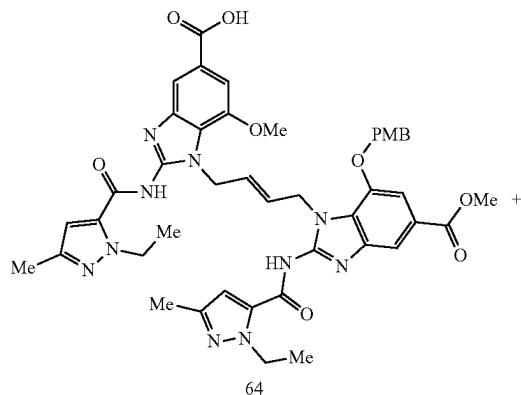
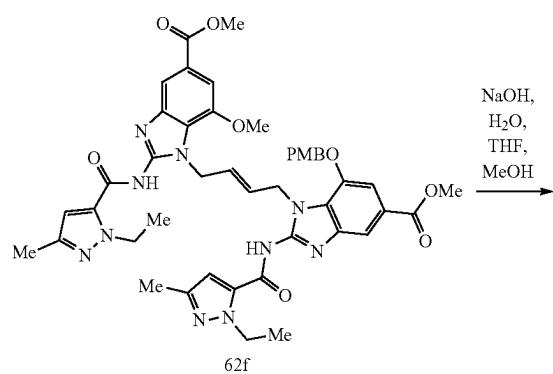
[1598] Compound 62f (100 mg, 0.115 mmols, 1 equiv.) was dissolved in acetonitrile (1 mL), 1M LiOH (1 mL, 1 mmol, 9 equiv.) was added and the solution was heated to 80° C. for 1 hour. The vial was cooled, solvent removed in vacuo and product purified by prepHPLC (Method I, 5-95% MeCN in water with 0.1% TFA) to give 63a (78 mg, 0.092 mmols, 97% yield) as a white solid. MS (Method D, ESI+): m/z [M+H]⁺=845.3 (theoretical); 845.8 (observed). HPLC retention time: 1.95 min.

Synthesis of 63

[1599] Compound 63 was prepared as previously described (see “Synthesis of 62”). MS (Method D, ESI+): m/z [M+H]⁺=725.3 (theoretical); 725.4 (observed). HPLC retention time: 1.83 min.

Synthesis of (E)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-hydroxy-5-(methoxycarbonyl)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-methoxy-1H-benzo[d]imidazole-5-carboxylic acid (Compound 64) and (E)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-5-(methoxycarbonyl)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-hydroxy-1H-benzo[d]imidazole-5-carboxylic acid Compound 65)

-continued



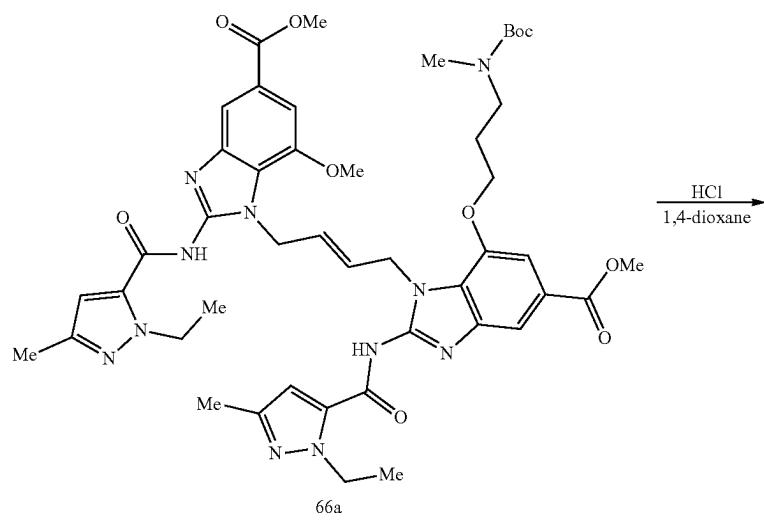
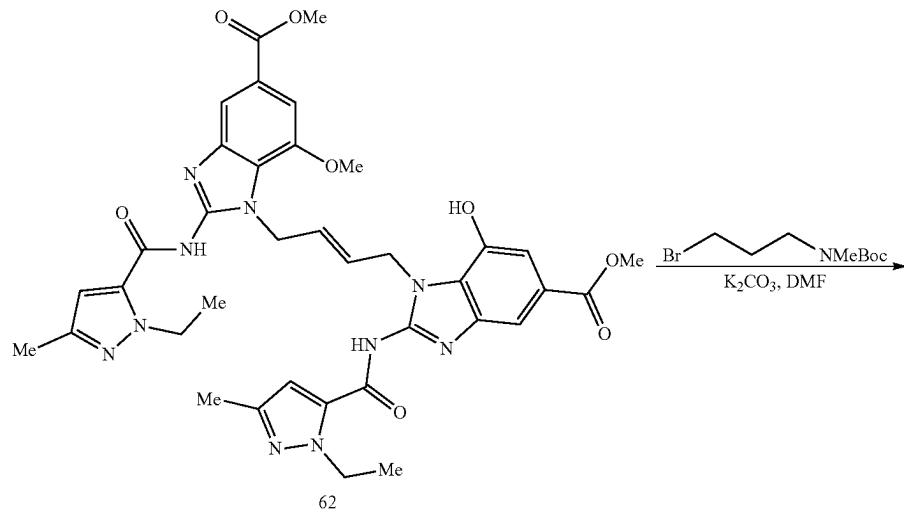
Synthesis of 64a and 65a

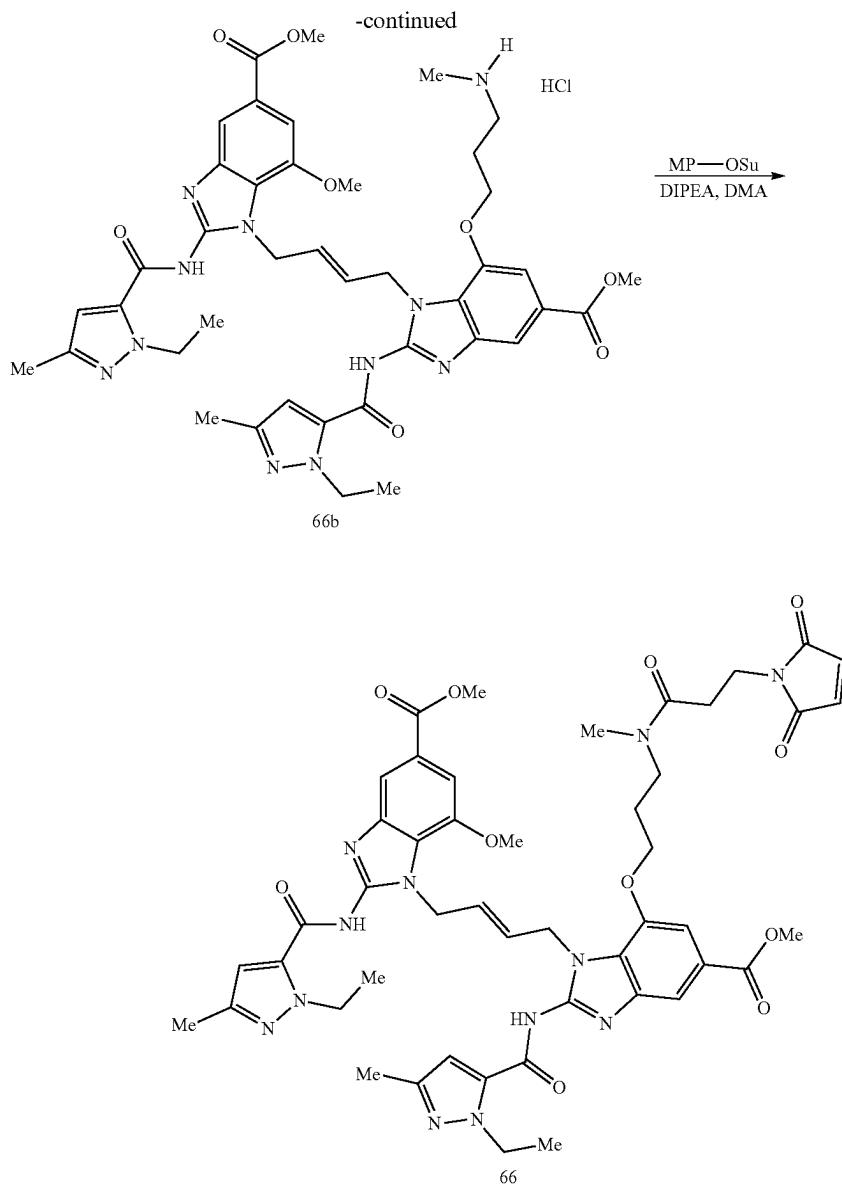
[1600] An inseparable 1:1 mixture of compounds 64a and 65a was prepared as previously described (see “Synthesis of 65a”) substituting sodium hydroxide for lithium hydroxide and quenching the reaction at 50% conversion followed by purification via prepHPLC (Method H with 0.1% FA). MS (Method D, ESI+): m/z [M+H]⁺=859.4 (theoretical); 859.5 (observed). HPLC retention time: 2.46 min.

Synthesis of 64 and 65

[1601] An inseparable 1:1 mixture of compounds 64a and 65a was prepared as previously described (see “Synthesis of 65a”). MS (Method D, ESI+): m/z [M+H]⁺=739.4 (theoretical); 739.4 (observed). HPLC retention time: 1.99 and 2.04 min.

Synthesis of methyl (E)-7-(3-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-N-methylpropanamido)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-5-(methoxycarbonyl)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazole-5-carboxylate (Compound 66)





Synthesis of 66a

[1602] Compound 62 (397 mg, 0.527 mmol, 1 equiv.), tert-butyl (3-bromopropyl)(methyl)carbamate (146 mg, 0.580 mmol, 1.1 equiv.) and potassium carbonate (218 mg, 1.58 mmol, 3 equiv.) were dissolved in DMF (5.3 mL) in a 20 mL vial. The reaction was stirred at 55° C. for 18 hours and then the mixture was filtered washing with methanol and the filtrate concentrated in vacuo. To the crude solid was added cold water and the precipitate isolated via filtration to give 66a (232 mg, 0.251 mmol, 48% yield). MS (Method E, ESI+): m/z [M+H]⁺ = 924.4 (theoretical); 924.9 (observed). HPLC retention time: 2.42 min.

Synthesis of 66b

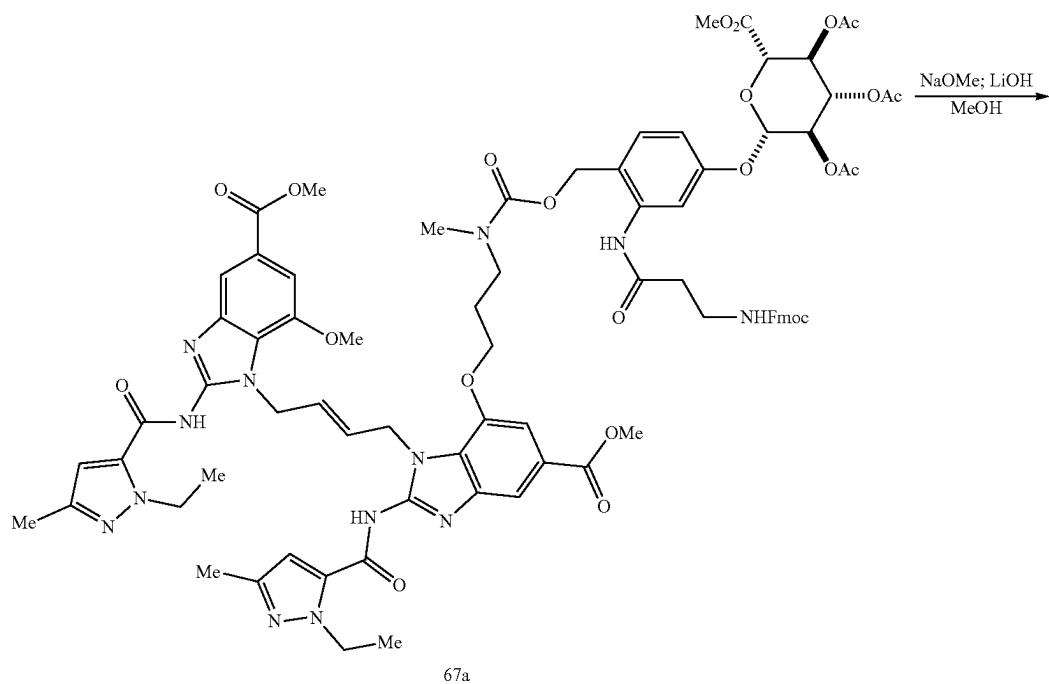
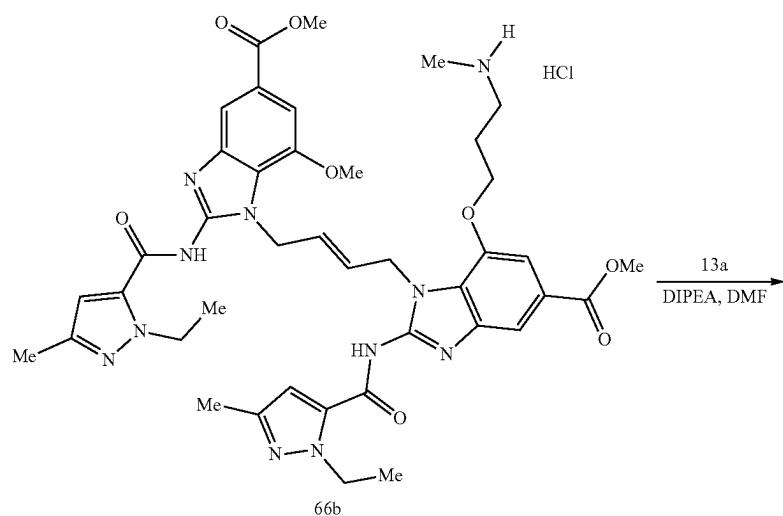
[1603] Compound 66a (232 mg, 0.251 mmol, 1 equiv.) was dissolved in methanol (2.5 mL) and 4M HCl in dioxane

was added (0.5 mL, 2.01 mmol, 8 equiv.). The reaction stirred at 30° C. for 90 minutes. The solvent was in vacuo and the crude product purified by prepHPLC (Method I with 0.05% TFA) to afford 66b (206 mg, 0.24 mmol, 96% yield). MS (Method E, ESI+): m/z [M+H]⁺ = 824.4 (theoretical); 824.9 (observed). HPLC retention time: 1.56 min.

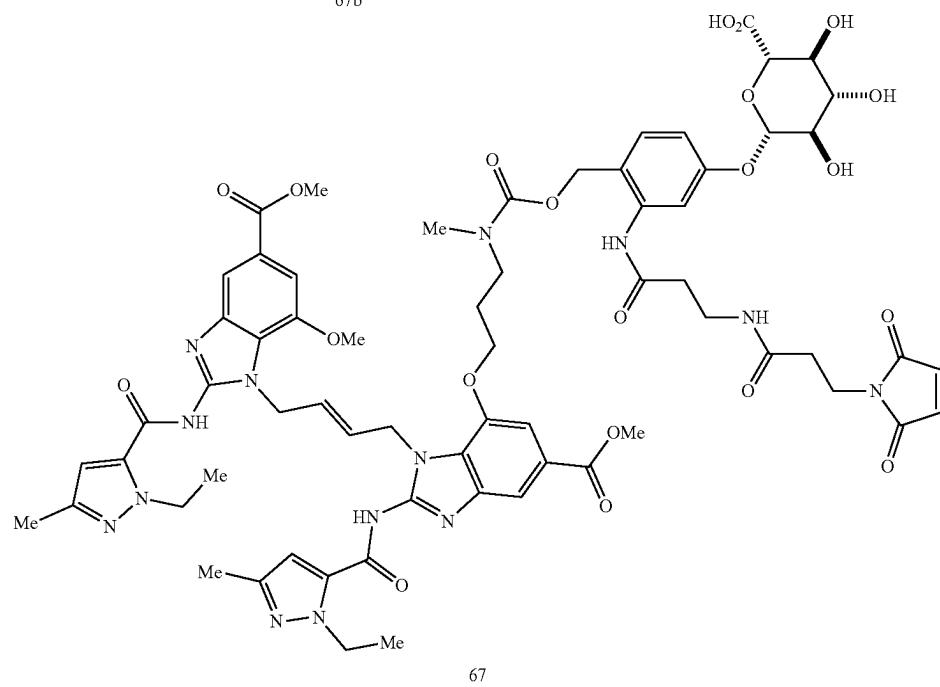
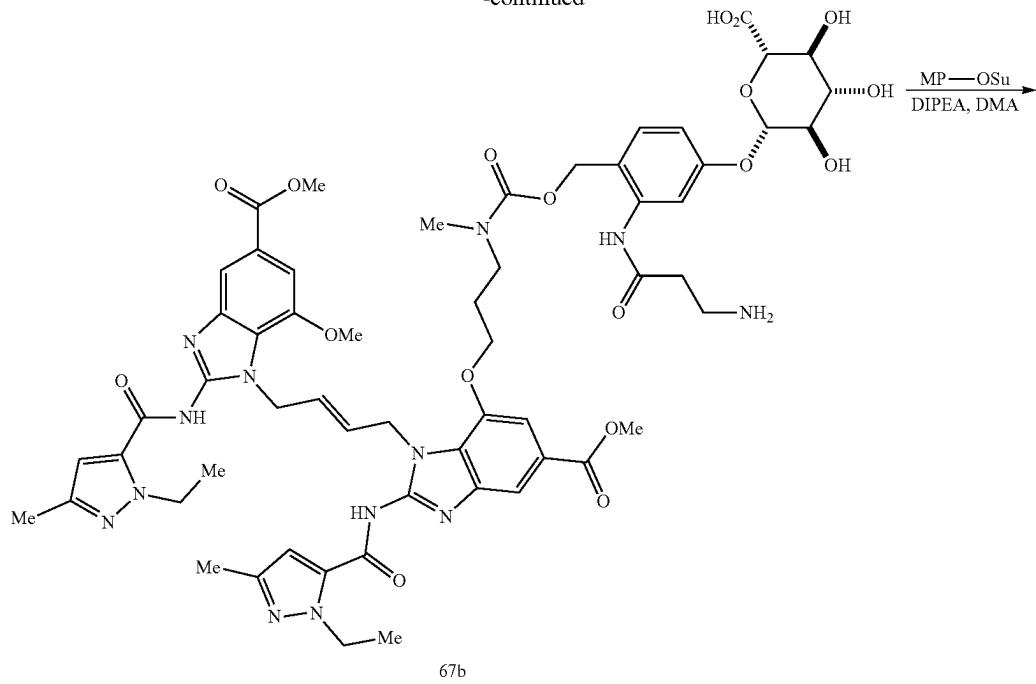
Synthesis of 66

[1604] Compound 66 (25 mg, 0.0291 mmol, 1 equiv.) and MP-OSu (11.6 mg, 0.0436 mmol, 1.5 equiv.) were dissolved in DMA (0.58 mL) and DIPEA (20 μL, 0.116 mmol) was added. The reaction was stirred at room temperature for 1 hour. The mixture was directly purified by prepHPLC (Method H, with 0.05% TFA) to afford 66 as a white solid (10.88 mg, 0.0112 mmol, 38% yield). MS (Method D, ESI+): m/z [M+H]⁺ = 975.4 (theoretical); 975.4 (observed). HPLC retention time: 2.24 min.

Synthesis of (2S,3S,4S,5R,6S)-6-(3-(3-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanamido)propanamido)-4-(((3-((2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-((E)-4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-5-(methoxycarbonyl)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-5-(methoxycarbonyl)-1H-benzo[d]imidazol-7-yl)oxy)propyl)(methyl)carbamoyl)oxy)methyl)phenoxy)-3,4,5-trihydroxytetrahydro-2H-pyran-2-carboxylic acid (Compound 67)



-continued



Synthesis of 67a

[1605] Compound 13a (65 mg, 0.0868 mmol, 1.4 equiv.) and bis(pentafluorophenyl) carbonate (120 mg, 0.304 mmol, 5 equiv.) were dissolved in DMA (0.43 mL) and DIPEA (70 μ L, 0.404 mmol, 6.7 equiv.) was added. The reaction was stirred for 30 minutes and then 66b (52 mg, 0.0607 mmol, 1 equiv.) was added. The reaction was stirred at room temperature for 18 hours. The solution was diluted with H_2O and extracted with EtOAc (3 \times), and the combined organics

were washed with 1M HCl (3 \times), dried with $MgSO_4$, filtered and solvent removed in vacuo to give a crude solid. This material was dissolved in DMSO and purified by prepHPLC (Method H, with 0.05% TFA) to give 67a as a white solid (33.1 mg, 0.0207 mmol, 34% yield). LCMS (Method D, ESI+) m/z [M+H]⁺ 1598.6 (theoretical), 1598.6 (observed). LCMS retention time 2.65 min.

[1606] MS (Method D, ESI+): m/z [M+H]⁺=1598.6 (theoretical); 1598.6 (observed). HPLC retention time: 2.65 min.

Synthesis of 67b

[1607] Compound 67a (33.1 mg, 0.0207 mmol) was dissolved in dry methanol (0.21 mL), cooled in an ice bath, and 0.5M NaOMe in MeOH (41.5 μ L, 0.0414 mmol, 2 equiv.) was added. The reaction was monitored by LCMS (Method D) and upon full acetate deprotection, 1M LiOH (62 μ L, 0.0621 mmol, 3 equiv.) was added. The reaction stirred at room temperature for 1h monitoring by LCMS (Method E). Upon full conversion, acetic acid (62 L) was added, solvent removed in vacuo and crude product purified via prepHPLC (Method H, with 0.05% TFA) to give 67b as a white solid (10.1 mg, 0.0075 mmol, 36% yield). LCMS (Method D, ESI+) m/z [M+H]⁺ 1236.5 (theoretical), 1236.5 (observed). LCMS retention time 2.31 min.

[1608] MS (Method D, ESI+): m/z [M+H]⁺=1236.5 (theoretical); 1236.5 (observed). HPLC retention time: 2.31 min.

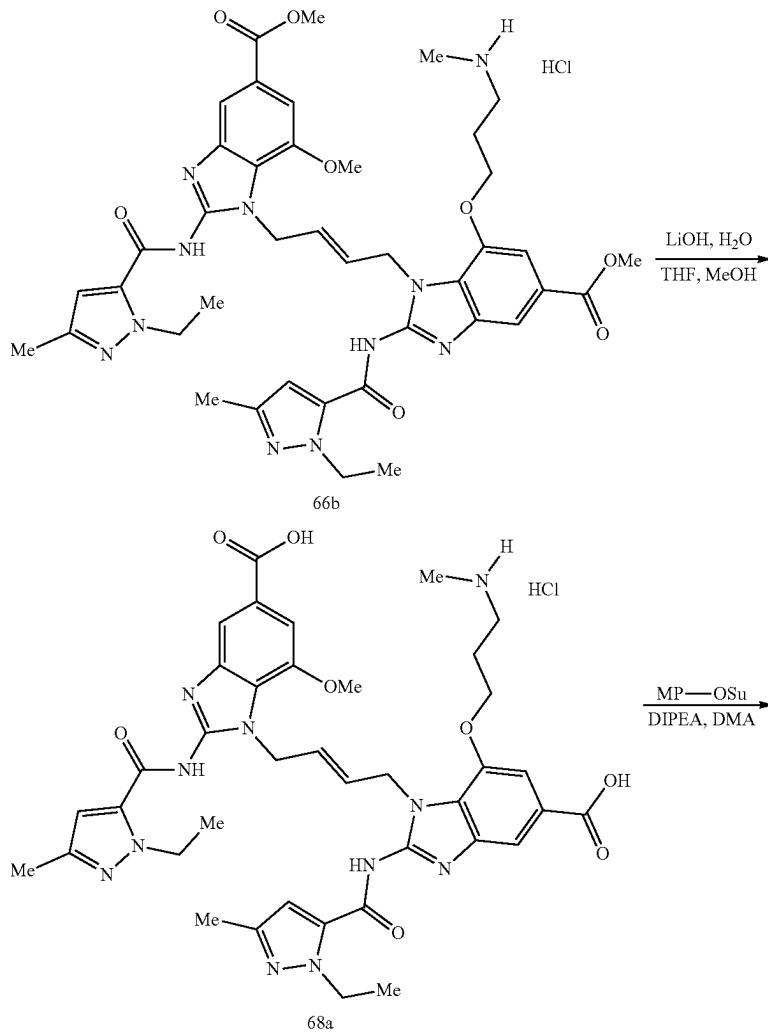
Synthesis of 67

[1609] Compound 67b (10.1 mg, 0.0075 mmol, 1 equiv.) and MP-OSu (3.0 mg, 0.0112 mmol, 1.5 equiv.) were

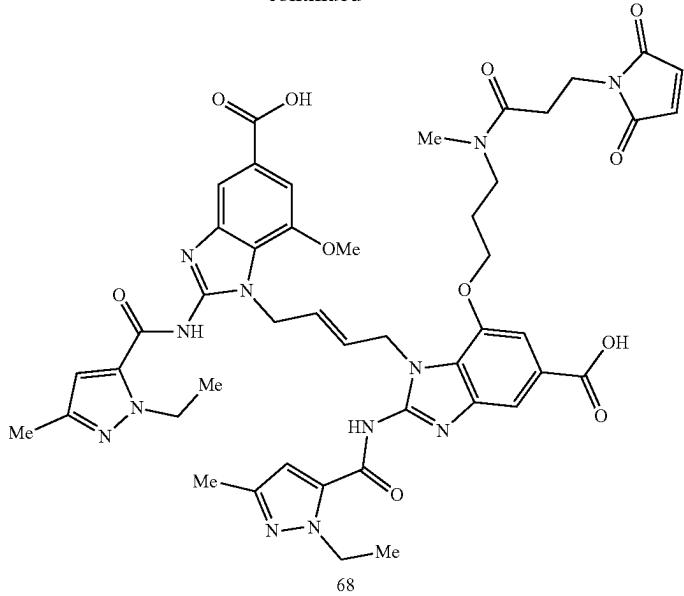
dissolved in DMA (150 μ L), DIPEA (4 μ L, 0.0224 mmol) was added. The reaction was stirred for 30 min at room temperature at which point acetic acid (4 μ L) was added, and the mixture was purified via prepHPLC (Method G, with 0.05% TFA) to obtain 67 as a white solid (3.3 mg, 0.0024 mmol, 32% yield). LCMS (Method E, ESI+) m/z [M+H]⁺ 1387.5 (theoretical), 1387.5 (observed). LCMS retention time 1.92 min.

[1610] MS (Method E, ESI+): m/z [M+H]⁺=1387.5 (theoretical); 1387.5 (observed). HPLC retention time: 1.92 min.

Synthesis of (E)-1-(4-(5-carboxy-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-N-methylpropanamido)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazole-5-carboxylic acid (Compound 68)



-continued



Synthesis of 68a

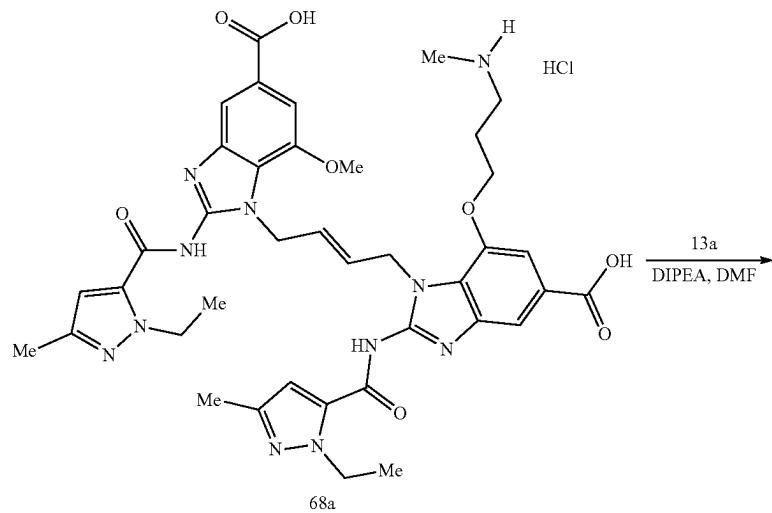
[1611] Compound 66b (30 mg, 0.032 mmol) was dissolved in methanol (0.32 mL) and 1M LiOH (0.256 mL, 0.256 mmols, 8 equiv.) was added. The mixture was stirred at 80° C. for 1h. The mixture was concentrated in vacuo and purified via prepHPLC (Method H with 0.05% TFA) to afford 68a as a white solid (17.4 mg, 0.0191 mmol, 60% yield). MS (Method D, ESI+): m/z [M+H]⁺=796.4 (theoretical); 796.4 (observed). HPLC retention time: 1.83 min.

Synthesis of 68

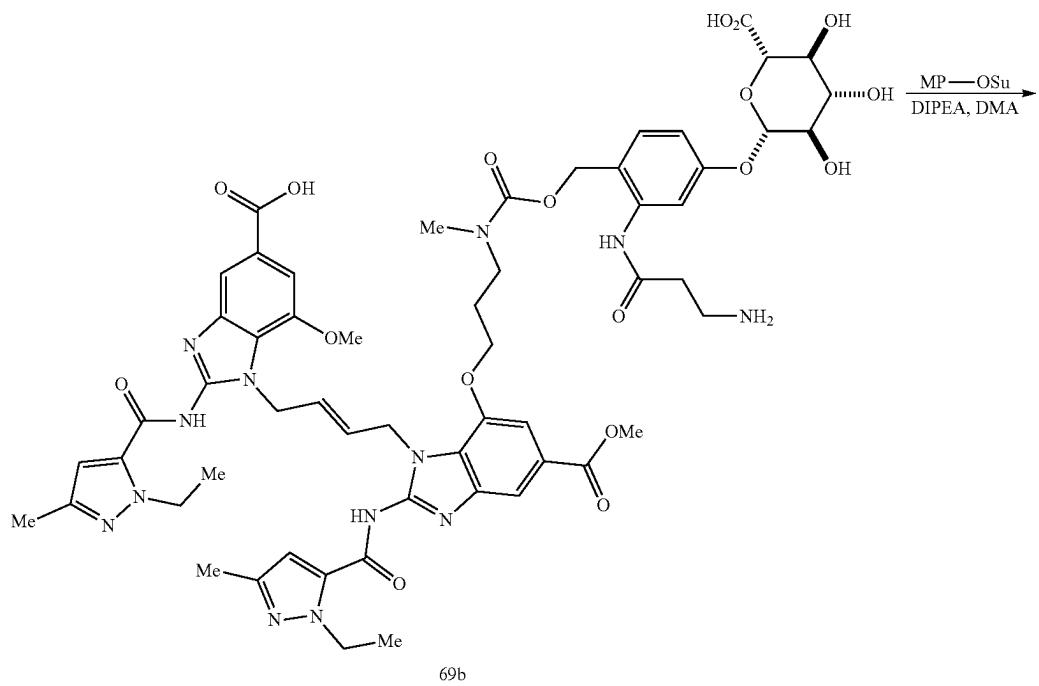
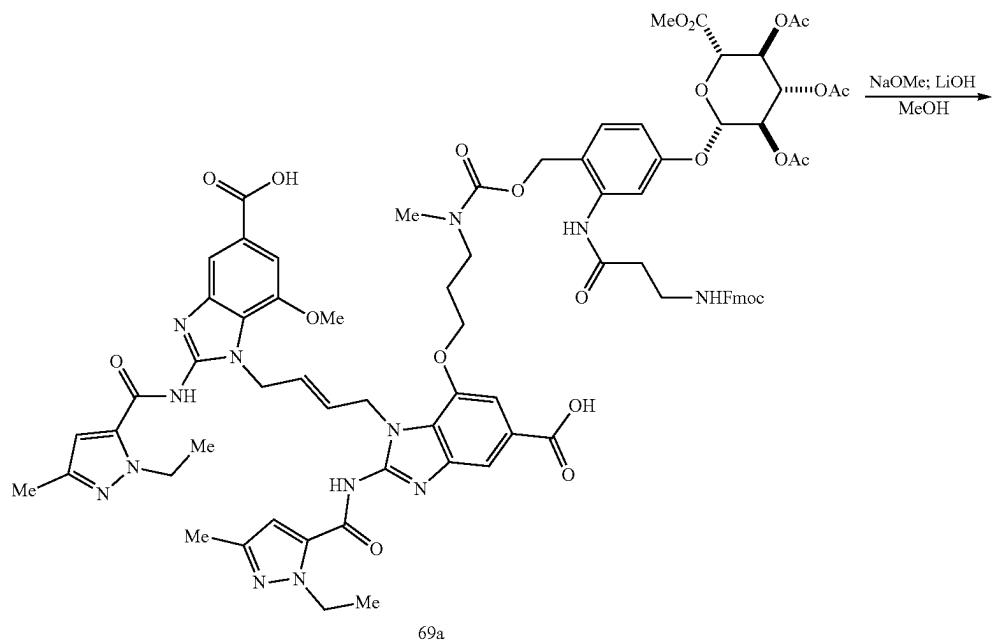
[1612] Compound 68a (16.7 mg, 0.0183 mmol, 1 equiv.) and MP-OSu (7.3 mg, 0.0275 mmol, 1.5 equiv.) were dissolved in DMA (0.37 mL) and DIPEA (10 μ L, 0.0574 mmol, 2 equiv.) was added. The reaction was stirred at room

temperature for 1 hour, AcOH (10 μ L) was added and the crude product was purified via prepHPLC (Method H with 0.05% TFA) to afford 68 as a white solid (7.6 mg, 0.0080 mmol, 44% yield). MS (Method D, ESI+): m/z [M+H]⁺=974.4 (theoretical); 974.4 (observed). HPLC retention time: 2.42 min.

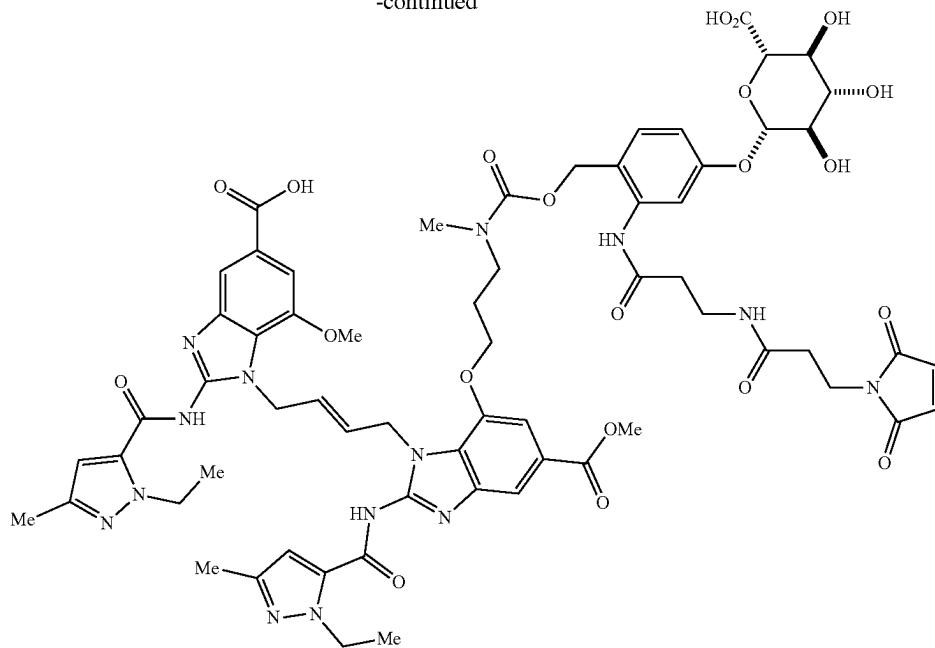
Synthesis of 1-((E)-4-(5-carboxy-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(3-(((4-((2S,3R,4S,5S,6S)-6-carboxy-3,4,5-trihydroxytetrahydro-2H-pyran-2-yl)oxy)-2-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanamido)propanamidobenzyl)oxy)carbonyl) (methyl)amino propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazole-5-carboxylic acid (Compound 69)



-continued



-continued



69

Synthesis of 69a

[1613] Compound 69a was prepared as previously described (see “Synthesis of 67a”). MS (Method E, ESI+): m/z [M+H]⁺=1570.6 (theoretical); 1570.4 (observed). HPLC retention time: 1.95 min.

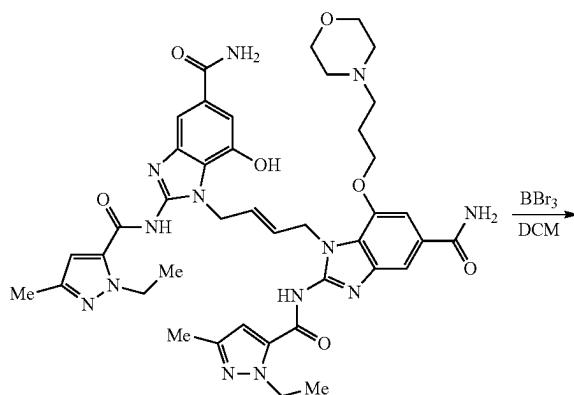
Synthesis of 69b

[1614] Compound 69b was prepared as previously described (see “Synthesis of 67b”). MS (Method E, ESI+): m/z [M+H]⁺=1208.5 (theoretical); 1208.3 (observed). HPLC retention time: 1.48 min.

Synthesis of 69

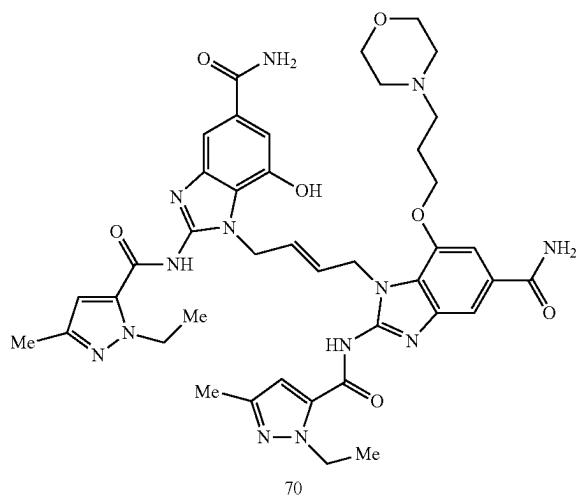
[1615] Compound 69 was prepared as previously described (see “Synthesis of 67”). MS (Method E, ESI+): m/z [M+H]⁺=1359.5 (theoretical); 1359.4 (observed). HPLC retention time: 1.68 min.

Synthesis of (E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-(3-morpholinopropoxy)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxamide (Compound 701)



-continued

Synthesis of 70



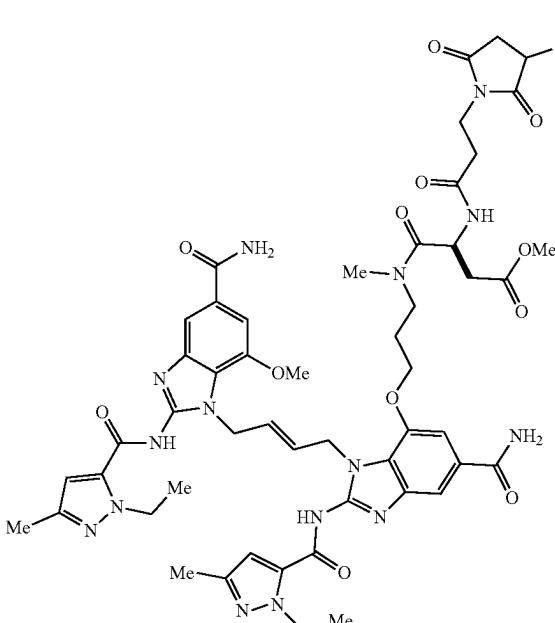
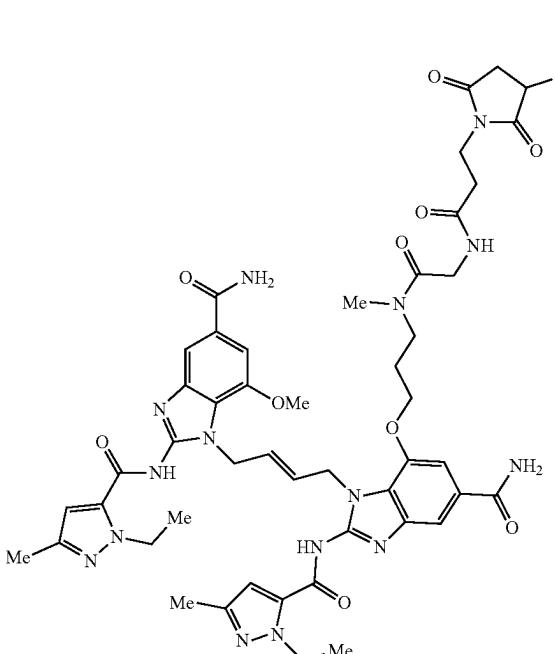
[1616] To a solution of compound A (6 mg, 0.00706 mmol) in dry DCM (0.10 mL) was added BBr_3 (0.04 mL, 1M in DCM) dropwise. The slurry that formed was stirred overnight at 30° C. under argon. The reaction was monitored by UPLC-MS. Upon completion, cold water (0.10 mL) was added and the mixture was stirred vigorously. After 30 min., the solvent was evaporated, and the product purified by prepHPLC (Method G) using formic acid as the additive. Pure fractions were collected, frozen, and lyophilized to afford compound 70 (5.14 mg, 0.00528 mmol, 75% yield) as a white solid. UPLC-MS (Method D, EST+): m/z [M+H]⁺ = 836.9 (theoretical), 836.6 (observed). HPLC retention time: 1.34 min.

[1617] The cysteine adducts of compounds 17-24 were prepared using the following method.

[1618] General Method 6. A 10 mM solution of maleimide was incubated with 1 equiv. of L-cysteine (100 mM in water) at 37° C. for 1 hour and the product used without any further purification.

Compound	Structure	LC-MS data
71		RT: 1.17 Theoretical: 1181.5 Observed: 1182.1

-continued

Compound	Structure	LC-MS data
72		RT: 1.21 Theoretical: 1195.5 Observed: 1195.7
73		RT: 1.17 Theoretical: 1123.5 Observed: 1124.0

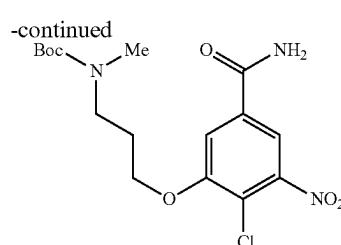
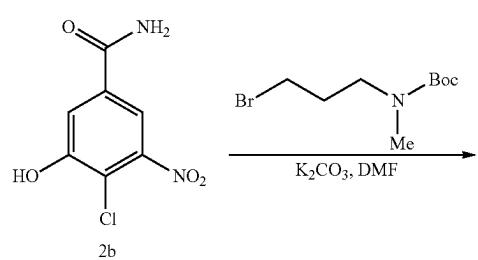
-continued

Compound	Structure	LC-MS data
74		RT: 1.19 Theoretical: 1137.5 Observed: 1137.9
75		RT: 1.16 Theoretical: 1153.5 Observed: 1153.8

-continued

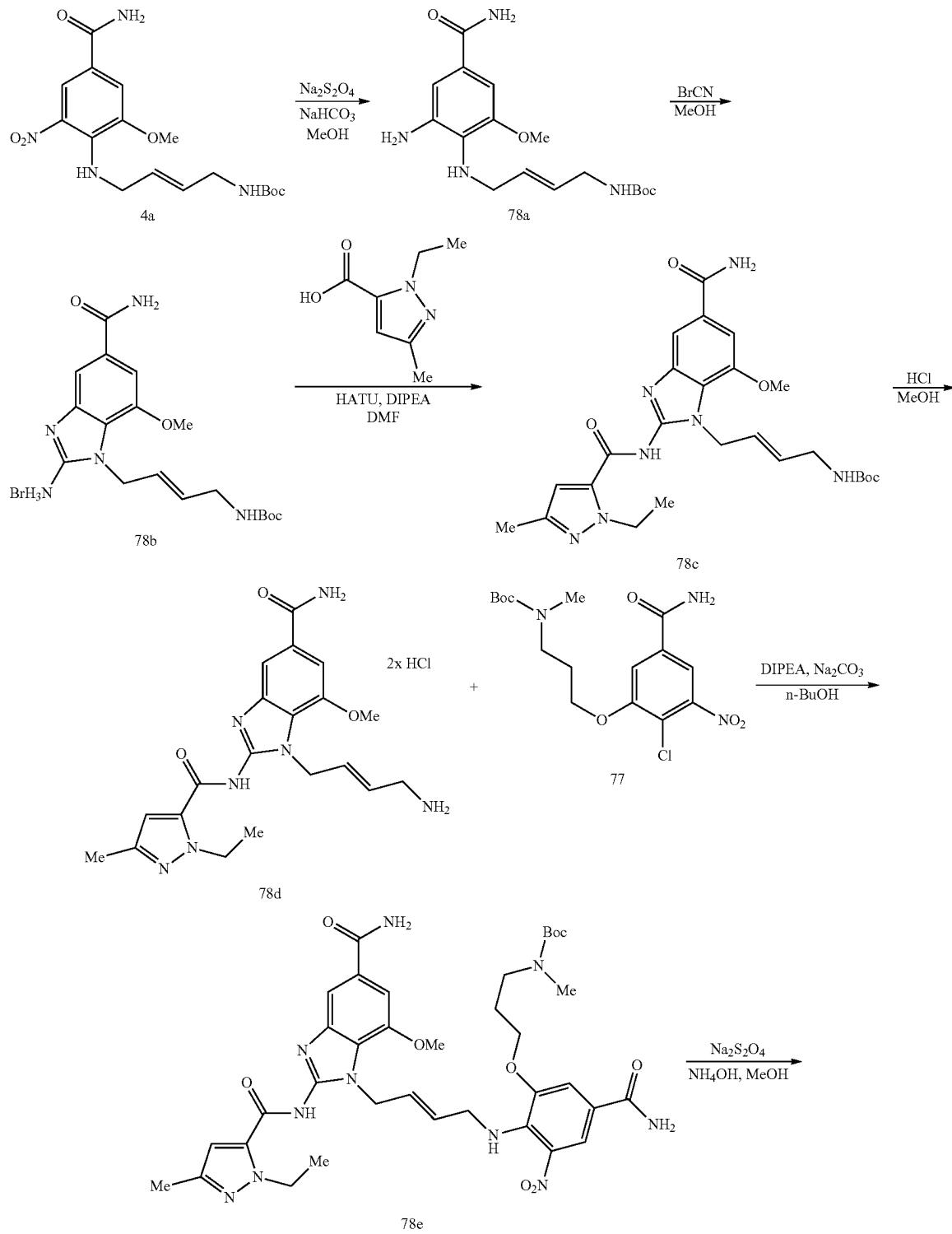
Compound	Structure	LC-MS data
76		RT: 1.19 Theoretical: 1167.5 Observed: 1168.0

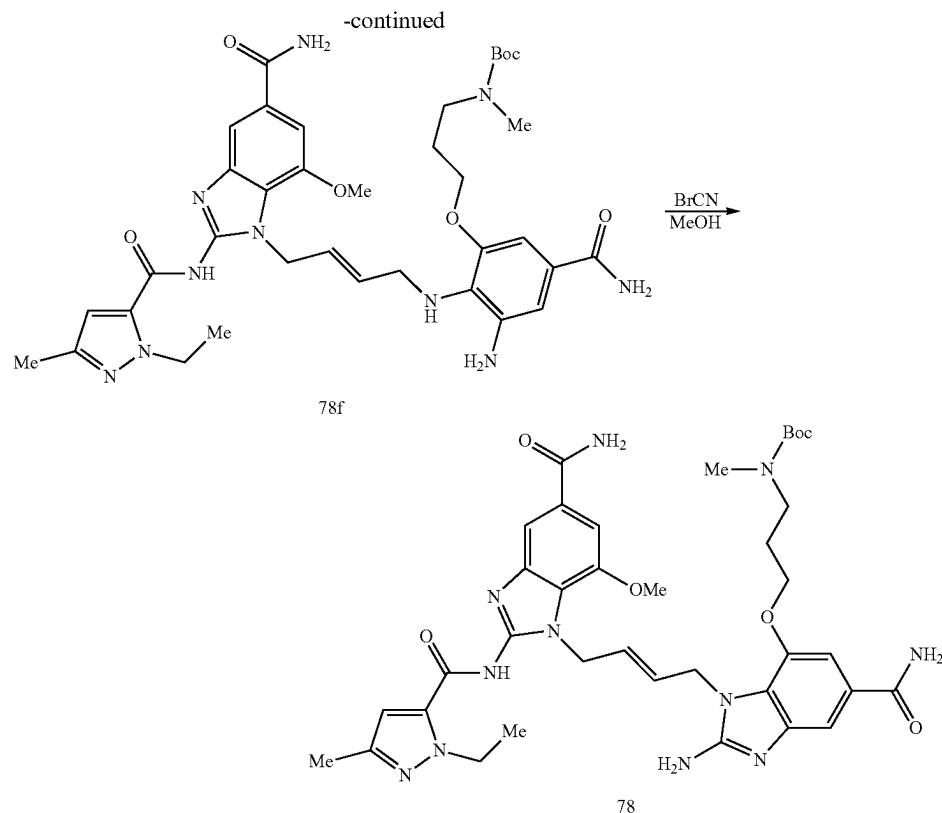
Synthesis of tert-butyl (3-(5-carbamoyl-2-chloro-3-nitrophenoxy)propyl)(methyl)carbamate (Compound 77)



[1619] A flame-dried 100 mL RB with stir bar was charged with a solution of 2b (1.0 g, 4.62 mmol, 1 equiv.) in DMF (10 mL), potassium carbonate (830 mg, 6.00 mmol, 1.3 equiv.) and a solution of tert-butyl N-(3-bromopropyl)-N-methyl-carbamate (1.20 eq, 1.40 g, 5.54 mmol, 1.20 equiv.) in DMF (5 mL). Additional DMF was added to bring the total volume to 45 mL and the reaction was heated to 70° C. for 24 hours. The reaction was cooled to room temperature and filtered over celite washing with DMF (3×10 mL). This solution was poured into ice water (900 mL), stirred for 90 minutes and crude product isolated via filtration. Finally, the filtrate was washed with cold water (300 mL) and dried in vacuo overnight to give 77 (1.23 g, 3.16 mmol, 68% yield).

Synthesis of tert-butyl (E)-(3-((2-amino-5-carbamoyl-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazol-7-yl)oxy)propyl)(methyl)carbamate (Compound 78)





Synthesis of 78a

[1620] A 500 mL round bottom flask with stir bar was charged with 4a (3.0 g, 7.9 mmol, 1 equiv.) and sodium bicarbonate (12.5 g, 148 mmol, 19 equiv.) and ethanol (105 mL) was added to give a heterogenous solution. This solution was cooled in an ice-bath and a solution of sodium hydrosulfite (25.8 g, 148 mmol, 19 equiv.) in 105 mL water was added dropwise at such a rate to keep the internal temperature below 10° C. The mixture was heated open to the atmosphere to 45° C. for 1 hour and cooled to room temperature. The mixture was filtered over celite, washing with EtOH (100 mL) and solvent removed in vacuo. The crude material was redissolved in 1:1 DCM:MeOH (200 mL), filtered over celite and solvent removed in vacuo. This procedure was repeated once more and then the crude product was loaded onto celite and purified by flash chromatography (50 g Sfar HC Duo, SiO₂ column, 0-40% 10:1 NH₄OH:MeOH in DCM) to give 78a (1.45 g, 4.13 mmol, 52% yield). MS (Method D, ESI+): m/z [M+H]⁺=351.2 (theoretical); 351.1 (observed). HPLC retention time: 1.53 min.

Synthesis of 78b

[1621] An oven-dried 200 mL round bottom flask was charged with 78a (1.95 g, 5.58 mmol, 1 equiv.) which was dissolved in methanol (45 mL) and cyanogen bromide (3M in DCM, 5.6 mL, 16.7 mmol, 3 equiv.) was added to give a yellow homogenous solution. The reaction was stirred at room temperature for 48 hours and solvent removed in vacuo to give 78b as the HBr salt (2.48 g, 5.44 mmol, 98%

yield). MS (Method D, ESI+): m/z [M+H]⁺=376.2 (theoretical); 376.1 (observed). HPLC retention time: 0.71 min.

Synthesis of 78c

[1622] A flame dried 40 mL vial with stir bar was charged with 78b HBr (867 mg, 1.90 mmol, 1 equiv.), 2-ethyl-5-methyl-pyrazole-3-carboxylic acid (879 mg, 5.70 mmol, 3 equiv.), and HATU (2.17 g, 5.70 mmol, 3 equiv.). The solids were dissolved in DMF (15 mL) and then DIPEA (2.0 mL, 11.4 mmol, 6 equiv.) was added. The vial was sealed and stirred at room temperature for 48 hours. The solution was poured into ice-cold water (450 mL) with NH₄OH (28% NH₃ in water, 10 mL) and allowed to precipitate at 4° C. overnight. The white precipitate was isolated via filtration and dried in vacuo overnight to give 78c (658 mg, 1.29 mmol, 68% yield). MS (Method D, ESI+): m/z [M+H]⁺=512.3 (theoretical); 512.2 (observed). HPLC retention time: 2.35 min.

Synthesis of 78d

[1623] An oven dried 8 mL vial with stir bar was charged with 78c (800 mg, 1.56 mmol, 3 equiv.) which was stirred in 3M HCl in MeOH (5.2 mL, 15.6 mmol HCl, 10 equiv.) for 1 hour. The solvent removed in vacuo to give 78d as the 2×HCl salt (700 mg, 1.56 mmol, quantitative yield). MS (Method D, ESI+): m/z [M+H]⁺=412.2 (theoretical); 412.5 (observed). HPLC retention time: 0.73 min.

Synthesis of 78e

[1624] An oven-dried 20 mL microwave vial was charged with 78e (700 mg, 1.56 mmol, 1 equiv.), 77 (909 mg, 2.34

mmol, 1.5 equiv.) and sodium carbonate (497 mg, 4.69 mmol, 3 equiv.) and to the mixture was added 1-butanol (15 mL) and DIPEA (1.6 mL, 9.38 mmol, 6 equiv.). The vial was sealed and heated in a microwave reactor at 140° C. for 3 hours to give a bright red heterogenous mixture. This mixture was poured into DCM (100 mL) and filtered over celite washing with DCM (50 mL) and MeOH (50 mL). The crude product was loaded onto celite and purified via flash chromatography (50 g Sfar HC Duo, SiO₂ column, 0-20% MeOH in DCM) to give 78e (569 mg, 0.746 mmol, 48% yield) as a bright red solid. MS (Method D, ESI+): m/z [M+H]⁺ 763.4 (theoretical); 763.4 (observed). HPLC retention time: 2.17 min.

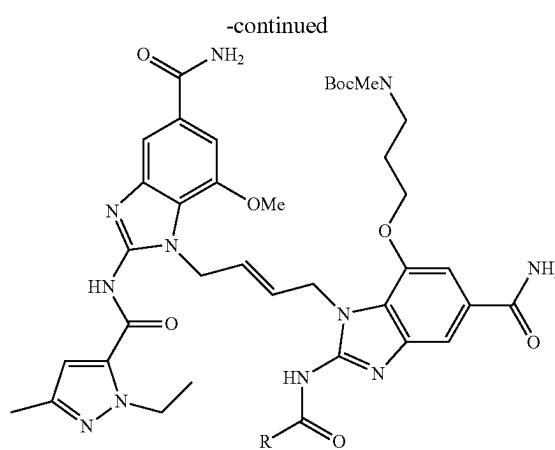
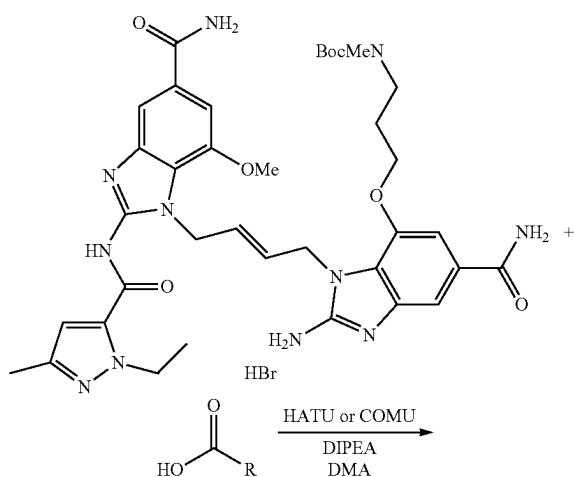
Synthesis of 78f

[1625] To a mixture of 78e (569 mg, 0.746 mmol, 1 equiv.) in methanol (8 mL) and NH₄OH (2.0 mL, 28% NH₃ in water) was added a solution of sodium hydrosulfite (2.34 g, 13.4 mmol, 18 equiv.) in water (8 mL). This solution was heated at 50° C. for 1 hour. The reaction was poured into a separatory funnel containing water (250 mL) and EtOAc (250 mL). The mixture was shaken, layers separated and the aqueous layer was further extracted with EtOAc (3×100 mL). The organics were combined, washed with brine (2×100 mL), dried with MgSO₄, filtered and solvent removed in vacuo to give 78f (400 mg, 0.546 mmol, 73% yield) as a tan solid. MS (Method D, ESI+): m/z [M+H]⁺ = 733.4 (theoretical); 733.6 (observed). HPLC retention time: 1.39 min.

Synthesis of 78

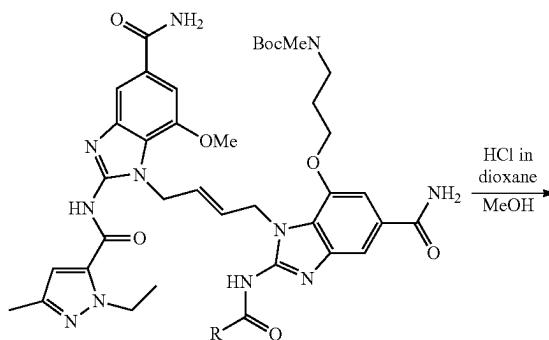
[1626] To a solution of 78f (1.00 eq, 400 mg, 0.546 mmol) in methanol (5.5 mL) was added cyanogen bromide (3M in DCM, 0.55 mL, 1.65 mmol, 3 equiv.) and the mixture was stirred at room temperature for 24 hours. The solvent was removed in vacuo to give 78 as the HBr salt (456 mg, 0.544 mmol, quantitative yield). MS (Method D, ESI+): m/z [M+H]⁺ = 758.4 (theoretical); 758.6 (observed). HPLC retention time: 1.19 min.

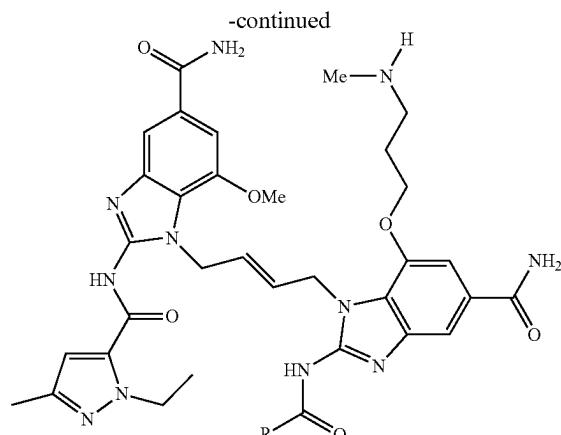
Library Synthesis of Amide Analogs, Group #2. Scheme and General Methods. Compounds 71-95.



[1627] COMU Couplings (General Method 7A): A 2 mL microwave vial was charged with a solution of compound 78 (20 mg, 0.0238 mmol, 1 equiv.) in DMA (0.50 mL). The respective carboxylic acid (2 equiv.), COMU (20.4 mg, 0.0477 mmol, 2 equiv.) and DIPEA (20.8 μL, 0.119 mmol, 5 equiv.) were added. The vial was sealed and heated to 80° C. in a microwave reactor for 1h. The reaction was monitored via UPLC-MS (Method E, ESI+). Upon completion, acetic acid (20 μL) was added and the resulting product was purified by prepHPLC (Method H) using 0.05% TFA as the additive. Pure fractions were collected, frozen, and lyophilized to afford product as a white solid.

[1628] HATU Couplings (General Method 7B): A 2 mL microwave vial was charged with a solution of compound 78 (20 mg, 0.0238 mmol, 1 equiv.) in DMA (0.50 mL). The respective carboxylic acid (4 equiv.), HATU (36.3 mg, 0.0954 mmol, 2 equiv.) and DIPEA (20.8 μL, 0.119 mmol, 5 equiv.) were added. The vial was sealed and heated to 80° C. a microwave reactor for 1h. The reaction was monitored via UPLC-MS (Method E, ESI+). Upon completion, acetic acid (20 L) was added and the resulting product was purified by prepHPLC (Method H) using 0.05% TFA as the additive. Pure fractions were collected, frozen, and lyophilized to afford product as a white solid.

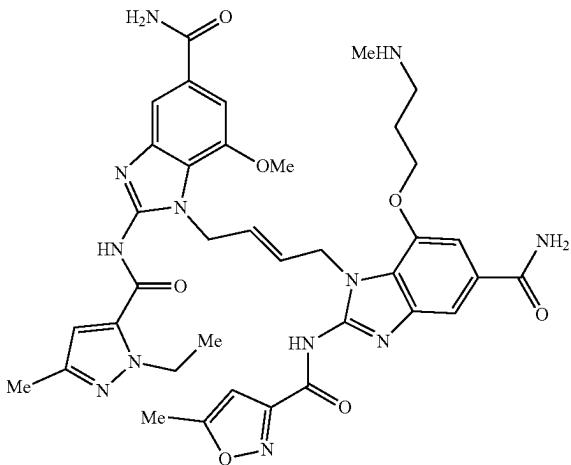
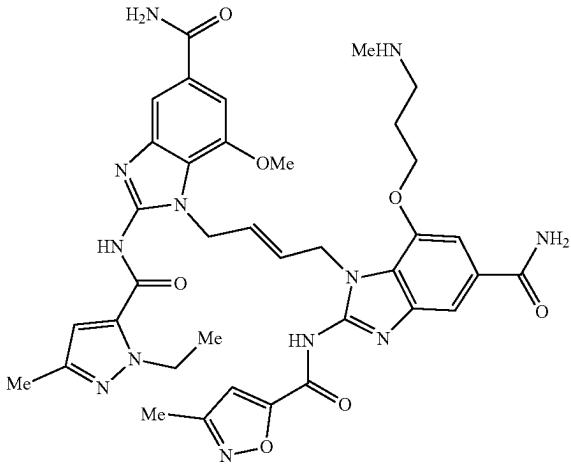
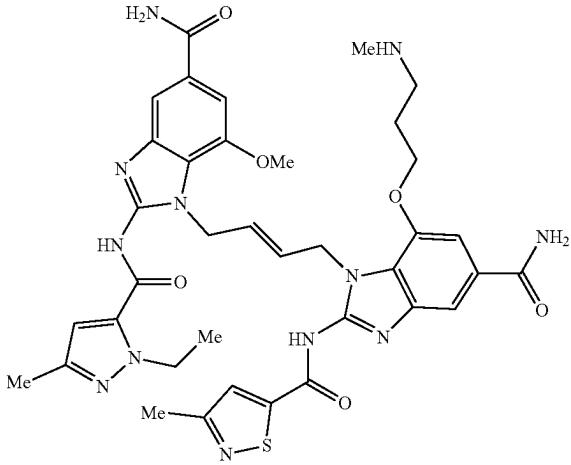




[1629] Boc Deprotection (General Method 8): The resulting product general method 7A or 7B was dissolved in MeOH (0.01 M), to which 4M HCl in dioxane (8 equiv.) was added. The solution stirred at room temperature for 30 min. The reaction was monitored via UPLC-MS (Method E, ESI+). Upon completion, the solution was concentrated, redissolved in DMSO, and purified via prepHPLC (Method G or H) using TFA as the additive. Pure fractions were collected, frozen, and lyophilized to afford product as a white solid.

Cmpd.	Structure	Method	Boc LC-MS data	Amine LC-MS data	Yield (over 2 steps)
79	<p>Detailed description: Compound 79 is a complex organic molecule. It consists of a purine core substituted with a 2-aminoethyl group (-NH2-CH2-), a 6-methoxy group (-OMe), and a 9-(2-((S)-2-methylpropyl)amino)ethyl side chain. The side chain includes a methylene group attached to a methyl group and an amino group, which is further linked to a propyl chain.</p>	7A	RT: 1.57 Theoretical: 864.4 Observed: 864.7	Theoretical: RT: 1.32 764.3 Observed: 764.4	17% 4.5 mg 0.00406 mmol
80	<p>Detailed description: Compound 80 is similar to compound 79 but with a different side chain. It features a purine core with a 2-aminoethyl group (-NH2-CH2-), a 6-methoxy group (-OMe), and a 9-(2-(4-pyridylmethyl)amino)ethyl side chain. The side chain includes a methylene group attached to a pyridyl ring and an amino group, which is further linked to a propyl chain.</p>	7A	RT: 2.18 Theoretical: 864.4 Observed: 864.4	Theoretical: RT: 1.24 764.3 Observed: 764.4	19% 5.0 mg 0.00455 mmol

-continued

Cmpd.	Structure	Method	Boc LC-MS data	Amine LC-MS data	Yield (over 2 steps)
81		7A	RT: 1.79 Theoretical: 867.4 Observed: 867.7	Theoretical: RT: 1.55 767.3 Observed: 767.3	18% 4.8 mg 0.00436 mmol
82		7A	RT: 1.83 Theoretical: 867.4 Observed: 967.4	Theoretical: RT: 1.37 767.3 Observed: 767.3	9% 2.4 mg 0.00216 mmol
83		7B	RT: 1.85 Theoretical: 883.4 Observed: 883.4	Theoretical: RT: 1.35 783.3 Observed: 783.3	10% 2.8 mg 0.00247 mmol

-continued

Cmpd.	Structure	Method	Boc LC-MS data	Amine LC-MS data	Yield (over 2 steps)
84		7A	RT: 1.69 Theoretical: 864.4 Observed: 864.4	Theoretical: RT: 1.18 764.3 Observed: 764.4	5% 1.2 mg 0.00110 mmol
85		7B	RT: 1.75 Theoretical: 894.4 Observed: 894.5	Theoretical: RT: 1.31 794.4 Observed: 794.4	3% 0.88 mg 0.00077 mmol
86		7B	RT: 1.59 Theoretical: 894.4 Observed: 894.5	Theoretical: RT: 1.19 794.4 Observed: 794.4	11% 3.1 mg 0.00270 mmol

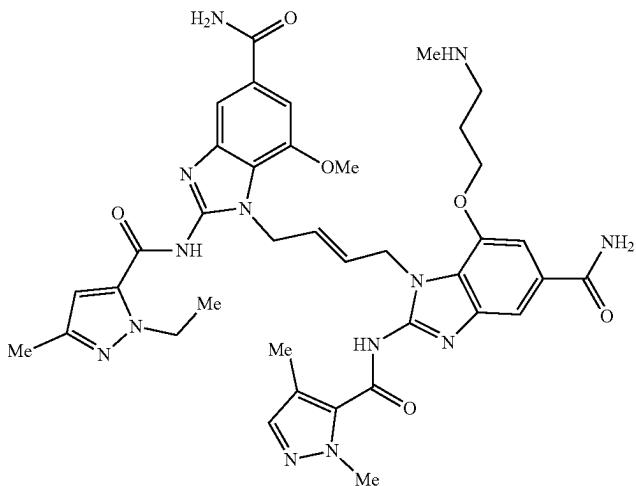
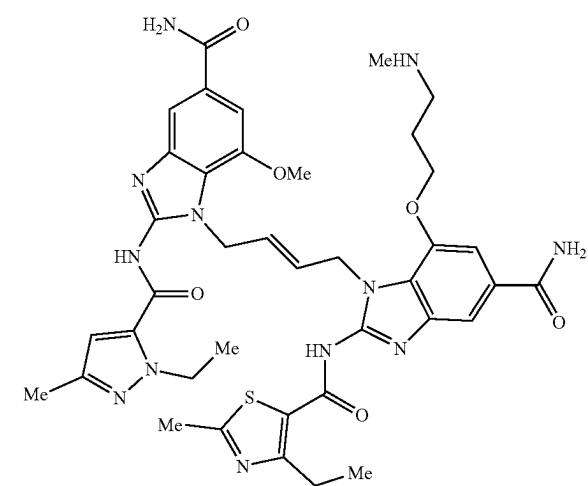
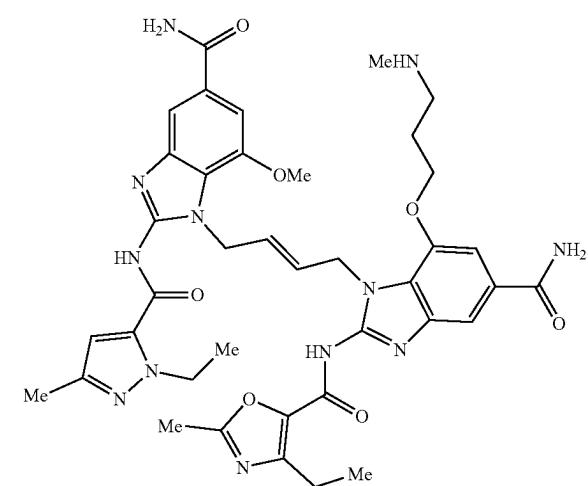
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Cmpd.	Structure	Method	Boc LC-MS data	Amine LC-MS data	Yield (over 2 steps)
87		7B	RT: 1.70 Theoretical: 894.4 Observed: 894.5	Theoretical: RT: 1.38 Observed: 794.4 Theoretical: RT: 1.38 Observed: 794.4	13% 3.5 mg 0.00307 mmol
88		7B	RT: 1.63 Theoretical: 880.4 Observed: 880.5	Theoretical: RT: 1.28 Observed: 780.4 Theoretical: RT: 1.28 Observed: 780.4	16% 4.4 mg 0.00391 mmol
89		7B	RT: 1.77 Theoretical: 894.4 Observed: 894.5	Theoretical: RT: 1.46 Observed: 794.4 Theoretical: RT: 1.46 Observed: 794.4	9% 2.4 mg 0.00211 mmol

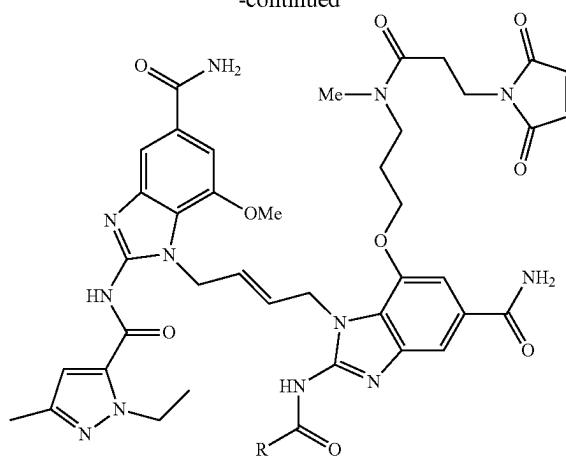
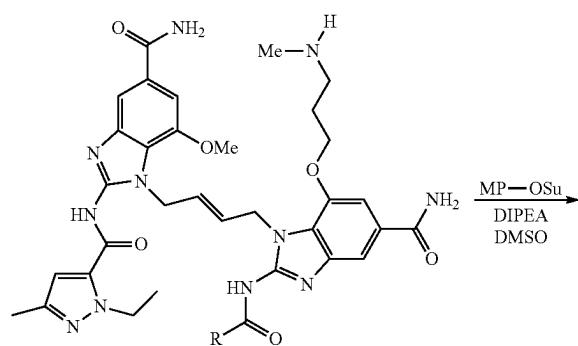
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Cmpd.	Structure	Method	Boc LC-MS data	Amine LC-MS data	Yield (over 2 steps)
90		7B	RT: 1.70 Theoretical: 883.4 Observed: 883.4	Theoretical: RT: 1.30 783.3 Observed: 783.4	17% 4.7 mg 0.00416 mmol
91		7B	RT: 1.65 Theoretical: 880.4 Observed: 880.5	Theoretical: RT: 1.32 780.4 Observed: 780.4	6% 1.7 mg 0.00153 mmol
92		7B	RT: 1.83 Theoretical: 948.4 Observed: 948.5	Theoretical: RT: 1.49 848.4 Observed: 848.4	10% 2.7 mg 0.00229 mmol

-continued

Cmpd.	Structure	Method	Boc LC-MS data	Amine LC-MS data	Yield (over 2 steps)
93		7B	RT: 1.74 Theoretical: 880.4 Observed: 880.5	Theoretical: RT: 1.37 780.4 Observed: 780.4	22% 5.9 mg 0.00529 mmol
94		7B	RT: 1.88 Theoretical: 911.4 Observed: 911.5	Theoretical: RT: 1.38 811.3 Observed: 811.4	30% 8.1 mg 0.00703 mmol
95		7B	RT: 1.86 Theoretical: 895.4 Observed: 895.5	Theoretical: RT: 1.41 795.4 Observed: 795.4	8% 2.1 mg 0.0018 mmol

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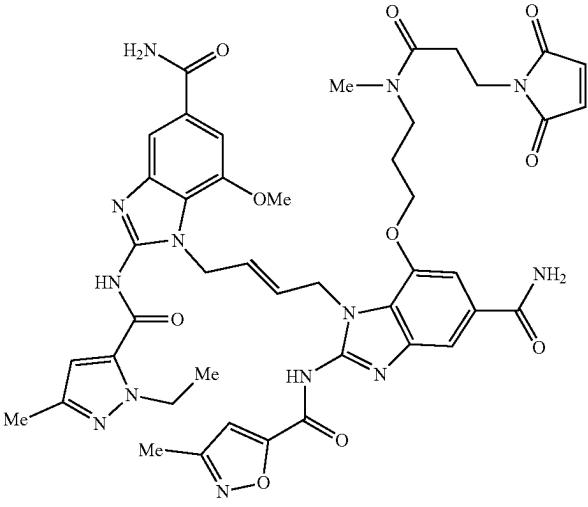
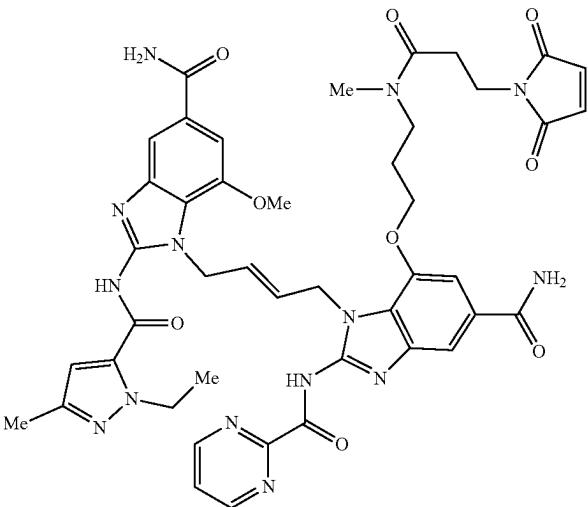
[1630] Maleimide Couplings (General Method 9): The resulting amine from the previous reaction (compounds 79-95) was dissolved in DMSO (0.01M), to which was added MP-OSu (2 equiv.) and DIPEA (5 equiv.). The mixture was stirred at 30° C. overnight, and monitored by UPLC-MS (Method E, ESI+). Upon completion, the resulting product was purified via prepHPLC (Method G) using 0.05% TEA as the additive.

Cmpd.	Structure	LC-MS data	
		$[\text{M} + \text{H}]^+$	Yield
96	 	RT: 1.38 Theoretical: 915.4 Observed: 915.4	68% 3.14 mg 0.0027 mmol

-continued

Cmpd.	Structure	LC-MS data [M + H] ⁺	Yield
97		RT: 1.65 Theoretical: 918.4 Observed: 918.4	62% 3.11 mg 0.0027 mmol
98		RT: 1.42 Theoretical: 915.4 Observed: 915.4	84% 4.38 mg 0.0038 mmol
99		RT: 1.47 Theoretical: 934.3 Observed: 934.4	31% 0.89 mg 0.0008 mmol

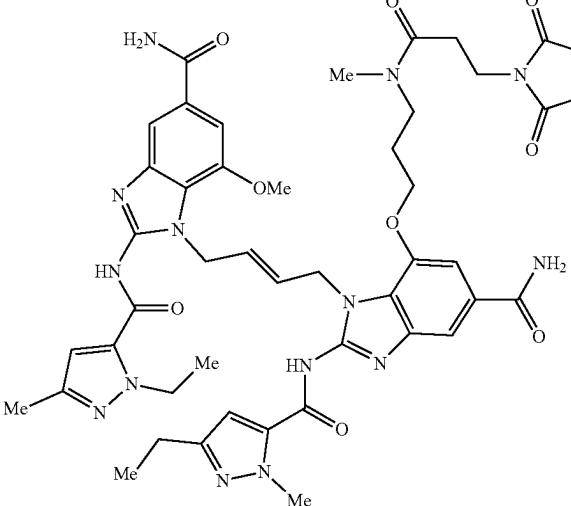
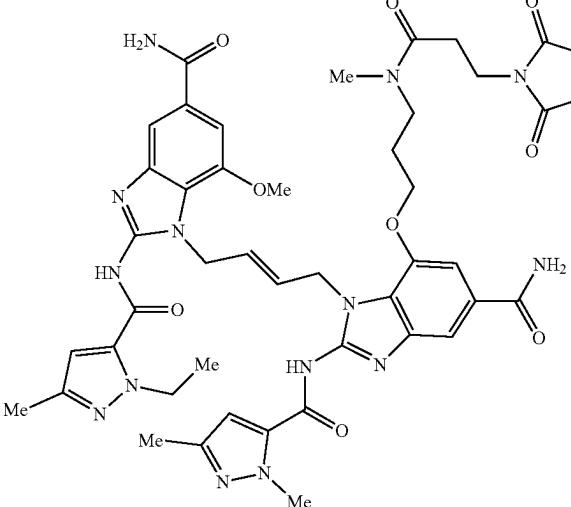
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Cmpd.	Structure	LC-MS data	
		[M + H] ⁺	Yield
100		RT: 1.50 Theoretical: 918.4 Observed: 918.4	53% 1.3 mg 0.0011 mmol
101		RT: 1.35 Theoretical: 915.4 Observed: 915.4	86% 5.88 mg 0.0051 mmol

-continued

Cmpd.	Structure	LC-MS data	
		[M + H] ⁺	Yield
102		RT: 1.45 Theoretical: 945.4 Observed: 945.4	40% 0.36 mg 0.0003 mmol
103		RT: 1.37 Theoretical: 945.4 Observed: 945.4	41% 1.29 mg 0.0011 mmol

-continued

Cmpd.	Structure	LC-MS data	
		[M + H] ⁺	Yield
104		RT: 1.67 Theoretical: 945.4 Observed: 945.5	52% 1.87 mg 0.0016 mmol
105		RT: 1.48 Theoretical: 931.4 Observed: 931.4	88% 4.00 mg 0.0035 mmol

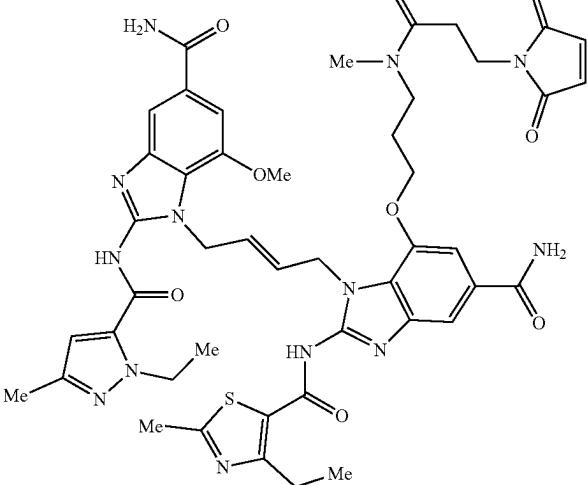
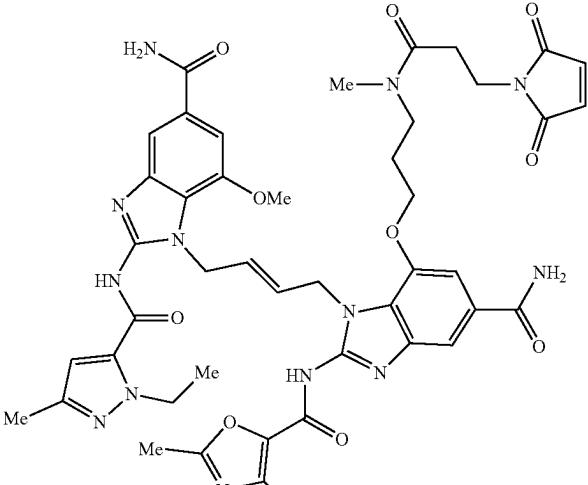
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Cmpd.	Structure	LC-MS data [M + H] ⁺	Yield
106		RT: 1.61 Theoretical: 945.4 Observed: 945.4	31% 0.76 mg 0.0006 mmol
107		RT: 1.45 Theoretical: 934.3 Observed: 934.4	51% 2.46 mg 0.0021 mmol
108		RT: 1.49 Theoretical: 931.4 Observed: 931.4	53% 0.94 mg 0.0008 mmol

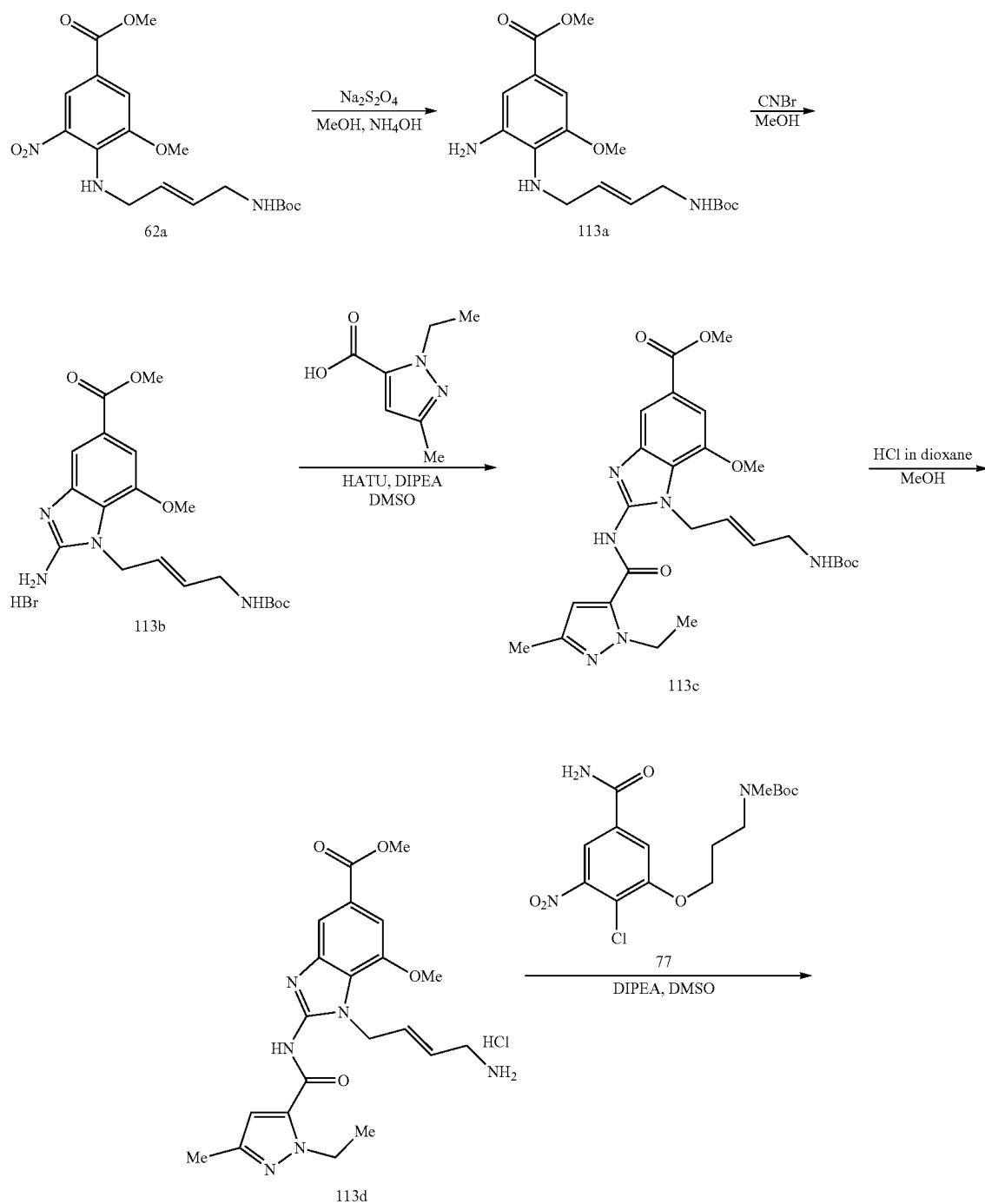
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Cmpd.	Structure	LC-MS data	
		[M + H] ⁺	Yield
109		RT: 1.83 Theoretical: 999.4 Observed: 999.4	51% 1.43 mg 0.0012 mmol
110		RT: 1.50 Theoretical: 931.4 Observed: 931.4	63% 3.86 mg 0.0033 mmol

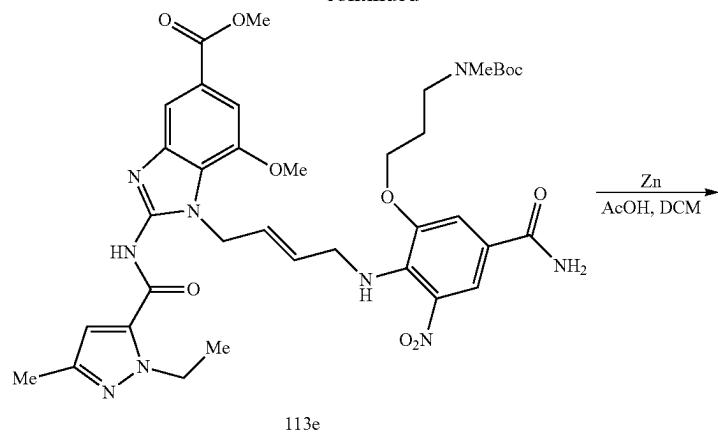
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Cmpd.	Structure	LC-MS data		Yield
		[M + H] ⁺		
111			RT: 1.50 Theoretical: 962.4 Observed: 962.4	40% 3.39 mg 0.0028 mmol
112			RT: 1.59 Theoretical: 946.4 Observed: 946.4	31% 0.67 mg 0.0006 mmol

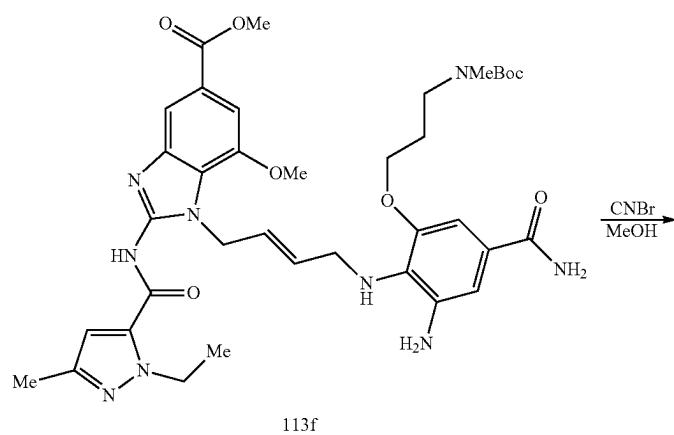
Synthesis of methyl (E)-1-(4-(5-carbamoyl-7-(3-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-N-methylpropanamido)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxylate (Compound 113)



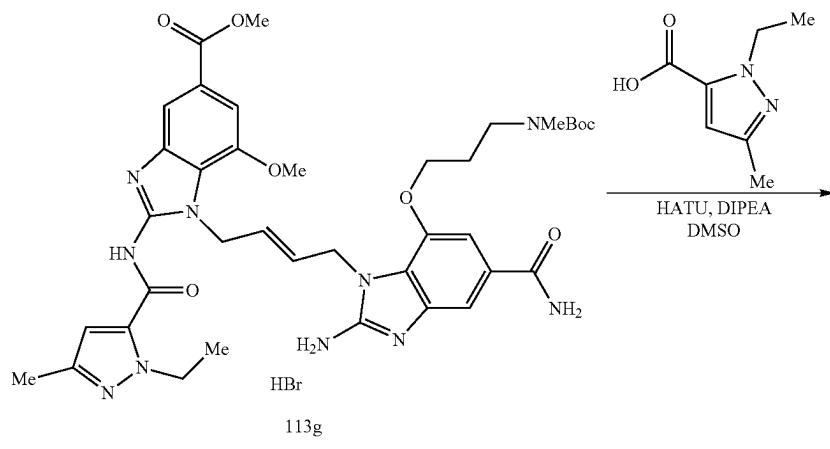
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113e

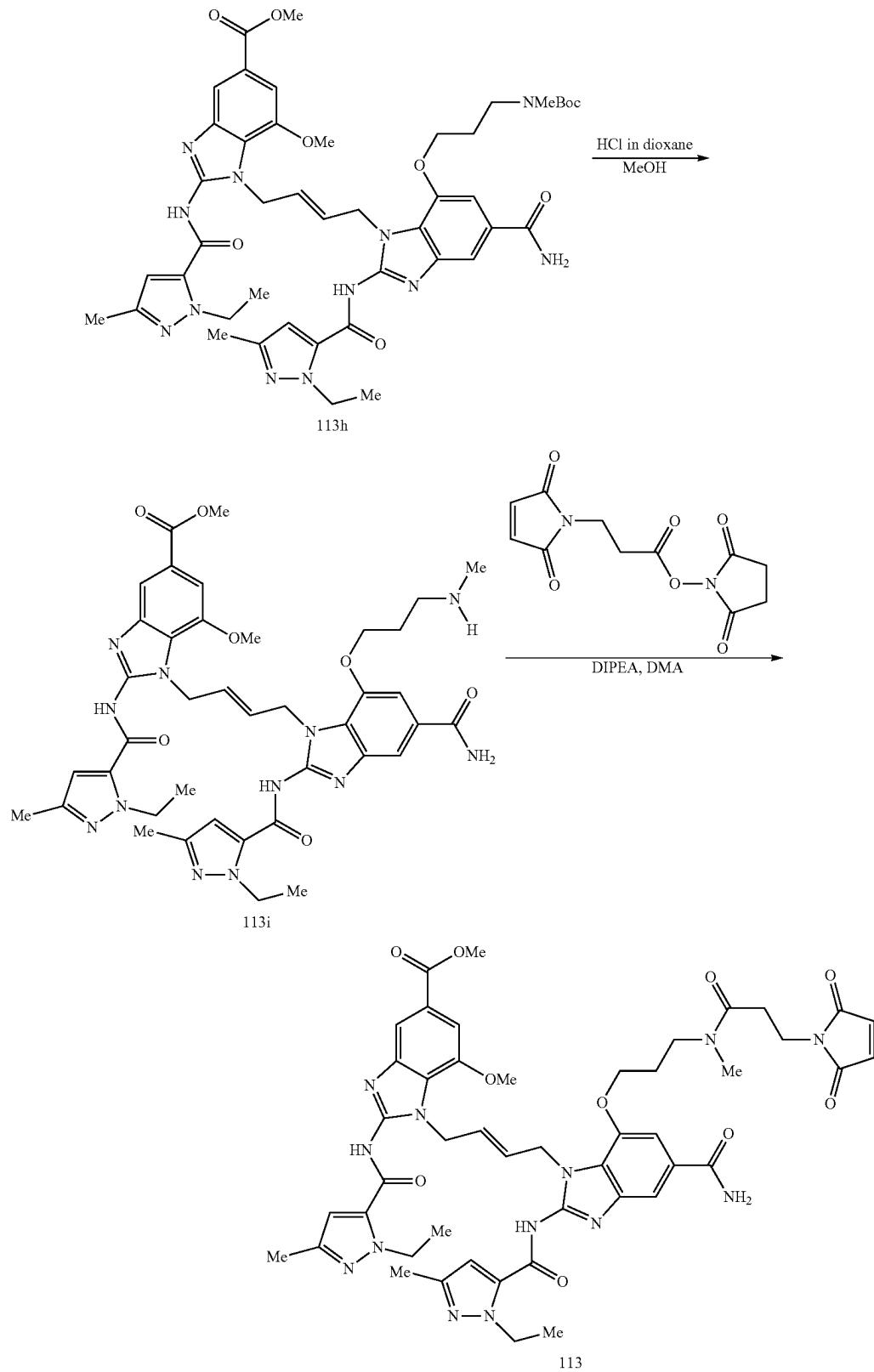


113f

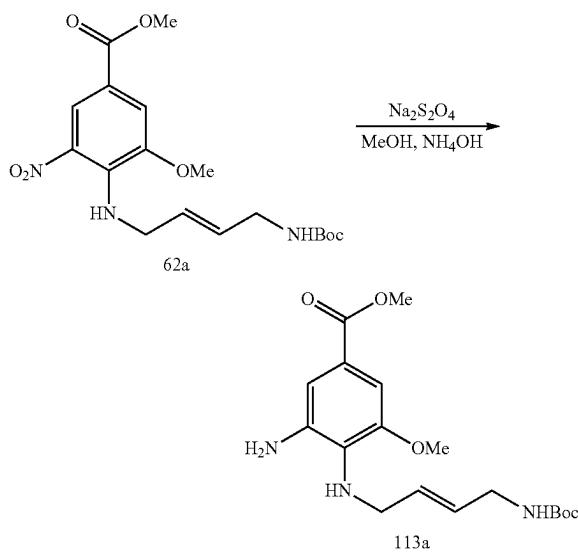


113g

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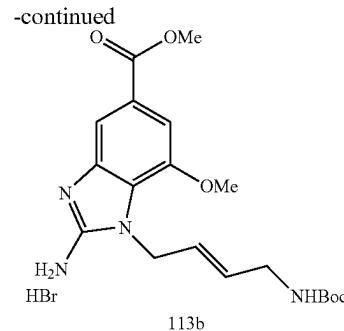
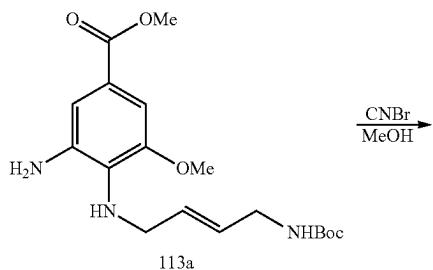


Synthesis of methyl (E)-3-amino-4-((4-((tert-butoxycarbonyl)amino)but-2-en-1-yl)amino)-5-methoxybenzoate (Compound 113a)



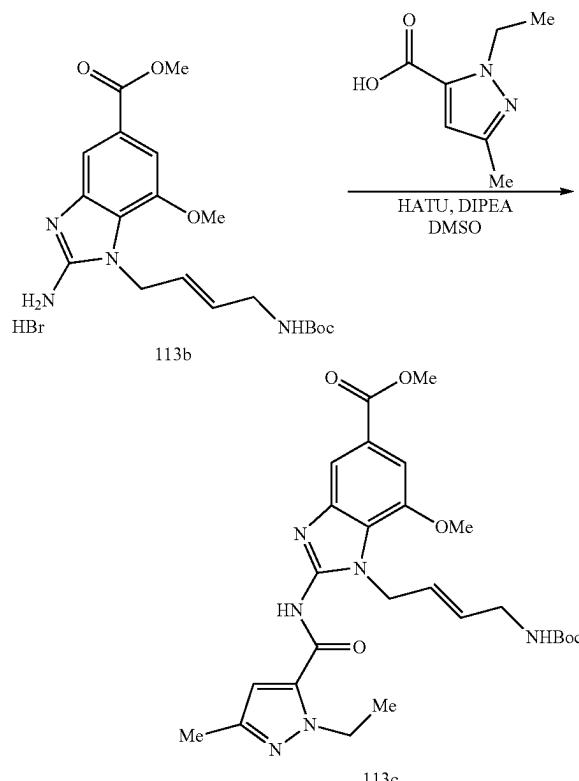
[1631] Compound 62a (500 mg, 1.26 mmol, 1 equiv.) was dissolved in MeOH (20 mL) and NH₄OH (6 mL). Na₂S₂O₄ (1.10 g, 6.32 mmol, 5 equiv.) in H₂O (5 mL) was slowly added and the mixture stirred at room temperature for 30 min. The reaction was monitored by UPLC-MS (Method E, ESI+). Upon completion, the mixture was filtered and concentrated. The resulting product was redissolved in EtOAc and washed with H₂O (\times 3). The organics were collected, dried with MgSO₄, filtered, and concentrated to afford compound 113a (343 mg, 0.938 mmol, 74% yield) as a yellow solid. The resulting product was used without further purification. UPLC-MS (Method E, ESI+): m/z [M+H]⁺ = 366.2 (theoretical), 366.2 (observed). HPLC retention time: 1.54 min.

Synthesis of methyl (E)-2-amino-1-(4-((tert-butoxycarbonyl)amino)but-2-en-1-yl)-7-methoxy-1H-benzo[d]imidazole-5-carboxylate hydrobromide (Compound 113b)



[1632] Compound 113a (343 mg, 0.938 mmol, 1 equiv.) was dissolved in MeOH (9.3 mL) to which CNBr (3 M in MeCN, 0.374 mL, 1.2 equiv.) was added. The reaction stirred for 18 h at room temperature, and monitored by UPLC-MS (Method E, ESI+). Upon completion, the solution was concentrated to afford compound 113b (402 mg, 0.853 mmol, 91% yield), which was used without further purification. UPLC-MS (Method E, EST+): m/z [M+H]⁺ = 391.2 (theoretical), 391.1 (observed). HPLC retention time: 1.51 min.

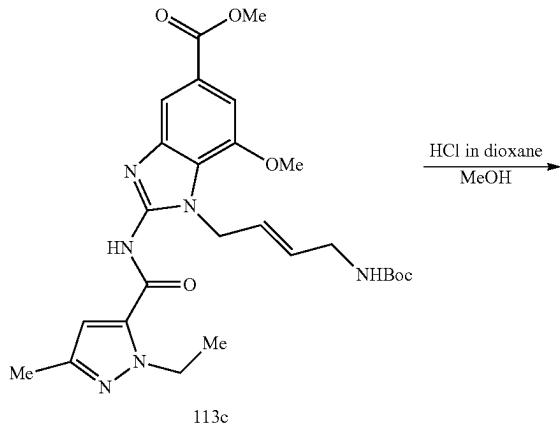
Synthesis of methyl (E)-1-(4-((tert-butoxycarbonyl)amino)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxylate (Compound 113c)



[1633] Compound 113b (402 mg, 0.853 mmol, 1 equiv.), 1-ethyl-3-methyl-1H-pyrazole-5-carboxylic acid (394 mg,

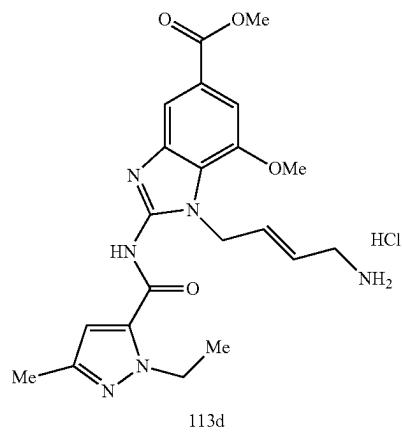
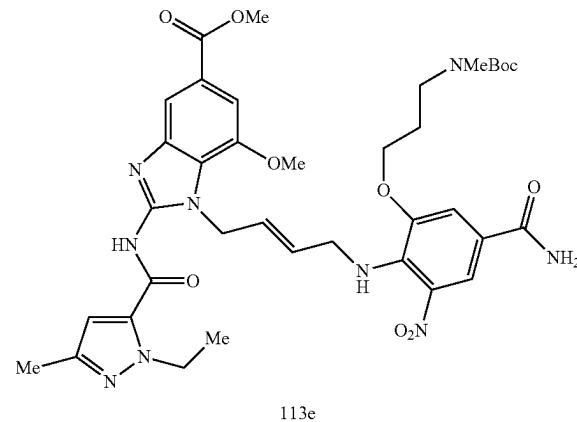
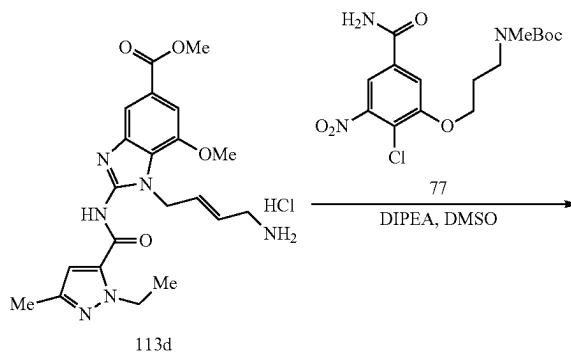
2.56 mmol, 3 equiv.) and HATU (973 mg, 2.56 mmol, 3 equiv.) were dissolved in DMA (1.7 mL) in a 5 mL microwave vial. DIPEA (0.74 mL, 4.26 mmol, 5 equiv.) was added, and the reaction was heated to 80° C. in a microwave reactor for 1 h. The reaction was monitored via UPLC-MS (Method E, ESI+). Upon completion, the reaction mixture was slowly added to ice-cold water (300 mL) to precipitate compound 113c (295 mg, 0.560 mmol, 66% yield), which was used without further purification. UPLC-MS (Method E, ESI+): m/z [M+H]⁺=527.3 (theoretical), 527.1 (observed). HPLC retention time: 2.30 min.

Synthesis of methyl (E)-1-(4-aminobut-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxylate (Compound 113d)



further purification. UPLC-MS (Method E, ESI+): m/z [M+H]⁺=427.2 (theoretical), 427.2 (observed). HPLC retention time: 1.54 min.

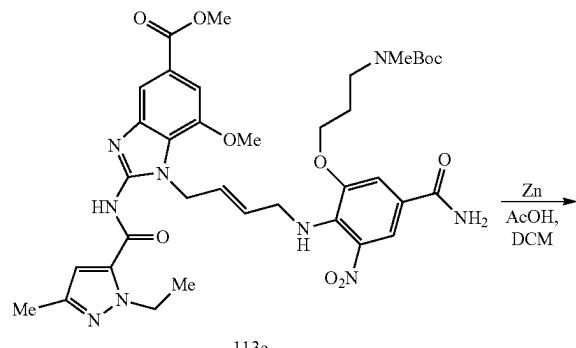
Synthesis of methyl (E)-1-((2-((tert-butoxy-carbonyl)(methyl)amino)propoxy)-4-carbamoyl-6-nitrophenyl)amino)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxylate (Compound 113e)



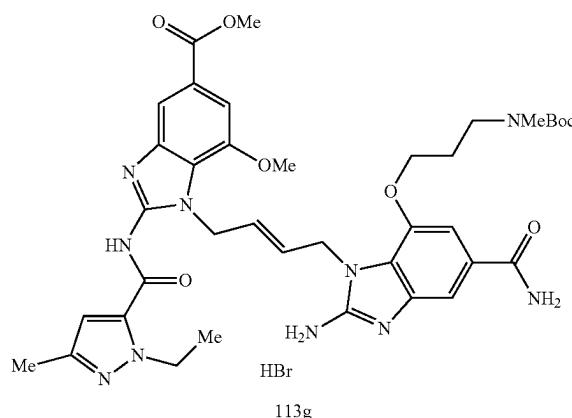
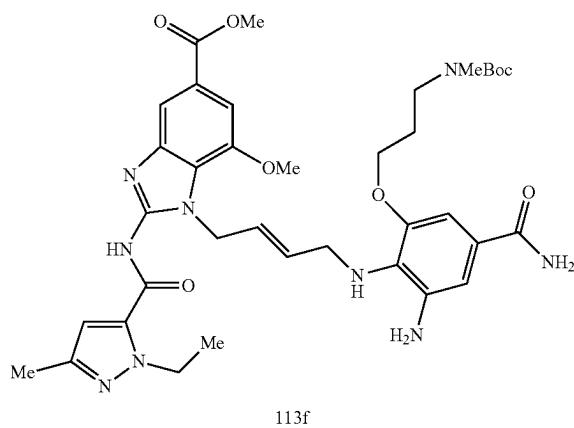
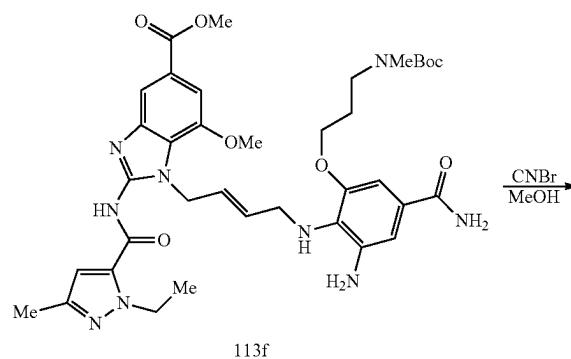
[1634] Compound 113c (319 mg, 0.606 mmol, 1 equiv.) was dissolved in MeOH (1 mL), to which HCl in dioxane (4 M, 1.2 mL, 4.85 mmol, 8 equiv.) was added. The reaction was stirred at room temperature for 30 min. and was monitored by UPLC-MS (Method E, ESI+). Upon completion, the solution was concentrated and compound 113d (280 mg, 0.605 mmol, quantitative yield) was used without

[1635] Compound 113d (280 mg, 0.605 mmol, 1 equiv.) and compound 77 (305 mg, 0.787 mmol, 1.3 equiv.) were dissolved in DMSO (3.0 mL) to which DIPEA (0.316 mL, 1.82 mmol, 3 equiv.) was added. The reaction stirred at 80° C. for 18 h and monitored via UPLC-MS (Method E, ESI+). Upon completion, AcOH (0.30 mL) was added, and the product was purified by prepHPLC (Method T) using 0.05% TFA as the additive. Pure fractions were collected, frozen, and lyophilized to afford compound 113e (58.6 mg, 0.0753 mmol, 12% yield) as an orange solid. UPLC-MS (Method E, ESI+): m/z [M+H]⁺=778.3 (theoretical), 778.4 (observed). HPLC retention time: 1.88 min.

Synthesis of methyl (E)-1-(4-((2-amino-6-(3-((tert-butoxycarbonyl)(methyl)amino)propoxy)-4-carbamoylphenyl)amino)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxylate (Compound 113f)



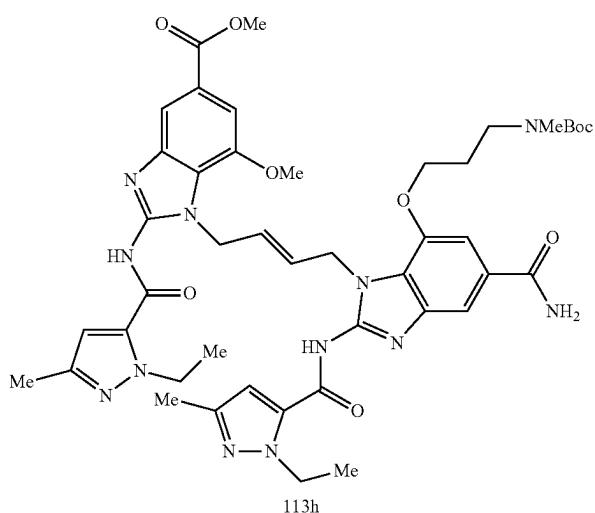
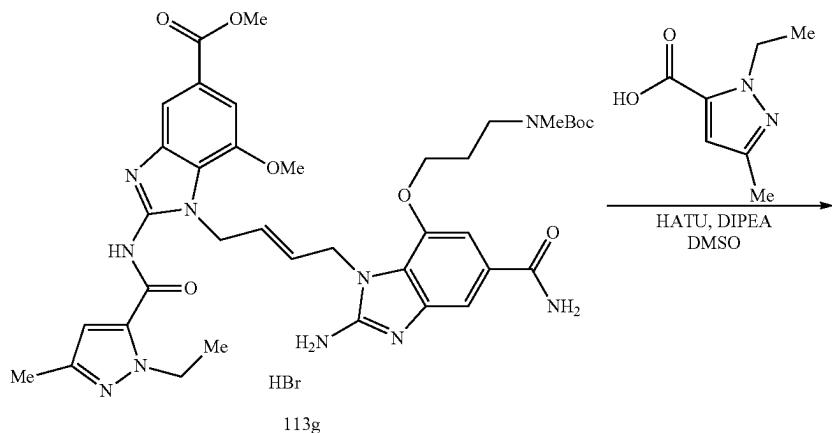
Synthesis of methyl (E)-1-(4-(2-amino-7-(3-((tert-butoxycarbonyl)(methyl)amino)propoxy)-5-carbamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxylate (Compound 113g)



[1636] Compound 113e (58.6 mg, 0.0753 mmol, 1 equiv.) was dissolved in a 1:1 mixture of AcOH/DCM (0.75 mL) and cooled to 0° C. Zn (49.2 mg, 0.753 mmol, 10 equiv.) was added and the mixture was allowed to warm to room temperature while stirring for 30 min. The reaction was monitored via UPLC-MS (Method E, ESI+). Upon completion, the solution was concentrated and redissolved in DCM to be purified by flash chromatography (25 g SiO₂ column, 0-40% MeOH:NH₄OH (10:1) in DCM) to afford compound 113f (28.3 mg, 0.378 mmol, 50% yield). UPLC-MS (Method E, ESI+): m/z [M+H]⁺=748.4 (theoretical), 748.4 (observed). HPLC retention time: 1.84 min.

[1637] Compound 113f (28.3 mg, 0.378 mmol, 1 equiv.) was dissolved in MeOH (0.38 mL) to which CNBr (3 M in MeCN, 15 µL, 0.0454 mmol, 1.2 equiv.) was added. The reaction stirred at room temperature for 18 h and was monitored via UPLC-MS (Method E, ESI+). Upon completion, the solution was concentrated to afford product 113g (30.7 mg, 0.360 mmol, quantitative yield), which was used without further purification. UPLC-MS (Method E, ESI+): m/z [M+H]⁺=773.4 (theoretical), 773.4 (observed). HPLC retention time: 1.53 min.

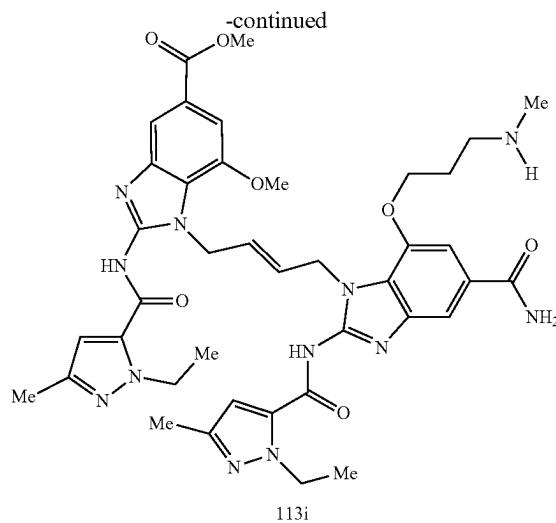
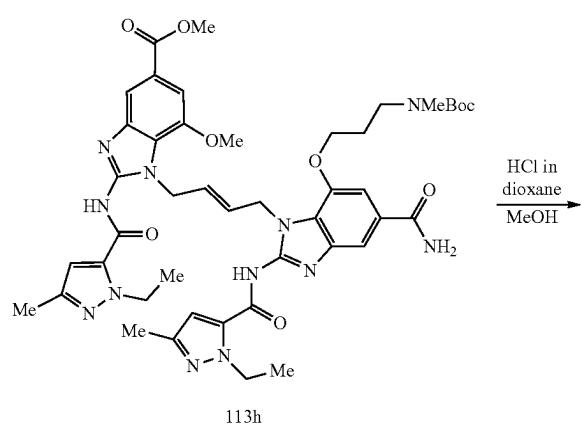
Synthesis of methyl (E)-1-(4-(7-(3-((tert-butoxycarbonyl)(methyl)amino)propoxy)-5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxylate (Compound H)



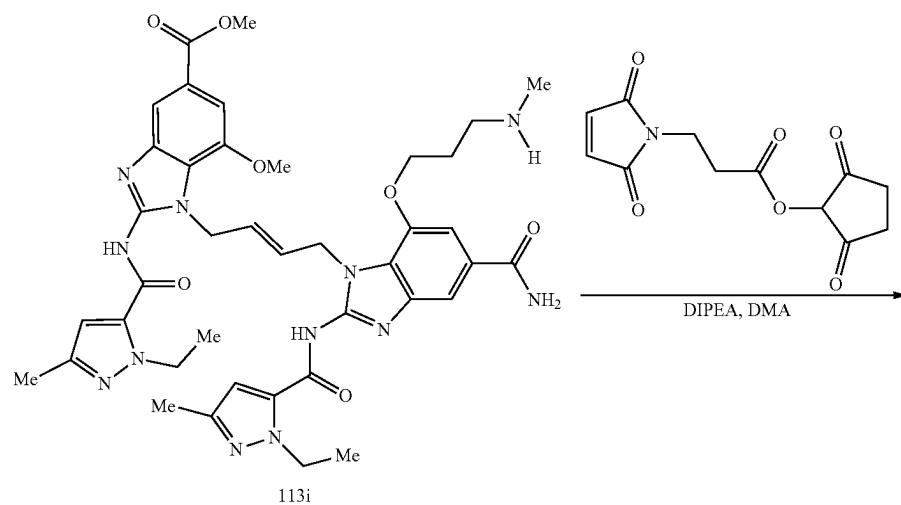
[1638] Compound 113g (30.7 mg, 0.0360 mmol, 1 equiv.), 1-ethyl-3-methyl-1H-pyrazole-5-carboxylic acid (22.1 mg, 0.144 mmol, 4 equiv.), and HATU (54.6 mg, 0.144 mmol, 4 equiv.) were dissolved in DMA (0.50 mL) in a 2 mL microwave vial. DIPEA (0.025 mL, 0.144 mmol, 4 equiv.) was added, and the reaction was heated in a microwave reactor at 80° C. for 1 h. The reaction was monitored via

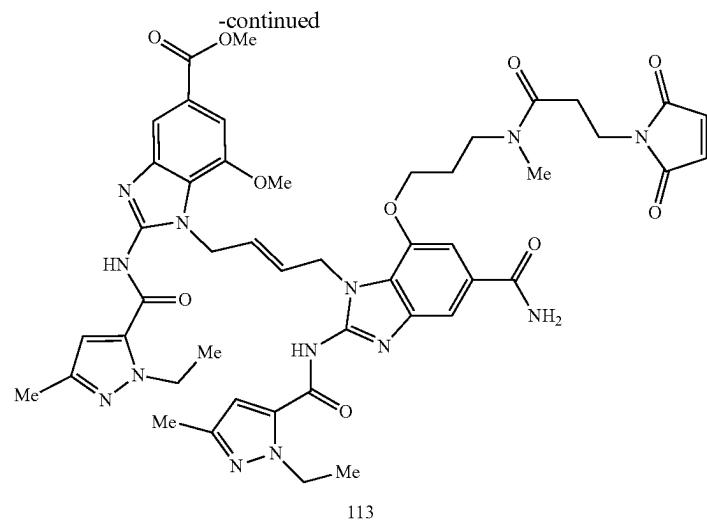
UPLC-MS (Method E, ESI+). Upon completion, the product was purified by prepHPLC (Method H) using 0.05% TFA as the additive. Pure fractions were collected, frozen, and lyophilized to afford compound 113h (6.52 mg, 0.0064 mmol, 18% yield) as a white solid. UPLC-MS (Method E, ESI+): m/z [M+H]⁺=909.4 (theoretical), 909.5 (observed). HPLC retention time: 1.90 min.

Synthesis of methyl (E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-(3-(methylamino)propoxy)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxylate (Compound 113i)



[1639] Compound 113h (3.02 mg, 0.0030 mmol, 1 equiv.) was dissolved in MeOH (0.30 mL) to which HCl in dioxane (4 M, 6.00 μ L, 0.0236 mmol, 8 equiv.) was added. The reaction stirred for 30 min at room temperature and monitored via UPLC-MS (Method E, ESI $^+$). Upon completion, the product was purified via prepHPLC (Method G) using 0.05% TFA as the additive. Pure fractions were collected, frozen, and lyophilized to afford compound 113i (1.35 mg, 0.0013 mmol, 44% yield) as a white solid. UPLC-MS (Method E, ESI $^+$): m/z [M+H] $^+$ =809.4 (theoretical), 809.4 (observed). HPLC retention time: 1.57 min.

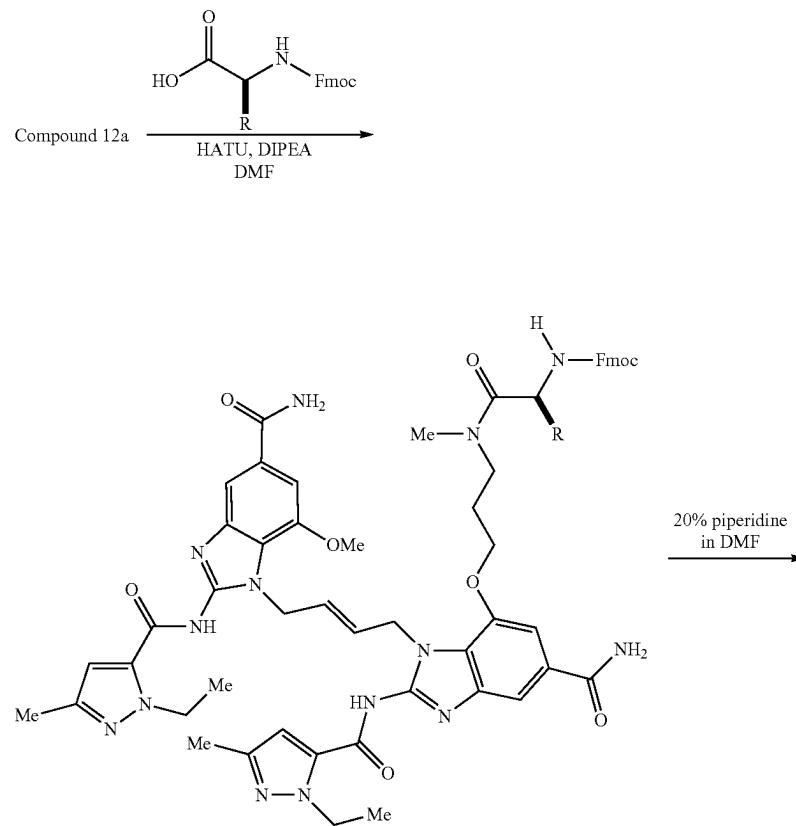




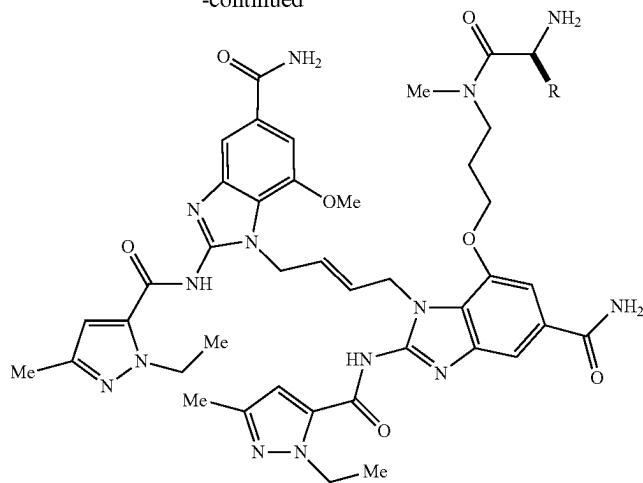
[1640] Compound 113i (7.53 mg, 0.0085 mmol, 1 equiv.) and MP-OSu (4.55 mg, 0.0171 mmol, 2 equiv.) were dissolved in DMA (0.854 mL), and DIPEA (42.7 μ L, 0.0074 mmol, 5 equiv.) was added. The reaction stirred at room temperature for 18 h and monitored by UPLC-MS (Method E, ESI+). Upon completion, AcOH (42 μ L) was added, and the product was purified via prepHPLC (Method G) using

0.05% TFA as the additive. Pure fractions were collected, frozen, and lyophilized to afford compound 113 (4.43 mg, 0.0041 mmol, 48% yield) as a white solid. UPLC-MS (Method E, ESI+): m/z [M+] H^+ =960.4 (theoretical), 960.5 (observed). HPLC retention time: 1.79 min.

Linker Library Synthesis (Compounds 114-124).



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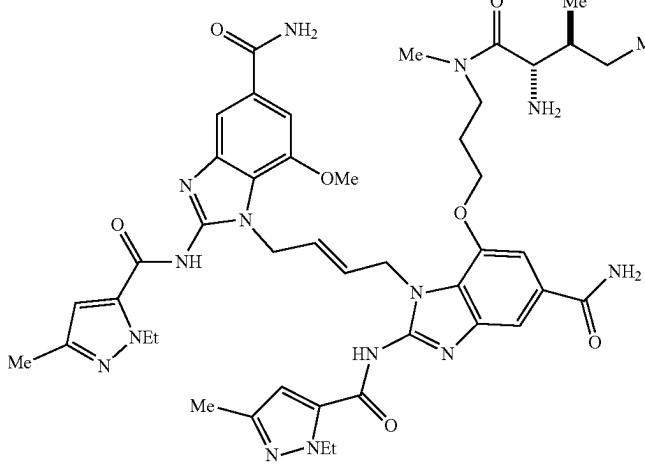
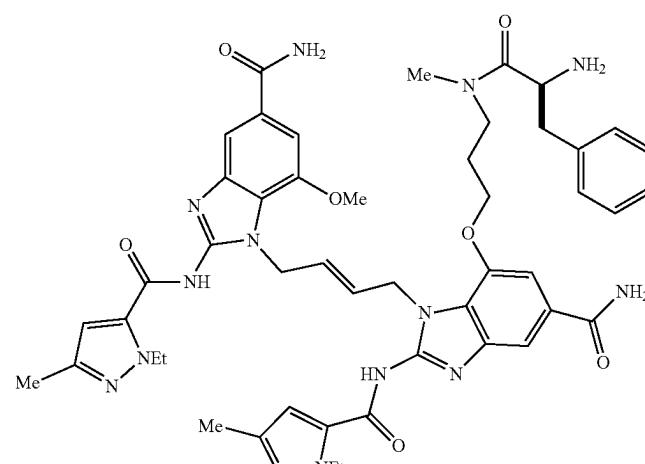


[1641] Amide coupling (General Method 10): A mixture of Compound 12a (1 equiv.), HATU (2 equiv.), DIPEA (5 equiv.), the appropriate L-amino acid (2 equiv.) was prepared in DMF (0.02 M in 12a) and stirred at room temperature overnight. The solvent was removed in vacuo, and resulting product used in the next step without further purification.

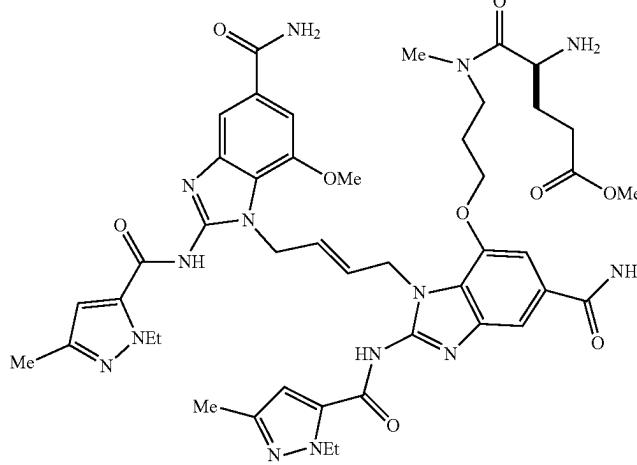
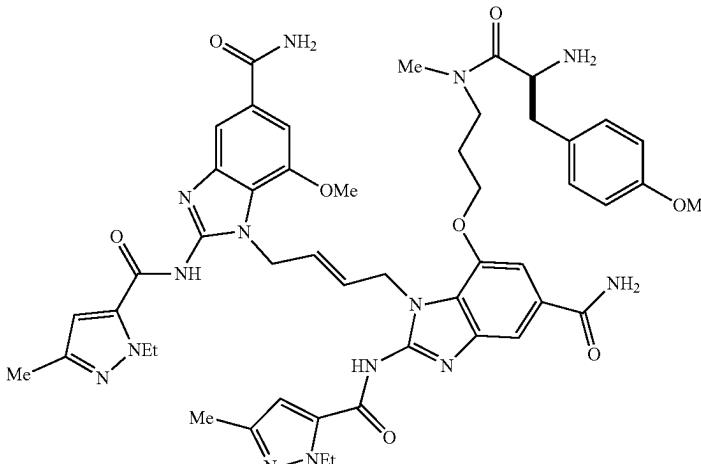
[1642] Fmoc deprotection (General Method 11): The resulting Fmoc-protected amine was dissolved in 20% piperidine in DMF (1 mL) and stirred at room temperature for 15 minutes. The solvent was removed in vacuo and the product purified via prep HPLC (Method H, 5-95% in MeCN in H₂O in 0.05% TFA).

Compound	UPLC-MS [M + H] ⁺	Yield
<p>The structure is identical to the one in entry 1641, except that the terminal amine group (-NH₂) is now protected as an Fmoc group (-NH-C(=O)-C₆H₄-CH₂-C₆H₃(CH₃)₂-). The rest of the molecule, including the four imidazole rings and their connecting linkages, remains the same.</p>	RT: 1.83 min Theoretical: 907.5 Observed: 907.5	18.6 mg (58%)

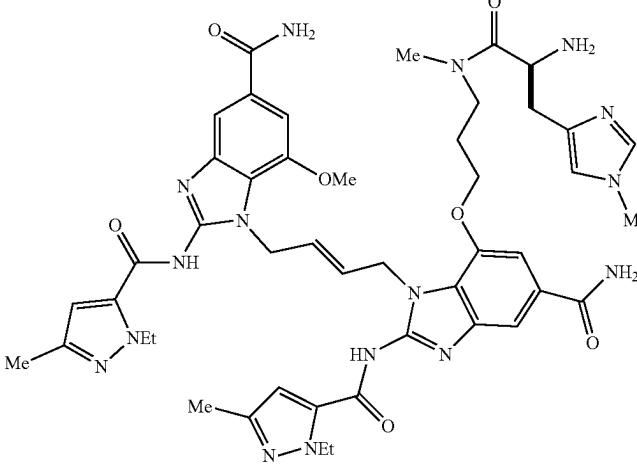
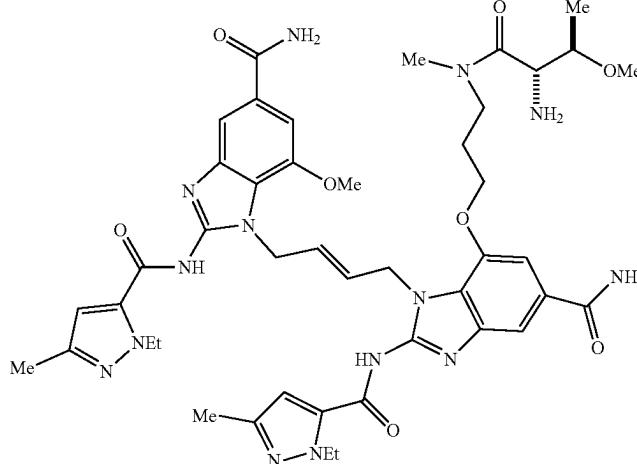
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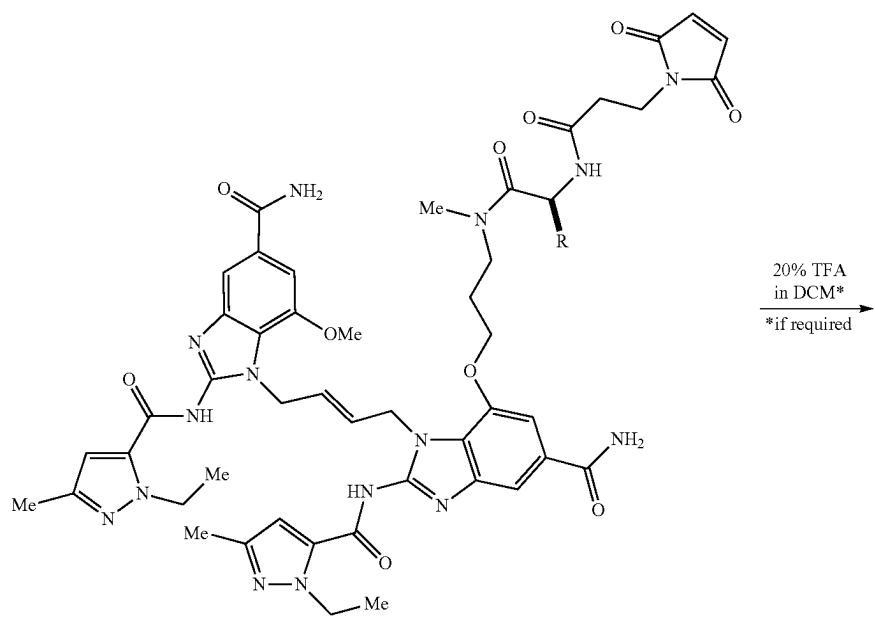
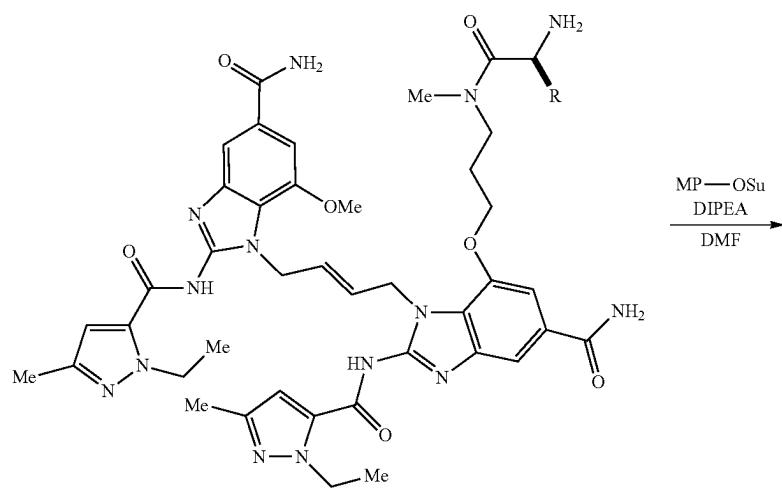
Compound	UPLC-MS [M + H] ⁺	Yield
 115	RT: 1.77 Theoretical: 907.5 Observed: 907.5	24.9 mg (78%)
 116	RT: 1.76 Theoretical: 941.5 Observed: 941.5	13.5 mg (28%)

-continued

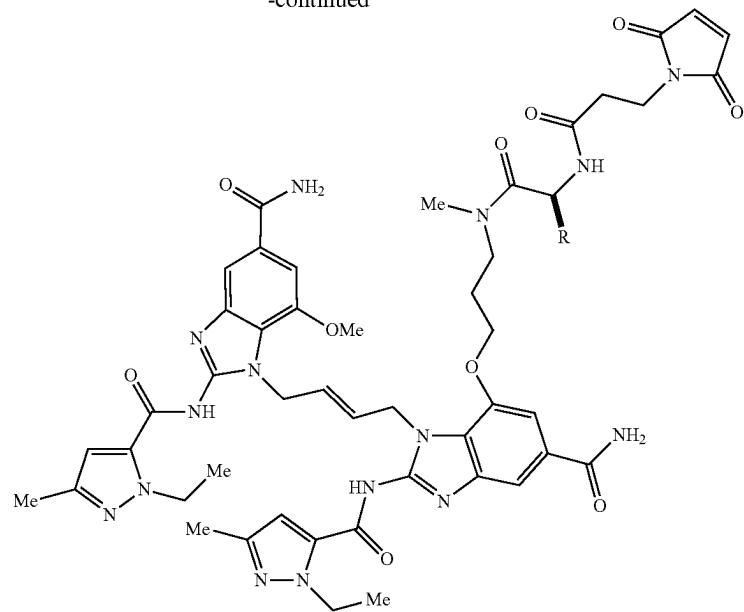
Compound	UPLC-MS [M + H] ⁺	Yield
 <p>117</p>	RT: 2.05 Theoretical: 937.4 Observed: 937.5	9.8 mg (35%)
 <p>118</p>	RT: 1.93 Theoretical: 971.5 Observed: 971.5	18.6 mg (64%)

-continued

Compound	UPLC-MS [M + H] ⁺	Yield
 119	RT: 1.93 Theoretical: 945.5 Observed: 945.5	19.4 (64%)
 120	RT: 2.05 Theoretical: 909.4 Observed: 909.5	24.5 mg (76.4%)



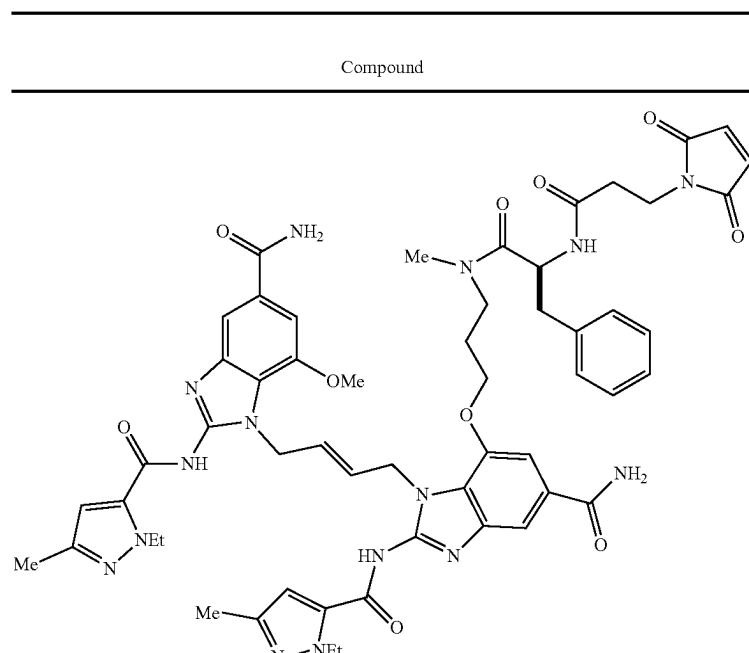
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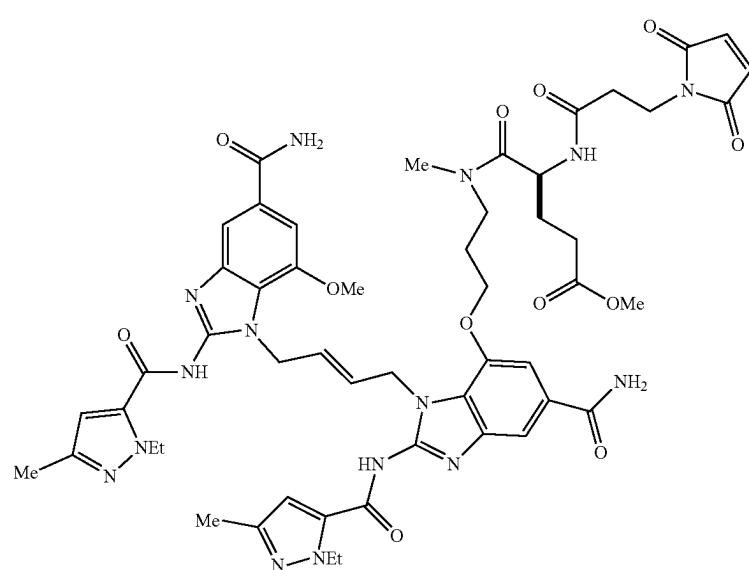
[1643] Synthesis of maleimide containing drug-linkers (compounds 121-125) was performed according to General Method 9.

Compound	UPLC-MS [M + H] ⁺	Yield
	RT: 2.16 Theoretical: 1058.5 Observed: 1058.5	1.5 mg (42%)

-continued

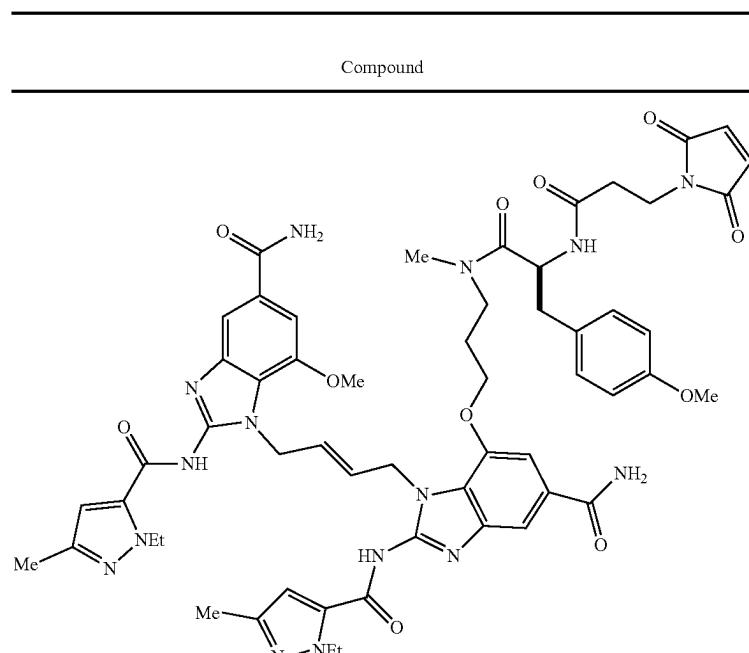
Compound	UPLC-MS [M + H] ⁺	Yield
	RT: 2.00 Theoretical: 1092.5 Observed: 1092.5	0.5 mg (21%)

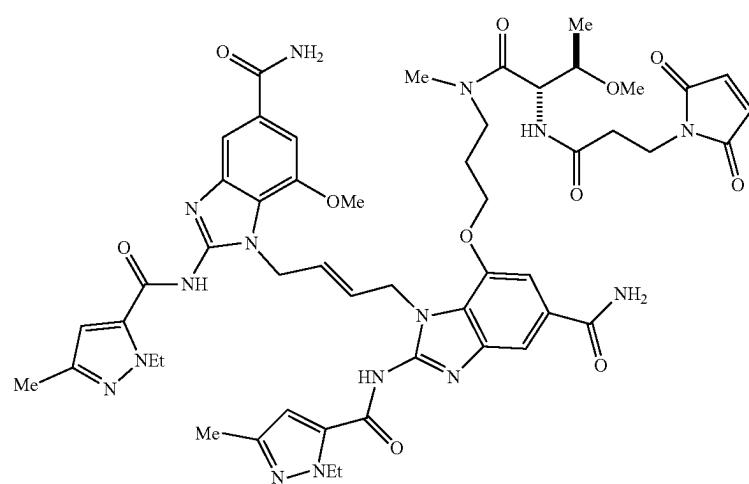
122

Compound	UPLC-MS [M + H] ⁺	Yield
	RT: 2.21 Theoretical: 1088.5 Observed: 1088.5	1.1 mg (32%)

123

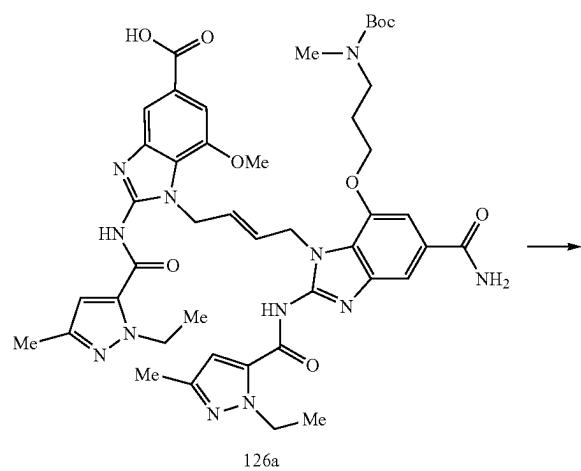
-continued

Compound	UPLC-MS [M + H] ⁺	Yield
 <p>124</p>	RT: 1.81 Theoretical: 1122.5 Observed: 1122.6	1.1 mg (32%)

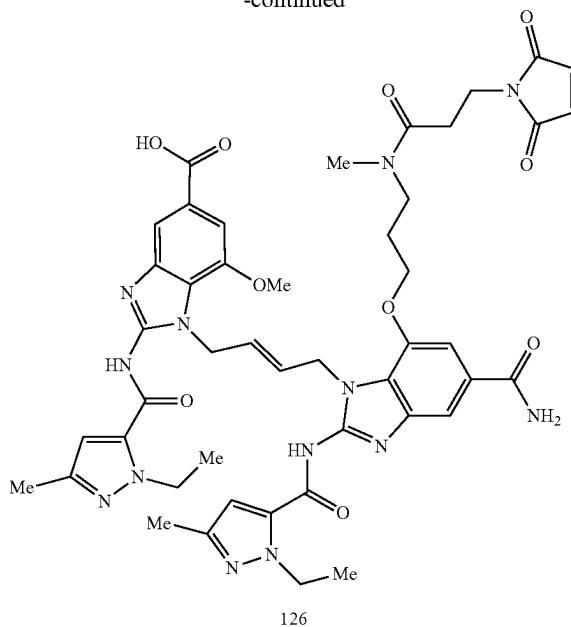
Compound	UPLC-MS [M + H] ⁺	Yield
 <p>125</p>	RT: 1.79 Theoretical: 1060.5 Observed: 1060.5	0.3 mg (8.6%)

(E)-1-(4-(5-carbamoyl-7-(3-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-N-methylpropanamido)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxylic acid (Compound 126)

113h →



-continued

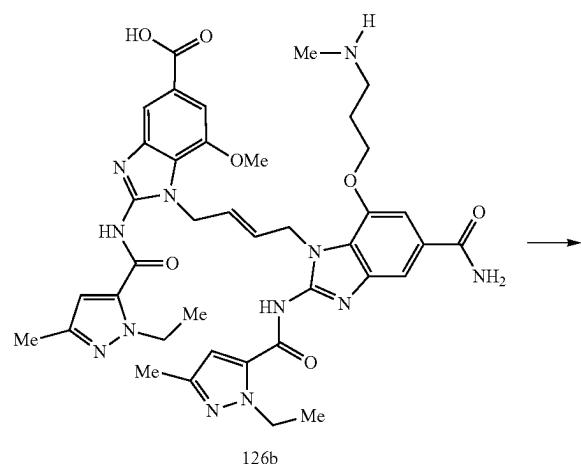


Synthesis of Compound 126a

[1644] Compound 113h (25.44 mg, 0.0249 mmol, 1 equiv.) was dissolved in MeOH (166 µL). An aqueous solution of 1M LiOH (200 µL, 8 equiv.) was added and the reaction was stirred at 80° C. for 2h. Upon completion, the solution was concentrated under reduced pressure and purified by prepHPLC (Method H) using 0.05% TFA as the additive. Pure fractions were collected, frozen, and lyophilized to afford compound 126a (7.1 mg, 0.0071 mmol, 28% yield) as a white solid. UPLC-MS (Method E, ESI+): m/z [M+H]⁺=895.4 (theoretical), 895.6 (observed). HPLC retention time: 1.97 min.

Synthesis of compound 126b

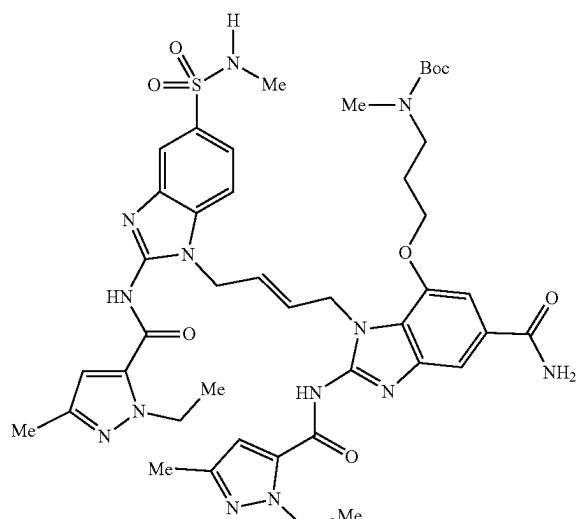
[1645] Compound 126b was prepared following the same procedure used to prepare compound 113i. UPLC-MS (Method E, ESI+): m/z [M+H]⁺=795.4 (theoretical), 795.6 (observed). HPLC retention time: 1.40 min.



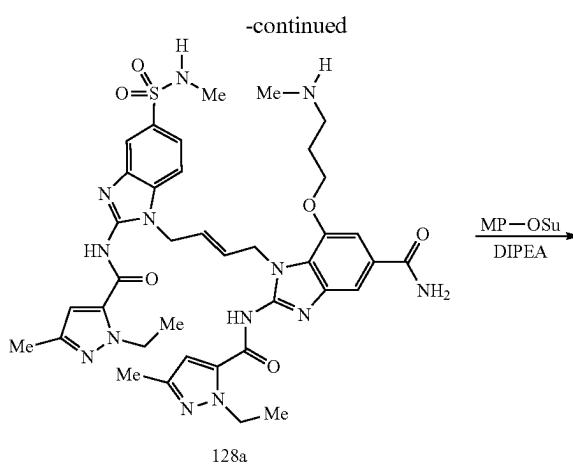
Synthesis of compound 126

[1646] Compound 126 was prepared following the same procedure used to prepare compound 113. UPLC-MS (Method E, ESI+): m/z [M+H]⁺=946.4 (theoretical), 946.6 (observed). HPLC retention time: 1.68 min.

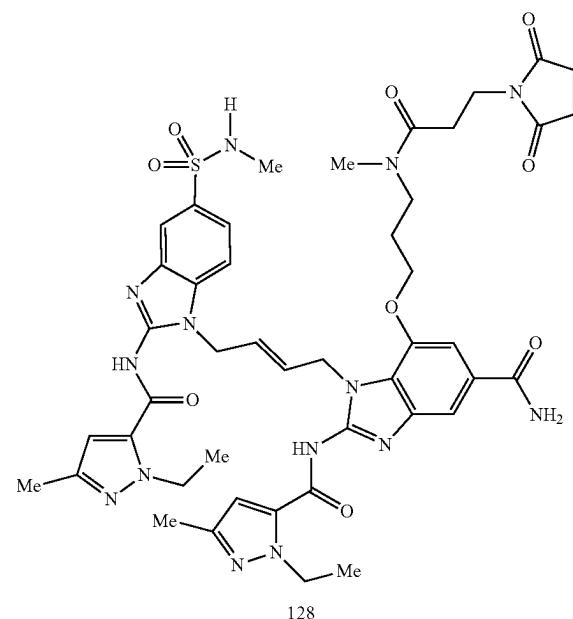
Synthesis of tert-butyl (E)-(3-((5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-(N-methylsulfamoyl)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazol-7-yl)oxy)propyl)(methyl)carbamate (Compound 127)



127



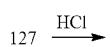
128a



128

[1647] Compound 127 was prepared following the same procedures as compound 25f substituting 4-chloro-N-methyl-3-nitrobenzenesulfonamide for 4-chloro-3-nitrobenzenesulfonamide. UPLC-MS (Method E, EST+): m/z [M+H]⁺=914.4 (theoretical), 914.6 (observed). HPLC retention time: 1.80 min.

Synthesis of (E)-7-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-N-methylpropanamido)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-(N-methylsulfamoyl)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazole-5-carboxamide (Compound 128)



Synthesis of 128a

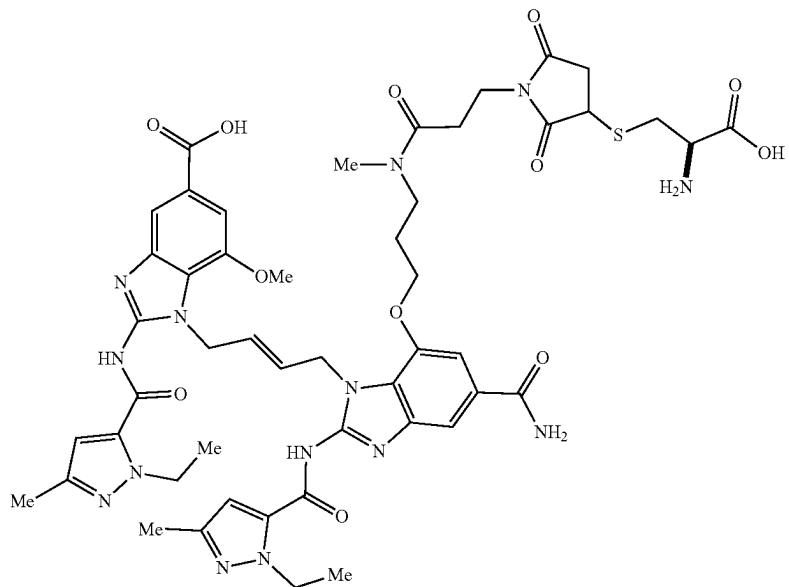
[1648] Compound 128a was prepared following the same procedure used to prepare compound 66b. UPLC-MS (Method E, ESI+): m/z [M+H]⁺=814.4 (theoretical), 814.5 (observed). HPLC retention time: 1.53 min.

Synthesis of 128

[1649] Compound 128 was prepared following the same procedure used to prepare compound 12. UPLC-MS (Method E, ESI+): m/z [M+H]⁺=965.4 (theoretical), 965.6 (observed). HPLC retention time: 1.60 min.

Synthesis of S-(1-(3-((3-((5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-((E)-4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-5-(methoxycarbonyl)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazol-7-yl)oxy)propyl) (methyl)amino)-3-oxopropyl)-2,5-dioxopyrrolidin-3-yl)-L-cysteine (Compound 129)

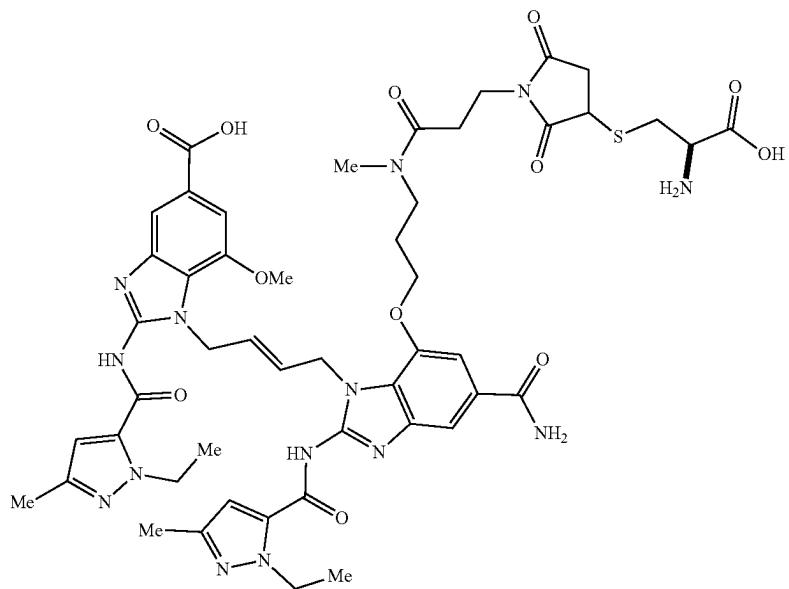
129



[1650] Compound 129 was prepared following General Method 6. UPLC-MS (Method E, ESI+); m/z [M+H]⁺ = 1081.4 (theoretical), 1081.6 (observed). HPLC retention time: 1.88 min.

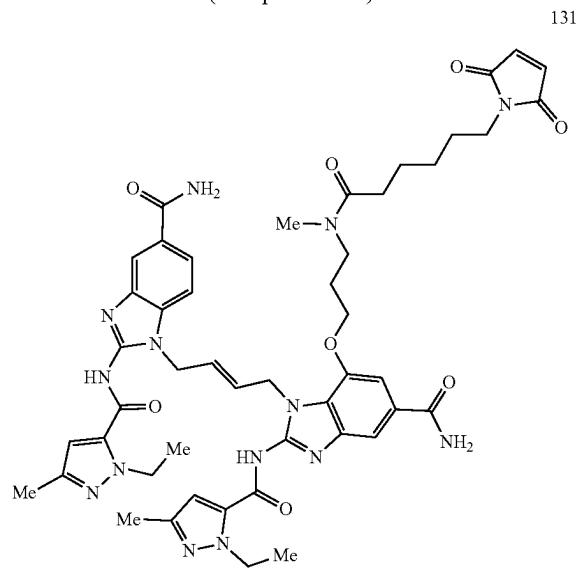
Synthesis of 1-((E)-4-(7-(3-((R)-2-amino-2-carboxyethyl)thio)-2,5-dioxopyrrolidin-1-yl)-N-methylpropanamido)propoxy)-5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxylic acid
(Compound 130)

130



[1651] Compound 130 was prepared following General Method 6. UPLC-MS (Method E, ESI+): m/z [M+H]⁺ =1067.4 (theoretical), 1067.6 (observed). HPLC retention time: 1.49 min.

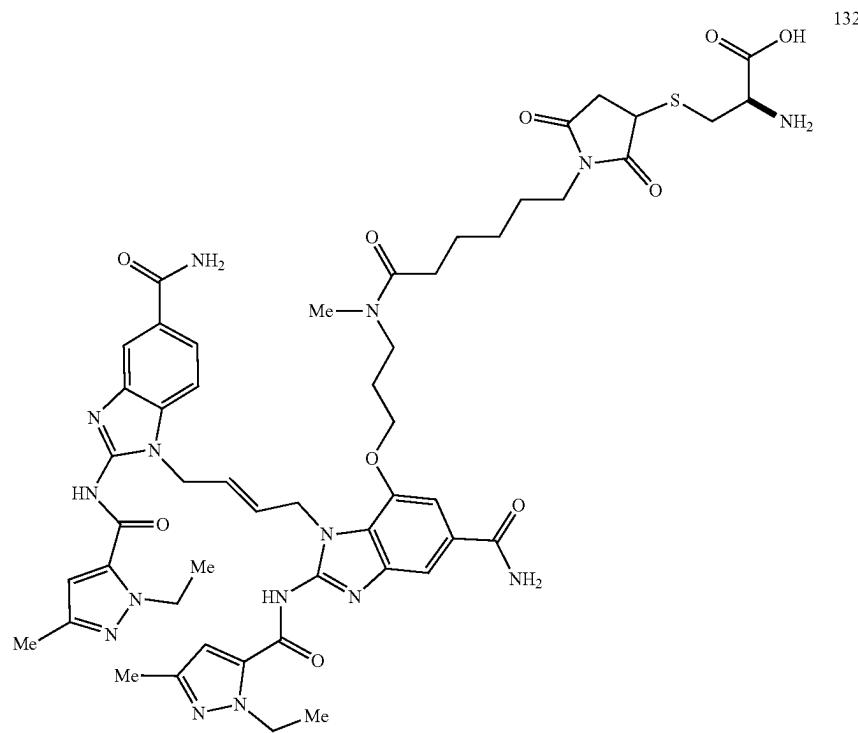
Synthesis of (E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(3-(6-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-N-methylhexanamido)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazole-5-carboxamide (Compound 131)



131

[1652] Compound 131 was prepared following the same procedure as compound 12 substituting 2,5-dioxopyrrolidin-1-yl 6-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)hexanoate for 2,5-dioxopyrrolidin-1-yl 3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoate. UPLC-MS (Method E, EST+): m/z [M+H]⁺=987.5 (theoretical), 987.7 (observed). HPLC retention time: 1.85 min.

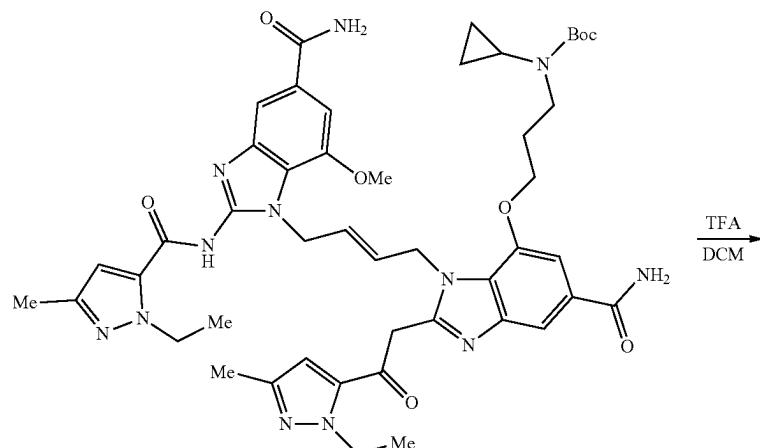
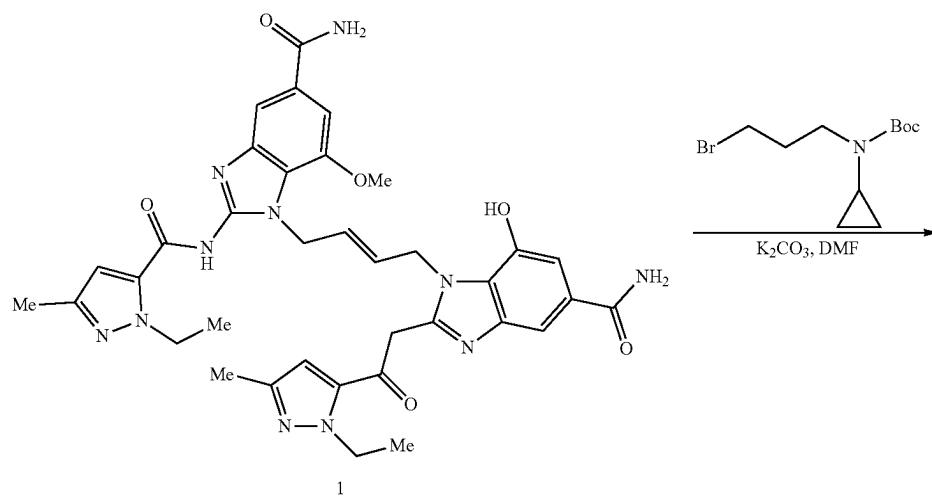
Synthesis of S-(1-((3-((5-carbamoyl-1-(E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)propyl)(methyl)amino)-6-oxohexyl)-2,5-dioxopyrrolidin-3-yl-L-cysteine (Compound 132)

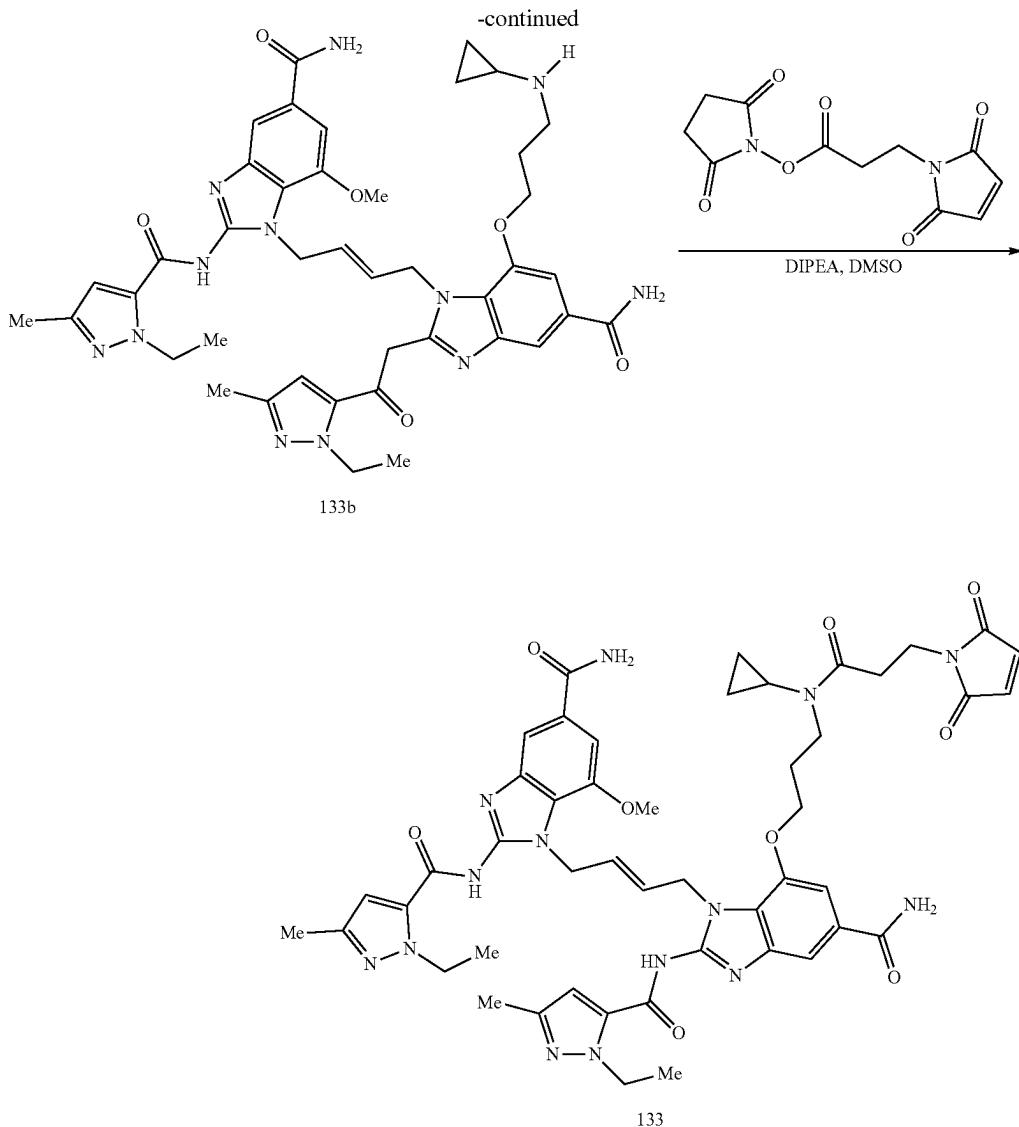


132

[1653] Compound 132 was prepared following General Method 6. UPLC-MS (Method E, ESI+): m/z [M+H]⁺ =1108.5 (theoretical), 1108.7 (observed). HPLC retention time: 1.42 min.

Synthesis of (E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(3-(N-cyclopropyl-3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanamido)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazole-5-carboxamide (Compound 133)





Synthesis of 133a

[1654] An oven-dried 4 mL vial was charged with 1 (10 mg, 0.0105 mmol, 1 equiv), potassium carbonate (7.3 mg, 0.0526 mmol, 5 equiv.), and tert-butyl N-(3-bromopropyl)-N-cyclopropyl-carbamate (0.49 mL of a 9 mg/mL solution in DMF, 0.0158 mmol, 1.50 equiv.) and starting materials were dissolved in DMF (0.50 mL). The reaction was stirred overnight at 55° C. and purified by preparatory HPLC (Method B), after which it was frozen and lyophilized to afford compound 133a (8.8 mg, 0.0077 mmol, 73% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=920.45 (theoretical), 920.64 (observed). HPLC retention time: 2.32 min.

Synthesis of 133b

[1655] An oven-dried 4 mL vial was charged with 133a (8.8 mg, 0.0077 mmol) and 20% TFA in DCM (100 μ L). The reaction was stirred for 30 minutes at room temperature and purified by preparatory HPLC (Method B), after which it

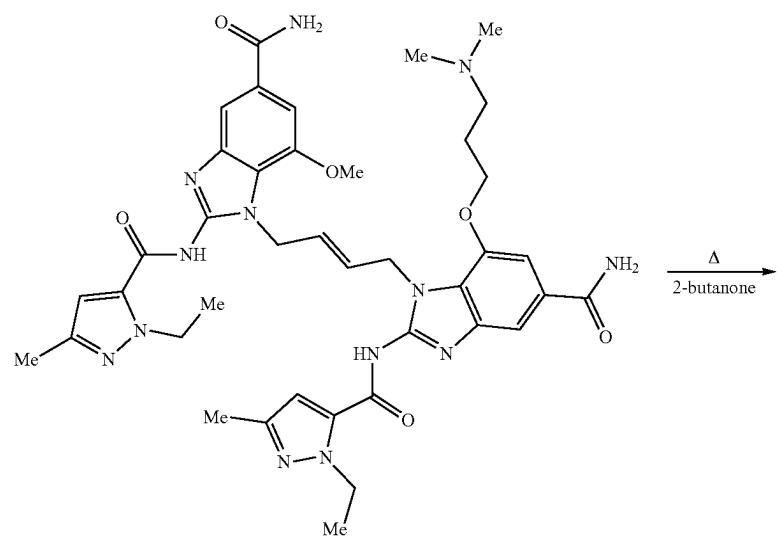
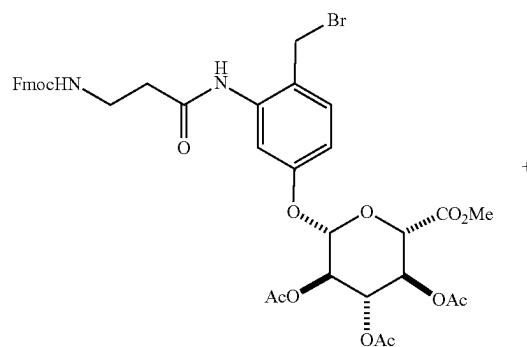
was frozen and lyophilized to afford compound 133b (5.0 mg, 0.0043 mmol, 56% yield). UPLC-MS (Method D, ESI+): m/z [M+H]⁺=820.40 (theoretical), 820.49 (observed). HPLC retention time: 1.29 min.

Synthesis of 133

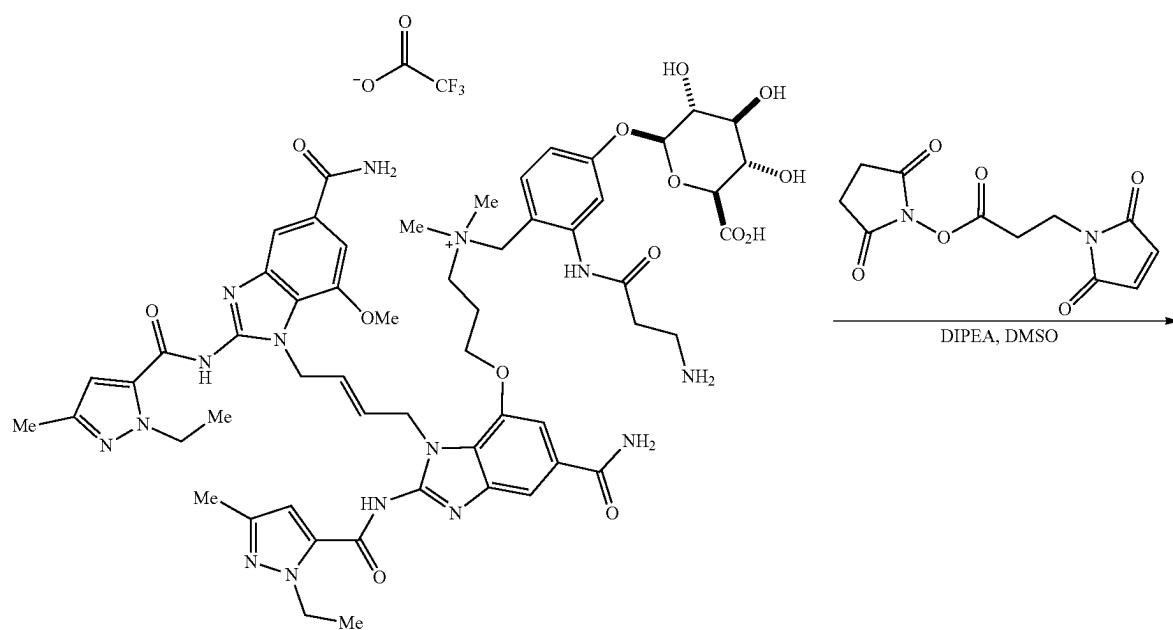
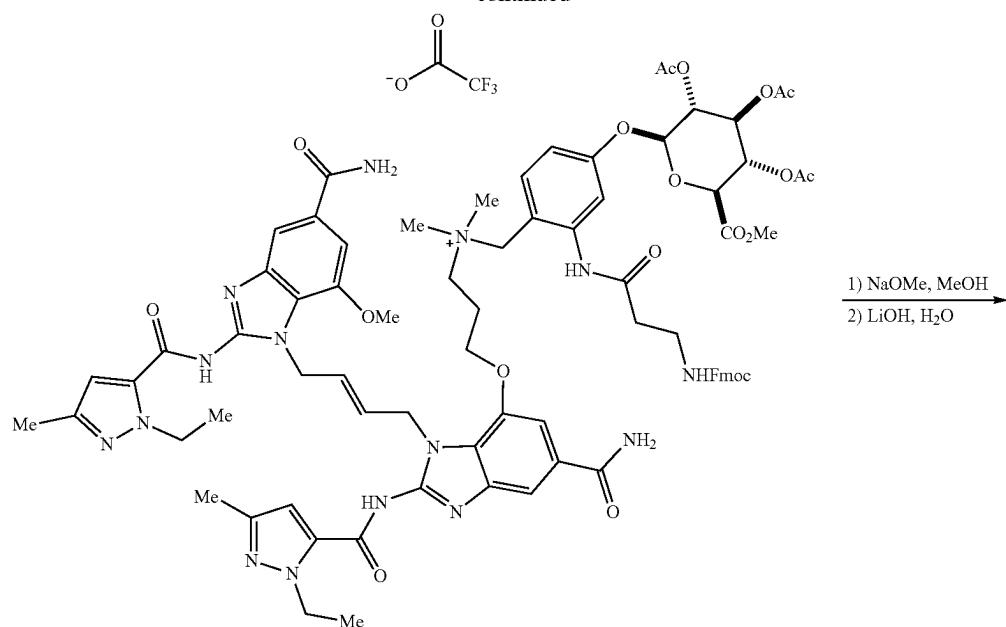
[1656] An oven-dried 8 mL vial was charged with 133b (3.3 mg, 0.0085 mmols, 1 equiv.) which was dissolved in DMSO (1 mL) and a solution of 2,5-dioxopyrrolidin-1-yl 3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoate in DMSO (10 mM in DMSO, 0.43 mL, 0.0043 mmol, 1.5 equiv.) and DIPEA (1.5 μ L, 0.00851 mmol, 3 equiv.). The reaction was heated to 30° C. overnight, quenched with acetic acid and purified by preparatory HPLC (Method B), after which the compound was frozen and lyophilized to afford 133 (1.9 mg, 0.00158 mmol, 56% yield).

[1657] UPLC-MS (Method D, ESI+): m/z [M+H]⁺=971.43 (theoretical), 971.48 (observed). HPLC retention time: 1.99 min.

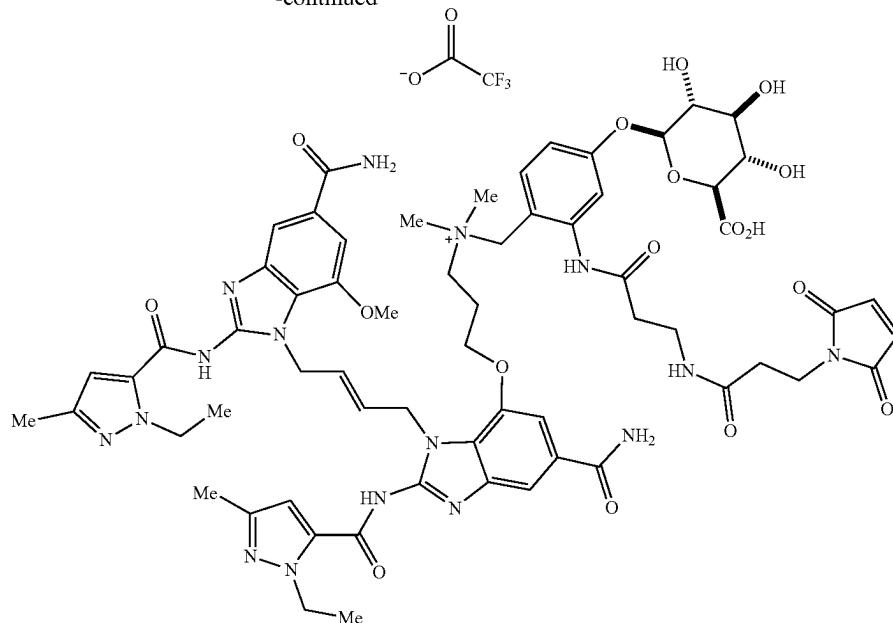
Synthesis of 3-((5-carbamoyl-1-((E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)-N-(4-(((2S,3R,4S,5S,6S)-6-carboxy-3,4,5-trihydroxytetrahydro-2H-pyran-2-yl)oxy)-2-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanamido)propanamido)benzyl)-N,N-dimethylpropan-1-aminium 2,2,2-trifluoroacetate (Compound 134)



-continued



-continued



134

Synthesis of 134a

[1658] An oven-dried 8 mL vial was charged with (E)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(3-(dimethylamino)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-5-carboxamide (20 mg, 0.0248 mmol, 1 equiv., prepared as previously described WO2017/175147, example 39, page 291) and (2S,3R,4S,5S,6S)-2-(3-(3-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)propanamido)-4-(bromomethyl)phenoxy)-6-(methoxycarbonyl)tetrahydro-2H-pyran-3,4,5-triyl triacetate (60.3 mg, 0.0743 mmol, 3 equiv, prepared as previously described, *Mol Cancer Ther* 2016 15(5), 938-945) and azeotroped with anhydrous acetonitrile. To the vial was added 2-butanone (2.5 mL) and the solution was heated to 100° C. overnight. The compound was directly purified by preparatory HPLC (Method B), frozen and lyophilized to afford 134a (11.3 mg, 0.0070 mmol, 28% yield). UPLC-MS (Method E, ESI+): m/z [M+H]⁺=1538.64 (theoretical), 1538.83 (observed). HPLC retention time: 2.55 min

Synthesis of 134b

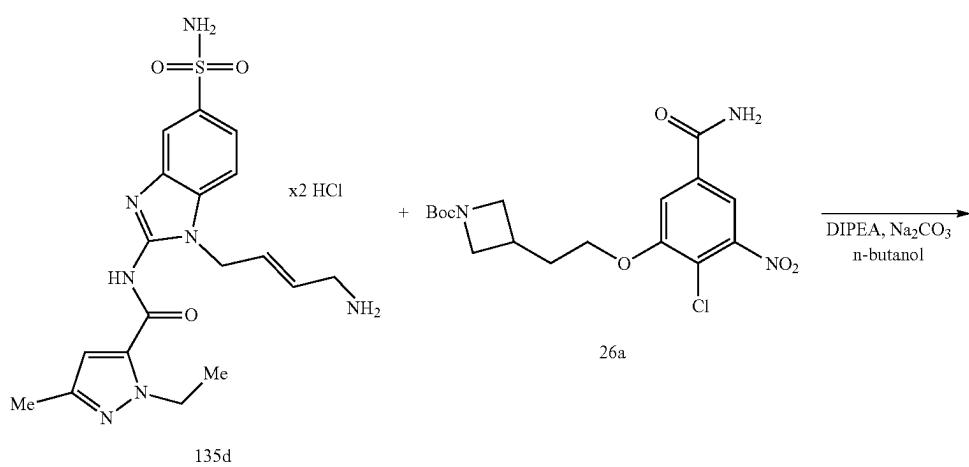
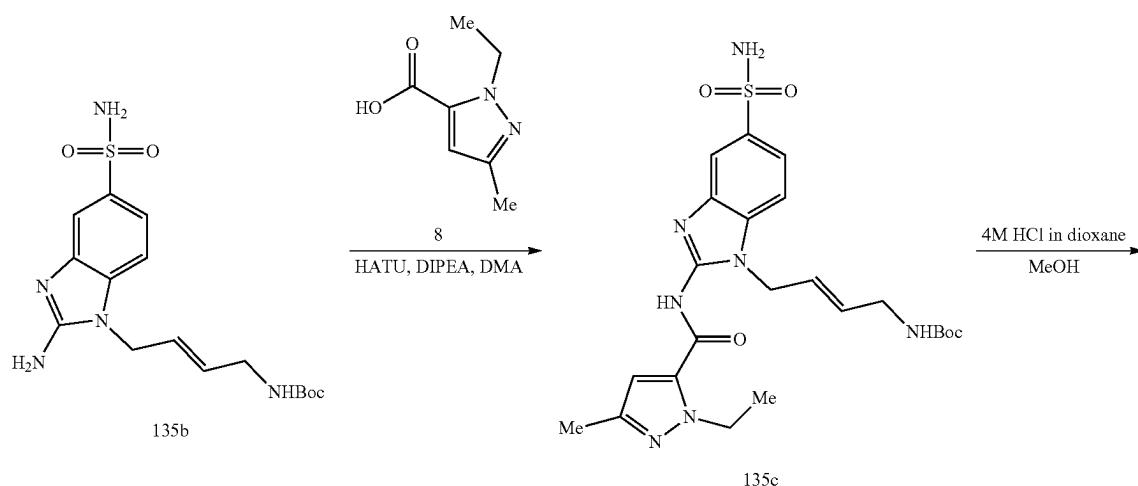
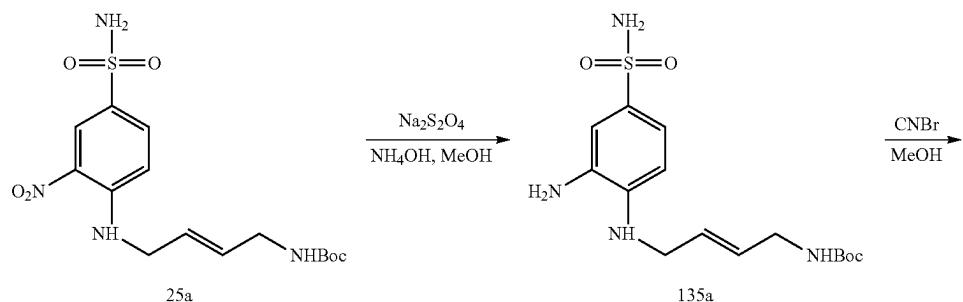
[1659] An oven-dried 4 mL vial was charged with 134a (4.5 mg, 0.0094 mmol, 1 equiv.) and dissolved in anhydrous

MeOH (0.5 mL). The vial was cooled in an acetonitrile/dry-ice bath at -40° C. and 0.5 M NaOMe (19 μL, 0.0094 mmol, 1 equiv) was added. The reaction was stirred for 1 hour before it was warmed to room temperature and LiOH (1 M in H₂O, 31 μL, 0.031 mmols, 3 equiv.) was added. The reaction was stirred at room temperature for 1 hour and then directly purified by preparatory HPLC (Method B) then frozen and lyophilized to afford 134b (5.8 mg, 0.0049 mmol, 48% yield). UPLC-MS (Method E, ESI+): m/z [M+H]⁺=1176.52 (theoretical), 1176.76 (observed). HPLC retention time: 1.29 min

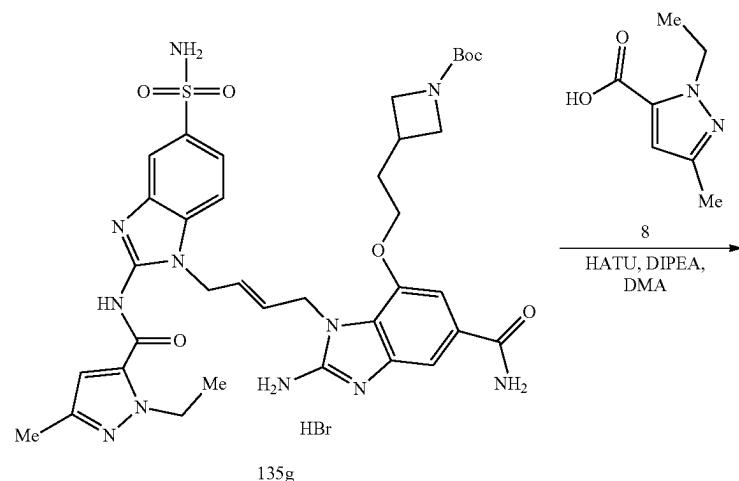
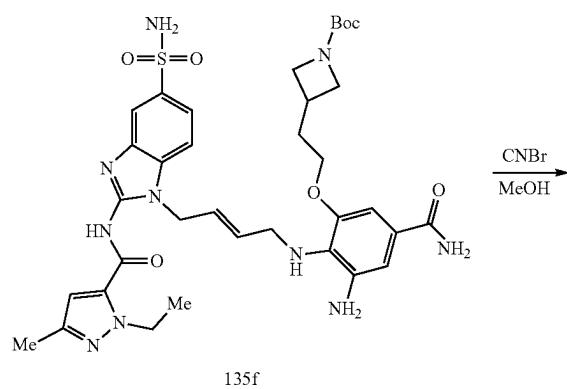
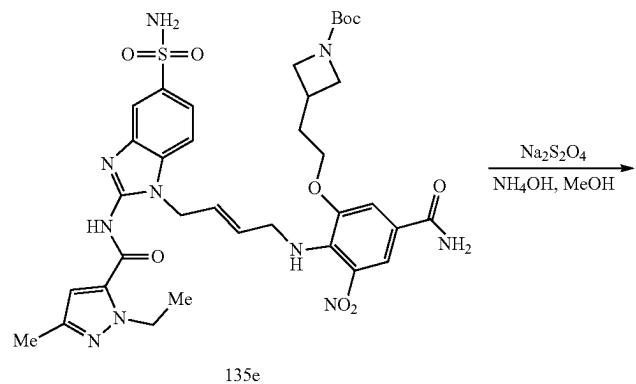
Synthesis of 134

[1660] 134b (5.8 mg, 0.0038 mmols, 1 equiv.) was added to an oven-dried 4 mL vial and dissolved in DMSO (1 mL) and then MP-OSu (10 mM in DMSO, 0.57 mL, 0.0057 mL, 1.5 equiv.) and DIPEA (2 μL, 0.0115 mmol, 3 equiv.) were added. The solution was stirred for 30 min, quenched with acetic acid and purified by preparatory HPLC (Method B), then frozen and lyophilized to afford 134 (3.6 mg, 0.0023 mmol, 61% yield). UPLC-MS (Method E, ESI+): m/z [M+H]⁺=1327.55 (theoretical), 1327.77 (observed). HPLC retention time: 1.38 min.

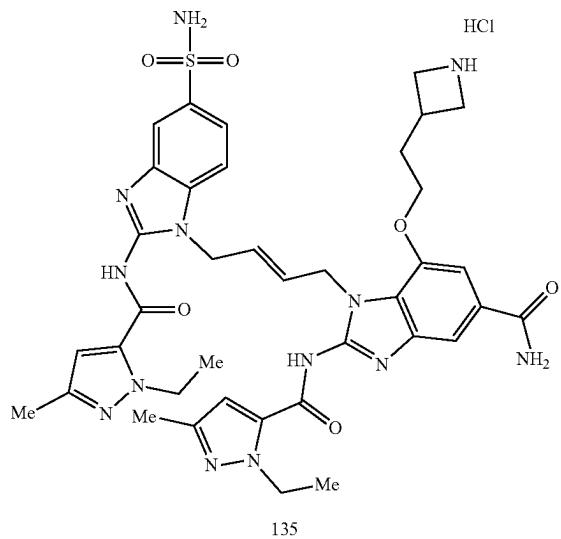
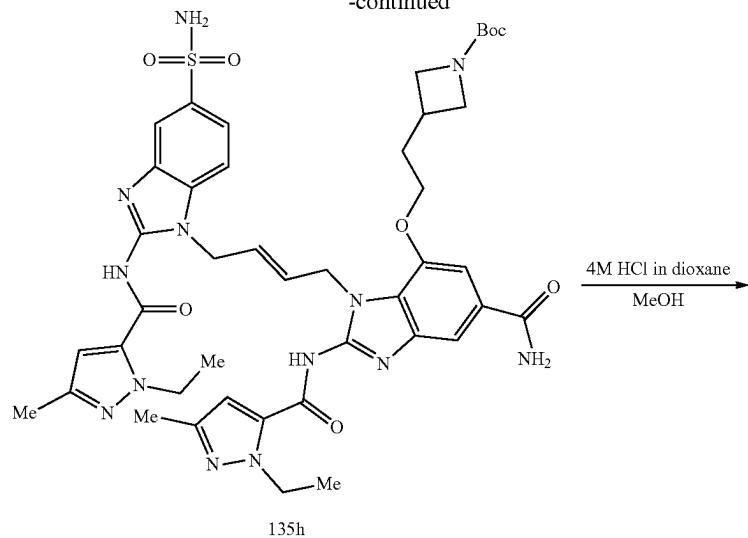
Synthesis of (E)-7-(2-(azetidin-3-yl)ethoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazole-5-carboxamide
(Compound 135)



-continued



-continued



Synthesis of 135a

[1661] To a solution of 25a (1.61 g, 4.18 mmol, 1 equiv.) in MeOH (63 mL) and aq. NH₄OH (21 mL) was added aq. Na₂S₂O₄ (1 M, 21 mL, 21 mmol, 5 equiv.). The mixture was stirred for 1 hour at 30° C., and the reaction was monitored by UPLC-MS (Method E, ESI+). Upon completion, the solution was filtered over celite and washed with MeOH. The filtrate was concentrated and the product was purified by flash chromatography (dry loaded on celite, Sfar HC Duo

SiO₂ column, 10:1 MeOH:NH₄OH gradient in DCM) to yield 135a (774 mg, 2.17 mmol, 52% yield). LC-MS (Method E, ESI+): m/z [M+H]⁺=357.2 (theoretical), 357.3 (observed). HPLC retention time: 1.44 min.

Synthesis of 135b

[1662] To a solution of compound 135a (774 mg, 2.17 mmol, 1 equiv.) in MeOH (4 mL) was added cyanogen bromide in MeCN (3 M, 1.5 mL, 4.35 mmol, 2 equiv.). The

solution stirred for 18 hours at 30° C. and was monitored via UPLC-MS (Method E, ESI+). Upon completion, solvent was removed in vacuo to yield 135b (1.0 g, 2.25 mmol, quantitative yield). LC-MS (Method E, ESI+): m/z [M+H]⁺ = 382.2 (theoretical), 382.2 (observed). HPLC retention time: 1.12 min.

Synthesis of 135c

[1663] A microwave vial was charged with a solution of 135b (1.0 g, 2.25 mmol, 1 equiv.) in DMA (11 mL), to which was added compound 8 (1.0 g, 6.74 mmol, 3 equiv.), HATU (2.6 g, 6.74 mmol, 3 equiv.) and DIPEA (1.2 mL, 6.74 mmol, 3 equiv.). This mixture was heated to 80° C. for 1 hour in a microwave reactor. Upon completion, 135c was isolated by precipitation with cold water (1.0 g, 1.93 mmol, 86% yield). LC-MS (Method E, ESI+): m/z [M+H]⁺ = 518.2 (theoretical), 518.3 (observed). HPLC retention time: 1.60 min.

Synthesis of 135d

[1664] To a solution of 135c (1.0 g, 1.93 mmol, 1 equiv.) in MeOH (3.3 mL) was added HCl in dioxane (4 M, 5.3 mL, 21 mmol, 8 equiv.). The mixture stirred for 1 hour at 30° C. Upon completion, solvent was removed in vacuo and 135d (1.2 g, 2.65 mmol, quantitative yield) was used without further purification. LC-MS (Method E, ESI+): m/z [M+H]⁺ = 418.2 (theoretical), 418.2 (observed). HPLC retention time: 1.09 min.

Synthesis of 135e

[1665] Compounds 135d (200 mg, 0.408 mmol, 1 equiv.) and 26a (245 mg, 0.612 mmol, 1.5 equiv.) were dissolved in n-butanol (2.0 mL) in a 5 mL microwave vial to which Na₂CO₃ (130 mg, 1.22 mmol, 3 equiv.) and DIPEA (0.36 mL, 2.04 mmol, 5 equiv.) were added. The reaction was heated via microwave reactor at 140° C. for 3 hours. The resulting product was filtered and washed with MeOH and DCM. The filtrate was concentrated and purified via flash chromatography (dry loaded on celite, Sfar HC Duo SiO₂ column, 10:1 MeOH:NH₄OH gradient in DCM) to yield 135e (51 mg, 0.0651 mmol, 16% yield). LC-MS (Method E, ESI+): m/z [M+H]⁺ = 781.3 (theoretical), 781.4 (observed). HPLC retention time: 1.72 min.

Synthesis of 135f

[1666] Compound 135f (30 mg, 0.0402 mmol, 62% yield) was prepared using the same procedure as 135a, using 135e (51 mg, 0.0651 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺ = 751.3 (theoretical), 751.4 (observed). HPLC retention time: 1.46 min.

Synthesis of 135g

[1667] Compound 135g (34 mg, 0.0394 mmol, quantitative yield) was prepared using the same procedure as 135b, using 135f (30 mg, 0.0402 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺ = 776.3 (theoretical), 776.4 (observed). HPLC retention time: 1.54 min.

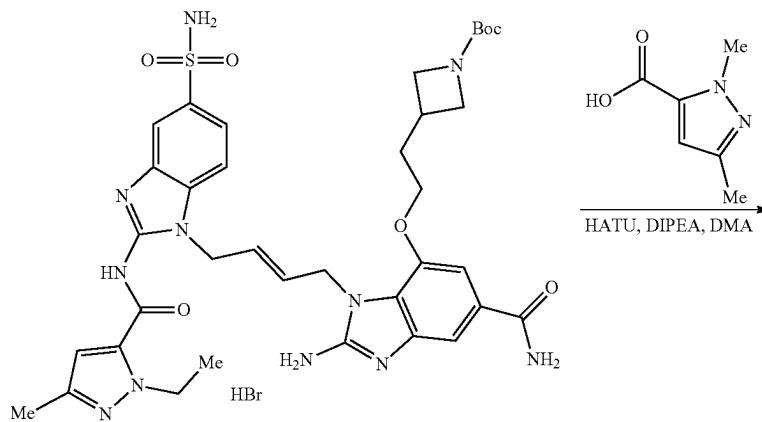
Synthesis of 135h

[1668] Compound 135h was prepared using the same procedure as 135c, using 135g (17 mg, 0.0197 mmol, 1 equiv.) as the starting material. Upon completion, the product was purified by preparatory HPLC (Method H). Pure fractions were collected, frozen and lyophilized to afford 135h (2.34 mg, 0.0021 mmol, 10% yield) as a white powder. LC-MS (Method E, ESI+): m/z [M+H]⁺ = 912.4 (theoretical), 912.5 (observed). HPLC retention time: 1.65 min.

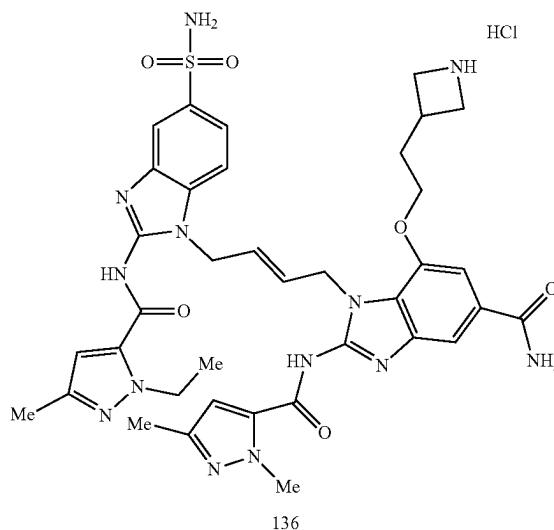
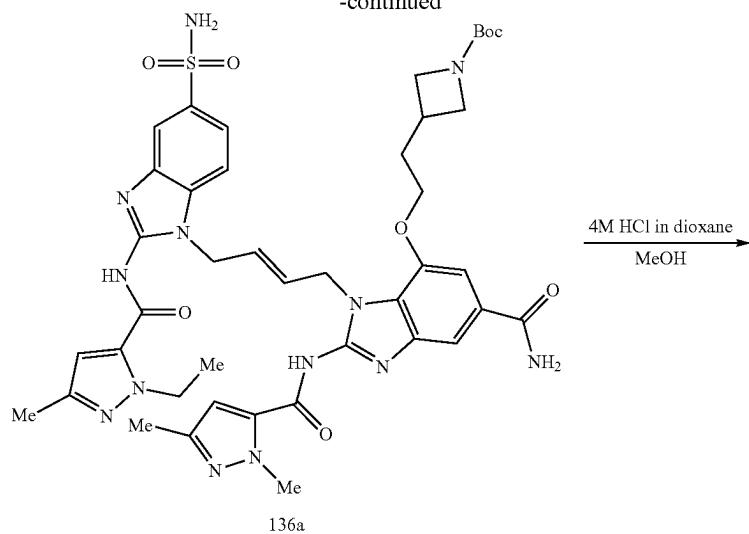
Synthesis of 135

[1669] Compound 135h (2.34 mg, 0.0021 mmol, 1 equiv.) was dissolved in MeOH (0.21 mL) and HCl in dioxane (4 M, 4.1 μL, 0.0164 mmol, 8 equiv.) was added. The solution was heated to 40° C. for 1 hour. Then solvent was removed in vacuo and 135 (1.86 mg, 0.0020 mmol, quantitative yield) was used without further purification. LC-MS (Method E, ESI+): m/z [M+H]⁺ = 812.3 (theoretical), 812.4 (observed). HPLC retention time: 1.26 min.

Synthesis of (E)-7-(2-(azetidin-3-yl)ethoxy)-2-(1,3-dimethyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazole-5-carboxamide (Compound 136)



-continued



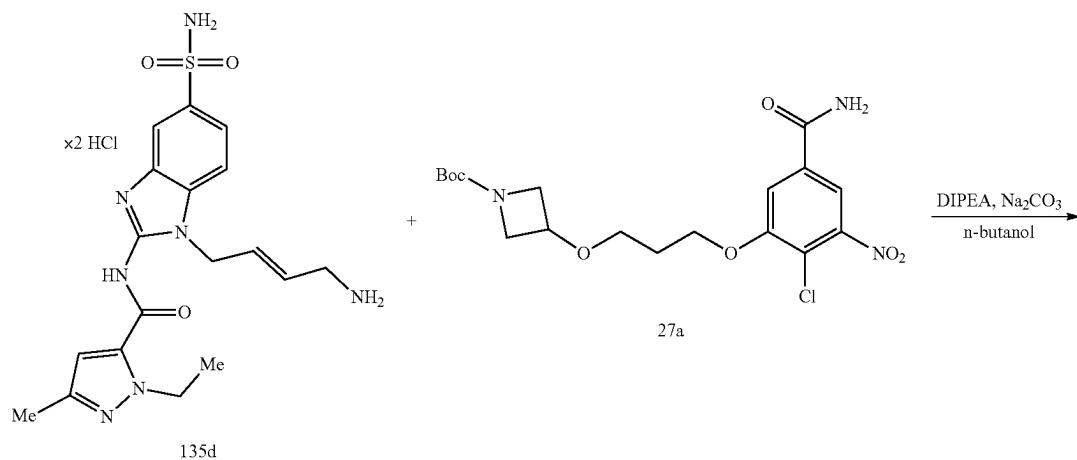
Synthesis of 136a

[1670] Compound 136a (3.15 mg, 0.0028 mmol, 14% yield) was prepared using the same procedure as 135h, using 135g (17 mg, 0.0197 mmol, 1 equiv.) and 1, 3-dimethyl-1H-pyrazole-5-carboxylic acid as the starting materials. LC-MS (Method E, ESI+): m/z [M+H]⁺=898.4 (theoretical), 898.5 (observed). HPLC retention time: 1.62 min.

Synthesis of 136

[1671] Compound 136 (2.09 mg, 0.0023 mmol, 82% yield) was prepared using the same procedure as 135, using 136a (3.15 mg, 0.0028 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=798.3 (theoretical), 798.4 (observed). HPLC retention time: 1.24 min.

Synthesis of (E)-7-(3-(azetidin-3-yloxy)propoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazole-5-carboxamide
(Compound 137)

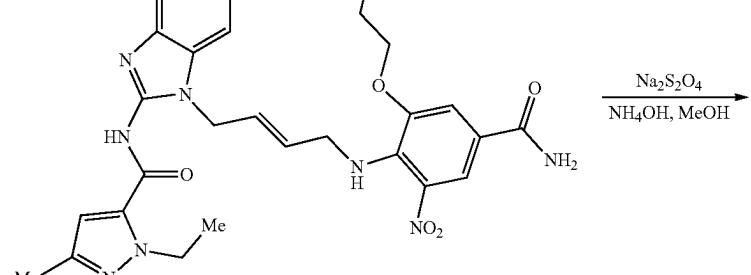


135d

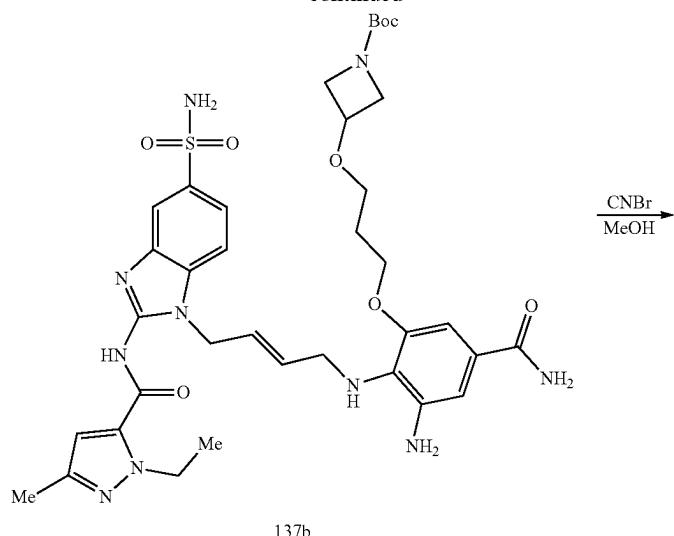
27a

DIPEA, Na_2CO_3
n-butanol

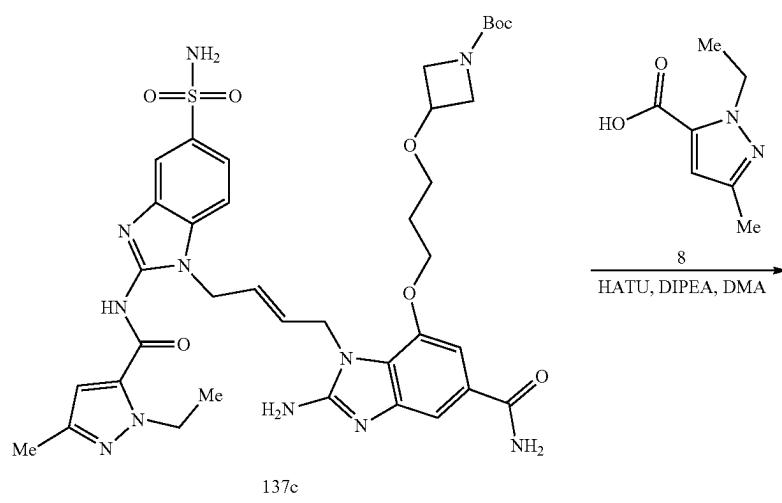
137a



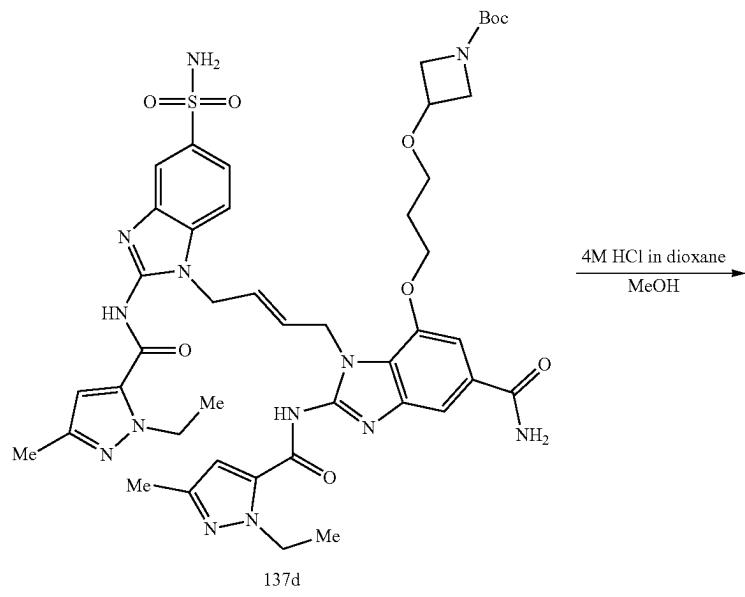
-continued



137b

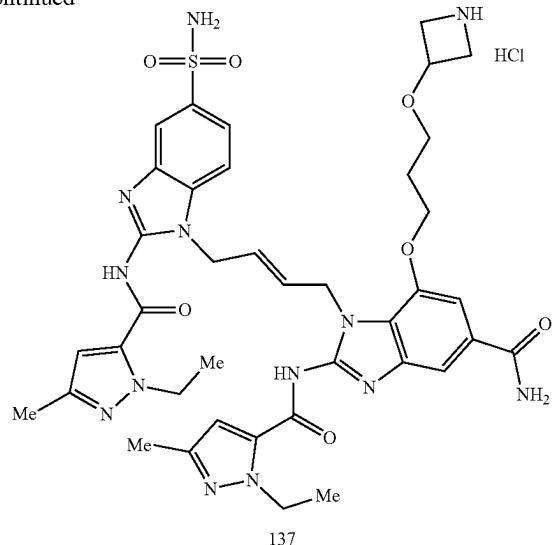


137c



137d

-continued

**Synthesis of 137a**

[1672] Compound 137a (72 mg, 0.0893 mmol, 22% yield) was prepared using the same procedure as 135e, using 135d (200 mg, 0.408 mmol, 1 equiv.) and 27a (263 mg, 0.612 mmol, 1.5 equiv.) as the starting materials. LC-MS (Method E, ESI+): m/z [M+H]⁺=811.3 (theoretical), 811.4 (observed). HPLC retention time: 1.72 min.

Synthesis of 137b

[1673] Compound 137b (30 mg, 0.0386 mmol, 43% yield) was prepared using the same method as 135a, using 137a (72 mg, 0.0893 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=781.3 (theoretical), 781.4 (observed). HPLC retention time: 1.46 min.

Synthesis of 137c

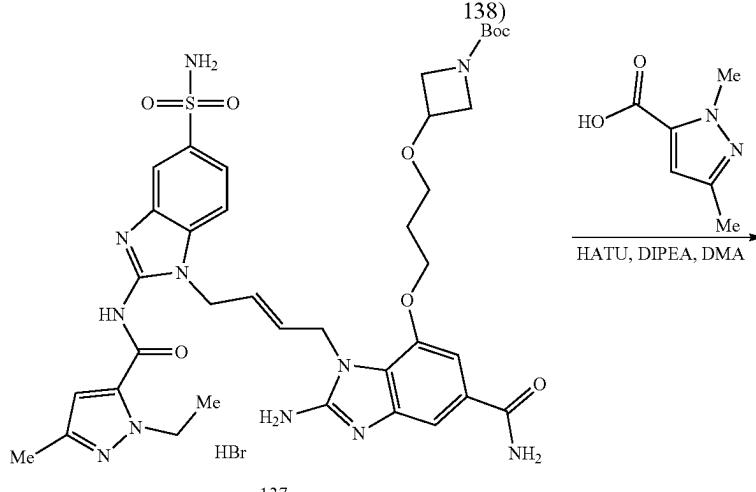
[1674] Compound 137c (34 mg, 0.0387 mmol, quantitative yield) was prepared using the same procedure as 135b, using 137b (30 mg, 0.03896 mmol, 1 equiv.) as the starting material. LC-MS (Method E, EST+): m/z [M+H]⁺=806.3 (theoretical), 806.4 (observed). HPLC retention time: 1.53 min.

Synthesis of 137d

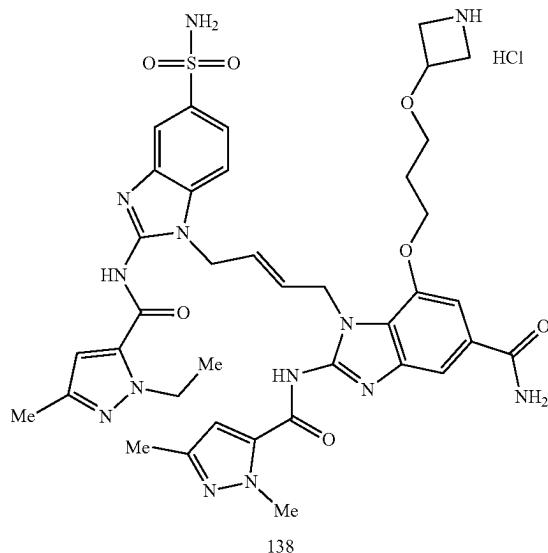
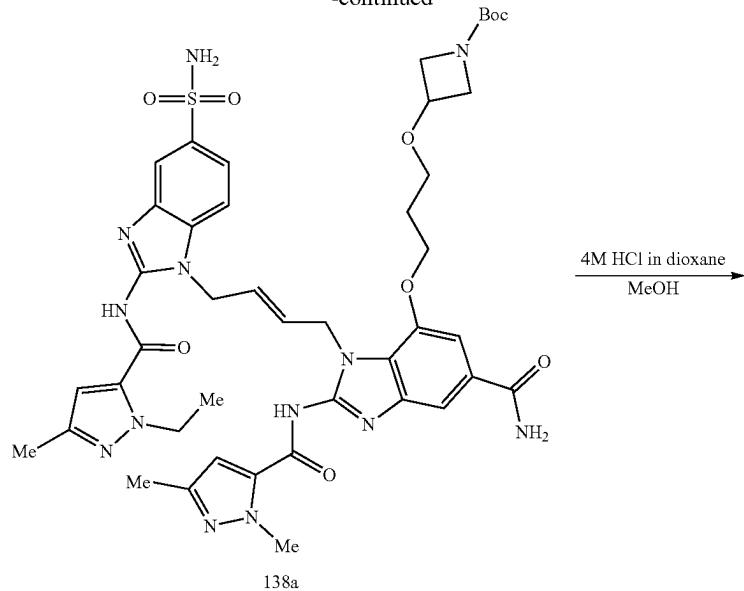
[1675] Compound 137d (4.21 mg, 0.0036 mmol, 19% yield) was prepared using the same procedure as 135h, using 137c (17 mg, 0.0194 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=942.4 (theoretical), 942.5 (observed). HPLC retention time: 1.65 min.

Synthesis of Compound 137

[1676] Compound 137 (3.35 mg, 0.0035 mmol, quantitative yield), was prepared using the same procedure as 135, using 137d (4.21 mg, 0.0036 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=842.3 (theoretical), 842.4 (observed). HPLC retention time: 1.29 min.

Synthesis of (E)-7-(3-(azetidin-3-yloxy)propoxy)-2-(1,3-dimethyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazole-5-carboxamide (Compound 138)

-continued



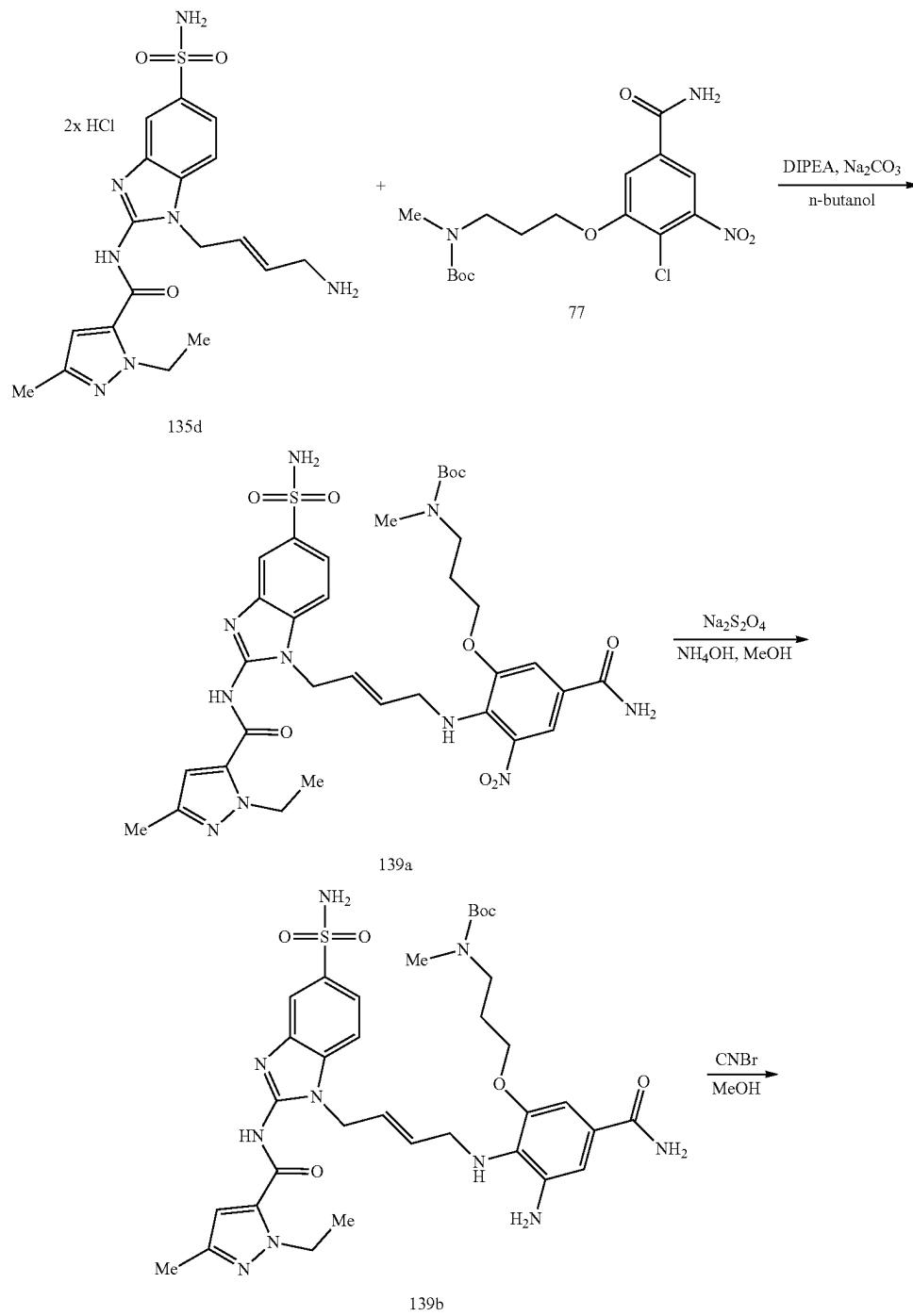
Synthesis of 138a

[1677] Compound 138a (3.00 mg, 0.0026 mmol, 13% yield) was prepared using the same procedure as 135h, using 137c (17 mg, 0.0197 mmol, 1 equiv.) and 1, 3-dimethyl-1H-pyrazole-5-carboxylic acid as the starting materials. LC-MS (Method E, EST+): m/z [M+H]⁺=928.4 (theoretical), 928.5 (observed). HPLC retention time: 1.62 min.

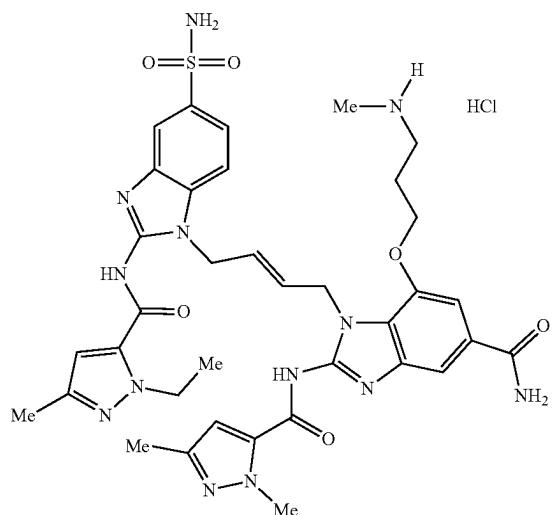
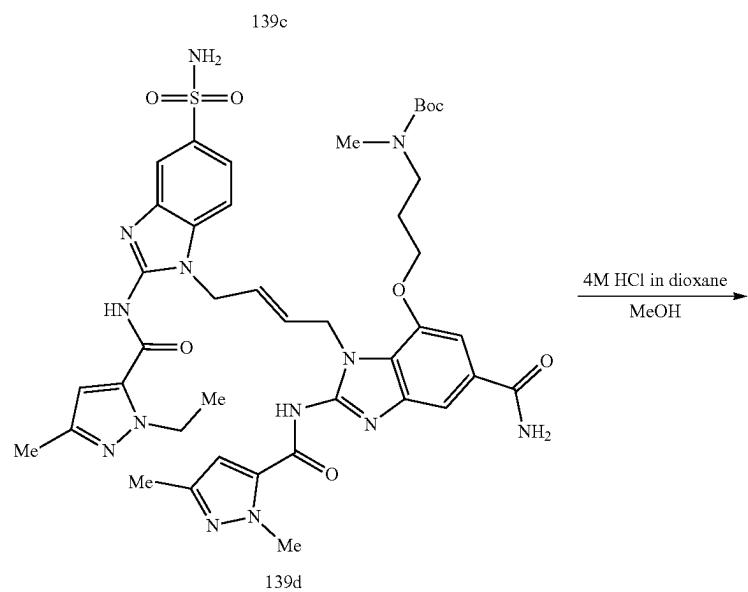
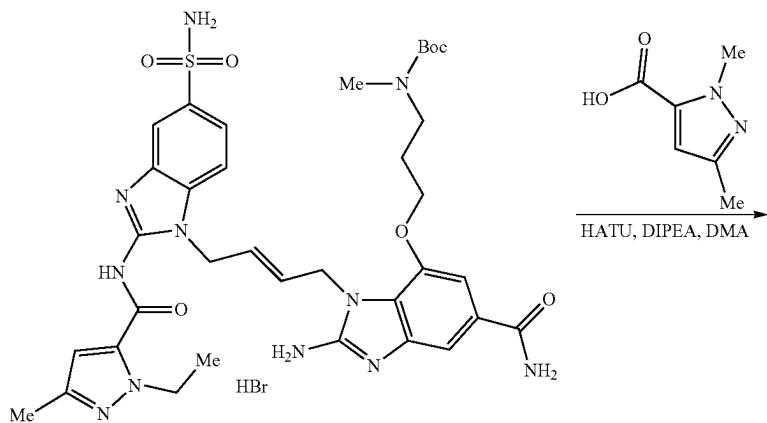
Synthesis of 138

[1678] Compound 138 (2.35 mg, 0.0025 mmol, quantitative yield), was prepared using the same procedure as 135, using 138a (3.00 mg, 0.0026 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=828.3 (theoretical), 828.4 (observed). HPLC retention time: 1.26 min.

Synthesis of (E)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(3-(methylamino)propoxy)-1H-benzo[d]imidazole-5-carboxamide (Compound 139)



-continued



Synthesis of 139a

[1679] Compound 139a (125 mg, 0.162 mmol, 29% yield) was prepared using the same procedure as 135e, using 135d (250 mg, 0.551 mmol, 1 equiv.) and 77 (320 mg, 0.826 mmol, 1.5 equiv.) as the starting materials. LC-MS (Method E, ESI+): m/z [M+H]⁺=769.3 (theoretical), 769.4 (observed). HPLC retention time: 1.67 min.

Synthesis of 139b

[1680] Compound 139b (51 mg, 0.0686 mmol, 42% yield) was prepared using the same procedure as 135a, using 139a (125 mg, 0.162 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=739.3 (theoretical), 739.4 (observed). HPLC retention time: 1.45 min.

Synthesis of 139c

[1681] Compound 139c (57 mg, 0.0670 mmol, quantitative yield) was prepared using the same procedure as 135b, using 139b (51 mg, 0.0686 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=764.3 (theoretical), 764.4 (observed). HPLC retention time: 1.31 min.

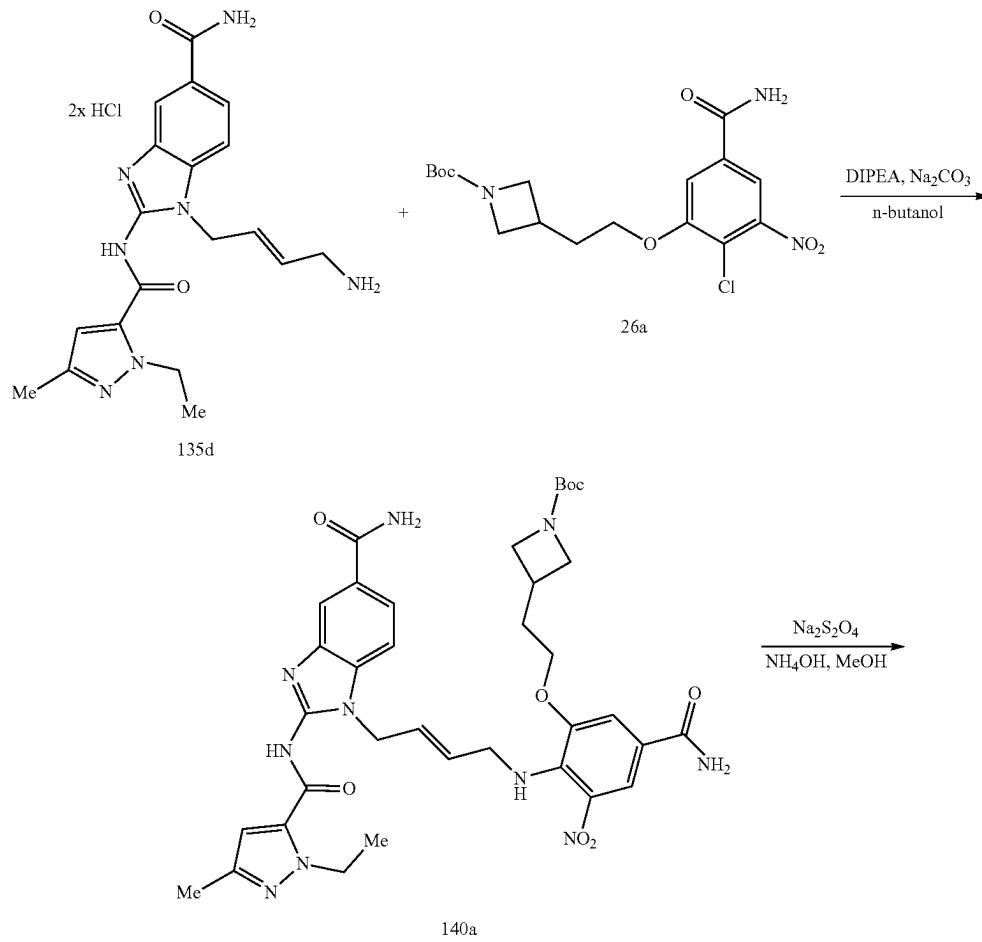
Synthesis of 139d

[1682] Compound 139d (34 mg, 0.0303 mmol, 45% yield) was prepared following the same procedure as 135h using 139c (57 mg, 0.0670 mmol, 1 equiv.) and 1, 3-dimethyl-1H-pyrazole-5-carboxylic acid as the starting materials. LC-MS (Method E, EST+): m/z [M+H]⁺=886.4 (theoretical), 886.5 (observed). HPLC retention time: 1.61 min.

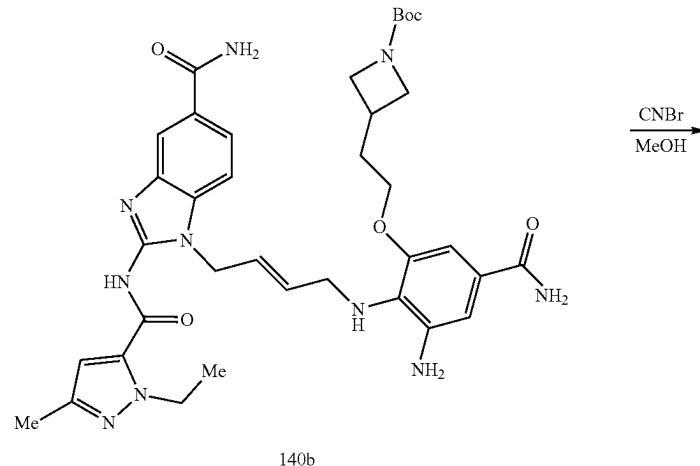
Synthesis of 139

[1683] Compound 139 (27 mg, 0.0291, quantitative yield) was prepared using the same procedure as 135, using 139d (34 mg, 0.0303 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=786.3 (theoretical), 786.4 (observed). HPLC retention time: 1.23 min.

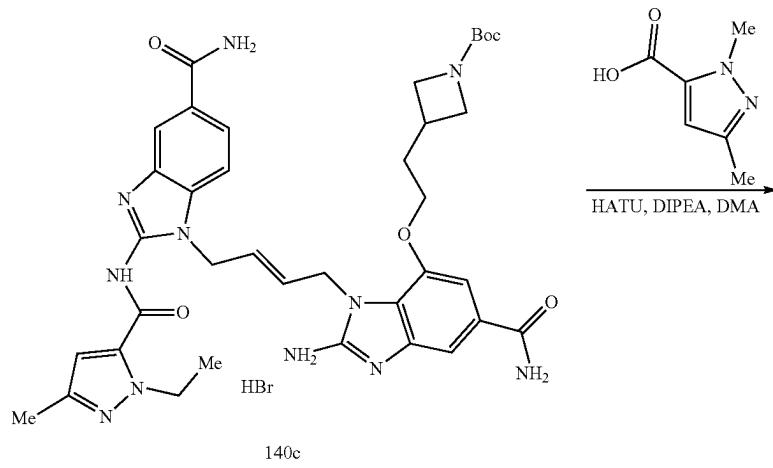
Synthesis of (E)-7-(2-(azetidin-3-yl)ethoxy)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1,3-dimethyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazole-5-carboxamide (Compound 140)



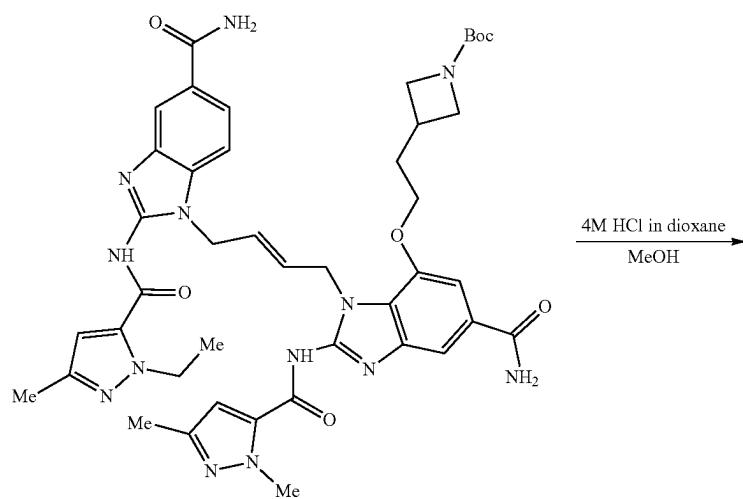
-continued



140b

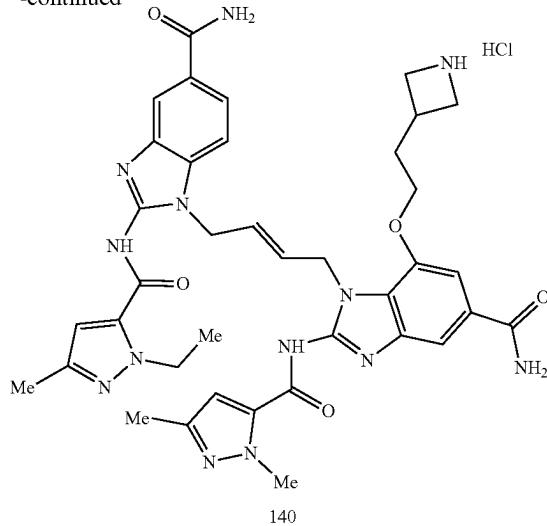


140c



140d

-continued



Synthesis of 140a

[1684] Compound 140a (380 mg, 0.490 mmol, 78% yield) was prepared using the same procedure as 135e, using 26a (250 mg, 0.625 mmol, 1 equiv.) and 78d (420 mg, 0.938 mmol, 1.5 equiv.) as the starting materials. The product was precipitated in cold water and used without further purification. LC-MS (Method E, ESI+): m/z [M+H]⁺=775.3 (theoretical), 775.4 (observed). HPLC retention time: 1.66 min.

Synthesis of 140b

[1685] Compound 140b (193 mg, 0.260 mmol, 53% yield) was prepared using the same procedure as 135a, using 140a (380 mg, 0.490 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=745.4 (theoretical), 745.5 (observed). HPLC retention time: 1.44 min.

Synthesis of 140c

[1686] Compound 140c (212 mg, 0.249 mmol, quantitative yield) was prepared using the same procedure as 135b, using 140b (193 mg, 0.260 mmol, 1 equiv.) as the starting

material. LC-MS (Method E, EST+): m/z [M+H]⁺=770.4 (theoretical), 770.5 (observed). HPLC retention time: 1.60 min.

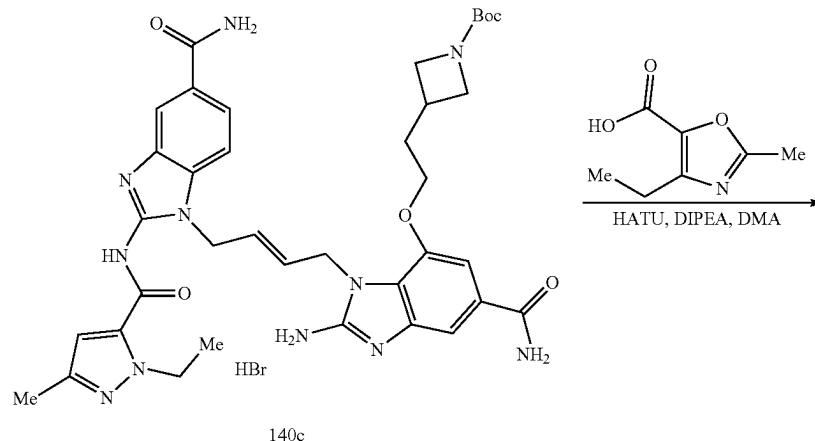
Synthesis of 140d

[1687] Compound 140d (38 mg, 0.0339 mmol, 27% yield) was prepared using the same procedure as 135h, using 140c (106 mg, 0.124 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=892.4 (theoretical), 892.5 (observed). HPLC retention time: 1.59 min.

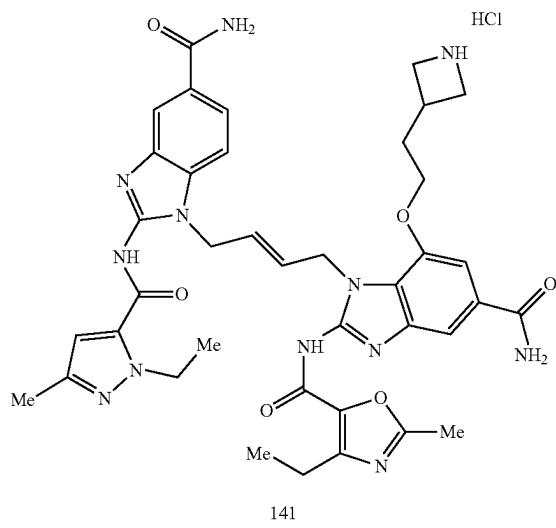
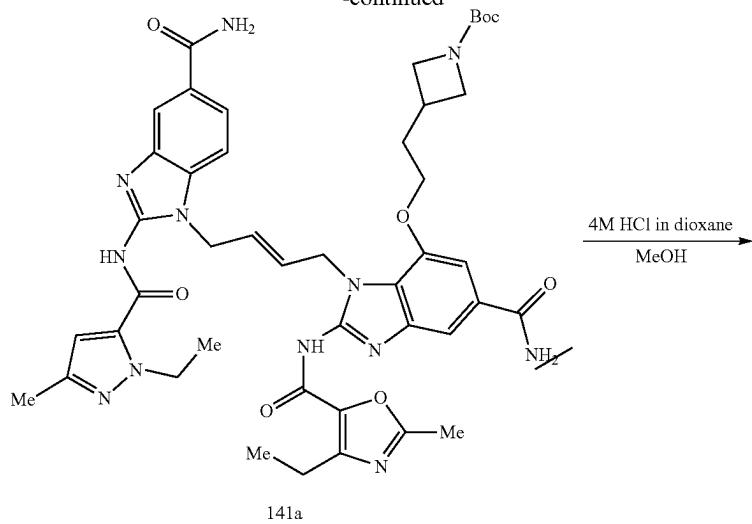
Synthesis of 140

[1688] Compound 140 (30 mg, 0.0334 mmol, quantitative yield) was prepared using the same procedure as 135, using 140d (38 mg, 0.0339 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=792.4 (theoretical), 792.5 (observed). HPLC retention time: 1.28 min.

Synthesis of (E)-N-(7-(2-(azetidin-3-yl)ethoxy)-5-carbamoyl-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazol-2-yl)-4-ethyl-2-methyloxazole-5-carboxamide (Compound 141)



-continued



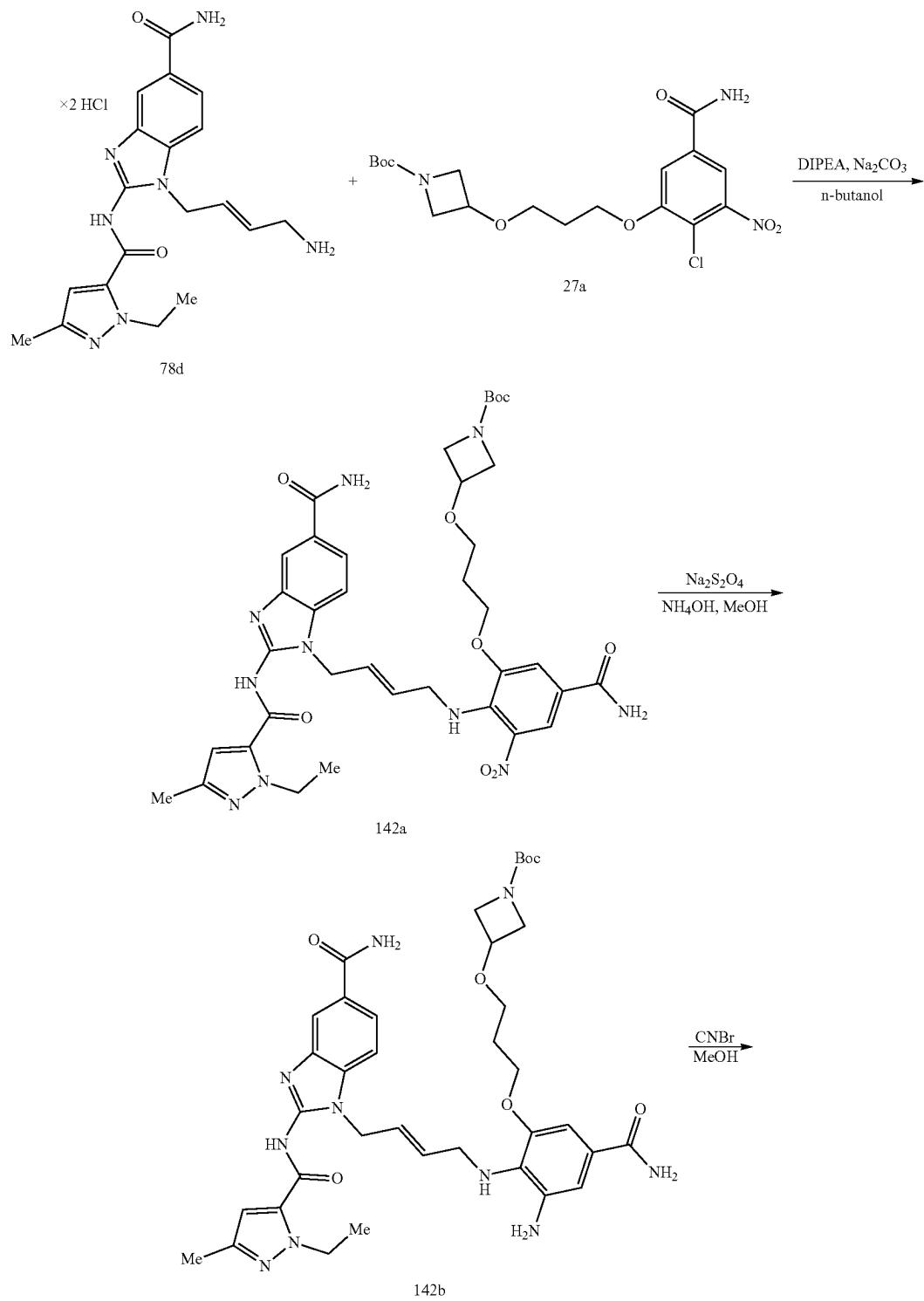
Synthesis of 141a

[1689] Compound 141a (27 mg, 0.0237 mmol, 19% yield) was prepared using the same procedure as 135h, using 140c (106 mg, 0.124 mmol, 1 equiv.) and 4-ethyl-2-methyl-oxazole-5-carboxylic acid as the starting materials. LC-MS (Method E, ESI+): m/z [M+H]⁺=907.4 (theoretical), 907.5 (observed). HPLC retention time: 1.57 min.

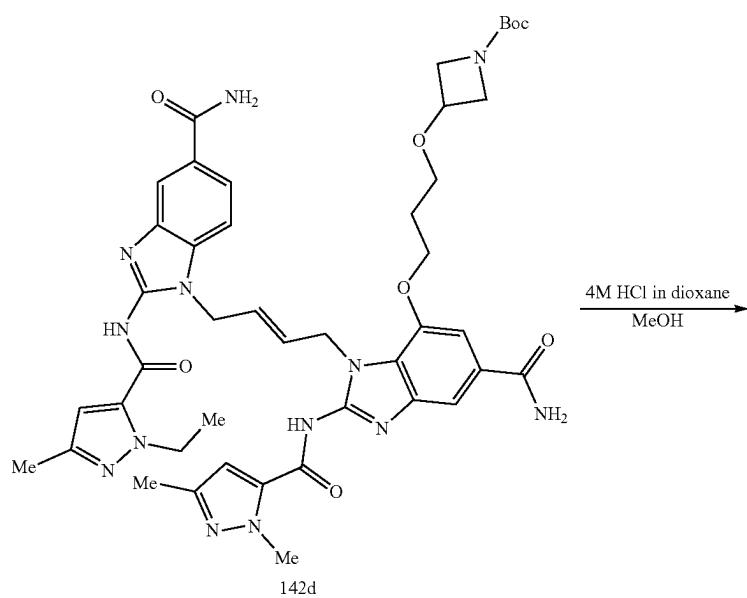
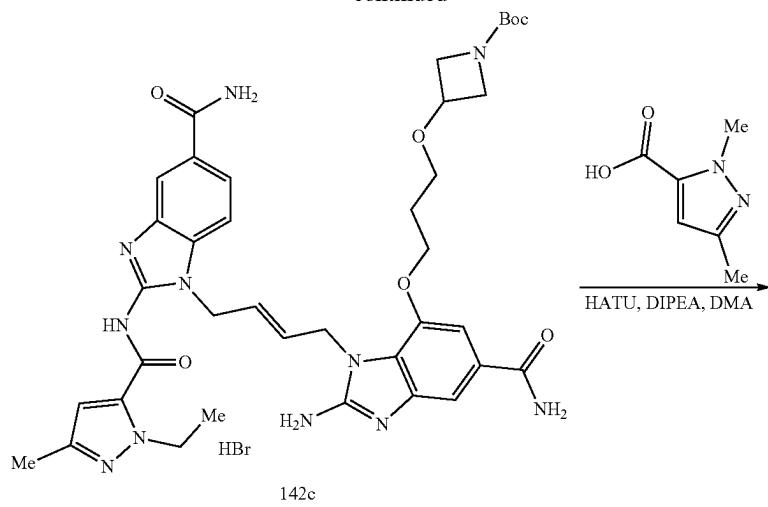
Synthesis of 141

[1690] Compound 141 (21 mg, 0.0230 mmol, quantitative yield), was prepared using the same procedure as 135, using 141a (27 mg, 0.0237 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=807.4 (theoretical), 807.5 (observed). HPLC retention time: 1.26 min.

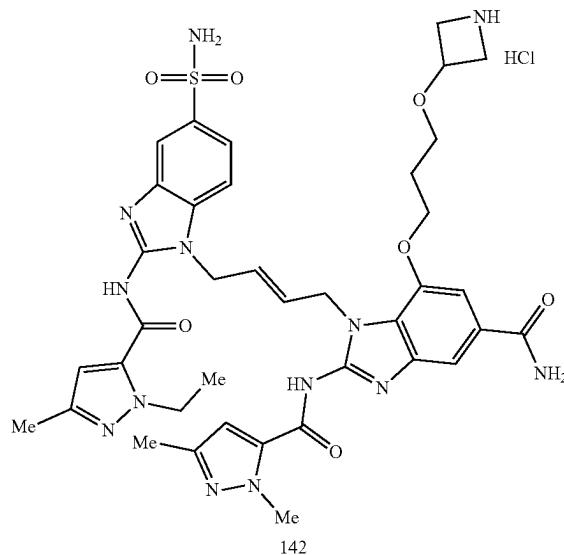
Synthesis of (E)-7-(3-(azetidin-3-yloxy)propoxy)-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1,3-dimethyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazole-5-carboxamide
(Compound 142)



-continued



-continued



Synthesis of 142a

[1691] Compound 142a was prepared using the same procedure as 135e, using 27a (250 mg, 0.582 mmol, 1 equiv.) and 78d (391 mg, 0.872 mmol, 1.5 equiv.) as the starting materials. The product was precipitated with cold water and used without further purification. LC-MS (Method E, ESI+): m/z [M+H]⁺=805.4 (theoretical), 805.4 (observed). HPLC retention time: 1.66 min.

Synthesis of 142b

[1692] Compound 142b (193 mg, 0.250 mmol, 37% yield over 2 steps) was prepared using the same procedure as 135a, using 142a (548 mg, 0.681 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=775.4 (theoretical), 775.5 (observed). HPLC retention time: 1.50 min.

Synthesis of 142c

[1693] Compound 142c (164 mg, 0.186 mmol, 75% yield) was prepared using the same procedure as 135b, using 142b

(193 mg, 0.260 mmol, 1 equiv.) as the starting material. LC-MS (Method E, EST+): m/z [M+H]⁺=800.4 (theoretical), 800.5 (observed). HPLC retention time: 1.33 min.

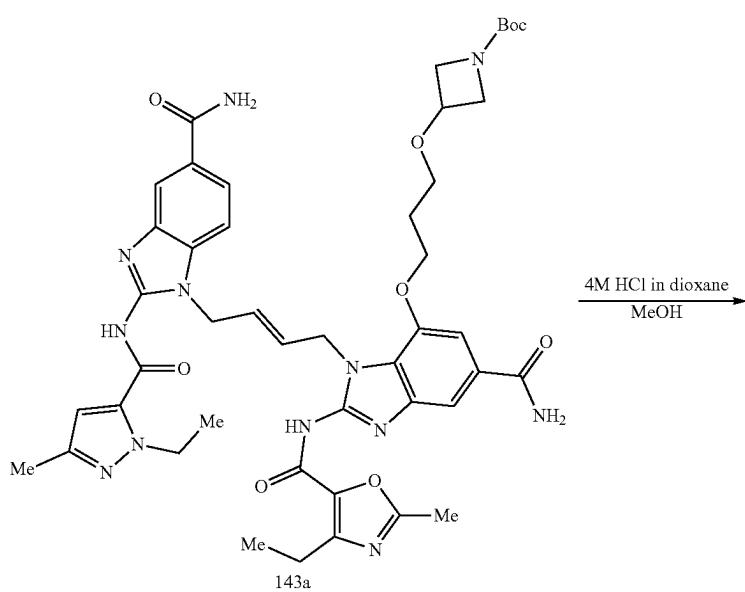
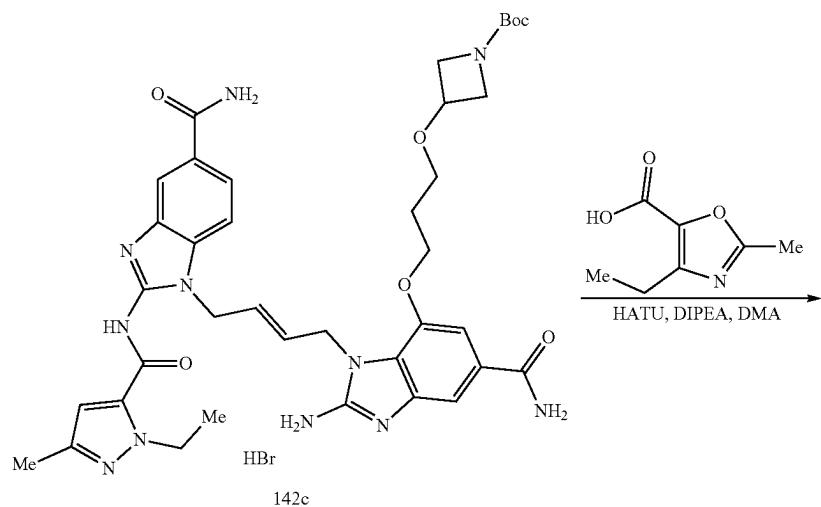
Synthesis of 142d

[1694] Compound 142d (40 mg, 0.0345 mmol, 37% yield) was prepared using the same procedure as 135h, using 142c (48 mg, 0.373 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=922.4 (theoretical), 922.5 (observed). HPLC retention time: 1.58 min.

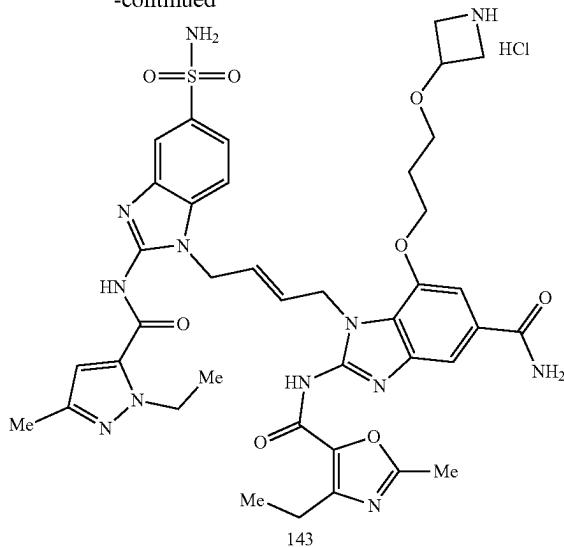
Synthesis of 142

[1695] Compound 142 (32 mg, 0.0323 mmol, quantitative yield) was prepared using the same procedure as 135, using 142d (40 mg, 0.0345 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=822.4 (theoretical), 822.5 (observed). HPLC retention time: 1.29 min.

Synthesis of (E)-N-(7-(3-(azetidin-3-yloxy)propoxy)-5-carbamoyl-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazol-2-yl)-4-ethyl-2-methyloxazole-5-carboxamide (Compound 143)



-continued



Synthesis of 143a

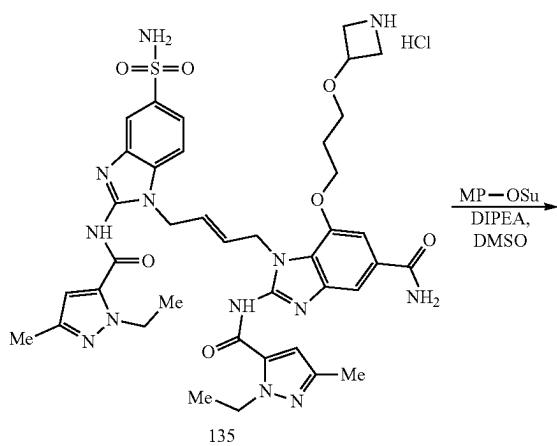
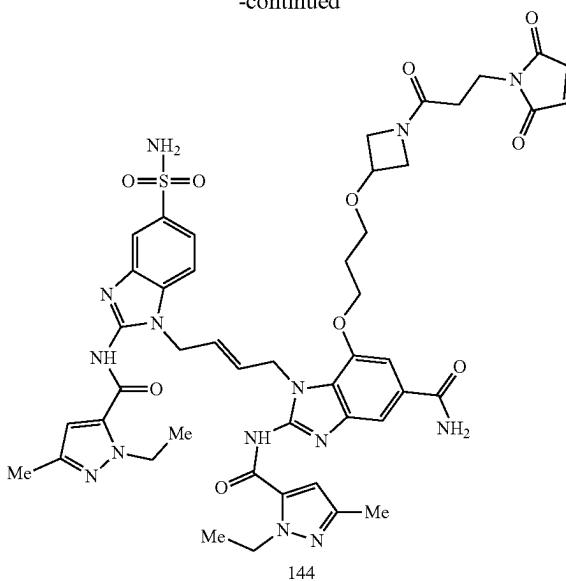
[1696] Compound 143a (31 mg, 0.0263 mmol, 28% yield) was prepared using the same procedure as 135h, using 142c (82 mg, 0.0931 mmol, 1 equiv.) and 4-ethyl-2-methyl-oxazole-5-carboxylic acid as the starting materials. LC-MS (Method E, ESI+): m/z [M+H]⁺=937.4 (theoretical), 937.5 (observed). HPLC retention time: 1.56 min.

Synthesis of 143

[1697] Compound 143 (25 mg, 0.0261 mmol, quantitative yield), was prepared using the same procedure as 135, using 141a (31 mg, 0.0263 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=837.4 (theoretical), 837.5 (observed). HPLC retention time: 1.29 min.

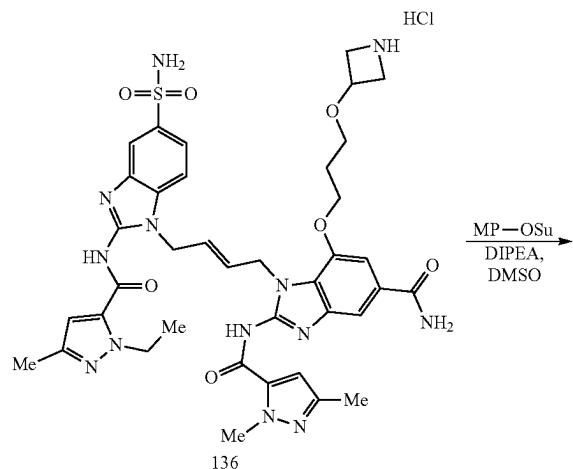
Synthesis of (E)-7-(2-(1-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)azetidin-3-yl)ethoxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazole-5-carboxamide (Compound 144)

-continued

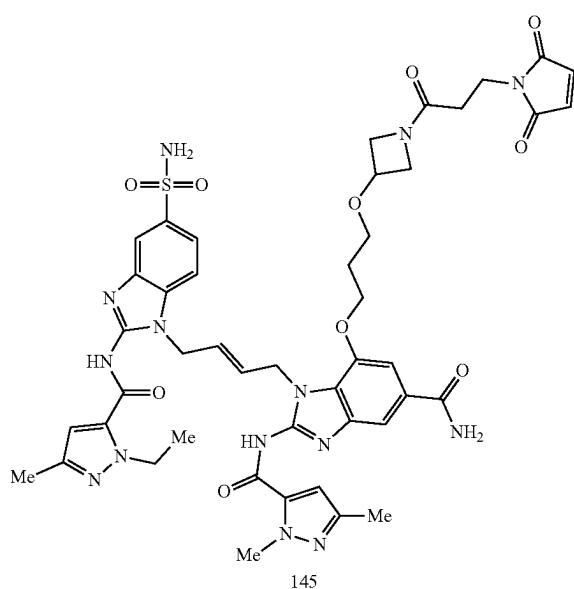
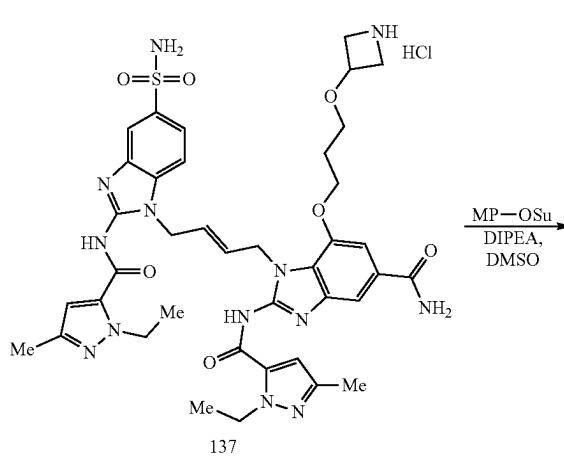


[1698] The $\times 2$ TFA salt of compound 144 (0.59 mg, 0.0005 mmol, 24% yield) was prepared according to general method 9, using compound 135 (1.86 mg, 0.0020 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=963.4 (theoretical), 963.5 (observed). HPLC retention time: 1.44 min.

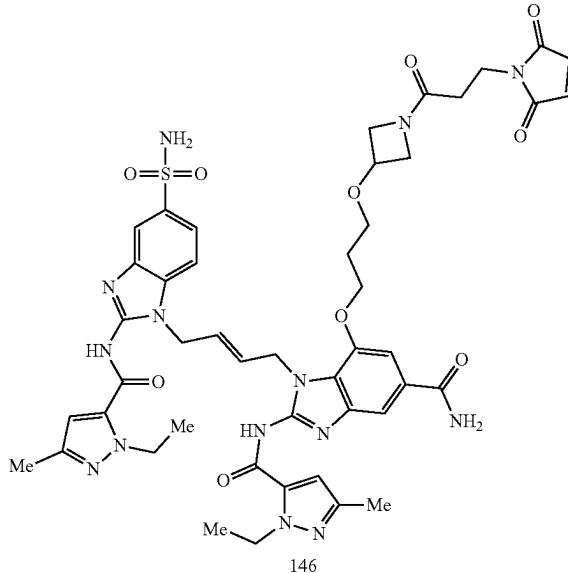
Synthesis of (E)-2-(1,3-dimethyl-1H-pyrazole-5-carboxamido)-7-(2-(1-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)azetidin-3-yl)ethoxy)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazole-5-carboxamide (Compound 145)



Synthesis of (E)-7-((1-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)azetidin-3-yl)oxy)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazole-5-carboxamide (Compound 146)

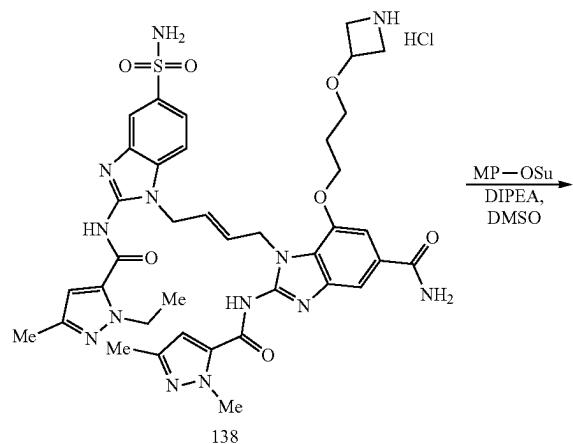


[1699] The $\times 2$ TFA salt of compound 145 (0.31 mg, 0.0003 mmol, 12% yield) was prepared according to general method 9, using compound 136 (2.09 mg, 0.0023 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI $^+$): m/z [M+H] $^+$ =949.3 (theoretical), 949.5 (observed). HPLC retention time: 1.40 min.

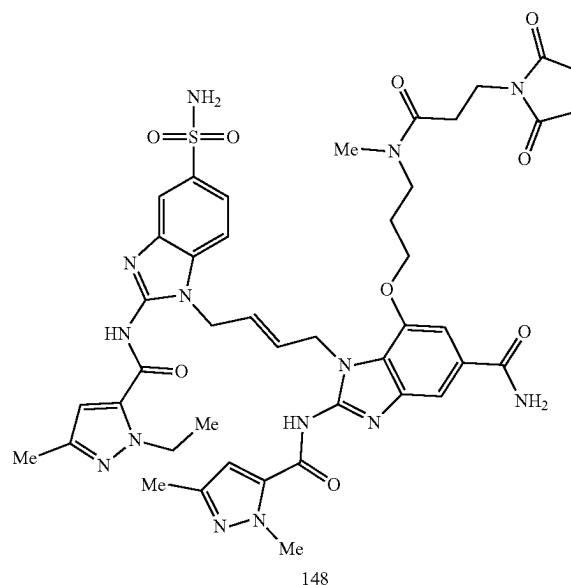
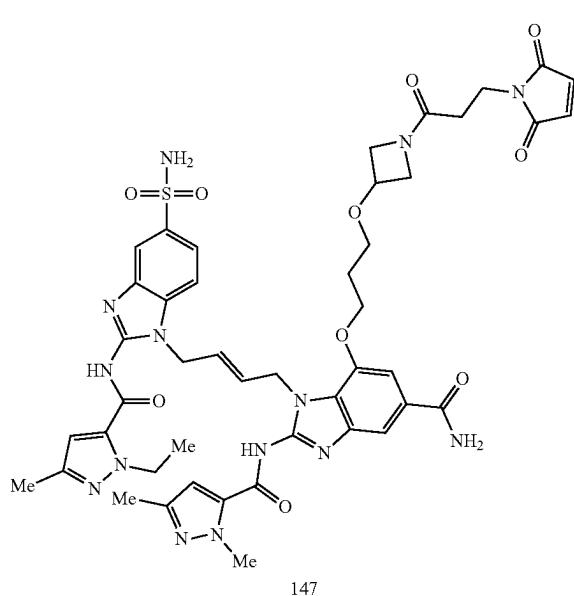
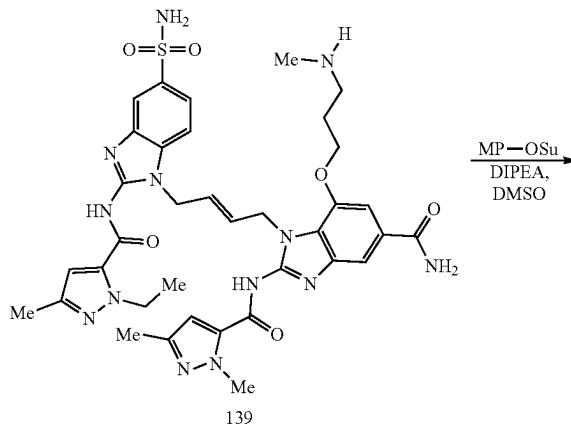


[1700] The $\times 2$ TFA salt of compound 146 (0.92 mg, 0.0008 mmol, 21% yield) was prepared according to general method 9, using compound 137 (3.35 mg, 0.0035 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI $^+$): m/z [M+H] $^+$ =993.4 (theoretical), 993.5 (observed). HPLC retention time: 1.43 min.

Synthesis of (E)-2-(1,3-dimethyl-1H-pyrazole-5-carboxamido)-7-(3-((1-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)azetidin-3-yl)oxy)propoxy)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazole-5-carboxamide (Compound 147)



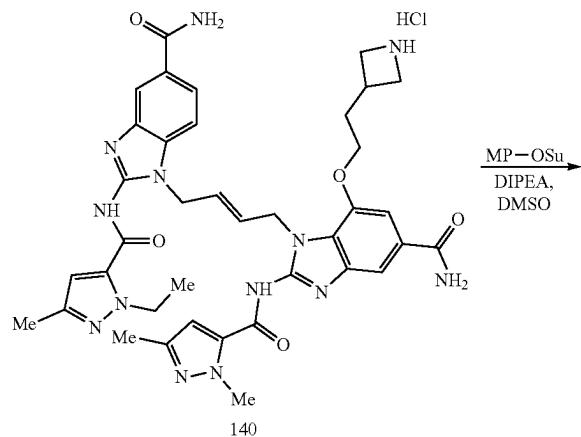
Synthesis of (E)-2-(1,3-dimethyl-1H-pyrazole-5-carboxamido)-7-(3-((1-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)azetidin-3-yl)oxy)propoxy)-1-(4-(2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-5-sulfamoyl-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-1H-benzo[d]imidazole-5-carboxamide
(Compound 148)



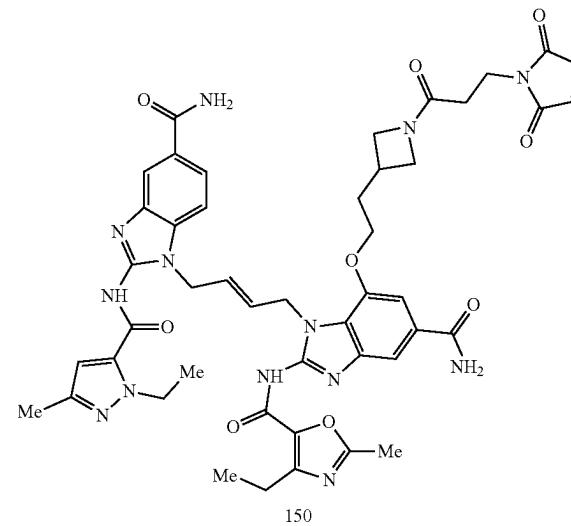
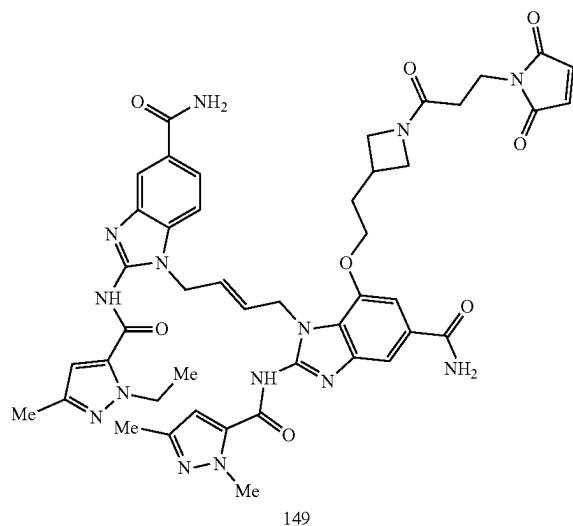
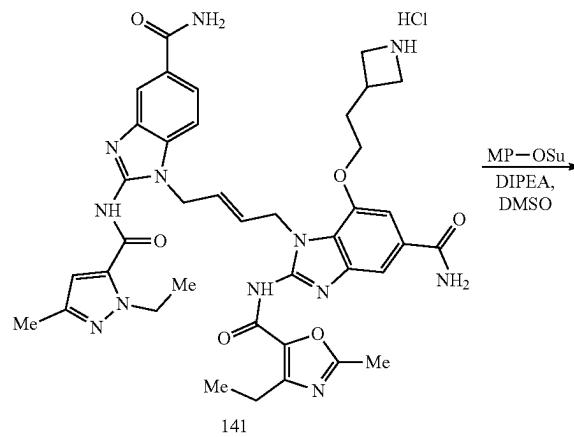
[1701] The $\times 2$ TFA salt of compound 147 (0.36 mg, 0.0003 mmol, 12% yield) was prepared according to general method 9, using compound 136 (2.83 mg, 0.0024 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI $^+$): m/z [M+H] $^+$ =979.4 (theoretical), 979.5 (observed). HPLC retention time: 1.41 min.

[1702] The $\times 2$ TFA salt of compound 148 (15 mg, 0.0129 mmol, 44% yield) was prepared according to general method 9, using compound 139 as the starting material. LC-MS (Method E, ESI $^+$): m/z [M+H] $^+$ =937.3 (theoretical), 937.4 (observed). HPLC retention time: 1.42 min.

Synthesis of (E)-1-(4-(5-carbamoyl-2-(1,3-dimethyl-1H-pyrazole-5-carboxamido)-7-(2-(1-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)azetidin-3-yl)ethoxy)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxamide
(Compound 149)



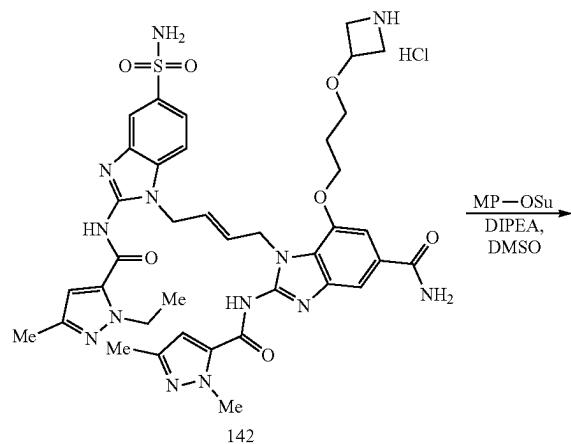
Synthesis of (E)-N-(5-carbamoyl-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(2-(1-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)azetidin-3-yl)ethoxy)-1H-benzo[d]imidazol-2-yl)-4-ethyl-2-methyloxazole-5-carboxamide (Compound 150)



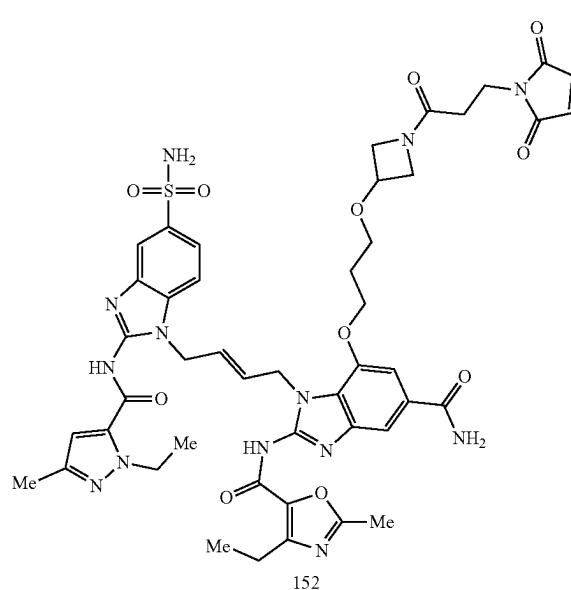
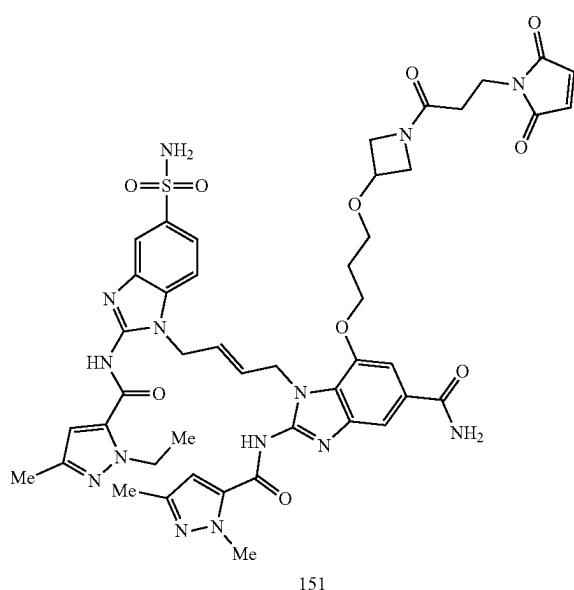
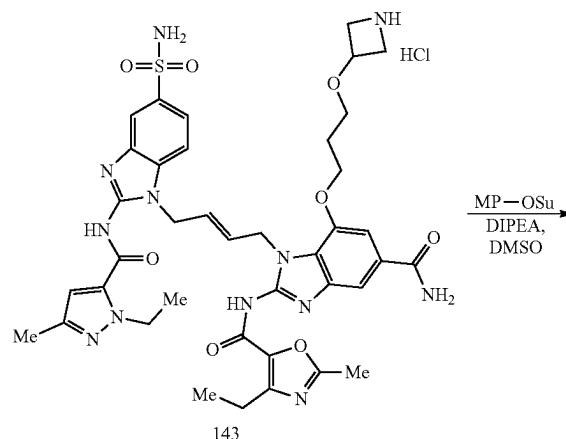
[1703] The $\times 2$ TFA salt of compound 149 (16 mg, 0.0136 mmol, 41% yield) was prepared according to general method 9, using compound 140 (30 mg, 0.0334 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI $^+$): m/z [M+H] $^+$ =943.4 (theoretical), 943.5 (observed). HPLC retention time: 1.41 min.

[1704] The $\times 2$ TFA salt of compound 150 (15 mg, 0.0123 mmol, 53% yield) was prepared according to general method 9, using compound 141 (21 mg, 0.0230 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI $^+$): m/z [M+H] $^+$ =943.4 (theoretical), 943.5 (observed). HPLC retention time: 1.41 min.

Synthesis of (E)-1-(4-(5-carbamoyl-2-(1,3-dimethyl-1H-pyrazole-5-carboxamido)-7-(3-((1-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)azetidin-3-yl)oxy)propoxy)-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazole-5-carboxamide (Compound 151)



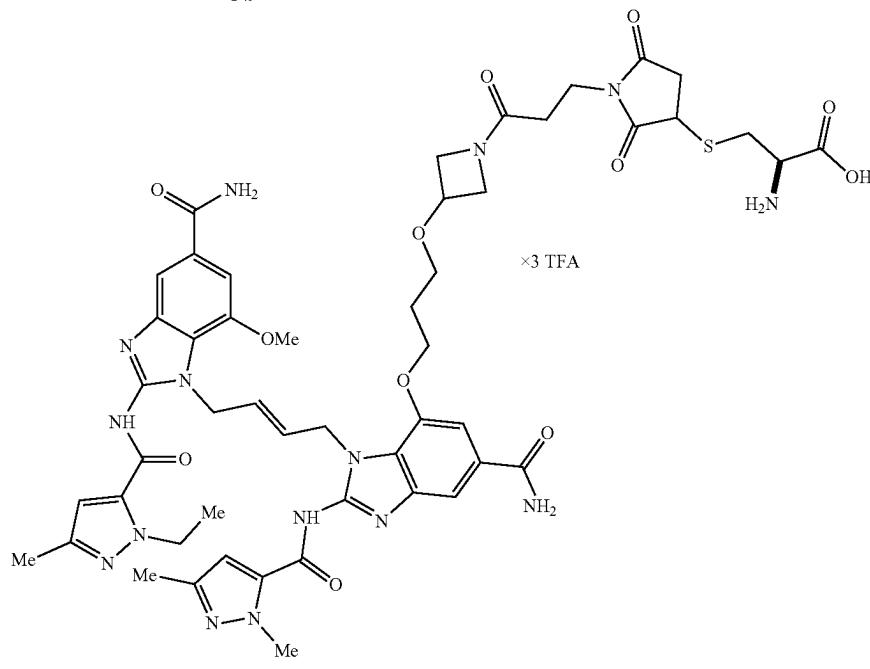
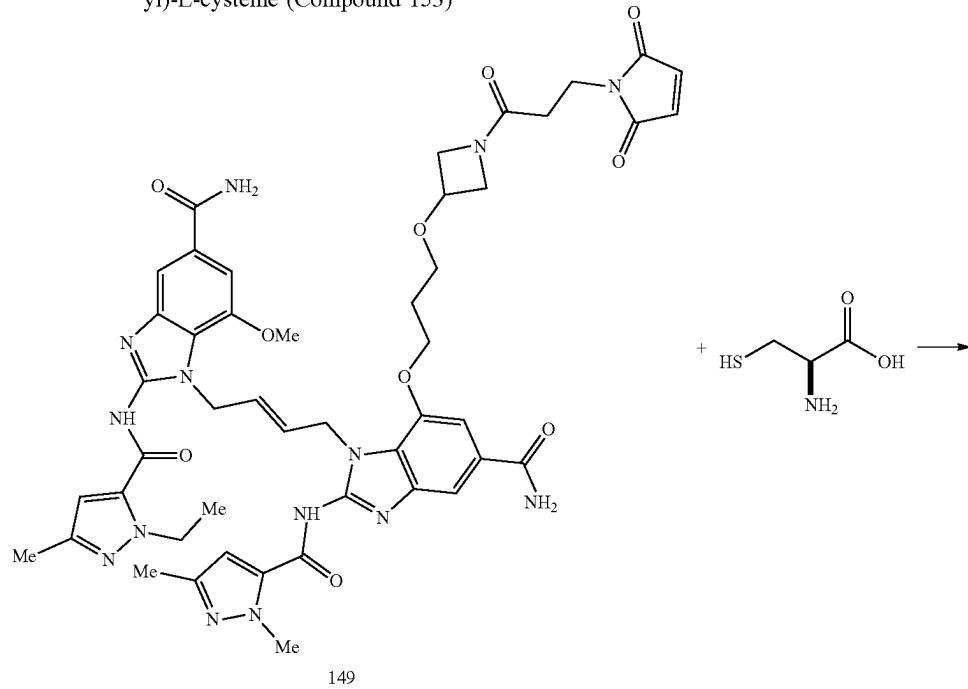
Synthesis of (E)-N-(5-carbamoyl-1-(4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-7-(3-((1-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)azetidin-3-yl)oxy)propoxy)-1H-benzo[d]imidazol-2-yl)-4-ethyl-2-methyloxazole-5-carboxamide (Compound 152)



[1705] The $\times 2$ TFA salt of compound 151 (22 mg, 0.0182 mmol, 56% yield) was prepared according to general method 9, using compound 142 (30 mg, 0.0323 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI $^+$): m/z [M+H] $^+$ =973.4 (theoretical), 973.5 (observed). HPLC retention time: 1.42 min.

[1706] The $\times 2$ TFA salt of compound 152 (20 mg, 0.0168 mmol, 43% yield) was prepared according to general method 9, using compound 143 (37 mg, 0.0388 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI $^+$): m/z [M+H] $^+$ =988.4 (theoretical), 988.5 (observed). HPLC retention time: 1.40 min.

Synthesis of S-(1-(3-(2-((5-carbamoyl-1-((E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1,3-dimethyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)ethyl)-azetidin-1-yl)-3-oxopropyl)-2,5-dioxopyrrolidin-3-yl)-L-cysteine (Compound 153)

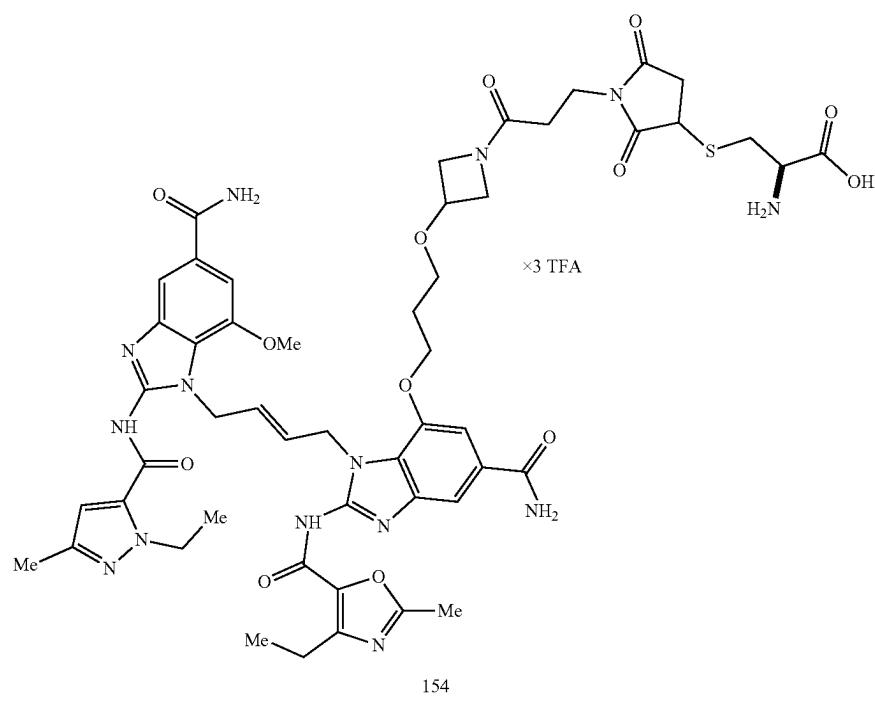
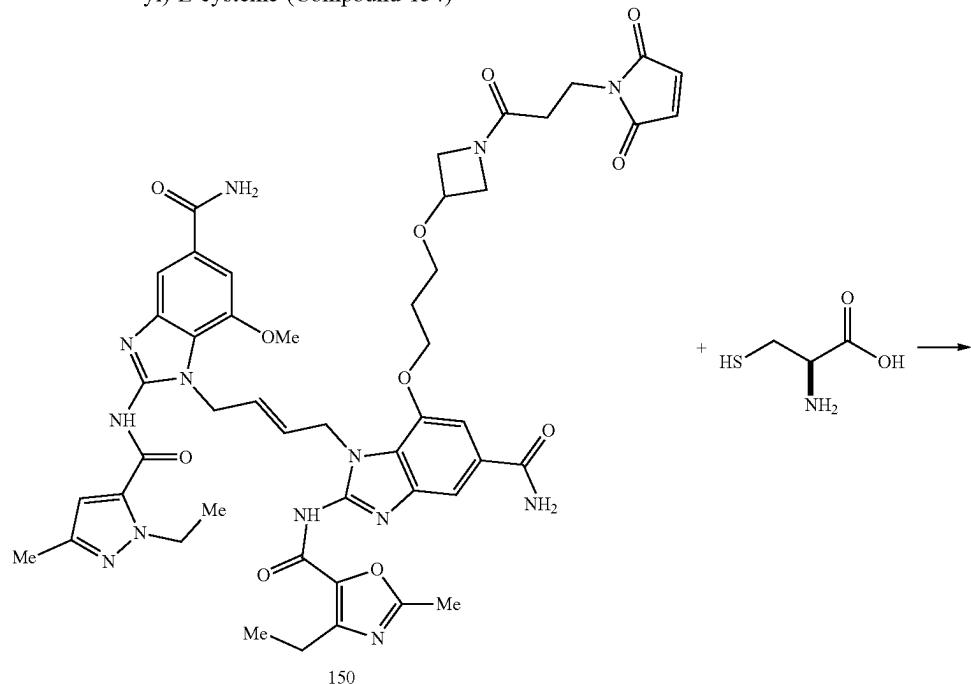


[1707] To a solution of compound 149 (10 mM in DMSO, 0.42 mL, 0.0042 mmol, 1 equiv.) was added 1-cysteine (0.1 M H₂O, 63 μL, 0.063 mmol, 1.5 equiv.). The reaction stirred at 30° C. for 1 h and was monitored by UPLC-MS. Upon

completion, the reaction mixture was purified directly by preparatory HPLC (method G). Pure fractions were collected, frozen, and lyophilized to yield compound 153 (2.17 mg, 0.0015 mmol, 36% yield). LC-MS (Method E, ESI+):

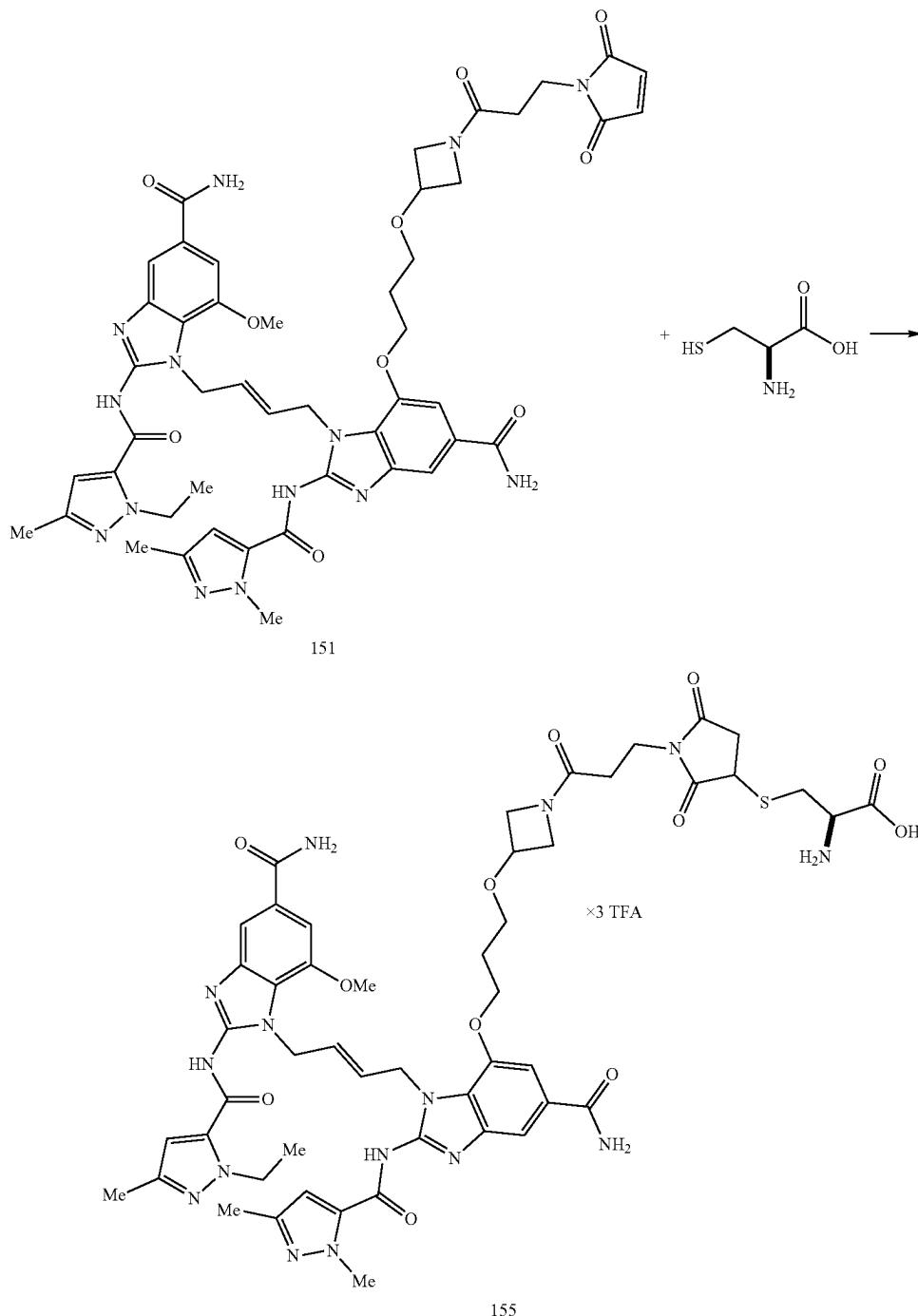
m/z [M+H]⁺=1079.4 (theoretical), 1079.5 (observed).
HPLC retention time: 1.28 min.

Synthesis of S-(1-(3-(3-(2-((5-carbamoyl-1-((E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(4-ethyl-2-methyloxazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)ethyl)azetidin-1-yl)-3-oxopropyl)-2,5-dioxopyrrolidin-3-yl)-L-cysteine (Compound 154)



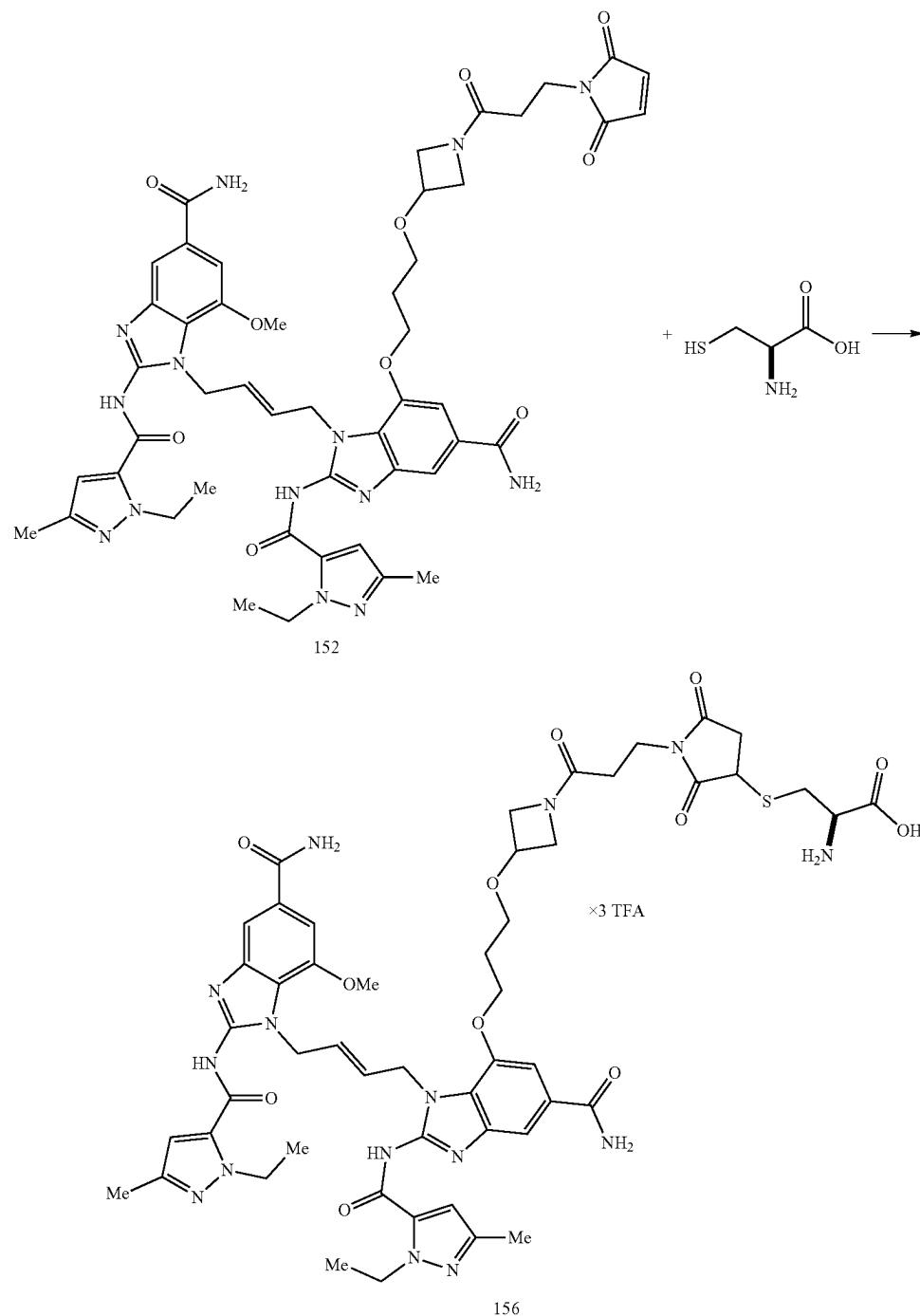
[1708] Compound 150 (2.35 mg, 0.0017 mmol, 39% yield) was prepared using the same procedure as compound 153, using compound 145 (10 mM in DMSO, 0.43 mL, 0.0043 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=1064.4 (theoretical), 1064.5 (observed). HPLC retention time: 1.29 min.

Synthesis of S-(1-(3-(3-((5-carbamoyl-1-((E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(1,3-dimethyl-1H-pyrazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)propoxy)azetidin-1-yl)-3-oxopropyl)-2,5-dioxopyrrolidin-3-yl)-L-cysteine (Compound 155)



[1709] Compound 155 (2.34 mg, 0.0016 mmol, 39% yield) was prepared using the same procedure as compound 153, using compound 151 (10 mM in DMSO, 0.41 mL, 0.0041 mmol, 1 equiv.) as the starting material. LC-MS (Method E, ESI+): m/z [M+H]⁺=1109.4 (theoretical), 1109.5 (observed). HPLC retention time: 1.30 min.

Synthesis of S-(1-(3-(3-((5-carbamoyl-1-((E)-4-(5-carbamoyl-2-(1-ethyl-3-methyl-1H-pyrazole-5-carboxamido)-7-methoxy-1H-benzo[d]imidazol-1-yl)but-2-en-1-yl)-2-(4-ethyl-2-methyloxazole-5-carboxamido)-1H-benzo[d]imidazol-7-yl)oxy)propoxy)azetidin-1-yl)-3-oxopropyl)-2,5-dioxopyrrolidin-3-yl)-L-cysteine (Compound 156)



[1710] Compound 156 (2.31 mg, 0.0016 mmol, 39% yield) was prepared using the same procedure as compound 153, using compound 152 (10 in mM DMSO, 0.42 mL, 0.0042 mmol, 1 equiv.) as the starting material. LC-MS (Method E, EST+): m/z [M+H]⁺=1094.4 (theoretical), 1094.5 (observed). HPLC retention time: 1.32 min.

General Procedures for the Preparation of ADCs:

[1711] ADCs were prepared as described previously (*Methods Enzymol.* 2012, 502, 123-138). Briefly, DAR (drug-to-antibody ratio) conjugates were prepared by partial reduction of the antibody inter-chain disulfide bonds using a sub-stoichiometric amount of tris(2-carboxyethyl)phosphine (TCEP). TCEP was added at approximately 2.2 molar equivalents relative to the antibody (TCEP:antibody) to a pre-warmed (37° C.) antibody stock solution in phosphate buffered saline, (PBS, Gibco, PN 10010023) and 1 M EDTA. The reduction reaction mixture was incubated at 37° C. for approximately 60 minutes. Conjugation of the partially-reduced antibody with maleimide drug-linker was carried out at room temperature by diluting the antibody with propylene glycol to improve drug solubility and adding 1.2 molar equivalents of the drug-linker per reduced cysteine. The propylene glycol was added to achieve a final co-solvent concentration of 40% (including addition of DMSO drug stock); half of the propylene glycol was added to the antibody and half to the drug stock before mixing to start the conjugation reaction. The conjugation reaction was allowed to proceed for 30 minutes at room temperature or until all available antibody cysteine thiols had been alkylated by drug-linker as indicated by reversed-phase HPLC (Method G). Removal of excess drug-linker was achieved by incubating the reaction mixture with 100% molar excess QuadraSil® MP resin (Millipore Sigma, PN 679526) for 30 minutes at room temperature. Buffer exchange into formulation buffer (PBS, Gibco, PN 10010023) was achieved by gel filtration chromatography using a prepakced PD-10 column (GE Life Sciences, PN 17043501) according to manufacturer's instructions. Further removal of residual drug-linker was achieved by repeated diafiltration (5-10 times) of the reaction mixture containing the ADCs in formulation buffer using a 30 kilodalton molecular weight cutoff centrifugal filter (Millipore Sigma, PN Z717185), until there was no detectable free drug-linker remaining, as indicated by HPLC analysis (Method K).

General Procedures for the Characterization of ADCs:

[1712] ADCs were characterized using the following methods:

[1713] Method I: Size-exclusion chromatography (SEC) was performed with a Waters ACQUITY UPLC system and an Acuity UPLC Protein BEH SEC Column, (200 Å, 1.7 m, 4.6×150 mm, PN: 186005225). The mobile phase used was 7.5% isopropanol in 92.5% aqueous (25 mM sodium phosphate, 350 mM NaCl, pH 6.8), v/v. Elution was performed isocratically at a flow rate of 0.4 mL/min at ambient temperature.

[1714] Method J: Reversed-phase chromatography (RP-HPLC) was performed on a Waters 2695 HPLC system and an Agilent PLRP-S column (1000 Å, 8 µm 50×2.1 mm, PN: PL1912-1802). ADCs were treated with 10 mM DTT to reduce disulfide bonds prior to analysis. Sample elution was done using Mobile Phase A (0.05% (v/v) TFA in water) and

Mobile Phase B (0.01% (v/v) TFA in MeCN) with a gradient of 25-44% B over 12.5 minutes at 80° C. The drug-to-antibody ratio (DAR) was calculated based on the integrated peak area measured at UV 280 nm.

Calculations of Molar Ratios

[1715] The average drug loading per antibody light-chain (MR_{DLC}) or antibody heavy-chain (MR_{DHC}) was calculated using the equations below:

$$MR_{DLC} = \frac{\sum (LC \% \text{ area}_n \times MR_n)}{100}$$

[1716] where MR_{DLC}=average drug-to-light chain ratio

[1717] LC % area_n=% area of the nth loaded light chain species

[1718] % areas based on light chain peaks only

[1719] MR_n=drug-to-antibody ratio of the nth loaded species

[1720] AND

$$MR_{DHC} = \frac{\sum (HC \% \text{ area}_n \times MR_n)}{100}$$

where MR_{DHC}=average drug-to-heavy chain ratio

[1721] HC % area_n=% area of the nth loaded heavy chain species

[1722] % areas based on heavy chain peaks only

[1723] MR_n=drug-to-antibody ratio of the nth loaded species

[1724] The average drug loading per antibody (MR_D) was calculated using the equation below:

$$MR_D = 2 \times (MR_{DLC} + MR_{DHC})$$

[1725] where MR_D=average drug-to-antibody ratio

[1726] MR_{DLC}=average drug-to-light chain ratio

[1727] MR_{DHC}=average drug-to-heavy chain ratio

[1728] Method K: Residual unconjugated drug linker was measured on a Waters ACQUITY UPLC system using an ACQUITY UPLC BEH C18 Column (130 Å, 1.7 µm, 2.1 mm×50 mm, PN: 186002350). ADC samples were treated with 2×volumes of ice-cold MeOH to induce precipitation and pelleted by centrifugation. The supernatant, containing any residual, unconjugated drug-linker, was injected onto the system. Sample elution was done using Mobile Phase A (0.05% (v/v) TFA in Water) and Mobile Phase B (0.01% TFA (v/v) in MeCN) with a gradient of 1-95% B over 2 minutes at 50° C. Detection was performed at 215 nm and quantitation of the residual drug-linker compound was achieved using an external standard of the corresponding linker.

Example 2

In Vitro Potency Evaluation of Sting Agonists and Corresponding ADCs

Experimental Procedures of In Vitro Biological Assays

THP1-Dual™ Cell Reporter Assay

[1729] Potency of compounds and ADCs was evaluated using the THP1-Dual™ cells (Invivogen PN: thpd-nfis [also referred to as THP1 dual reporter cells]), which contain an IRF-Lucia luciferase reporter. Cells were cultured in RPMI-1640 (Gibco) with 10% heat-inactivated fetal bovine serum, Pen-Strep (100 U/mL-100 g/mL, Gibco), HEPES (10 mM, Gibco)), sodium pyruvate (1 mM, Gibco), MEM non-essential amino acids (1x, Gibco), GlutaMAX (1x, Gibco), and beta-mercaptoethanol (55 μM, Gibco). Cells were plated in a 96-well flat bottom tissue culture-treated clear polystyrene plate (Corning Costar #3596) at ~100,000 cells per well in 200 μL with the indicated concentration of the compound or ADC. The supernatant was harvested at 24 hours (compounds) or 48 hours (ADC) post plating for the reporter assay, or as indicated. To measure Lucia reporter signal, 10 L of the supernatant was combined with 40 L of QUANTI-Luc™ Luminescence assay reagent (Invivogen PN: rep-qlc1) in a 96-well clear flat bottom tissue culture-treated black polystyrene plate (Corning Costar #3603) and read on a Perkin Elmer Envision plate reader. In some experiments, HEK 293T cells engineered to express a murine protein typically expressed by immune cells (target antigen C an immune cell antigen) were plated as above instead of Renca tumor cells.

Bone Marrow-Derived Macrophage Assay

[1730] Potency of the compounds described herein was evaluated using mouse bone-marrow derived macrophages cultured from wild type (C57BL/6J, the Jackson Laboratory #000664) or STING-deficient (C57BL/6J-Sting^{1g/J}, the Jackson Laboratory #017537) mice. Briefly, mouse bone marrow cells were cultured for 7-10 days in RPMI-1640 (Gibco) with 10% heat-inactivated fetal bovine serum, Pen-Strep (100 U/mL-100 g/mL, Gibco), HEPES (10 mM, Gibco), sodium pyruvate (1 mM, Gibco), GlutaMAX (1x, Gibco), beta-mercaptoethanol (55 M, Gibco) and 20-40 ng/mL murine M-CSF (Peprotech, #315-02). Cells were plated in a 96-well flat bottom tissue culture-treated clear polystyrene plate (Corning Costar #3596) at ~100,000 cells per well in 200 μL with the indicated concentration of the compound. The supernatant was harvested at 24 hours and cytokines were measured using a Milliplex MAP mouse cytokine/chemokine magnetic bead panel assay kit (MCY-TOMAG-70k custom 11-plex kit: MCP1, MIP1α, MIP1β, TNFα, IFNγ, IL-10, IL-12p70, IL-1β, IL-6, IP10, RANTES) and analyzed using a Luminex™ MAGPIX™ Instrument System.

Bystander Activity Assay

[1731] Bystander activity of ADCs was evaluated using Renca cancer cells and THP1-Dual™ cells (InvivoGen) which contain an IRF-Lucia luciferase reporter. Cells were cultured in RPMI-1640 (Gibco) with 10% heat-inactivated fetal bovine serum, Pen-Strep (100 U/ml-100 μg/ml, Gibco), HEPES (10 mM, Gibco), sodium pyruvate (1 mM, Gibco), MEM non-essential amino acids (1x, Gibco), GlutaMAX (1x, Gibco), and beta-mercaptoethanol (55 μM, Gibco). Renca cells were plated in a 96-well flat bottom tissue culture-treated clear polystyrene plate (Corning Costar

#3596) at 50,000 cells per well in 100 μL. On the day following the initial plating, 50,000 THP1-Dual™ cells were added to each well with the indicated concentration of ADC in a total volume of 200 μL. Supernatant was harvested at 48 hours post addition of the THP1-Dual™ cells. To measure Lucia reporter signal, 10 μL of supernatant was combined with 40 μL of QUANTI-Luc™ Luminescence assay reagent (Invivogen PN: rep-qlc1) in a 96-well clear flat bottom tissue culture-treated black polystyrene plate (Corning Costar PN: 3603) and read on a Perkin Elmer Envision plate reader. In some experiments, HEK 293T cells engineered to express a murine protein typically expressed by immune cells (target antigen C an immune cell antigen) were plated as above instead of Renca tumor cells.

Cancer Cell Direct Cytotoxicity Assay

[1732] Cancer cells were counted and plated in 40 μL complete growth media in 384-well, white-walled tissue culture treated plates (Corning). Cell plates were incubated at 37° C. and with 5% CO₂ overnight to allow the cells to equilibrate. Stock solutions containing ADCs or free drugs were serially diluted in RPMI-1640+20% fetal bovine serum (FBS). 10 μL of each concentration were then added to each cell plate in duplicate. Cells were then incubated at 37° C. and with 5% CO₂ for 96 hours, upon which, the cell plates were removed from the incubator and allowed to cool to room temperature for 30 minutes prior to analysis. CellTiter-Glo® luminescent assay reagent (Promega Corporation, Madison, WI) was prepared according to Promega's protocol. 10 μL of CellTiter-Glo® were added to assay plates using a Formulatrix Tempest liquid handler (Formulatrix) and the plates were protected from light for 30 minutes at room temperature. The luminescence of the samples was measured using an EnVision Multimode plate reader (Perkin Elmer, Waltham, MA). Raw data were analyzed in Graphpad Prism (San Diego, CA) using a nonlinear, 4-parameter curve fit model [$Y = Bottom + (Top - Bottom) / (1 + 10^{(Log EC50 - X) * HillSlope})$]. Results are reported as X50 values, which are defined as the concentration of ADC or free drug required to reduce cell viability to 50%.

SU-DHL-1 Assay

[1733] Potency of ADCs was evaluated using the SU-DHL-1 lymphoma cells. Cells were cultured in RPMI-1640 (Gibco) with 10% heat-inactivated fetal bovine serum, Pen-Strep (100 U/mL-100 g/mL, Gibco), HEPES (10 mM, Gibco)), sodium pyruvate (1 mM, Gibco), MEM non-essential amino acids (1x, Gibco), GlutaMAX (1x, Gibco), and beta-mercaptoethanol (55 M, Gibco). Cells were plated in a 96-well flat bottom tissue culture-treated clear polystyrene plate (Corning Costar #3596) at ~100,000 cells per well in 200 L with the indicated concentration of ADC. After 48 hours, the 50 μL supernatant was harvested and cytokine production was evaluated using a MILLIPLEX MAP Human Cytokine/Chemokine Magnetic Bead panel (HCY-TOMAG-60K custom 8-plex kit: IL-6, IL-8, MCP1, TNFα, GRO, IP-10, MIP1α, and MIP1β). Cell viability was evaluated by adding 100 μL CellTiter-Glo® luminescent assay reagent (Promega Corporation, Madison, WI) to remaining 150 μL of cells in the plate and transferring the mixture to a 96-well black-walled plate (Corning Costar #3603). Plates were protected from light for 30 minutes at room tempera-

ture, and the luminescence of the samples was measured using an EnVision Multimode plate reader (Perkin Elmer, Waltham, MA).

Tumor/PBMC Co-Culture Assay

[1734] Tumor cells were transfected with Incucyte® Cytolight red lentivirus per manufacturer's instructions and stable polyclonal cell populations expressing mKate2 (red fluorescent protein, RFP) were generated under puromycin selection. Live-cell killing assays were performed by seeding RFP+ tumor cells (MDA-MB-468, HCT 15, HT-1080) in 96-well flat bottom plates (Corning #3603) at a variety of densities (1×10^4 or 2.5×10^3) and grown overnight. The following day, PBMCs isolated from healthy donors were added at 10:1 or 40:1 E:T ratios and cultures were treated with the indicated small molecule drugs or ADCs. Automated cell imaging was performed at 10-fold magnification using an IncuCyte S3 live-cell analysis system (Sartorius). Images were acquired in approximately 2-to-3-hour intervals with four fields of view per well for 3-4 days. Data were analyzed using the IncuCyte® analysis software. Area (μm^2) and red mean intensity (RCU) filter thresholds were enforced to remove debris and red fluorescent anomalies. Tumor cell killing was quantified by calculating the confluence of red fluorescent tumor cells (normalized to t=0) at 72- or 96-hours. Molar concentrations of unconjugated compound 16, compound 12 mAb conjugate, or unconjugated mAb (adjusted to equivalent payload concentration) were plotted.

[1735] To determine STING pathway activation and quantify T cell numbers, identical tumor-immune cell (MDA-MB-468 tumor cells and PBMCs) cocultures were established in tandem. At 48-hours post treatment, supernatants were harvested and CXCL10/IP-10 production was evaluated by ELISA (ThermoFisher, #CHC2363). Optical density (450 nm) was measured using a SpectraMax M3 (Molecular Devices) microplate reader. Following supernatant harvest, cells were dissociated (TrypLE Express, Gibco) and dead cells were stained with LIVE/DEAD Fixable Near-JR Dead Cell Stain Kit (ThermoFisher, L34994) per manufacturer's instructions. After the viability stain, Fc-gamma receptors were blocked using human TruStain FcX (Biolegend, 422302). Cells were washed 1x with cell staining buffer (BD, 554657) and subsequently stained (30 min, at 4° C.) with antibodies for detection of surface antigens. The following antibodies were used: CD8 V450 (clone RPA-T8, BD), CD14 BV650 (clone M5E2, Biolegend), CD19 SB702 (clone HIB19, ThermoFisher), CD4 FITC (clone OKT4, Tonbo), CD56 PerCP-eF710 (clone TULY56, ThermoFisher), CD69 PE-Cy7 (clone FN50, Biolegend), CD86 APC (clone IT2.2, ThermoFisher), and HLA-DR A700 (clone LN3, ThermoFisher). Following the final wash, cell pellets were resuspended in 200 μL staining buffer and analyzed on an NXT Attune flow cytometer (ThermoFisher). Flow cytometry data were analyzed using FlowJo software and CD8+ T cells were quantified by counting the total number of CD8+ cell events within the RFP—/live/CD19—/CD14—/CD56— gate.

[1736] MDA-MB-468 and HCT15 tumor cells were cultured in RPMI-1640 (Gibco) with 10% heat-inactivated fetal bovine serum, Pen-Strep (100 U/mL-100 mg/mL, Gibco), HEPES (10 mM, Gibco), sodium pyruvate (1 mM, Gibco), MEM non-essential amino acids (1x, Gibco), GlutaMAX (1x, Gibco), and beta-mercaptoproethanol (55 μM , Gibco).

HT-1080 cells were cultured in DMEM (Gibco) with 10% heat-inactivated fetal bovine serum, Pen-Strep (100 U/mL-100 mg/mL, Gibco), HEPES (10 mM, Gibco)), sodium pyruvate (1 mM, Gibco), MEM non-essential amino acids (1x, Gibco), GlutaMAX (1x, Gibco), and beta-mercaptoproethanol (55 μM , Gibco).

Results from In Vitro Biological Assays

[1737] STING agonist compounds were assessed for their ability to activate THP1-Dual™ reporter cells, a human monocytic cell line in which type I interferon (IRF) signaling can be monitored via a secreted luciferase reporter protein (Lucia). THP1-Dual™ cells were treated with increasing concentrations of the agonists for 24 h, then supernatants were harvested and the Lucia reporter signal was quantified using QUANTI-Luc™ Luminescence assay reagent. Compound A and compound 1 were significantly more potent than (2', 3')-Rp,Rpc-diAMPS disodium (Compound B) and activated the Lucia reporter with EC₅₀ values of 3 and 5 nM respectively. Compound 12a was less potent than compound 1 and compound A (FIG. 1, EC₅₀ value of 21 nM). Both compound 1 and 12a induced cytokine production when used to stimulate wild type (WT), but not STING-deficient, murine bone marrow-derived macrophages, indicating the activity of these compounds is STING-dependent (FIG. 2).

[1738] The STING agonist compounds were conjugated to both targeted and non-binding antibodies and the resulting ADCs were assessed for their ability to activate THP1-Dual™ reporter cells. Compound 1 was conjugated using a cleavable glucuronide-based linker (11). Compound 12a was conjugated using a non-cleavable, cleavable peptide-based, and cleavable glucuronide-based linker (Compounds 12, 14 and 13, respectively). THP1-Dual™ cells were treated with increasing concentrations of ADCs with a non-binding or targeted mAb conjugated to a compound for 48h, then supernatants were harvested, and the Lucia reporter signal was quantified using QUANTI-Luc™ Luminescence assay reagent. Although compound 12a was less potent than compound 1 as a free drug (FIG. 1), compound 12a was more potent when conjugated to a targeted mAb via a cleavable glucuronide linker (13) than the similar compound 1 conjugate (11). Furthermore, compound 12a was more potent when conjugated to a targeted mAb via a non-cleavable linker (12) than either cleavable linker 13 or 14 (FIG. 3), demonstrating that conjugation of STING agonist small molecules to an antibody can increase their potency.

[1739] Compound 12 and the cysteine adduct (compound 16) that is released upon cleavage of the mAb conjugate in the endo-lysosome were assessed for their ability to activate THP1-Dual™ reporter cells. THP1-Dual™ cells were treated with increasing concentrations of the compounds for 24 h, then supernatants were harvested and the Lucia reporter signal was quantified using QUANTI-Luc™ Luminescence assay reagent. Both compound 12 and compound 16 were active with EC₅₀ values (37 nM and 34 nM, respectively) similar to the parent free drug 12a (21 nM, FIG. 4 and FIG. 1).

[1740] Compound 15b was also evaluated, both as a free drug and when conjugated to a targeted antibody using a non-cleavable linker (15). THP1-Dual™ cells were treated with increasing concentrations of free drug or ADCs with a non-binding or targeted mAb conjugated to a compound for 48h; then supernatants were harvested, and the Lucia

reporter signal was quantified using QUANTI-LucTM Luminescence assay reagent. Compound 15b was more potent than 12a, while the potency of the ADC of 15 was similar to that of the ADC of 12 when linked to the same targeted mAb (FIG. 5).

[1741] Compound 12a was conjugated to both targeted and non-binding antibodies using a variety of non-cleavable linkers (12, 17, 19-24) and the resulting ADCs were assessed for their ability to activate THP1-DualTM reporter cells. All conjugates with the targeted mAb were active with EC50 values ranging from ~1.7-7.3 ng/mL (Table 1). We also evaluated the ability of these linkers to directly kill cancer cells when conjugated to targeted mAbs binding tumor antigen A or antigen B (CD30). All conjugates were active in a subset of cancer cell lines (regardless of target antigen expression), indicating target-independent killing of some cancer cells; compounds 1, 12a, and 16 also demonstrated direct cytotoxic activity on a subset of cancer cell lines (Table 2; targeted mAb A conjugates comprise a mAb targeting the tumor antigen A conjugated to various drug linker compounds; targeted mAb B conjugates comprise the cAC10 mAb targeting CD30 conjugated to various drug linkers).

TABLE 1

Activity of target STING agonist ADCs in THP1-Dual TM reporter cells.	
Compound	EC ₅₀ (ng/mL)**
12	4.2
17	2.2
19	7.3
20	1.7
21	4.2
22	4.7
23	2.4
24	2.1
25	307
26	14.4
27	10.4
66	>10,000
67	>10,000

TABLE 1-continued

Activity of target STING agonist ADCs in THP1-Dual TM reporter cells.	
Compound	EC ₅₀ (ng/mL)**
68	>10,000
69	>10,000
96	>10,000
97	*
98	>10,000
99	*
100	*
101	>10,000
102	>10,000
103	>10,000
104	>10,000
105	52.5
106	>10,000
107	>10,000
108	63.5
109	>10,000
110	>10,000
111	13.2
112	2
121	3.0
122	5.6
123	1.6
124	9.1
125	1.4
126	>10,000
128	>10,000
131	3.6
133	12.2
134	10.3
144	>10,000
145	>10,000
146	>10,000
147	>10,000
148	>10,000
149	>10,000
150	7.9
151	>10,000
152	6.5

*ADCs with >10% aggregate were not evaluated

**For some compounds, EC50 values comprise the average value from multiple experiments

TABLE 2

Direct cytotoxicity data of various ADCs and compounds on human cancer cell lines.											
Target A expression	+	+	+	+	+	+	+	+	+	+	+
	-	-	-	+	+	+	+	-	-	-	-
786-O	A2058	BxPC3	DEL	DELBVR	Karpas299	L540cy	Ls174T	MDAMB231	MOLM-13	SU-DHL-4	
ADC X50 (ng/mL)											
Targeted mAb A 12 (8 load)	>1K	>1K	>1K	0.01	0.04	1	1	>1K	>1K	1	>1K
Targeted mAb A 12 (4 load)	>1K	>1K	>1K	0.012	0.03	3	2	>1K	>1K	12	>1K
Targeted mAb B 12 (8 load)	>1K	>1K	>1K	<0.004	0.004	1	1	>1K	>1K	2	>1K
Targeted mAb B 12 (4 load)	>1K	>1K	>1K	0.01	0.1	2	1	>1K	>1K	7	>1K
Targeted mAb A 17 (8 load)	>1K	>1K	>1K	<0.004	0.004	1	1	>1K	>1K	2	>1K
Targeted mAb A 17 (4 load)	>1K	>1K	>1K	0.1	0.03	5	2	>1K	>1K	26	>1K
Targeted mAb B 17 (8 load)	>1K	>1K	>1K	<0.004	<0.004	1	0.2	>1K	>1K	2	>1K
Targeted mAb B 17 (4 load)	>1K	>1K	>1K	0.004	0.01	1	1	>1K	>1K	25	>1K
Targeted mAb A 21 (8 load)	>1K	>1K	>1K	0.01	0.03	4	1	>1K	>1K	2	>1K
Targeted mAb A 21 (4 load)	>1K	>1K	>1K	0.1	0.2	7	2	>1K	>1K	20	>1K
Targeted mAb B 21 (8 load)	>1K	>1K	>1K	<0.004	0.01	1	0.4	>1K	>1K	2	>1K
Targeted mAb A 22 (6 load)	>1K	>1K	>1K	0.02	0.1	2	1	>1K	>1K	2	>1K
Targeted mAb A 22 (2 load)	>1K	>1K	>1K	0.03	0.2	29	4	>1K	>1K	29	>1K
Targeted mAb B 22 (6 load)	>1K	>1K	>1K	0.01	0.1	1	1	>1K	>1K	3	>1K
Targeted mAb A 19 (8 load)	>1K	>1K	>1K	<0.004	0.02	1	1	>1K	>1K	1	>1K

TABLE 2-continued

Direct cytotoxicity data of various ADCs and compounds on human cancer cell lines.											
	Compound X50 (nM)										
Targeted mAb A 19 (4 load)	>1K	>1K	>1K	0.01	0.1	3	5	>1K	>1K	13	>1K
Targeted mAb B 19 (8 load)	>1K	>1K	>1K	<0.004	0.01	0.3	0.3	>1K	>1K	0.4	>1K
Targeted mAb B 19 (4 load)	>1K	>1K	>1K	<0.004	0.02	0.5	1	>1K	>1K	1	>1K
Targeted mAb A 20 (8 load)	>1K	>1K	>1K	0.01	0.02	0.2	0.3	>1K	>1K	1	>1K
Targeted mAb A 20 (4 load)	>1K	>1K	>1K	0.01	0.02	1	1	>1K	>1K	10	>1K
Targeted mAb B 20 (8 load)	>1K	>1K	>1K	<0.004	<0.004	0.1	0.1	>1K	>1K	0.2	>1K
Targeted mAb B 20 (4 load)	>1K	>1K	>1K	<0.004	0.02	0.1	0.5	>1K	>1K	1	>1K
Targeted mAb A 24 (8 load)	>1K	>1K	>1K	<0.004	0.01	0.3	1	>1K	>1K	1	>1K
Targeted mAb A 24 (4 load)	>1K	>1K	>1K	0.01	0.01	1	4	>1K	>1K	11	>1K
Targeted mAb B 24 (8 load)	>1K	>1K	>1K	<0.004	0.01	0.03	0.5	>1K	>1K	1	>1K
Targeted mAb B 24 (4 load)	>1K	>1K	>1K	<0.004	0.01	0.2	2	>1K	>1K	4	>1K
Targeted mAb A 23 (8 load)	>1K	>1K	>1K	0.01	0.03	1	1	>1K	>1K	1	>1K
Targeted mAb A 23 (4 load)	>1K	>1K	>1K	0.02	0.05	4	5	>1K	>1K	8	>1K
Targeted mAb B 23 (8 load)	>1K	>1K	>1K	<0.004	0.01	0.1	0.2	>1K	>1K	0.3	>1K
Targeted mAb B 23 (4 load)	>1K	>1K	>1K	0.002	0.02	0.3	0.3	>1K	>1K	2	>1K

[1742] Multiple additional compounds were synthesized and evaluated for their ability activate THP1-Dual™ reporter cells. Several compounds were active with EC50 values ranging from 1.3 nM (compound 27e) to 6337 nM (compound 126a, Table 3). Compounds with minimal activity up to 10 µM are listed in Table 3 as having an EC59 value of >10,000 nM. Several compounds were conjugated to targeted (Table 1) and non-binding antibodies (not shown) via cleavable or non-cleavable drug linkers and the resulting ADCs were assessed for their ability to activate THP1-Dual™ reporter cells. Conjugates with drug linkers 25-27, 105, 108, 111-112, 121-125, 131-134, 150, and 152 were active with EC51 values ranging from 1.4 to 307 ng/mL (Table 1). All other conjugates tested were not active up to 10 µg/mL in this assay, including conjugates with drug linkers derived from active small molecules (Table 3, Table 1) thus highlighting the challenges of developing active ADCs targeting the STING pathway.

TABLE 3

Activity of STING agonist small molecules in THP1-Dual™ reporter cells.		
Compound	EC ₅₀ (nM)**	EC ₅₀ (nM)**
A	3	175.6
1	5	44.5
12	37	>10,000
12a	21	>10,000
15b	5.8	>10,000
16	52/34	>10,000
17	66.28	>10,000
19	190.2	>10,000
20	53.91	>10,000
21	2632	2508
23	62.55	388.3
24	83.29	1159
25f	12	2238
25g	1576	216.25
26e	5	35.98
26f	69	57.73
27e	1.3	58.8
27f	38	>10,000
28	954	>10,000
29	52	>10,000
30	87	>10,000

TABLE 3-continued

Activity of STING agonist small molecules in THP1-Dual™ reporter cells.

Compound	EC ₅₀ (nM)**
31	175.6
32	44.5
33	>10,000
35	>10,000
37	>10,000
38	>10,000
39	>10,000
40	>10,000
41	>10,000
42	>10,000
43	>10,000
44	>10,000
45	>10,000
46	>10,000
47	>10,000
48	>10,000
49	>10,000
50	>10,000
51	>10,000
52	>10,000
53	>10,000
54	>10,000
55	>10,000
56	>10,000
57	>10,000
58	>10,000
59	>10,000
60	>10,000
62	>10,000
63	2508
64/65	388.3
66b	1159
68a	2238
70	1.6
71	70.11
72	275.3
73	216.25
74	35.98
75	57.73
76	58.8
79	>10,000
80	>10,000
81	>10,000
82	>10,000

TABLE 3-continued

Compound	EC ₅₀ (nM)**
83	>10,000
84	>10,000
85	>10,000
86	2465
87	>10,000
88	394
89	1324
90	>10,000
91	350
92	1190
93	>10,000
94	132.8
95	12.9
114	9.4
115	17.4
116	11.6
117	14.6
118	23.6
119	49.9
120	5.2
126a	6337
126b	>10,000
127	301
128a	>10,000
129	836
130	2260
132	37.4
135	2011
136	>5,000
137	1685
138	>5,000
139	>4,000
140	1793
141	159
142	1123
143	155
154	>10,000
155	94
156	1561
157	51

**For some compounds, EC₅₀ values comprise the average value from multiple experiments

[1743] Compound 1 was conjugated to a non-binding antibody as well as antigen C and PD-L1-targeted mAbs using the cleavable linker 11 and the resulting ADCs were assessed for their ability to induce cytokine production and direct cytotoxicity by SU-DHL-1 cells. Conjugates targeting antigen C and PD-L1, but not the non-binding conjugate, induced robust production of the cytokine MIP-1 α and led to SU-DHL-1 cell death (FIG. 6A and FIG. 6B).

[1744] The ability of conjugates to activate THP1 dual reporter immune cells in a bystander manner was evaluated. Conjugates consisting of an antibody targeting antigen C with a hIgG1 LALAPG Fc backbone conjugated to compound 12, 13, and 14 demonstrated some bystander activity when THP1 dual cells were co-cultured with HEK 293T cells engineered to express antigen C (FIG. 7). Conjugates consisting of the h1C1 antibody targeting EphA2 with a mIgG2a WT or LALAPG Fc backbone (see, e.g., Schlothauer et al., Protein Engineering, Design and Selection, 2016, 29(10):457-466; and Hezareh et al., Journal of Virology, 2001, 75(24):12161-12168, each of which is incorporated herein by reference in its entirety) conjugated to compound 12 also demonstrated bystander activity when THP1 dual cells were co-cultured with murine Renca tumor

cells. Markedly enhanced bystander activity was observed with conjugates with an intact WT Fc backbone (FIG. 8).

[1745] The ability of compound 12-mAb conjugates to elicit immune-mediated tumor cell killing in vitro compared to compound 16 was evaluated by co-culturing RFP+ MDA-MB-468 tumor cells and human peripheral blood mononuclear cells (PBMCs). Tumor cell killing was measured by quantifying the RFP confluence, and immune activation was evaluated by quantifying the number of CD8 T cells in each culture as well as IP-10 cytokine secretion. All compounds led to tumor cell killing (FIG. 9A), with the B7-H4-targeted conjugates demonstrating more potent tumor cell killing compared to the non-binding conjugates and compound 16. Moreover, the B7-H4-targeted conjugates with a WT Fc backbone demonstrated more potent tumor cell killing compared to the same conjugates with an Fc effector function null LALA-KA backbone (FIGS. 9A and 10). B7-H4-targeted conjugates with a WT Fc backbone also led to increased CD8 T cell counts (FIG. 9B) and secretion of the cytokine IP-10 (FIG. 9C) compared to the other conjugates and compound 16. α v β 6-targeted conjugates were also evaluated and demonstrated greater tumor cell killing activity than compound 16 (FIG. 10). Finally, α v β 6-targeted and CD228-targeted conjugates demonstrated more potent tumor cell killing compared to compound 16 when used to treat co-cultures of RFP+ HCT15 (FIG. 11) or HT 1080 (FIG. 12) tumor cells and PBMCs, respectively. CD228-targeted conjugates with a WT Fc backbone demonstrated more potent tumor cell killing compared to the same conjugates with an Fc effector function null LALAKA backbone (FIG. 13). This suggests that targeted conjugates with a WT Fc backbone (FIG. 9A, 10, and 13) drive increased tumor cell killing in vitro compared to conjugates with an Fc effector function null LALAKA backbone.

[1746] The ability of CD228-targeted conjugates of compound 12 (non-cleavable linker) to elicit tumor cell killing in vitro was also evaluated compared to CD228-targeted conjugates of compounds 11, 13, and 14 (cleavable linkers) as well as compound 25. Similar to experiments described above, CD228-targeted conjugates with a WT Fc backbone elicited more potent cell killing compared to conjugates with an Fc effector function null LALAKA backbone (FIG. 35). Consistent with the reduced potency of conjugates of 11 and 25 in the THP1 dual assay (FIG. 3 and Table 1), CD228-targeted conjugates of 11 and 25 elicited reduced tumor cell killing in the tumor/PBMC co-culture assay compared to CD228-targeted conjugates of compound 12 (FIG. 35). However, interestingly, in contrast to the modest decrease in potency of conjugates of 13 and 14 in the THP1 dual assay (FIG. 3 and Table 1), CD228-targeted conjugates of 13 and 14 elicited similar tumor cell killing in the tumor/PBMC coculture assay compared to CD228-targeted conjugates of compound 12 (FIG. 35).

Example 3

In Vivo Evaluation of Anti-Tumor Immune Responses Induced by Sting Agonist ADCS

Experimental Procedures for In Vivo Studies

In Vivo Cytokine Assay

[1747] Cytokines were measured in mouse plasma harvested at 3, 6, 24, or 48 hours after treatment with com-

pounds or ADCs using a Milliplex MAP mouse cytokine/chemokine magnetic bead panel assay kit (MCYTOMAG-70k custom 11-plex kit: MCP1, MIP1 α , MIP1(3, TNF α , IFN γ , IL-10, IL-12p70, IL-6, IL-1 β , IP10, RANTES) and analyzed using a Luminex™ MAGPIX™ Instrument System. Values that were outside of the standard curve range (<3.2 or >10,000 μ g/mL) were either excluded from calculation of the mean values or, when indicated, converted to 3.2 or 10,000 μ g/mL for calculation of the mean values.

In Vivo Anti-Tumor Activity Studies

Renca Cancer Cells

[1748] Renca cancer cells (ATCC) were cultured in RPMI-1640 (ATCC) with 10% heat-inactivated fetal bovine serum, Pen-Strep (100 U/mL-100 μ g/mL), MEM non-essential amino acids (1x), sodium pyruvate (1 mM), and L-glutamine (2 mM). Renca cancer cells were implanted (2×10^6 cells in 200 μ L 25% Matrigel) subcutaneously into Balb/c female mice. In some experiments, Renca tumor cells were engineered to express the indicated murine or human target antigen.

[1749] When tumor volumes reached 100 mm 3 , the mice were dosed with either compounds or ADCs by intraperitoneal or intravenous injection at the indicated dosing schedule and tumor volumes were monitored twice weekly. Compounds were formulated in 40% PEG400 in saline.

CT26 Cancer Cells

[1750] CT26 cancer cells (ATCC) were cultured in RPMI 1640 modified with 1 mM Sodium Pyruvate, 10 mM HEPES, 2.8 mL 45% Glucose (1.25 g) and supplemented with 10% fetal bovine serum and 1% Pen/Strep/Glutamine. CT26 cancer cells were implanted (0.5×10^6 cells in 200 μ L serum-free RPMI 1640) subcutaneously into Balb/c mice.

MC38 Cancer Cells

[1751] MC38 cancer cells (Kerafast) were cultured in DMEM with 10% heat-inactivated fetal bovine serum, Pen-Strep (100 U/mL-100 g/mL), MEM non-essential amino acids (1x), sodium pyruvate (1 mM), and L-glutamine (2 mM). MC38 cancer cells were implanted (1×10^6 cells in 100 μ L 25% Matrigel) subcutaneously into C57BL/6 mice.

[1752] In some experiments, tumor-bearing mice that achieved complete tumor regression following ADC treatment were “rechallenged” with MC38 tumor cells; MC38 cancer cells were implanted (1×10^6 cells in 100 μ L 25% Matrigel) subcutaneously into the opposite flank of C57BL/6 mice.

4T1 Cancer Cells

[1753] 4T1 cancer cells (ATCC) were cultured in RPMI with 10% heat-inactivated fetal bovine serum and implanted (0.02×10^6 cells in 200 μ L plain RPMI) subcutaneously into Balb/c mice.

α v β 6-CT26 Tumor Cells

[1754] CT26 cancer cells (ATCC) were engineered using lentiviral transduction to express murine integrin α v β 6. CT26 cells were cultured in RPMI 1640 modified with MEM Non-essential amino acids (1x), 1 mM Sodium Pyruvate, 2 mM Glutamax, 10 mM HEPES, beta mercaptoethanol (55 μ M) and supplemented with 10% fetal bovine serum. CT26 cancer cells were implanted (0.1×10^6 cells in 100 μ L

25% Matrigel in serum-free RPMI 1640) subcutaneously into Balb/c mice. When tumor volumes reached 100 mm 3 , the mice were dosed with either compounds or ADCs by intraperitoneal or intravenous injection at the indicated dosing schedule and tumor volumes were monitored twice weekly.

mB7-H4-Renca Tumor Cells

[1755] Renca cancer cells were engineered using lentiviral transduction to express murine B7-H4. Renca cells were cultured in High glucose RPMI-1640 (ATCC) with 10% heat-inactivated fetal bovine serum, MEM non-essential amino acids (1x), sodium pyruvate (1 mM), and L-glutamine (2 mM). Renca cancer cells were implanted (2×10^6 cells in 200 μ L 25% Matrigel in RPMI 1640 medium) subcutaneously into Balb/c female mice. When tumor volumes reached 100 mm 3 , the mice were dosed with either compounds or ADCs by intraperitoneal or intravenous injection at the indicated dosing schedule and tumor volumes were monitored twice weekly.

mB7-H4-EMT6 Tumor Cells

[1756] EMT6 cancer cells were engineered using lentiviral transduction to express murine B7-H4. EMT6 cells were cultured in Dulbecco's Modified Eagle Medium with MEM Non-essential Amino Acids (1x), Sodium Pyruvate (1 mM), Glutamax (2 mM), HEPES (10 mM), beta mercaptoethanol (55 μ M) and supplemented with 10% heat-inactivated fetal bovine serum. EMT6 cancer cells were implanted (0.5×10^6 cells in 100 μ L 25% Matrigel in serum-free RPMI 1640) subcutaneously into Balb/c female mice. When tumor volumes reached 100 mm 3 , the mice were dosed with either compounds or ADCs by intraperitoneal or intravenous injection at the indicated dosing schedule and tumor volumes were monitored twice weekly.

hCD228-LL2 Tumor Cells

[1757] LL2 cancer cells were engineered using lentiviral transduction to express human CD228. LL2 cells were cultured in DMEM (ATCC) with 10% heat-inactivated fetal bovine serum. Female C57BL/6 mice were implanted with 1×10^6 hCD228-LL2 tumor cells in 100 μ L 25% Matrigel in RPMI 1640 medium subcutaneously. Once tumor volumes reached 100 mm 3 , mice were randomized into treatment groups and dosed as indicated. Tumor volumes were measured twice per week, and animals were euthanized when tumor volumes reached 750-1000 mm 3 . Stock concentrations of mAb or conjugates were diluted to a desired concentration (with 20 mM His, 6% Trehalose or 0.01% Tween20 in PBS) and injected intraperitoneally (i.p.) or intravenously (i.v.) as indicated. The small molecule was formulated in 40% PEG400 in saline and injected i.v.

Evaluation of Conjugate Pk in Lewis Lung Tumor Model

[1758] Pharmacokinetic profiles were analyzed following administration of a single 1, 5, or 10 mg/kg dose of ADCs comprising a CD228-targeted mAb (WT hlgG1 Fc) conjugated to compound 12, 13, or 14 (delivered intravenously or intraperitoneally, as indicated) to female C57BL/6 mice bearing hCD228-expressing LL2 tumors. Plasma was collected and analyzed for generic total antibody (gTAB) by immunoassay. TAB concentrations in mouse K2EDTA plasma were determined by a Gyros flow-through immunoassay platform. Samples and standards were diluted in assay buffer and incubated with a solution containing biotinylated murine anti-human kappa light chain antibody and fluorescent goat anti-human IgG Fcg F(ab') $_2$ antibody fragment in

a sandwich format. The resulting immunocomplexes were bound to the streptavidin-coated beads in the affinity column of the compact disc (CD). The CD was read by a laser that excites the fluorescent detection reagent, producing a signal that is directly proportional to the concentration of test article in the C57BL/6 female mouse plasma sample. Non-compartmental analysis was applied to pooled animal plasma concentration data (serial (FIG. 31) or sparse (FIG. 33) sampling) using Phoenix WinNonlin 8.2 (Certara, USA). Concentration values below the limit of quantitation (BLQ) were treated as zero for analysis. Nominal doses and sampling times were used.

MDAMB468 Tumor Model

[1759] MDA-MB-468 cells were cultured in RPMI with 10% fetal bovine serum (FBS) and sodium pyruvate. Female Nude mice were implanted with 1×10^6 MDA-MB-468 cells in 25% Matrigel HC (Corning #354248) subcutaneously. Once tumor volumes reached 100 mm^3 , mice were randomized into treatment groups of 8-10 mice each and dosed with a single 3 mg/kg dose of ADCs. Tumor volumes were measured twice per week; animals were euthanized when tumor volume reached $700\text{-}1000 \text{ mm}^3$. Tumors were harvested from some animals 3 days post-dose at necropsy and processed for immunohistochemical staining. Stock concentrations of ADC were diluted to desired concentration (with 0.01% Tween20 in PBS) and injected i.p. into each treatment group.

Results from In Vivo Studies

Renca Cancer Cells

[1760] A syngeneic system was used to assess the ability of the STING agonist ADCs to induce immune responses in vivo and drive an anti-tumor immune response. The Renca system is a subcutaneous, mouse renal adenocarcinoma model. Female Balb/c mice were implanted with 2×10^6 Renca cells subcutaneously in the flank on day 0. When mean tumor size of 100 mm^3 (measured by using the formula Volume (mm^3)= $0.5 \times \text{Length} \times \text{Width}^2$ where length is the longer dimension) was reached mice were randomized into treatment groups of ≥ 5 mice per group. Animals were then treated intraperitoneally (ADCs or compounds) or intravenously (compounds) with the indicated treatment every 7 days, for 3 doses total (or as indicated). Tumor length and width and the weight of the animals was measured throughout the study and tumor volume was calculated using the formula above. Animals were followed until the tumor volume reached $\sim 1000 \text{ mm}^3$; animals were then euthanized.

[1761] The anti-tumor activity of compound 1 compared to the cleavable linker 11 conjugated to a non-binding or EphA2-targeted mAb (mIgG2a LALAPG backbone; see, e.g., Schlothauer et al., Protein Engineering, Design and Selection, 2016, 29(10):457-466; and Hezareh et al., Journal of Virology, 2001, 75(24):12161-12168, each of which is incorporated herein by reference in its entirety) was evaluated; note that all EphA2-targeted mAb conjugates described herein consist of the h1C1 mIgG2a mAb conjugated to various drug linker compounds. When animals were treated with the Compound 1 or the non-binding mAb conjugate of 11, some tumor growth delay was observed; however, tumor growth delay was significantly enhanced with the EphA2-targeted mAb conjugate of 11, especially at

the higher 12 mg/kg dose (FIG. 14A), clearly demonstrating the anti-tumor benefit of delivering STING agonists using a targeted ADC.

[1762] In the next in vivo study, the anti-tumor activity of the non-cleavable linker compound 12 conjugated to a non-binding or EphA2-targeted mAb (mIgG2a LALAPG backbone) was evaluated. The EphA2-targeted mAb conjugate of 12 exhibited robust anti-tumor activity and was surprisingly more active than the ADC of 11 conjugated to the same EphA2-targeted mAb (FIG. 15A). In the next in vivo study, the anti-tumor activity of the non-cleavable linker 15 conjugated to a non-binding or EphA2-targeted mAb (mIgG2a WT backbone) was evaluated. EphA2-targeted mAb conjugates of 15 exhibited robust anti-tumor activity that was similar to the corresponding ADC of 12 (FIG. 16A). In this study, the activity of 12 conjugated to an EphA2-targeted antibody with a mIgG2a WT and LALAPG backbone was also evaluated, and both conjugates were similarly active. This was a surprising finding, given that the in vitro bystander assay indicates that an intact WT Fc backbone significantly enhances bystander immune cell activation compared to LALAPG Fc backbone (FIG. 8).

[1763] Compound 1 and all antibody conjugates of 11 and 12 on a mIgG2a LALAPG backbone were well tolerated—average weight loss was $<-5\%$ after the 1st and 2nd dose of the treatment. The STING agonist compound A was less well tolerated—with mice exhibiting on average 6.2% weight loss after the 2nd dose (FIG. 14B, 15B, and 16B). Moreover, EphA2-targeted mAb conjugates of 12 and 15 with a mIgG2a WT backbone at the 3 mg/kg dose level were less well tolerated than the conjugate of 12 with a LALAPG backbone—with mice treated with targeted WT backbone ADCs exhibiting ~8% weight loss (FIG. 16B).

[1764] In the next in vivo study, the anti-tumor activity of the non-cleavable linker compound 12 conjugated to an EphA2-targeted mAb (mIgG2a LALAPG backbone) as well as unconjugated Compound 12a was evaluated. The EphA2-targeted mAb conjugates of 12 exhibited robust anti-tumor activity at doses of 1 mg/kg and 3 mg/kg, while Compound 12a had limited anti-tumor efficacy (FIG. 17). Collectively, this suggests that STING agonist compounds (e.g., compounds 1 and 12a) that are minimally active in vivo in tumor models can be converted into active therapeutics by conjugation to an antibody (e.g., targeted mAb conjugates of 11 and 12).

[1765] Systemic cytokine production in response to the free drugs and conjugates was measured as a proxy for systemic activity. Compound 1 and all antibody conjugates of 11, 12 and 15 induced very little pro-inflammatory cytokine (IL-6 and TNF) production. On the other hand, compound A and compound 12a induced robust production of IL-6 and TNF (Table 4, Table 5, and Table 6). Moreover, EphA2-targeted conjugates of 11 and 12 with a WT Fc backbone induced more systemic MIP1 α , MIP1 β , and MCP-1 expression than the conjugate of 12 with a LALAPG Fc backbone. This indicates that, in the Renca tumor model with the specific EphA2-targeted antibodies described in FIGS. 15A-17 dosed at 3 mg/kg q7dx3, a LALAPG Fc backbone may reduce on-target toxicity (systemic cytokines/weight loss), without impacting anti-tumor efficacy. This also indicates that conjugation of a STING agonist compound (e.g., compound 12a vs. the targeted mAb conjugate of 12) may improve both efficacy and safety (reduce systemic cytokines).

TABLE 4

	Time (h)	3 mg/kg control	3 mg/kg non-binding mAb 11	3 mg/kg non-binding mAb 12	3 mg/kg targeted mAb 11	3 mg/kg targeted mAb 12	2.4 mg/kg control	2.4 mg/g non-binding mAb 11	12 mg/kg targeted mAb 11	1.48 mg/kg Compound 1	1.86 mg/kg Compound A
IFNγ	3	<3.2	1.1	0.4	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	0.3
	6	<3.2	15.6	7.1	8.5	22.6	<3.2	<3.2	1.3	4.3	0.2
	24	<3.2	<3.2	1.4	<3.2	3.0	<3.2	<3.2	0.9	<3.2	<3.2
IL1β	3	3.2	5.3	4.3	4.3	5.3	0.4	0.3	0.5	0.3	1.5
	6	3.2	4.3	4.3	5.3	6.4	0.3	1.7	0.3	1.8	0.6
	24	3.2	4.3	4.8	4.3	5.8	0.3	0.3	0.3	0.3	0.3
IL-6	3	9.2	120.1	23.8	150.5	109.5	154.7	14.3	5.5	37.7	95.7
	6	26.9	472.1	176.6	305.6	404.4	0.7	162.2	81.9	303.4	6.8
	24	33.2	12.0	58.6	28.0	75.3	7.7	19.6	4.8	27.0	13.5
IL-10	3	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	1.5	48.8
	6	<3.2	3.9	4.3	4.8	6.4	<3.2	<3.2	<3.2	<3.2	0.5
	24	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	0.8	<3.2
IL12p70	3	<3.2	5.9	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	17.6	174.5
	6	<3.2	<3.2	<3.2	<3.2	3.1	<3.2	<3.2	<3.2	<3.2	0.2
	24	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	23.4	140.0
IP10	3	235.3	973.2	402.4	1069.7	1094.1	59.8	176.7	80.5	295.4	702.8
	6	179.7	2976.0	2783.5	2963.1	3037.2	37.0	3977.4	4205.6	7374.2	3391.5
	24	192.3	1129.0	2329.0	1019.3	2564.0	71.5	559.7	358.1	1524.0	551.1
MCP-1	3	50.2	138.6	97.6	152.5	166.5	67.8	21.6	10.0	65.2	167.8
	6	35.8	1168.1	615.0	1727.0	7542.0	19.7	3822.7	1811.8	10211.9	795.6
	24	50.2	157.0	2374.8	284.9	7777.1	26.9	238.0	161.9	1486.0	332.6
MIP1α	3	<3.2	26.1	<3.2	26.1	<3.2	24.1	3.0	13.9	10.0	55.6
	6	<3.2	36.4	44.5	38.4	67.1	10.0	49.1	24.0	108.5	38.9
	24	<3.2	<3.2	62.9	62.9	36.4	33.9	10.0	49.4	29.9	69.9
MIP1β	3	<3.2	78.2	40.4	66.6	53.3	6.4	11.3	6.4	45.4	362.3
	6	<3.2	736.5	697.0	657.3	1267.3	<3.2	469.0	197.9	1170.5	6365.1
	24	<3.2	61.8	439.4	35.9	705.5	<3.2	35.6	26.4	270.7	2153.8
RANTES	3	4.4	6.4	1.3	7.8	5.3	2.9	2.2	1.7	3.4	10.6
	6	<3.2	14.9	3.4	13.2	34.1	2.7	19.9	11.9	57.3	91.6
	24	4.3	25.5	186.5	22.3	239.1	3.5	18.2	11.9	90.6	18.4
TNFα	3	<3.2	3.2	<3.2	<3.2	<3.2	1.6	1.4	1.3	2.5	3.6
	6	<3.2	12.9	7.2	10.2	4.6	0.8	3.8	2.1	6.2	1.9
	24	<3.2	<3.2	3.2	<3.2	8.2	1.3	1.4	1.3	3.1	2.0

TABLE 5

Cytokine production in peripheral blood (plasma) in engineered Renca tumor-bearing mice upon treatment with various ADCs comprising a non-binding or EphA2-targeted mAb with either a mIgG2a wild type (WT) or a mIgG2a											
	Time (h)	3 mg/kg control	3 mg/kg non-targeted mAb 12 (LALAPG)	3 mg/kg non-targeted mAb 12 (WT)	3 mg/kg targeted mAb 12 (LALAPG)	3 mg/kg targeted mAb 12 (WT)	3 mg/kg non-targeted mAb 15 (WT)	3 mg/kg targeted mAb 15 (WT)			
IFNγ	3	1.1	1.2	2.2	0.7	1.2	1.3	1.8			
	6	0.8	8.9	5.2	12.1	19.3	8.5	17.5			
	24	1.3	7.1	6.1	18.8	27.0	6.6	21.1			
	48	2.0	1.5	2.0	2.1	2.0	1.8	2.0			
IL1β	3	8.8	12.7	26.0	19.	7.8	15.9	30.3			
	6	8.8	35.5	14.7	<3.2	27.0	27.3	19.0			
	24	10.7	12.2	22.7	4.9	10.7	10.8	7.8			
	48	<3.2	4.9	22.7	7.8	2.1	13.7	10.7			
IL-6	3	5.1	12.7	12.6	71.6	61.6	12.0	105.8			
	6	5.5	55.3	47.3	327.4	279.5	82.4	475.4			
	24	3.5	33.4	25.2	61.1	80.8	41.3	63.0			
	48	2.3	5.0	5.8	29.9	15.6	11.5	17.9			
IL-10	3	2.6	4.0	4.4	4.1	2.2	5.9	5.1			
	6	2.5	8.2	4.8	5.2	9.6	8.4	6.3			
	24	1.6	3.2	2.7	4.9	5.5	4.9	7.3			
	48	0.6	0.6	2.7	1.7	1.0	2.6	2.1			
IL12p70	3	12.1	5.0	31.9	26.6	<3.2	23.3	12.5			
	6	0.9	48.9	13.7	<3.2	23.5	29.0	10.3			
	24	0.9	10.5	7.1	4.0	0.9	10.5	4.0			
	48	<3.2	0.9	20.1	<3.2	0.9	7.1	0.9			

TABLE 5-continued

Cytokine production in peripheral blood (plasma) in engineered Renca tumor-bearing mice upon treatment with various ADCs comprising a non-binding or EphA2-targeted mAb with either a mIgG2a wild type (WT) or a mIgG2a

Time (h)	control	3 mg/kg	3 mg/kg	3 mg/kg	3 mg/kg	non- targeted	3 mg/kg	3 mg/kg
		mAb 12 (LALAPG)	mAb 12 (WT)	mAb 12 (LALAPG)	mAb 12 (WT)	mAb 15 (WT)	mAb 15 (WT)	
IP10	3	99.4	134.0	104.9	335.5	371.9	185.4	637.3
	6	71.0	2469.9	2651.6	2757.9	3219.0	2885.3	3422.1
	24	86.3	1798.9	1652.7	2219.9	2004.1	2616.0	2324.1
	48	127.6	738.5	822.9	824.4	819.2	1052.2	935.8
MCP-1	3	63.2	120.4	165.9	135.5	96.9	142.7	276.1
	6	72.1	1368.6	1195.0	915.2	4492.9	1764.0	6594.8
	24	57.0	2083.8	1878.0	6406.5	8018.1	9546.4	15026.1
	48	42.1	285.6	599.9	794.1	934.2	1629.3	2234.6
MIP1 α	3	137.3	142.9	205.0	166.4	101.3	187.3	163.7
	6	101.3	178.8	130.0	61.4	284.3	133.8	271.9
	24	133.8	120.7	153.3	101.3	227.0	193.7	205.2
	48	<3.2	101.3	140.2	101.3	101.3	140.2	166.4
MIP1 β	3	<3.2	<3.2	78.1	<3.2	349.4	49.8	942.0
	6	<3.2	578.4	850.5	735.3	2898.1	677.8	4342.5
	24	<3.2	425.4	456.2	661.8	1493.2	1561.0	1387.7
	48	<3.2	178.9	227.9	221.2	309.4	567.1	378.3
RANTES	3	5.6	8.0	11.0	9.1	6.7	10.1	11.0
	6	6.6	24.5	18.9	14.4	168.0	37.5	206.6
	24	5.6	77.1	52.5	338.9	174.8	335.7	772.2
	48	6.6	21.3	43.9	69.6	59.2	140.4	190.4
TNF α	3	4.6	6.2	6.8	7.7	4.3	11.0	9.8
	6	2.7	15.0	5.8	3.5	16.5	9.9	22.9
	24	5.4	7.7	7.7	6.6	8.8	13.3	11.0
	48	1.9	5.4	6.5	5.4	6.6	7.6	

TABLE 6

Cytokine production in peripheral blood (plasma) in Renca tumor-bearing mice upon treatment with ADCs comprising an EphA2-targeted mAb with mIgG2a LALAPG backbone conjugated to compound 12 or compound 12a.

Dose #	Time (h)	Untreated	Vehicle	0.2 mg/kg Compound 12a	0.6 mg/kg Compound 12a	1.8 mg/kg Compound 12a	0.3 mg/kg targeted mAb 12 (LALAPG)	1.0 mg/kg targeted mAb 12 (LALAPG)	3.0 mg/kg targeted mAb 12 (LALAPG)
IFNg	1	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2
	1	<3.2	<3.2	4.6	18.3	36.4	<3.2	<3.2	9.4
	1	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	5.8	5.3
	1	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2
	2	<3.2	<3.2	16.5	41.5	80.4	0.0	1.7	20.1
IL-1b	1	0.7	0.7	0.7	0.7	7.5	3.2	0.7	0.7
	1	0.7	<3.2	0.7	5.7	0.7	3.2	11.0	5.7
	1	24	7.0	3.2	3.2	1.6	3.2	0.7	3.2
	1	48	3.2	5.7	0.7	5.7	3.2	3.2	5.8
	2	<3.2	<3.2	2.7	5.8	4.6	2.7	2.7	<3.2
IL-6	1	3.3	16.6	780.0	1899.7	4314.6	5.8	13.9	17.8
	1	6	0.4	4.9	266.1	424.0	543.0	25.0	28.3
	1	24	2.8	1.5	4.1	6.1	6.8	22.5	74.1
	1	48	0.9	0.9	5.6	1.8	1.5	1.9	1.8
	2	6	2.2	5.1	410.9	516.9	1681.6	13.6	53.2
IL-10	1	<3.2	<3.2	15.6	30.4	27.3	<3.2	<3.2	<3.2
	1	<3.2	<3.2	<3.2	3.8	9.9	<3.2	<3.2	3.8
	1	24	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	3.8
	1	48	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2
	2	<3.2	<3.2	1.2	<3.2	7.7	<3.2	1.2	<3.2
IL12p70	1	<3.2	9.4	<3.2	<3.2	3.1	<3.2	<3.2	9.4
	1	6	<3.2	<3.2	3.2	3.1	<3.2	<3.2	<3.2
	1	24	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	3.1
	1	48	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2
	2	<3.2	<3.2	<3.2	28.4	28.4	<3.2	<3.2	12.1
IP10	1	3	88.9	124.3	1989.6	4826.2	8222.7	122.1	200.3
	1	6	95.4	116.3	8985.4	8828.3	7589.2	4294.0	5279.6
	1	24	102.2	78.1	257.9	381.8	595.6	1123.5	4251.8

TABLE 6-continued

Cytokine production in peripheral blood (plasma) in Renca tumor-bearing mice upon treatment with ADCs comprising an EphA2-targeted mAb with mIgG2a LALAPG backbone conjugated to compound 12 or compound 12a.										
	Dose #	Time (h)	Untreated	Vehicle	0.2 mg/kg Compound 12a	0.6 mg/kg Compound 12a	1.8 mg/kg Compound 12a	0.3 mg/kg targeted mAb 12 (LALAPG)	1.0 mg/kg targeted mAb 12 (LALAPG)	3.0 mg/kg targeted mAb 12 (LALAPG)
MCP-1	1	48	80.8	85.1	172.8	218.4	223.5	317.8	566.2	1631.2
	2	6	139.5	191.4	>10000	3996.6	4151.5	1451.7	2590.8	2963.6
	1	3	17.3	65.0	333.3	1547.8	5805.3	21.8	48.1	50.2
	1	6	11.9	62.8	7790.8	12898.6	13861.5	518.9	311.8	1080.9
	1	24	24.4	2.0	53.0	141.5	143.9	283.5	694.9	5104.5
	1	48	29.3	19.4	56.8	40.0	2.0	118.0	108.0	530.5
MIP1a	2	6	51.7	87.7	5244.6	9761.2	17185.9	175.5	338.2	592.4
	1	3	<3.2	<3.2	10.3	251.5	1052.6	<3.2	<3.2	10.3
	1	6	<3.2	10.3	101.9	137.2	172.2	10.3	10.3	100.5
	1	24	10.3	<3.2	<3.2	<3.2	10.3	<3.2	<3.2	92.5
	1	48	<3.2	<3.2	10.3	10.3	<3.2	10.3	<3.2	<3.2
	2	6	32.6	32.6	104.9	115.5	209.9	52.2	32.6	99.2
MIP1b	1	3	<3.2	<3.2	727.2	2471.0	7438.6	<3.2	<3.2	<3.2
	1	6	<3.2	<3.2	670.7	1050.0	1162.7	155.7	256.7	695.2
	1	24	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	497.5
	1	48	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	157.8
	2	6	<3.2	<3.2	718.6	837.6	1407.7	<3.2	216.1	449.7
	1	3	<3.2	<3.2	<3.2	20.1	51.2	<3.2	5.0	<3.2
RANTES	1	6	20.3	<3.2	130.3	255.0	526.2	14.7	17.1	23.2
	1	24	<3.2	<3.2	3.2	46.2	48.8	11.3	34.5	131.7
	1	48	9.2	<3.2	<3.2	5.0	<3.2	7.9	17.1	79.4
	2	6	8.2	2.9	133.8	621.6	892.1	12.5	15.6	45.8
	1	3	<3.2	4.3	9.1	21.0	46.4	3.2	3.2	4.5
	1	6	<3.2	3.2	8.1	15.6	21.2	3.2	10.6	7.3
TNFa	1	24	7.3	3.2	3.2	5.2	3.2	5.2	5.9	15.2
	1	48	<3.2	5.4	4.3	<3.2	3.2	5.2	7.3	8.9
	2	6	<3.2	<3.2	10.0	16.7	46.4	3.2	3.2	3.2

[1766] The anti-tumor activity of the cleavable linker 11 conjugated to a non-binding mAb, PD-L1-targeted mAb (tumor and/or immune cell-targeted), or antigen C-targeted mAb (immune cell-targeted) was also evaluated in Renca tumor-bearing mice. All conjugates demonstrated tumor growth delay compared to untreated tumors. The PD-L1-targeted mAb conjugate of 11 demonstrated enhanced anti-tumor activity compared to an unconjugated PD-L1-targeted mAb. This demonstrates the anti-tumor benefit of delivering STING agonists using an ADC targeting antigens C and PD-L1 (FIG. 18). The anti-tumor activity of the non-cleavable linker 12 conjugated to a PD-L1-targeted mAb was also evaluated in Renca tumor-bearing mice; these conjugates induced tumor growth delay, though were less well tolerated than PD-L1 targeted mAb conjugates of 11.

CT26 Cancer Cells

[1767] The anti-tumor activity of compound 1 compared to the cleavable linker 11 conjugated to a non-binding mAb,

antigen C-targeted mAb, PD-L1-targeted mAb, or EphA2-targeted mAb was evaluated in CT26 tumor-bearing mice. When animals were treated with compound 1 or the unconjugated PD-L1-targeted mAb, minimal tumor growth delay was observed. Modest tumor growth delay was observed with the non-binding mAb conjugate of 11. In contrast, significant tumor growth delay was observed following treatment with all three targeted mAb conjugates of 11. This demonstrates the anti-tumor benefit of delivering STING agonists using an ADC targeting a variety of antigens, including an immune cell-targeted conjugate (antigen C), immune and/or tumor-targeted conjugate (PD-L1), and tumor-targeted conjugate (EphA2) (FIG. 19). Results of cytokine production in peripheral blood plasma is presented in Table 7.

TABLE 7

Cytokine production in peripheral blood (plasma) in CT26 tumor-bearing mice upon treatment with various ADCs comprising a mAb conjugated to compound 11.										
	Time (h)	Untreated		1.86 mg/kg Compound 1		12 mg/kg EphA2-targeted mAb 11 (mIgG2a LALAPG)				
IL-6	3	0.5	3.2	3.2	622.1	781.4	1128.3	185.8	0.5	217.7
	6	2.7	3.2	0.2	2652.5	2393.5	2412.7	2677.9	1790.2	2777.7
	24	5.7	5.4	0.6	44.5	31.8	36.5	72.8	0.2	67.6
	48	26.5	262.8	7.6	47.8	142.7	29.2	214.1	61.7	80.4

TABLE 7-continued

Cytokine production in peripheral blood (plasma) in CT26 tumor-bearing mice upon treatment with various ADCs comprising a mAb conjugated to compound 11.										
	3	3.2	3.2	3.2	0.2	2.3	1.2	3.2	3.2	1.2
IL-10	6	3.2	3.2	3.2	7.8	9	4.4	7.2	2	4.3
	24	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	1.5
	48	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2
IP-10	3	242.4	109.7	200.2	1439.4	1501.7	1160.7	592.6	125.9	377.2
	6	174.7	117.4	188.2	2610.8	2133.6	2473.4	2039.3	2711.3	2008.6
	24	272.5	134.4	201.1	1121.6	1025.3	696.2	1468.5	145	1900.5
	48	122.9	155.8	74.7	560.1	398.8	560	1293.4	541.3	716.9
MCP-1	3	2.7	3.2	3.2	73.7	78.6	110.3	36.4	2.7	23.1
	6	7.2	7.2	3.2	3185.3	2816.3	1634.8	6186.6	3754.5	3698.6
	24	3.2	3.2	3.2	397.7	294.7	305.9	765.3	3.2	821
	48	13.5	18.6	3.2	93.1	20.9	41.4	207.4	85.1	108.7
MIP-1a	3	3.2	3.2	3.2	3.9	3.2	3.2	3.9	3.2	3.2
	6	3.9	3.2	3.2	94.6	93.6	73.9	222.1	127.3	261.8
	24	3.2	3.2	3.2	12.7	25.1	3.2	21.7	3.2	21.7
	48	3.2	3.2	3.2	3.9	12.7	3.2	3.9	3.2	3.9
MIP1b	3	3.2	1.6	3.2	297.7	336.8	224	311.6	3.2	185.9
	6	3.2	3.2	3.2	925.8	369.7	1161.4	1679.2	1460.7	1237.9
	24	3.2	3.2	3.2	127.6	125.3	55.3	268.8	3.2	356.8
	48	3.2	14.8	3.2	61.1	10.8	57.6	66.7	26.9	56.9
TNF α	3	3.2	3.2	3.2	3.2	4.9	4.3	1.4	3.2	3.2
	6	3.2	3.2	3.2	16.9	16.6	10	29.1	26.2	34.8
	24	3.2	3.2	3.2	0.4	0.7	3.2	4.3	3.2	3.2
	48	3.2	3.2	3.2	1.1	3.2	3.2	1.4	3.2	3.2
	2.4 mg/kg				2.4 mg/kg				2.4 mg/kg	
Time	EphA2-targeted				Antigen C-targeted				Non-binding	
(h)	mAb 11 (mIgG2a LALAPG)				mAb 11 (mIgG2a LALAPG)				mAb 11 (mIgG2a LALAPG)	
IL-6	3	17.8	27.7	23.4	483.9	182.4	442.5	1.4	100.6	56.5
	6	168.7	303.4	304.8	1821.4	2769.8	2324.8	123.7	151.3	266.9
	24	16.2	143.2	16.1	9.4	34.4	126.9	5	16.9	3.2
	48	6.5	39.1	7.8	48.9	32.2	19.5	2.9	2.9	2.3
IL-10	3	3.2	3.2	3.2	0.9	3.2	0.4	3.2	3.2	3.2
	6	4	1.2	1.6	1.2	3.7	4.3	0.4	0.4	2
	24	3.2	3.2	3.2	0.4	3.2	3.2	3.1	3.2	3.2
	48	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2
IP-10	3	198.1	190.9	196.9	1271.3	629.1	627.8	109.4	450	308.7
	6	2327.7	2740.5	1949.2	2062.9	2328	2713.5	1779.6	1376.6	2092
	24	1189.9	1094.8	1089	2565	1994.5	1329.8	246.4	693.7	3.2
	48	307.2	167.2	250.2	448.8	273.5	378	107.3	235.9	319.2
MCP-1	3	3.2	10.5	2.7	393.2	69.9	78.6	3.2	46.2	2.7
	6	656.5	578.3	382.2	10207.3	4960.7	37687.1	162	556.2	425
	24	99.1	99.1	99.1	1009.2	637.8	194	3.2	55.1	3.2
	48	27.2	10.5	13.5	39.8	34.7	365.9	3.2	2.7	20.9
MIP-1a	3	3.2	3.2	3.2	217.7	103.1	139.8	3.2	3.2	3.2
	6	12.7	3.9	3.2	144	152.7	82.1	17.7	12.7	3.9
	24	3.2	3.2	3.2	17.7	21.7	12.7	3.2	3.2	3.2
	48	3.2	3.2	3.2	3.2	3.2	17.7	3.2	3.2	3.2
MIP1b	3	26.9	19.7	5.4	1600.5	682.1	991.5	3.2	31.2	7.2
	6	367.2	264.6	356.3	1377.1	1236.6	1740.4	137.2	215.4	203.6
	24	84.9	63.2	51.3	197.4	142.2	127.5	3.2	26.9	3.2
	48	11.4	3.2	8.8	13.8	13.2	69	3.2	3.2	3.2
TNF α	3	3.2	3.2	3.2	31	25.6	27.6	3.2	3.2	3.2
	6	6.2	3.8	2.6	31	45.5	39.5	3.2	4.3	3.2
	24	3.2	2.9	8.5	2	7	3.8	3.2	1.4	3.2
	48	3.2	3.2	3.2	3.2	1.7	3.2	3.2	3.2	3.2

TABLE 7-continued

Cytokine production in peripheral blood (plasma) in CT26 tumor-bearing mice upon treatment with various ADCs comprising a mAb conjugated to compound 11.

	Time (h)	2.4 mg/kg PD-L1-targeted mAb 11			2.4 mg/kg PD-L1-targeted mAb		
IL-6	3	18.1	56.9	3.3	25.6	0.6	5.8
	6	119.4	72.6	162.5	3.2	3.2	1
	24	23.8	21.8	5.2	21.2	6.5	216.8
	48	26.6	26.8	89.7	1.4	3.2	12.2
IL-10	3	3.2	3.2	3.2	33.8	3.2	3.2
	6	0.4	0	0	3.2	3.2	3.2
	24	3.2	3.2	3.2	26.2	3.2	3.2
	48	3.2	3.2	0.4	3.2	3.2	3.2
IP-10	3	163.9	154.4	178.3	105.7	190.4	96.1
	6	1814.4	1744	1389.4	130.6	151.9	110.7
	24	717.5	1002.6	833.1	247.7	689.9	166.7
	48	748.1	599.3	580.4	128.1	183.3	135.9
MCP-1	3	18.9	13.8	3.2	169.8	3.2	3.2
	6	143.3	133	252	3.1	7.5	7.5
	24	129.2	191.4	98	129.2	7.5	3.2
	48	135.9	127.3	253.1	7.5	13.8	16.4
MIP-1a	3	3.2	3	3.2	3	3	3
	6	11.2	3	3	3	3	11.2
	24	3	3	3	3	11.2	24
	48	11.2	11.2	3	3	7.9	3
MIP1b	3	3.2	5.4	9.9	3.2	3.2	3.2
	6	70	61.7	85.7	3.2	3.2	3.2
	24	3.2	19.3	32	3.2	3.2	46.1
	48	26.5	23.5	30	3.2	3.2	3.2
TNFa	3	5.8	3.2	3.2	75.5	3.2	3.2
	6	3.2	3.2	3.2	3.2	3.2	3.2
	24	6.4	3.2	3.2	58.6	3.2	3.2
	48	3.6	3.2	3.2	3.2	3.2	3.2

MC38 Cancer Cells

[1768] The anti-tumor activity of the cleavable linker 12 conjugated to a non-binding mAb or EphA2-targeted mAb with a LALAPG mIgG2a Fc backbone was evaluated in MC38-tumor bearing wild type (WT) or STING-deficient (*Tmem173^{ge}*) mice. Animals treated with 3 weekly doses of 1 mg/kg non-binding conjugates of 12 or 0.1 mg/kg targeted conjugates of 12 demonstrated modest and minimal tumor growth delay, respectively, in WT but not STING-deficient tumor bearing mice. Animals treated with 3 weekly doses of 1 mg/kg targeted conjugates of 12 demonstrated robust tumor growth delay in WT but not STING-deficient tumor bearing mice. This demonstrates that in MC38 tumor-bearing mice STING signaling is required in non-tumor cells in the tumor microenvironment for anti-tumor activity (FIGS. 20A and 20C).

[1769] Animals treated with a single dose of 1 mg/kg EphA2-targeted conjugates of 12 also demonstrated robust tumor growth delay in WT tumor bearing mice, demonstrating that a single dose of EphA2-targeted conjugates of 12 is sufficient to drive complete tumor regression (FIG. 20A).

[1770] Mice that achieved complete tumor regression in response to a single dose or 3 weekly doses of ADC were rechallenged with MC38 tumor cells on the opposite flank and tumor growth was monitored. All rechallenged mice—but not all naïve untreated mice challenged with MC38 tumor cells—were protected from rechallenge, suggesting that targeted conjugates of 12 elicit immune memory (FIG. 20D).

4T1 Cancer Cells

[1771] The anti-tumor activity of the cleavable linker 12 conjugated to a non-binding or EphA2-targeted mAb with a LALAPG mIgG2a Fc backbone was evaluated in 4T1 tumor-bearing mice. All conjugates of compound 12 led to significant tumor growth delay at the doses tested, with the targeted mAb conjugate of compound 12 demonstrating enhanced tumor growth delay compared to the non-binding conjugate (FIG. 21A), with minimal weight loss observed (FIG. 21B). This demonstrates that EphA2-targeted mAb conjugates of compound 12 are active in multiple tumor models (FIGS. 17-21B).

B7-H4-Targeted Conjugates

[1772] B7-H4-targeted conjugates were evaluated in a Renca tumor model engineered via lentiviral transduction to express murine B7-H4 (mB7-H4). mB7-H4-expressing Renca tumor-bearing mice were treated with 3 weekly doses of 1 mg/kg of unconjugated mAb or ADC. Non-binding mAb conjugates of compound 12 led to modest tumor growth delay, while the B7-H4-targeted mAb conjugates of compound 12 led to robust tumor growth delay. B7-H4-targeted conjugates with a WT mIgG2a Fc backbone led to slightly enhanced tumor growth delay compared to those with a Fc effector function null LALA-KA mIgG2a Fc backbone (see, e.g., Schlothauer et al., Protein Engineering, Design and Selection, 2016, 29(10):457-466; and Hezareh et al., Journal of Virology, 2001, 75(24):12161-12168, each of which is incorporated herein by reference in its entirety). This suggests that the B7-H4-targeted ADCs elicit robust anti-tumor responses. Moreover, this suggests that in the

Renca tumor model, B7-H4-targeted mAb conjugates with a WT Fe backbone drive slightly more robust anti-tumor responses than those with a LALA-KA Fe null backbone (FIG. 22A). Importantly, all conjugates were tolerated, though slightly more weight loss was observed following treatment with ADCs with a WT Fe backbone (FIG. 22B). Cytokine production is provided in Table 8.

TABLE 8

Time (h)	control	1 mg/kg B7-h4- targeted mAb		1 mg/kg non- binding mAb 12 (WT)		1 mg/kg B7-h4- targeted mAb 12 (LALAPG)		1 mg/kg non- binding mAb 12 (LALAKA)		1 mg/kg B7-h4- targeted mAb 12 (LALAPG)	
		1 mg/kg B7-h4- targeted mAb	1 mg/kg non- binding mAb 12 (WT)	1 mg/kg B7-h4- targeted mAb 12 (LALAPG)	1 mg/kg non- binding mAb 12 (LALAKA)	1 mg/kg B7-h4- targeted mAb 12 (LALAPG)	1 mg/kg EphA2- targeted mAb 12 (LALAPG)				
IFN γ	3	3.5	0.5	3.2	4.3	2.0	1.2	2.1			
	6	3.4	1.2	5.8	6.3	1.6	1.8	2.9			
IL1 β	3	56.7	25.4	50.5	58.5	48.5	23.9	27.9			
	6	50.9	62.3	66.1	38.4	15.9	27.7	51.0			
IL-6	3	12.6	12.3	19.9	35.1	15.0	11.4	27.7			
	6	138.4	64.3	85.2	206.2	153.5	135.4	71.1			
IL-10	3	17.3	24.8	32.8	26.8	23.4	11.2	9.4			
	6	23.4	35.0	35.0	23.0	14.8	12.8	11.0			
IL12p70	3	44.9	53.6	55.1	44.8	42.0	33.4	24.3			
	6	60.8	79.4	79.5	38.5	19.7	33.4	35.8			
IP10	3	158.7	100.3	172.0	205.7	167.7	132.6	308.9			
	6	108.8	72.5	630.2	1498.6	1134.8	617.0	1295.5			
MCP-1	3	101.5	122.3	175.8	171.3	146.5	97.1	81.7			
	6	142.1	192.9	297.2	863.5	213.6	146.5	180.9			
MIP1 α	3	150.5	161.6	171.4	200.8	179.9	136.8	118.3			
	6	223.3	268.0	221.6	151.7	98.9	131.8	84.1			
MIP1 β	3	29.4	30.4	80.8	66.4	52.0	18.0	30.8			
	6	39.6	65.9	86.1	164.4	43.2	40.4	47.2			
RANTES	3	14.5	13.9	13.6	17.5	14.2	12.1	6.6			
	6	15.0	16.5	18.8	20.7	9.3	11.5	11.7			
TNF α	3	16.6	13.5	16.8	18.0	13.0	3.8	4.7			
	6	12.2	21.4	24.1	13.3	6.3	16.6	12.3			

[1773] B7-H4-targeted ADCs were also evaluated in an EMT6 tumor model engineered via lentiviral transduction to express murine B7-H4 (mB7-H4). mB7-H4-expressing EMT6 tumor-bearing mice were treated with 3 weekly doses of 1 or 0.5 mg/kg of STING ADCs or a single dose of 1 mg/kg of ADCs. Non-binding mAb conjugates of compound 12 led to modest tumor growth delay, while the B7-H4-targeted mAb conjugates of compound 12 led to robust tumor growth delay in a dose-dependent manner (FIG. 23A). B7-H4-targeted conjugates with a WT mIgG2aFc backbone led to enhanced tumor growth delay compared to those with a Fc effector function null LALA-KA mIgG2aFc backbone. This suggests that B7-H4-targeted ADCs elicit robust anti-tumor responses in this mB7-H4-expressing EMT6 tumor model. Moreover, these data demonstrate that B7-H4-targeted ADCs with a WT Fc backbone drive more robust anti-tumor responses than those with a LALA-KA Fc null backbone. Importantly, all conjugates were tolerated, as there was no significant weight loss observed in any treatment group (FIG. 23B).

α v β 6-Targeted ADCs

[1774] Integrin α v β 6-targeted ADCs were evaluated in a CT26 tumor model engineered via lentiviral transduction to express murine integrin α v and β 6 (α v β 6). Murine α v β 6-expressing CT26 tumor bearing mice were treated with 3 weekly doses of 0.5, 1, or 3 mg/kg of ADCs or a single dose of 1 mg/kg of ADCs. Non-binding mAb conjugates of

compound 12 led to modest tumor growth delay, while the α v β 6-targeted conjugates of compound 12 led to robust tumor growth delay in a dose-dependent manner (FIG. 24). α v β 6-targeted ADCs with a WT mIgG2a Fc backbone elicited similar tumor growth delay compared to those with an Fc effector function null LALA-KA mIgG2a Fc backbone, though there was a slight trend towards modestly

enhanced anti-tumor activity with the WT backbone (FIG. 24). There was no significant weight loss observed in any treatment group. Overall, this demonstrates that α v β 6-targeted ADCs are active in this murine α v β 6-expressing CT26 tumor model.

Evaluation of CD228-Targeted ADCs in hCD228-LL2 Tumor-Bearing Mice

[1775] CD228-targeted ADCs were evaluated in a LL2 tumor model engineered via lentiviral transduction to express human CD228 (hCD228). hCD228-expressing LL2 tumor-bearing mice were treated with non-binding or CD228-targeted mAb conjugates of compound 12 (5 mg/kg single dose, 3 mg/kg Q4Dx2, or 3 mg/kg Q7Dx3), compound A (0.08 or 1.5 mg/kg Q4Dx3), or an anti-PD1 mAb (10 mg/kg Q4Dx3) alone or in combination when tumors were 100 mm³. Tumor volume was measured twice weekly. Some ADCs were prepared using antibodies with a human IgG1 backbone; therefore, shortened dosing schedules were selected to avoid anti-drug antibody (ADA) responses that can occur in immunocompetent mice upon repeat dosing.

[1776] Treatment with the CD228-targeted ADCs, but not the non-binding ADCs, resulted in robust tumor growth delay (FIG. 25, FIG. 26). Moreover, while treatment with an anti-PD1 mAb alone was inactive, combination of an anti-PD1 mAb with CD228-targeted ADCs resulted in enhanced tumor growth delay compared to either alone (FIG. 26). All

ADCs were tolerated; no significant weight loss was observed in any treatment group.

[1777] CD228-targeted ADCs with a mIgG2a backbone were also evaluated and demonstrated more robust antitumor activity compared to those on a hIgG1 backbone (FIG. 26 and FIG. 27A). Moreover, CD228-targeted STING IDCs with a mIgG2a WT Fc backbone demonstrated significantly more antitumor activity than those with an Fc effector function null LALAKA Fc backbone (FIG. 28A), without impacting weight loss or increasing systemic cytokine levels after the 1st or 2nd dose (FIG. 28B and Table 9). Thus, consistent with *in vitro* data (FIG. 13), CD228-targeted STING IDCs with a WT Fc backbone drive enhanced anti-tumor activity compared to those with a LALAKA Fc null backbone. Finally, intravenous dosing of CD228-targeted STING IDCs led to more robust anti-tumor activity compared to intraperitoneal dosing, suggesting that the route of IDC delivery impacts antitumor activity (FIG. 28A).

[1778] The ability of CD228-targeted conjugates of compound 12 (non-cleavable linker) to elicit antitumor activity was then evaluated compared to conjugates of compounds 13 and 14 (cleavable linkers). Although CD228-targeted conjugates of compounds 12, 13, and 14 elicited similar tumor cell killing *in vitro* in a tumor/PBMC co-culture assay (FIG. 35), *in vivo* CD228-targeted conjugates of compound 12 elicited more robust antitumor activity compared to

conjugates of compounds 13 or 14 (FIG. 30). All three conjugates had a similar Pk profile, with comparable exposures over the first 4 days after intravenous dosing (FIG. 31). Moreover, the reduced antitumor activity of conjugates of compounds 13 and 14 was accompanied by a trend towards higher levels of several cytokines 6 hours after dosing (e.g. IFNg, IL-6, IP10, MIP1a, MIP1b, RANTES) and a slight reduction in cytokines 24 hours after dosing. This suggests that the kinetics of the systemic cytokine response to IDCs may vary depending on the drug linker properties—*independent* of the Pk profile—and this in turn may impact antitumor activity (Table 10). Moreover, this suggests that the antitumor activity of conjugates *in vivo* cannot be predicted simply based on *in vitro* potency.

[1779] The antitumor activity and pharmacokinetic profile of CD228-targeted conjugates of compound 12 were also evaluated across a range of dose levels. Antitumor activity increased with increasing dose of ADC (FIG. 32). Consistent with dose-dependent antitumor activity, systemic exposure was also dose-dependent (FIG. 33), with the maximum observed concentration (C_{max}) increasing proportionally with increasing dose of ADC. The area under the concentration time curves from time 0 to 7 days (AUC_{0-7d}) and from time 0 to 10 days (AUC_{0-10d}) increased less than proportionally with increasing dose of ADC, potentially due to anti-drug antibodies elicited by the human Fc backbone in immunocompetent mice.

TABLE 9

Cytokine production in peripheral blood (plasma) in engineered LL2 tumor-bearing mice upon treatment with various ADCs comprising a non-binding, CD228-targeted, or EphA2-targeted mAb with either a mIgG2a wild type (WT) or a mIgG2a LALAKA backbone conjugated to compound 12.

	Dose	Time (h)	CD228-targeted mAb 12 (WT hIgG1 Fc) Q4Dx2 i.p.	CD228-targeted mAb 12 (WT mIgG2a Fc) Q7dx3 i.v.	CD228-targeted mAb 12 (WT mIgG2a Fc) Q7dx3 i.p.	CD228-targeted mAb 12 (LALAKA mIgG2a Fc) Q7dx3 i.p.	EphA2-targeted mAb 12 (WT mIgG2a Fc) Q7dx3 i.p.	Non-binding mAb 12 (WT mIgG2a Fc) Q7dx3 i.p.	Compound A (1.5 mg/kg Q7Dx3 i.v.)	Compound A (0.08 mg/kg Q7Dx3 i.v.)
IFNg	1	3	3.2							
	1	6	6.0	62.8	9.9	5.4	29.2	<3.2	392.4	9.8
	2	3	8.7							
	2	6	12.2	59.2	8.0	21.4	22.3	33.0	1550.6	11.7
	1	24	10.2							
	3	6		11.5	25.2	17.6	38.1	2.5	1236.8	21.9
IL1b	1	3	32.0							
	1	6	33.4	38.3	22.1	16.0	24.8	12.1	38.0	12.1
	2	3	12.1							
	2	6	24.8	32.0	54.0	33.1	37.3	2670.8	57.4	26.2
IL-6	1	24	38.3							
	3	6		64.9	1006.6	29.1	42.3	11.0	36.8	66.6
	1	3	79.9							
	1	6	689.2	2388.9	450.3	398.7	1671.2	108.9	10532.0	346.7
	2	3	70.1							
IL-10	2	6	166.5	363.0	478.0	892.5	2984.4	848.6	22725.1	936.6
	1	24	306.6							
	3	6		209.0	684.8	685.8	1750.7	133.6	14635.1	1494.7
	1	3	9.8							
	1	6	41.5	24.8	27.9	33.5	41.7	9.8	71.5	15.8
IL-12p70	2	3	12.8							
	2	6	24.5	36.4	27.2	35.4	49.5	294.1	92.3	9.5
	1	24	20.4							
	3	6		73.8	305.7	36.0	76.2	26.6	62.8	36.3
	1	3	2.8							
	1	6	34.3	28.5	9.3	3.0	16.1	3.0	32.3	3.0
	2	3	15.5							
IL-12p70	2	6	15.3	9.3	99.6	15.0	21.8	3005.9	75.4	9.7
	1	24	32.9							
	3	6		43.9	1537.3	15.5	12.9	2.8	43.9	220.3

TABLE 9-continued

Cytokine production in peripheral blood (plasma) in engineered LL2 tumor-bearing mice upon treatment with various ADCs comprising a non-binding, CD228-targeted, or EphA2-targeted mAb with either a mIgG2a wild type (WT) or a mIgG2a LALAKA backbone conjugated to compound 12.

	Dose	Time (h)	CD228-targeted mAb 12 (WT) hIgG1 Fc) Q4Dx2 i.p.	CD228-targeted mAb 12 (WT) mIgG2a Fc) Q7dx3 i.v.	CD228-targeted mAb 12 (WT) mIgG2a Fc) Q7dx3 i.p.	CD228-targeted mAb 12 (LALAKA) mIgG2a Fc) Q7dx3 i.p.	EphA2-targeted mAb 12 (WT) mIgG2a Fc) Q7dx3 i.p.	Non-binding mAb 12 (WT) mIgG2a Fc) Q7dx3 i.p.	Compound A (1.5 mg/kg Q7Dx3 i.v.)	Compound A (0.08 mg/kg Q7Dx3 i.v.)
IP10	1	3	459.9							
	1	6	6335.8	9573.5	6777.7	8402.9	8605.7	3525.7	>10000	7501.0
	2	3	1192.3							
	2	6	1323.4	8091.7	3979.4	6251.2	6699.0	2025.2	>10000	9045.3
	1	24	2189.6							
	3	6		3410.9	6519.3	4653.6	7420.3	1435.8	>10000	7718.5
MCP-1	1	3	258.6							
	1	6	5512.0	8936.7	5632.5	3576.4	6704.7	3335.2	10000.0	3780.5
	2	3	776.5							
	2	6	808.2	2864.3	2355.9	4122.0	4369.8	3250.3	>10000	7114.6
	1	24	4295.5							
	3	6		2776.1	7830.5	2043.7	7114.1	383.7	>10000	5009.1
MIP1a	1	3	158.2							
	1	6	170.4	343.8	135.7	193.2	512.4	114.4	574.2	107.1
	2	3	102.7							
	2	6	102.7	231.5	232.0	311.5	366.4	515.7	846.6	206.0
	1	24	145.3							
	3	6		230.0	333.6	264.0	423.0	80.8	743.4	270.0
MIP1b	1	3	49.9							
	1	6	903.3	2671.2	1074.9	1126.5	3471.4	193.5	4253.1	474.6
	2	3	51.7							
	2	6	124.2	1435.1	887.2	1461.3	1765.7	453.7	5235.4	1550.3
	1	24	325.2							
	3	6		703.1	1415.0	743.6	2507.7	205.1	4517.1	1009.6
RANTES	1	3	11.0							
	1	6	14.4	161.6	29.1	16.8	43.6	4.7	1705.3	33.9
	2	3	20.6							
	2	6	11.2	80.7	44.7	103.8	95.5	313.0	1906.1	236.6
	1	24	109.0							
	3	6		102.9	264.4	57.5	275.4	19.5	2533.7	172.9
TNFa	1	3	18.2							
	1	6	16.0	46.3	18.8	13.3	41.2	3.3	95.7	11.0
	2	3	8.5							
	2	6	8.5	29.9	38.5	37.3	54.2	204.1	204.0	18.4
	1	24	22.7							
	3	6		43.3	176.8	16.8	58.7	11.0	195.3	29.6

*Values out of standard curve range (e.g. >10,000 or <3.2) were converted to 10,000 or 3.2 pg/mL respectively to calculate mean cytokine; if all 3 values were out of range, they are plotted as <10,000 or <3.2 pg/mL.

TABLE 10

		CD228-targeted mAb-12 (WT) hIgG1, i.v.)	CD228-targeted mAb-13 (WT) hIgG1, i.v.)	CD228-targeted mAb-14 (WT) hIgG1, i.v.)	CD228-targeted mAb-12 (WT) hIgG1, i.p.)
IFNg	6 h	3.2	53.4	138.9	166.9
	24 h	3.2	16.5	11.2	8.0
IL1b	6 h	18.9	31.6	44.4	50.8
	24 h	18.9	22.1	25.3	25.3
IL-6	6 h	78.5	1939.1	3407.3	2422.3
	24 h	27.9	459.6	197.2	117.4
IL-10	6 h	3.8	26.1	49.1	23.4
	24 h	3.2	3.2	14.5	9.2
IL12p70	6 h	7.0	25.6	35.8	33.1
	24 h	8.9	5.0	25.2	17.1
IP10	6 h	206.8	7593.2	9554.3	9735.5
	24 h	197.2	2894.2	2013.7	1426.2
MCP-1	6 h	135.5	12716.4	17729.6	24776.7
	24 h	109.8	4183.4	1962.1	1979.7
					4222.1

TABLE 10-continued

Cytokine production in peripheral blood (plasma) in human CD228-LL2 tumor-bearing mice upon treatment with various ADCs comprising a CD228-targeted mAb (hIgG1 WT) conjugated to compounds 12, 13, or 14.

		CD228-targeted mAb-12 (WT hIgG1, i.v.)	CD228-targeted mAb-13 (WT hIgG1, i.v.)	CD228-targeted mAb-14 (WT hIgG1, i.v.)	CD228-targeted mAb-12 (WT hIgG1, i.p.)
	Untreated				
MIP1a	6 h	69.4	315.3	791.1	622.8
	24 h	116.5	205.8	221.5	139.5
MIP1b	6 h	3.2	2692.2	4311.9	4274.3
	24 h	17.4	503.8	313.4	219.4
RANTES	6 h	7.5	178.1	627.4	609.8
	24 h	6.0	264.6	203.2	154.6
TNF α	6 h	6.4	41.3	67.6	69.1
	24 h	8.6	7.8	12.5	13.8
					15.6

*Values out of standard curve range (e.g. >10,000 or <3.2) were converted to 10,000 or 3.2 pg/mL respectively to calculate mean cytokine.

Evaluation of STING IDCs in a Xenograft Model of Breast Cancer

[1780] The ability of B7-H4 and $\alpha\beta\delta$ -targeted conjugates of compound 12 to elicit antitumor activity in immunodeficient Nude mice bearing MDA-MB-468 tumors was then evaluated. B7-H4-targeted conjugates of 12 (with both a WT and LALAKA Fc backbone) elicited robust anti-tumor activity. Similarly, human $\alpha\beta\delta$ -targeted conjugates of compound 12 (h2A2 mAb with both a WT and aglycosylated Fc backbone that reduces Fc γ R binding) elicited strong tumor

growth delay. Finally, the human/mouse $\alpha\beta\delta$ -targeted conjugates of compound 12 (h15H3 mAb with both a WT and LALAKA Fc backbone) elicited modest tumor growth delay, similar to the non-binding conjugate of compound 12. This demonstrates the ability of tumor-targeted conjugates of compound 12 to elicit antitumor activity in the absence of cytotoxic T cells and independent of engagement of innate immune cells via Fc γ R binding. Systemic cytokines elicited by these conjugates was also evaluated and is shown in Table 11.

TABLE 11

Cytokine production in peripheral blood (plasma) in human MDA-MB-468 tumor-bearing mice upon treatment with various ADCs comprising a B7-H4 or $\alpha\beta\delta$ -targeted mAb conjugated to compound 12.

		Non-binding mAb-12 (WT hIgG2a)	B7-H4-targeted mAb-12 (LALAKA Fc hIgG2a)	$\alpha\beta\delta$ -targeted mAb-12 (h15H3 WT hIgG2a)	$\alpha\beta\delta$ -targeted mAb-12 (h15H3 LALAKA hIgG2a)	$\alpha\beta\delta$ -targeted mAb-12 (h2A2 WT hIgG2a)	$\alpha\beta\delta$ -targeted mAb-12 (h2A2 aglycosylated hIgG2a)
	Untreated						
IFNg	3 h	2.9	3.2	3.2	3.2	3.2	3.2
	6 h	3.2	11.6	5.8	10.1	30.5	2.9
IL1b	3 h	10.5	16.6	16.5	19.4	27.5	18.6
	6 h	5.6	13.7	20.5	35.7	27.6	15.4
IL-6	3 h	12.3	30.9	29.0	24.6	25.3	16.3
	6 h	762.2	768.5	581.3	895.9	900.3	1001.9
IL-10	3 h	10.4	131.0	10.4	25.9	15.9	10.4
	6 h	3.2	97.1	33.2	46.9	50.2	3.2
IL12p70	3 h	16.4	20.5	16.4	25.1	27.2	18.4
	6 h	3.2	14.3	16.4	33.4	31.5	3.2
IP10	3 h	172.7	221.9	217.3	185.5	342.3	189.0
	6 h	135.7	5612.7	5400.7	5730.7	6171.4	6085.6
MCP-1	3 h	125.2	131.4	161.8	165.7	274.0	169.8
	6 h	73.1	2015.6	1195.0	2487.6	3820.9	3180.1
MIP1a	3 h	150.7	184.1	174.7	155.0	226.1	206.2
	6 h	98.3	197.1	221.0	230.8	411.5	259.2
MIP1b	3 h	16.7	3.2	17.8	28.8	459.9	34.9
	6 h	3.2	560.1	716.0	853.8	2526.3	1171.0
RANTES	3 h	3.2	2.1	3.5	3.2	2.8	2.5
	6 h	3.2	6.4	9.9	11.2	49.3	9.5
TNF α	3 h	9.6	4.8	4.8	14.4	18.2	8.7
	6 h	3.2	12.8	12.8	29.0	26.2	21.7

Rat Tolerability Study:

[1781] The nonclinical safety profile of compound 12 conjugated to non-binding antibodies with a WT Fc backbone, non-binding antibodies with an Fe null backbone, targeted antibodies with a WT Fe backbone, and targeted antibodies with an Fe null backbone was evaluated in non-GLP rat toxicology studies. All conjugates with the compound 12 drug linker (both non-binding and targeted, WT and null Fc backbone) were tolerated in rat at doses higher than the minimally efficacious dose in mouse tumor models.

Example 4

In Vivo Pharmacokinetic Study

Methods

[1782] Pharmacokinetic profiles were analyzed following administration of two weekly 1 mg/kg doses of an ADC comprising a [deglycosylated]non-binding mAb conjugated to compound 12 to male C57BL/6 mice. Plasma was collected and analyzed for generic total antibody (gTAb) by immunoassay. TAb concentrations in mouse K2EDTA plasma were determined by a Gyros flow-through immunoassay platform. Samples and standards were diluted in assay buffer and incubated with a solution containing biotinylated murine anti-human kappa light chain antibody and fluorescent goat anti-human IgG Fc_γ F(ab')₂ antibody fragment in a sandwich format. The resulting immunocomplexes were bound to the streptavidin-coated beads in the affinity column of the compact disc (CD). The CD was read by a laser that

excites the fluorescent detection reagent, producing a signal that is directly proportional to the concentration of test article in the C57BL/6 male mouse plasma sample. Non-compartmental analysis was applied to pooled animal plasma concentration data (sparse sampling) using Phoenix WinNonlin 8.2 (Certara, USA). Concentration values below the limit of quantitation (BLQ) were treated as zero for analysis. Nominal doses and sampling times were used.

Results

[1783] Pharmacokinetic profiles were analyzed following administration of two weekly 1 mg/kg doses of an ADC comprising a [deglycosylated]non-binding mAb conjugated to compound 12 to male C57BL/6 mice. The maximum observed concentration (Cmax) after the first and second dose was 40500 and 52400 ng/mL, respectively. The area under the concentration-time curve from time 0 through 7 days (AUC0-7d) was 85600 d*ng/mL. This suggests that the total antibody exposure for the non-binding conjugate of compound 12 was higher than the small molecule exposure of published small molecule STING agonists (FIG. 29) (See, e.g., Ramanjulu et al., 2018, Nature 564, 439-443).

[1784] The contents of each of the references cited in the present disclosure are hereby incorporated by reference in their entirety.

[1785] A number of embodiments of the present disclosure have been described. Nevertheless, it will be understood that various modifications may be made without departing from the spirit and scope of the present disclosure. Accordingly, other embodiments are within the scope of the following claims.

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	organism = synthetic construct				
SEQUENCE: 12					
HYMMA					5
SEQ ID NO: 13	moltype = AA length = 17				
FEATURE	Location/Qualifiers				
source	1..17				
	mol_type = protein				
	organism = synthetic construct				
SEQUENCE: 13					
RIGPSGGPTH YADSVKG					17
SEQ ID NO: 14	moltype = AA length = 19				
FEATURE	Location/Qualifiers				
source	1..19				
	mol_type = protein				
	organism = synthetic construct				
SEQUENCE: 14					
YDSGYDYVAV AGPAEYFQH					19
SEQ ID NO: 15	moltype = AA length = 11				
FEATURE	Location/Qualifiers				
source	1..11				
	mol_type = protein				
	organism = synthetic construct				
SEQUENCE: 15					
RASQSISTWL A					11
SEQ ID NO: 16	moltype = AA length = 7				
FEATURE	Location/Qualifiers				
source	1..7				
	mol_type = protein				
	organism = synthetic construct				
SEQUENCE: 16					
KASNLTHT					7
SEQ ID NO: 17	moltype = AA length = 9				
FEATURE	Location/Qualifiers				
source	1..9				
	mol_type = protein				
	organism = synthetic construct				
SEQUENCE: 17					
QQYNNSYRT					9
SEQ ID NO: 18	moltype = AA length = 128				
FEATURE	Location/Qualifiers				
source	1..128				
	mol_type = protein				
	organism = synthetic construct				
SEQUENCE: 18					
EVLQLESGGG LVQPGGSLRL SCAASGFTFS HYMMAWVRQA PGKGLEWVSR IGPSGGPTHY	60				
ADSVVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAGYD SGYDYVAVAG PAEYFQHWGQ	120				
GTLVTVSS	128				
SEQ ID NO: 19	moltype = AA length = 107				
FEATURE	Location/Qualifiers				
source	1..107				
	mol_type = protein				
	organism = synthetic construct				
SEQUENCE: 19					
DIGMTQSPSS LSASVGDRVT ITCRASQSIIS TWLAWYQQKP GKAPKLLIYK ASNLTHTGVPS	60				
RFSGSGSGTE FSLTISGLQP DDFATYYCQQ YNSYSRTFGQ GTKVEIK	107				
SEQ ID NO: 20	moltype = AA length = 458				
FEATURE	Location/Qualifiers				
source	1..458				
	mol_type = protein				
	organism = synthetic construct				
SEQUENCE: 20					
EVQLLESGGG LVQPGGSLRL SCAASGFTFS HYMMAWVRQA PGKGLEWVSR IGPSGGPTHY	60				
ADSVVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAGYD SGYDYVAVAG PAEYFQHWGQ	120				
GTLVTVSSAS TKGPSVFPLA PSSKSTSGGT AALGCLVKDY FPEPVTVSWN SGALTSGVHT	180				
GPAVLQSSGL YSLSSVVTVP SSSLGTQTYI CNVNHKPSNT KVDKKVEPKS CDKTHTCP	240				
PAPELLGGPS VFLFPPPKKD TLMIISRTEV TCVVVDSHE DPEVKFNWYV DGVEVHN	300				

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KPREEQYNST YRVVSLVTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY	360
TLPSSRDELT KNQVSLTCLV KGFYPSDIAV EWESNGOPEN NYKTPPVLD SDGSFFLYSK	420
LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPGK	458
SEQ ID NO: 21 moltype = AA length = 457	
FEATURE Location/Qualifiers	
source 1..457	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 21	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS HYMMAWRQA PGKGLEWVR IGPGGGPTHY	60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAGYD SGYDYVAVAG PAEYQHWGQ	120
GTLVTVSSA TKGPSVPLA PSSKSTSGGT AALGCLVKDY FPEPVTVSN SGALTSGVHT	180
FPAVLQSSGL YSLSSVTVP SSSLTQTYI CNVNHKPSNT KVDKKVEPKS CDKTHTCPPC	240
PAPELLGGPS VFLFPKPKD TLMISRTEV TCVVVDVSHE DPEVKFNWYV DGVEVHNAKT	300
KPREEQYNST YRVVSLVTVL HQDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY	360
TLPPSSRDELT KNQVSLTCLV KGFYPSDIAV EWESNGOPEN NYKTPPVLD SDGSFFLYSK	420
LTVDKSRWQQ GNVFSCSVMH EALHNHYTQK SLSLSPG	457
SEQ ID NO: 22 moltype = AA length = 214	
FEATURE Location/Qualifiers	
source 1..214	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 22	
DIQMTQSPSS LSASVGDRVT ITCRASQSI TWLAWYQQKP GKAPKLLIYK ASNLLHTGVPS	60
RFGSGSGSTE FSLTISGLQP DDFATYYCQQ YNSYSRTFGQ GTKVEIKRTV AAPSVFIFPP	120
SDBQLKSGTA SVVCLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSTLT	180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGE	214
SEQ ID NO: 23 moltype = AA length = 458	
FEATURE Location/Qualifiers	
source 1..458	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 23	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS HYMMAWRQA PGKGLEWVR IGPGGGPTHY	60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAGYD SGYDYVAVAG PAEYQHWGQ	120
GTLVTVSSA TTAPSVDGSS VTLGCLVKGY FPEPVTLTWN SGSLSSGVHT	180
FPAVLQSDLY TLSSSVTVTS STWPSQSITC NVAHPASSTK VDKKIEPRGP TIKPCPPCKC	240
PAPNLLGGPS VFIFPPKIKD VLMIISLPIV TCVVVDVSED DPDVQISWVF NNVEVHTAQ	300
QTHREDYNST LRVVSALPIQ HQDWMSGKEF KCKVNNNKDLP APIERTISK P KGSVRAPQVY	360
VLPPPEEEMT KKQVTLTCMV TDFMPEDIYV EWTNNGKTEL NYKNTEPVLD SDGSYFMYSK	420
LRVEKKNWVE RNSYSCSVVH EGLHNHHTTK SFSRTPG	458
SEQ ID NO: 24 moltype = AA length = 457	
FEATURE Location/Qualifiers	
source 1..457	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 24	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS HYMMAWRQA PGKGLEWVR IGPGGGPTHY	60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAGYD SGYDYVAVAG PAEYQHWGQ	120
GTLVTVSSA TTAPSVDGSS VTLGCLVKGY FPEPVTLTWN SGSLSSGVHT	180
FPAVLQSDLY TLSSSVTVTS STWPSQSITC NVAHPASSTK VDKKIEPRGP TIKPCPPCKC	240
PAPNLLGGPS VFIFPPKIKD VLMIISLPIV TCVVVDVSED DPDVQISWVF NNVEVHTAQ	300
QTHREDYNST LRVVSALPIQ HQDWMSGKEF KCKVNNNKDLP APIERTISK P KGSVRAPQVY	360
VLPPPEEEMT KKQVTLTCMV TDFMPEDIYV EWTNNGKTEL NYKNTEPVLD SDGSYFMYSK	420
LRVEKKNWVE RNSYSCSVVH EGLHNHHTTK SFSRTPG	457
SEQ ID NO: 25 moltype = AA length = 214	
FEATURE Location/Qualifiers	
source 1..214	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 25	
DIQMTQSPSS LSASVGDRVT ITCRASQSI TWLAWYQQKP GKAPKLLIYK ASNLLHTGVPS	60
RFGSGSGSTE FSLTISGLQP DDFATYYCQQ YNSYSRTFGQ GTKVEIKRAD AAPTVSIFPP	120
SSEQLTSGGA SVVCLNNFY PKDINVWKI DGSERQNGVL NSWTDQDSKD STYSMSSTLT	180
LTKDEYERHN SYTCEATHKT STSPIVKSFN RNEC	214
SEQ ID NO: 26 moltype = AA length = 458	
FEATURE Location/Qualifiers	
source 1..458	
mol_type = protein	
organism = synthetic construct	

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SEQUENCE: 26			
EVOLLESGGG LVQPGGSLRL SCAASGFTFS HYMMAWVRQA PGKGLEWCSR IGPSGGPTHY	60		
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAGYD SGYDYVAVAG PAEYFQHWGQ	120		
GTLVTVSSAK TTAPSVYPLA PVCGDTTGSS VTLGCLVKGY FPEPVTLTWN SGSLSSGVHT	180		
FPAVLQSDLY TLSSSVTVTS STWPSQSITC NVAHPASSTK VDKKIEPRGP TIKPCPPCKC	240		
PAPNAAGGPS VFIFPPKIKD VLMISLSPIV TCVVVDVSED DPDVQISWFV NNVEVHTAQ	300		
QTHREDYNST LRVVSALPIQ HQDWMSGKEF KCKVNNKDLG APIERTISKP KGSRAPQVY	360		
VLPPEEEEMT KKQVTLTCMV TDFMPEDIYV EWTNNGKTEL NYKNTEPVLD SDGSYFMYSK	420		
LRVEKKNWVE RNSYSCSVVH EGLHNHHHTK SFSRTPGK	458		
 SEQ ID NO: 27	moltype = AA length = 457		
FEATURE	Location/Qualifiers		
source	1..457		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 27			
EVOLLESGGG LVQPGGSLRL SCAASGFTFS HYMMAWVRQA PGKGLEWCSR IGPSGGPTHY	60		
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAGYD SGYDYVAVAG PAEYFQHWGQ	120		
GTLVTVSSAK TTAPSVYPLA PVCGDTTGSS VTLGCLVKGY FPEPVTLTWN SGSLSSGVHT	180		
FPAVLQSDLY TLSSSVTVTS STWPSQSITC NVAHPASSTK VDKKIEPRGP TIKPCPPCKC	240		
PAPNAAGGPS VFIFPPKIKD VLMISLSPIV TCVVVDVSED DPDVQISWFV NNVEVHTAQ	300		
QTHREDYNST LRVVSALPIQ HQDWMSGKEF KCKVNNKDLG APIERTISKP KGSRAPQVY	360		
VLPPEEEEMT KKQVTLTCMV TDFMPEDIYV EWTNNGKTEL NYKNTEPVLD SDGSYFMYSK	420		
LRVEKKNWVE RNSYSCSVVH EGLHNHHHTK SFSRTPGK	457		
 SEQ ID NO: 28	moltype = AA length = 214		
FEATURE	Location/Qualifiers		
source	1..214		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 28			
DIQMTQSPSS LSASVGDRVT ITCRASQSIIS TWLAWYQQKP GKAPKLLIYK ASNLLHTGVPS	60		
RFSGSGSGTE FSLTISGLQP DDFATYYCQQ YNSYSRTFGQ GTKVEIKRAD AAPTVSIFPP	120		
SSEQLTSGGA SVCFLNNFY PKDINVWKI DGSERQNGVLS NSWTDQDSKD STYSMSSTLT	180		
LTKDEYERHN SYTCEATHKT STSPIVKSFN RNEC	214		
 SEQ ID NO: 29	moltype = AA length = 5		
FEATURE	Location/Qualifiers		
source	1..5		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 29			
SGYWN		5	
 SEQ ID NO: 30	moltype = AA length = 16		
FEATURE	Location/Qualifiers		
source	1..16		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 30			
YISDSDGITYYY NPSLKS		16	
 SEQ ID NO: 31	moltype = AA length = 11		
FEATURE	Location/Qualifiers		
source	1..11		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 31			
RTLATYYAMD Y		11	
 SEQ ID NO: 32	moltype = AA length = 16		
FEATURE	Location/Qualifiers		
source	1..16		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 32			
RASQSLVHSD GNTYLN		16	
 SEQ ID NO: 33	moltype = AA length = 7		
FEATURE	Location/Qualifiers		
source	1..7		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 33			
RVSNRFS		7	

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SEQ ID NO: 34	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 34	
SQSTHVPPT	9
SEQ ID NO: 35	moltype = AA length = 119
FEATURE	Location/Qualifiers
source	1..119
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 35	
QVQLQESGPG LVKPSETLSL TCTVSGDSIT SGYWNWIROQ PGKGLEYIIGY ISDSGITYYN 60	
PSLKSRTVIS RDTSKNQYSR KLSSVTAADT AVYYCARRTL ATYYAMDYWG QGTLTVSSA 119	
SEQ ID NO: 36	moltype = AA length = 112
FEATURE	Location/Qualifiers
source	1..112
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 36	
DVFMQTSPSLS LPVTLGQPAS ISCRASQSLV HSDGNTYLHW YQQRPGQSPR LLIYRVSNRF 60	
SGVPDRFSGS GSGTDFTLKI SRVEAEDGVV YYCSQSTHVP PTFGQQGTKE IK 112	
SEQ ID NO: 37	moltype = AA length = 449
FEATURE	Location/Qualifiers
source	1..449
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 37	
QVQLQESGPG LVKPSETLSL TCTVSGDSIT SGYWNWIROQ PGKGLEYIIGY ISDSGITYYN 60	
PSLKSRTVIS RDTSKNQYSR KLSSVTAADT AVYYCARRTL ATYYAMDYWG QGTLTVSSA 120	
STKGPSVFL APSSKSTSGG TAALGCLVKD YFPEPVTVSW NSGALTSGVH TFPAVLQSSG 180	
LYSLSSVVTV PSSSLGTQTY ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPAPELLGGP 240	
SVFLFPPPKP DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAAK TKPREEQYNS 300	
TYRVSVSLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV YTLPPSRDEL 360	
TKNQVSLTCL VKGFYPSDIA VEWESENQPE NNYKTPPVL DSDGSFFLYS KLTVDKSRWQ 420	
QGNVFSCSVM HEALHNHYTQ KSLSLSPGK 449	
SEQ ID NO: 38	moltype = AA length = 448
FEATURE	Location/Qualifiers
source	1..448
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 38	
QVQLQESGPG LVKPSETLSL TCTVSGDSIT SGYWNWIROQ PGKGLEYIIGY ISDSGITYYN 60	
PSLKSRTVIS RDTSKNQYSR KLSSVTAADT AVYYCARRTL ATYYAMDYWG QGTLTVSSA 120	
STKGPSVFL APSSKSTSGG TAALGCLVKD YFPEPVTVSW NSGALTSGVH TFPAVLQSSG 180	
LYSLSSVVTV PSSSLGTQTY ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPAPELLGGP 240	
SVFLFPPPKP DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAAK TKPREEQYNS 300	
TYRVSVSLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV YTLPPSRDEL 360	
TKNQVSLTCL VKGFYPSDIA VEWESENQPE NNYKTPPVL DSDGSFFLYS KLTVDKSRWQ 420	
QGNVFSCSVM HEALHNHYTQ KSLSLSPG 448	
SEQ ID NO: 39	moltype = AA length = 219
FEATURE	Location/Qualifiers
source	1..219
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 39	
DVFMQTSPSLS LPVTLGQPAS ISCRASQSLV HSDGNTYLHW YQQRPGQSPR LLIYRVSNRF 60	
SGVPDRFSGS GSGTDFTLKI SRVEAEDGVV YYCSQSTHVP PTFGQQGTKE IKRTVAAPSV 120	
FIFPPPSDEQL KSGTASVVCL LNNFYPREAK VQWKVDNALQ SGNSQESVTE QDSKDSTYSL 180	
STTLTLSKAD YEKHKVYACE VTHQGLSSPV TKSFNRGEC 219	
SEQ ID NO: 40	moltype = AA length = 449
FEATURE	Location/Qualifiers
source	1..449
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 40	
QVQLQESGPG LVKPSETLSL TCTVSGDSIT SGYWNWIROQ PGKGLEYIIGY ISDSGITYYN 60	
PSLKSRTVIS RDTSKNQYSR KLSSVTAADT AVYYCARRTL ATYYAMDYWG QGTLTVSSA 120	
STKGPSVFL APSSKSTSGG TAALGCLVKD YFPEPVTVSW NSGALTSGVH TFPAVLQSSG 180	

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LYSLSSVVTV PSSSLGTQTY ICNVNHKPSN TKVDKKVEPK SCDKTHCPP CPAPEAAGGP 240	
SVFLFPPKPK DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VGVEVHNAAK TKPREEQYNS 300	
TYRVVSVLTV LHQDWLNGKE YKCAVSNKAL PAPIEKTIISK AKGQPREPQV YTLPPSRDEL 360	
TKNQVSLTCL VKGFYPSDIA VEWESENQPE NNYKTTPPVVL DSDGSFFLYS KLTVDKSRWQ 420	
QGNVFSCSVM HEALHNHYTQ KSLSLSPKG 449	
 SEQ ID NO: 41 moltype = AA length = 448	
FEATURE Location/Qualifiers	
source 1..448	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 41	
QVQLQESGPG LVKPSETLSL TCTVSGDSIT SGYWNWIROQ PGKGLEIYG ISDSGITYYN 60	
PSLKSRTVIS RDTSKNQYS KLSSVTAADT AVYYCARRTL ATYYAMDYWG QGTLVTVSSA 120	
STKGPSVFL APSSKSTSGG TAALGCLVKD YFPEPVTVSW NSGALTSGVH TFPAVLQSSG 180	
LYSLSSVVTV PSSSLGTQTY ICNVNHKPSN TKVDKKVEPK SCDKTHCPP CPAPEAAGGP 240	
SVFLFPPKPK DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VGVEVHNAAK TKPREEQYNS 300	
TYRVVSVLTV LHQDWLNGKE YKCAVSNKAL PAPIEKTIISK AKGQPREPQV YTLPPSRDEL 360	
TKNQVSLTCL VKGFYPSDIA VEWESENQPE NNYKTTPPVVL DSDGSFFLYS KLTVDKSRWQ 420	
QGNVFSCSVM HEALHNHYTQ KSLSLSPKG 448	
 SEQ ID NO: 42 moltype = AA length = 219	
FEATURE Location/Qualifiers	
source 1..219	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 42	
DVMTQSPS LPPVTLGQSPAS ISCRAQSLSV HSDGNTYLHW YQQRPGQSPR LLIYRVSNRF 60	
SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCSQSTHVP PTFGQGTKLE IKRTVAAPSV 120	
FIPPPSDEQL KSGTASVVCL LNNFYPREAK VQWKVDNALQ SGNSQESVTE QDSKDSTYSL 180	
SSTLTLASKAD YEKHKVYACE VTHQGLSSPV TKSFNRGEC 219	
 SEQ ID NO: 43 moltype = AA length = 5	
FEATURE Location/Qualifiers	
source 1..5	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 43	
DYNVN 5	
 SEQ ID NO: 44 moltype = AA length = 17	
FEATURE Location/Qualifiers	
source 1..17	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 44	
VINPKYGTTR YNQKFKG 17	
 SEQ ID NO: 45 moltype = AA length = 7	
FEATURE Location/Qualifiers	
source 1..7	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 45	
GLNAWDY 7	
 SEQ ID NO: 46 moltype = AA length = 11	
FEATURE Location/Qualifiers	
source 1..11	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 46	
GASENIYGAL N 11	
 SEQ ID NO: 47 moltype = AA length = 7	
FEATURE Location/Qualifiers	
source 1..7	
mol_type = protein	
organism = synthetic construct	
SEQUENCE: 47	
GATNLED 7	
 SEQ ID NO: 48 moltype = AA length = 9	
FEATURE Location/Qualifiers	
source 1..9	
mol_type = protein	

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SEQUENCE: 48          organism = synthetic construct
QNVLTTPYT                                         9

SEQ ID NO: 49          moltype = AA  length = 116
FEATURE                                         Location/Qualifiers
source                                           1..116
mol_type = protein
organism = synthetic construct

SEQUENCE: 49
QFQLVQSGAE VKKPGASVKV SCKASGYSFT DYNVNWVRQA PGQGLEWIGV INPKYGTTRY 60
NQKFKGRATL TVDKSTSTAY MELSSLRSED TAVYYCTRGL NAWDYWGQGT LVTVSSASTK 116

SEQ ID NO: 50          moltype = AA  length = 107
FEATURE                                         Location/Qualifiers
source                                           1..107
mol_type = protein
organism = synthetic construct

SEQUENCE: 50
DIQMTQSPSS LSASVGDRVT ITCGASENIY GALNWyQQKP GKAPKLLIYG ATNLEDGVPS 60
RFSGSGSGRD YTFTISSLQP EDIATYYCQN VLTPYTFQG GTKLEIK 107

SEQ ID NO: 51          moltype = AA  length = 446
FEATURE                                         Location/Qualifiers
source                                           1..446
mol_type = protein
organism = synthetic construct

SEQUENCE: 51
QFQLVQSGAE VKKPGASVKV SCKASGYSFT DYNVNWVRQA PGQGLEWIGV INPKYGTTRY 60
NQKFKGRATL TVDKSTSTAY MELSSLRSED TAVYYCTRGL NAWDYWGQGT LVTVSSASTK 120
GPSVFPLAPS SKSTSGGTA A LGCLVKDYFP EPVTWSWNNG ALTSGVHTFP AVLQSSGLYS 180
LSSVVTVPSS SLGTQTYICN VNHKPSNTKV DKKVEPKSCD KTHTCPCCPA PELLGGPSVF 240
LFPPPKPDTL MISRTPEVTC VVVDSHEDP EVKFNWYVDG VEVHNAAKTKP REEQYNSTYR 300
VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG QPREPVQVTL PPSRDELTKN 360
QVSLTCLVKG FYPDSIAVEW ESNGQPENNY KTPPPVLDSD GSFFFLYSKLT VDKSRWQGN 420
VFSCSVMHEA LHNHYTQKSL SLSPKG 446

SEQ ID NO: 52          moltype = AA  length = 445
FEATURE                                         Location/Qualifiers
source                                           1..445
mol_type = protein
organism = synthetic construct

SEQUENCE: 52
QFQLVQSGAE VKKPGASVKV SCKASGYSFT DYNVNWVRQA PGQGLEWIGV INPKYGTTRY 60
NQKFKGRATL TVDKSTSTAY MELSSLRSED TAVYYCTRGL NAWDYWGQGT LVTVSSASTK 120
GPSVFPLAPS SKSTSGGTA A LGCLVKDYFP EPVTWSWNNG ALTSGVHTFP AVLQSSGLYS 180
LSSVVTVPSS SLGTQTYICN VNHKPSNTKV DKKVEPKSCD KTHTCPCCPA PELLGGPSVF 240
LFPPPKPDTL MISRTPEVTC VVVDSHEDP EVKFNWYVDG VEVHNAAKTKP REEQYNSTYR 300
VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG QPREPVQVTL PPSRDELTKN 360
QVSLTCLVKG FYPDSIAVEW ESNGQPENNY KTPPPVLDSD GSFFFLYSKLT VDKSRWQGN 420
VFSCSVMHEA LHNHYTQKSL SLSPKG 445

SEQ ID NO: 53          moltype = AA  length = 214
FEATURE                                         Location/Qualifiers
source                                           1..214
mol_type = protein
organism = synthetic construct

SEQUENCE: 53
DIQMTQSPSS LSASVGDRVT ITCGASENIY GALNWyQQKP GKAPKLLIYG ATNLEDGVPS 60
RFSGSGSGRD YTFTISSLQP EDIATYYCQN VLTPYTFQG GTKLEIKRTV AAPSVFIFPP 120
SDBQLKSGTA SVVCLNNFY PREAKVQWKV DNALQSGNSQ E SVNTEQDSKD STYSLSTLT 180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGE 214

SEQ ID NO: 54          moltype = AA  length = 446
FEATURE                                         Location/Qualifiers
source                                           1..446
mol_type = protein
organism = synthetic construct

SEQUENCE: 54
QFQLVQSGAE VKKPGASVKV SCKASGYSFT DYNVNWVRQA PGQGLEWIGV INPKYGTTRY 60
NQKFKGRATL TVDKSTSTAY MELSSLRSED TAVYYCTRGL NAWDYWGQGT LVTVSSASTK 120
GPSVFPLAPS SKSTSGGTA A LGCLVKDYFP EPVTWSWNNG ALTSGVHTFP AVLQSSGLYS 180
LSSVVTVPSS SLGTQTYICN VNHKPSNTKV DKKVEPKSCD KTHTCPCCPA PEAAGGPPSF 240
LFPPPKPDTL MISRTPEVTC VVVDSHEDP EVKFNWYVDG VEVHNAAKTKP REEQYNSTYR 300
VVSVLTVLHQ DWLNGKEYKC AVSNKALPAP IEKTISKAKG QPREPVQVTL PPSRDELTKN 360
QVSLTCLVKG FYPDSIAVEW ESNGQPENNY KTPPPVLDSD GSFFFLYSKLT VDKSRWQGN 420

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VFSCSVMHEA LHNHYTQKSL SLSPKG	446
SEQ ID NO: 55	moltype = AA length = 445
FEATURE	Location/Qualifiers
source	1..445
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 55	
QFQLVQSGAE VKKPGASVKV SCKASGYSFT DYNVNWVRQA PGQGLEWIGV INPKYGTTRY	60
NQKFKGRTATL TVDKSTSTAY MELSSLRSED TAVYYCTRGL NAWDYWGQGT LVTVSSASTK	120
GPSVFPPLAPS SKSTSGGTAAC LCCLVKDYPF EPVTVSNNGC ALTSGVHTFP AVLQSSGLYS	180
LSSVVTVPSS SLGTQTYICN VNHKPSNTKV DKKVEPKSCD KTHTCPPCPA PEAAGGPSPF	240
LFPPPKPDKTL MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTP REEQYNSTYR	300
VVSVLTVLHQ DWLNGKEYCA AVSNKALPAP IEKTISKAKG QPREPVYTL PPSRDELTKN	360
QVSLTCLVKG FYPSDIAVEW ESNGQPENNY KTPPPVLDSD GSFFLYSKLT VDKSRWQQGN	420
VFSCSVMHEA LHNHYTQKSL SLSPG	445
SEQ ID NO: 56	moltype = AA length = 214
FEATURE	Location/Qualifiers
source	1..214
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 56	
DIGMTQSPSS LSASVGDRVT ITCGASENIY GALNWYQQKP GKAPKLLIYG ATNLEDGVPS	60
RFSGSGSGRD YTFTISSLQP EDIATYYCQN VLTPPYTFQG GTKLEIKRTV AAPSVFIFPP	120
SDEQLKSGTA SVVCLNNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSTLT	180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEC	214
SEQ ID NO: 57	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 57	
SGSYWG	7
SEQ ID NO: 58	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 58	
NIYYSGSTYY NPSSLRS	16
SEQ ID NO: 59	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 59	
EGSYPNQFDP	10
SEQ ID NO: 60	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 60	
RASQSVSSNL A	11
SEQ ID NO: 61	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 61	
GASTRAT	7
SEQ ID NO: 62	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 62	
QQYHSFPFT	9

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SEQ ID NO: 63      moltype = AA length = 120
FEATURE          Location/Qualifiers
source           1..120
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 63
QLQLQESGPG LVKPSETLSL TCTVSGGSIK SGSYYWGWIR QPPGKGLEWI GNIYYSGSTY 60
YNPSLRSRVT ISVDTSKNQF SLKLSSVTA DTAVYYCARE GSYPNQFDPW GQGTLTVSS 120
RFSFGSGSGTE FTLTISLQS EDFAVYYCQQ YHSFPFTFGG GTKVEIKRTV 107

SEQ ID NO: 64      moltype = AA length = 107
FEATURE          Location/Qualifiers
source           1..107
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 64
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKP QOAPRLLIYG ASTRATGIPA 60
RFSFGSGSGTE FTLTISLQS EDFAVYYCQQ YHSFPFTFGG GTKVEIKRTV 107

SEQ ID NO: 65      moltype = AA length = 450
FEATURE          Location/Qualifiers
source           1..450
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 65
QLQLQESGPG LVKPSETLSL TCTVSGGSIK SGSYYWGWIR QPPGKGLEWI GNIYYSGSTY 60
YNPSLRSRVT ISVDTSKNQF SLKLSSVTA DTAVYYCARE GSYPNQFDPW GQGTLTVSS 120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYPPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTQT YICCNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG 240
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTI KAKGQPREPQ VYTLPSSRDE 360
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW 420
QQGNVFSCSV MHEALHNHYT QKSLSLSPKG 450

SEQ ID NO: 66      moltype = AA length = 449
FEATURE          Location/Qualifiers
source           1..449
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 66
QLQLQESGPG LVKPSETLSL TCTVSGGSIK SGSYYWGWIR QPPGKGLEWI GNIYYSGSTY 60
YNPSLRSRVT ISVDTSKNQF SLKLSSVTA DTAVYYCARE GSYPNQFDPW GQGTLTVSS 120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYPPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTQT YICCNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG 240
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTI KAKGQPREPQ VYTLPSSRDE 360
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW 420
QQGNVFSCSV MHEALHNHYT QKSLSLSPKG 449

SEQ ID NO: 67      moltype = AA length = 214
FEATURE          Location/Qualifiers
source           1..214
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 67
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKP QOAPRLLIYG ASTRATGIPA 60
RFSFGSGSGTE FTLTISLQS EDFAVYYCQQ YHSFPFTFGG GTKVEIKRTV AAPSVFIFPP 120
SDBQLKSGTA SVVCLNNFY PREAKVQWK DNALQSGNSQ ESVTEQDSKD STYSLSTLT 180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGECA 214

SEQ ID NO: 68      moltype = AA length = 450
FEATURE          Location/Qualifiers
source           1..450
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 68
QLQLQESGPG LVKPSETLSL TCTVSGGSIK SGSYYWGWIR QPPGKGLEWI GNIYYSGSTY 60
YNPSLRSRVT ISVDTSKNQF SLKLSSVTA DTAVYYCARE GSYPNQFDPW GQGTLTVSS 120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYPPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTQT YICCNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPEAAGG 240
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCAVSNKA LPAPIEKTI KAKGQPREPQ VYTLPSSRDE 360
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW 420
QQGNVFSCSV MHEALHNHYT QKSLSLSPKG 450

SEQ ID NO: 69      moltype = AA length = 449
FEATURE          Location/Qualifiers

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source          1..449
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 69
QLQLQESGPG LVKPSETLSL TCTVSGGSIK SGSYWGWIR QPPGKGLEWI GNIYSGSTY 60
YNPSLRSRVT ISVDTSKNQF SLKLSSVTAA DTAVYYCARE GSYPNQFDPW GQGTLTVVSS 120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTQI YICNVNHKPS NTKVDKKVEP KSCDKTHTCPC PCPAPEAAGG 240
PSVFLFPKPK KDTLMSRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVRVSVLT VLHQDWLNQF EYKCAVSNKA LPAPIEKTIS KAKGQPREPQ VYTLEPSRDE 360
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW 420
QQGNVFCSCV MHEALHNHYT QKSLSLSPG 449

SEQ ID NO: 70      moltype = AA length = 214
FEATURE           Location/Qualifiers
source            1..214
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 70
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKP GQAPRLLIYG ASTRATGIPA 60
RFSGSGSGTE FTLTISLQS EDFAVYYCQQ YHSFPFTFGV GTKVEIKRTV AAPSVFIFPP 120
SDBQLKSGTA SVVCLLNNFY PREAKVQWK DNALQSGNSQ ESVTEQDSKD STYSLSSTLT 180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEc 214

SEQ ID NO: 71      moltype = AA length = 11
FEATURE           Location/Qualifiers
source            1..11
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 71
GSISSSYYW G 11

SEQ ID NO: 72      moltype = AA length = 16
FEATURE           Location/Qualifiers
source            1..16
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 72
NIYSGSTYY NPSLKS 16

SEQ ID NO: 73      moltype = AA length = 12
FEATURE           Location/Qualifiers
source            1..12
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 73
AREGSYPNWF DP 12

SEQ ID NO: 74      moltype = AA length = 11
FEATURE           Location/Qualifiers
source            1..11
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 74
RASQSVSSNL A 11

SEQ ID NO: 75      moltype = AA length = 7
FEATURE           Location/Qualifiers
source            1..7
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 75
GASTRAT 7

SEQ ID NO: 76      moltype = AA length = 9
FEATURE           Location/Qualifiers
source            1..9
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 76
QQYHSFPFT 9

SEQ ID NO: 77      moltype = AA length = 120
FEATURE           Location/Qualifiers
source            1..120
               mol_type = protein

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SEQUENCE: 77          organism = synthetic construct
QLQLQESGPG LVKPSETLSL TCTVSGGSIS SSSYYWGWR QPPGKGLEWI GNIYYSGSTY  60
YNPSLRSRVT ISVDTSKNQF SLKLSSVTAA DTAVYYCARE GSYPNWFDPW GQGTLTVSS 120

SEQ ID NO: 78          moltype = AA length = 107
FEATURE
source
1..107
mol_type = protein
organism = synthetic construct

SEQUENCE: 78
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKP QQAPRLLIYG ASTRATGIPA  60
RFSGSGSGTE FTLTISLQS EDFAVYYCQQ YHSFPFTFGG GTKVEIK 107

SEQ ID NO: 79          moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct

SEQUENCE: 79
GSIKGSGSHYW G 11

SEQ ID NO: 80          moltype = AA length = 16
FEATURE
source
1..16
mol_type = protein
organism = synthetic construct

SEQUENCE: 80
NIYYSGSTYY NPSLR 16

SEQ ID NO: 81          moltype = AA length = 12
FEATURE
source
1..12
mol_type = protein
organism = synthetic construct

SEQUENCE: 81
AREGSYPNWF DP 12

SEQ ID NO: 82          moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct

SEQUENCE: 82
RASQSVSSNL A 11

SEQ ID NO: 83          moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 83
GASTRAT 7

SEQ ID NO: 84          moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 84
QQYHSFPFT 9

SEQ ID NO: 85          moltype = AA length = 120
FEATURE
source
1..120
mol_type = protein
organism = synthetic construct

SEQUENCE: 85
QLQLQESGPG LVKPSETLSL TCTVSGGSIK SGSHYWGWR QPPGKGLEWI GNIYYSGSTY  60
YNPSLRSRVT ISVDTSKNQF SLKLSSVTAA DTAVYYCARE GSYPNWFDPW GQGTLTVSS 120

SEQ ID NO: 86          moltype = AA length = 107
FEATURE
source
1..107
mol_type = protein
organism = synthetic construct

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SEQUENCE: 86
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKP GQAPRLLIYG ASTRATGIPA 60
RFSGSGSGTE FTLTISQLQS EDFAVYYCQQ YHSFPFTFGG GTKVEIK 107

SEQ ID NO: 87      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 87
GSIKSGSHYW G 11

SEQ ID NO: 88      moltype = AA length = 16
FEATURE
source
1..16
mol_type = protein
organism = synthetic construct
SEQUENCE: 88
NIYYSGSTYY NPSLKS 16

SEQ ID NO: 89      moltype = AA length = 12
FEATURE
source
1..12
mol_type = protein
organism = synthetic construct
SEQUENCE: 89
AREGSYPNWL DP 12

SEQ ID NO: 90      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 90
RASQSVSSNL A 11

SEQ ID NO: 91      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 91
GASTRAT 7

SEQ ID NO: 92      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 92
QQYHSFPFT 9

SEQ ID NO: 93      moltype = AA length = 120
FEATURE
source
1..120
mol_type = protein
organism = synthetic construct
SEQUENCE: 93
QLQLQESGPG LVKPSETLSL TCTVSGGSIK SGSHYWGIR QPPGKGLEWI GNIYYSGSTY 60
YNPSLKSRTV ISVDTSKNQF SLKLSSVTAA DTAVYYCARE GSYPNWLDPW GQGTLVTVSS 120

SEQ ID NO: 94      moltype = AA length = 107
FEATURE
source
1..107
mol_type = protein
organism = synthetic construct
SEQUENCE: 94
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKP GQAPRLLIYG ASTRATGIPA 60
RFSGSGSGTE FTLTISQLQS EDFAVYYCQQ YHSFPFTFGG GTKVEIK 107

SEQ ID NO: 95      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 95

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GSIKSGSYW G	11
SEQ ID NO: 96 FEATURE source	moltype = AA length = 16 Location/Qualifiers 1..16 mol_type = protein organism = synthetic construct
SEQUENCE: 96 NIYYSGSTYY NPSLKS	16
SEQ ID NO: 97 FEATURE source	moltype = AA length = 12 Location/Qualifiers 1..12 mol_type = protein organism = synthetic construct
SEQUENCE: 97 AREGSYPNQF DP	12
SEQ ID NO: 98 FEATURE source	moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct
SEQUENCE: 98 RASQSVSSNL A	11
SEQ ID NO: 99 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct
SEQUENCE: 99 GASTRAT	7
SEQ ID NO: 100 FEATURE source	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct
SEQUENCE: 100 QQYHSPFPFT	9
SEQ ID NO: 101 FEATURE source	moltype = AA length = 120 Location/Qualifiers 1..120 mol_type = protein organism = synthetic construct
SEQUENCE: 101 QLQLQESCPG LVKPSETLSL TCTVSGGSIK SGSYYWGWIR QPPGKGLEWI GNIYYSGSTY 60 YNPSLKSRTV ISVDTSKNQF SLKLSSVTAA DTAVYYCARE GSYPNQFDPW GQGILTVSS 120	
SEQ ID NO: 102 FEATURE source	moltype = AA length = 107 Location/Qualifiers 1..107 mol_type = protein organism = synthetic construct
SEQUENCE: 102 EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKP GQAPRLLIYG ASTRATGIPA 60 RGSGSGSGTE FTLTISSLQS EDFAVYYCQQ YHSFPFTFGG GTKVEIK 107	
SEQ ID NO: 103 FEATURE source	moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct
SEQUENCE: 103 GSIKSGSHY W G	11
SEQ ID NO: 104 FEATURE source	moltype = AA length = 16 Location/Qualifiers 1..16 mol_type = protein organism = synthetic construct
SEQUENCE: 104 NIYYSGSTYY NPSLKS	16

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SEQ ID NO: 105	moltype = AA length = 12
FEATURE	Location/Qualifiers
source	1..12
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 105	
AREGSYPNWF DP	12
SEQ ID NO: 106	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 106	
RASQSVSTNL A	11
SEQ ID NO: 107	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 107	
DASARVT	7
SEQ ID NO: 108	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 108	
QQYHSPFPT	9
SEQ ID NO: 109	moltype = AA length = 120
FEATURE	Location/Qualifiers
source	1..120
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 109	
QLQLQESPGP LVKPSETLSL TCTVSGGSIK SGSHYWGIR QPPGKGLEWI GNIYYSGSTY	60
YNPSLKSRTV MSVDTSKNQF SLKLSSVTAA DTAVYYCARE GSYPNWFDPW GQGTLVTVSS	120
SEQ ID NO: 110	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 110	
EIVMTQSPAT LSVSPGERAT LSCRASQSVS TNLAWYQQKP GQAPRLLIYD ASARVTGIPA	60
RFGSGSGSGTE FTLTISLQS EDFAVYYCQQ YHSFPFTFGG GTKVEIK	107
SEQ ID NO: 111	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 111	
GSISSSSYYW G	11
SEQ ID NO: 112	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 112	
NIYYSGSTYY NPSLKS	16
SEQ ID NO: 113	moltype = AA length = 12
FEATURE	Location/Qualifiers
source	1..12
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 113	
AREGSYTTVL NV	12
SEQ ID NO: 114	moltype = AA length = 12
FEATURE	Location/Qualifiers

-continued

source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 114		
RASQSVSSSY LA		12
SEQ ID NO: 115	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 115		
GASSRAT		7
SEQ ID NO: 116	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 116		
QQAASYPLT		9
SEQ ID NO: 117	moltype = AA length = 120	
FEATURE	Location/Qualifiers	
source	1..120	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 117		
QLQLQESPGV LVKPSETLSL TCTVSGGSIS SSSYYWGWR QPPGKGLEWI GNIYYSGSTY	60	
YNPSLKSRTV ISVDTSKNQF SLKLSSVTA DTAVYYCARE GSYTTVLNVW GQGTMVTVSS	120	
SEQ ID NO: 118	moltype = AA length = 108	
FEATURE	Location/Qualifiers	
source	1..108	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 118		
EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSYLAWSYQQK PGQAPRLLIY GASSRATGIP	60	
DRFGSGSGGT DFTLTISRLE PEDFAVYYCQ QAASYPLTFG GGTKVEIK	108	
SEQ ID NO: 119	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 119		
GSIGRGSYYW G		11
SEQ ID NO: 120	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
source	1..16	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 120		
NIYYSGSTYY NPSLKS		16
SEQ ID NO: 121	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 121		
AREGSYTTVL NV		12
SEQ ID NO: 122	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 122		
RASQSVASSH LA		12
SEQ ID NO: 123	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	

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SEQUENCE: 123	organism = synthetic construct	
DAVSRAT		7
SEQ ID NO: 124	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 124		
QQAASYPLT		9
SEQ ID NO: 125	moltype = AA length = 120	
FEATURE	Location/Qualifiers	
source	1..120	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 125		
QLQLQESPGV LVKPSETLSL TCTVSGGSIG RGSYYWGWIR QPPGKGLEWI GNIYYSGSTY 60		
YNPSLKSRTV ISVDTSKNQF SLKLSSVTAA DTAVYYCARE GSYTTVLNVV GQGTMVTVSS 120		
SEQ ID NO: 126	moltype = AA length = 108	
FEATURE	Location/Qualifiers	
source	1..108	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 126		
EIVLTQSPGT LSLSPGERAT LSCRASQSVA SSHLAWYQQK PGQAPRLLIY DAVSRATGIP 60		
DRFGSGSGSGT DFTLTISRLE PEDFAVYYCQ QAASYPLTFG GGTKVEIK		108
SEQ ID NO: 127	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 127		
GSISSGGYYW S		11
SEQ ID NO: 128	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
source	1..16	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 128		
NIYYSGSTYY NPSLKS		16
SEQ ID NO: 129	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 129		
ARESSTISAD FDL		13
SEQ ID NO: 130	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 130		
RASQGISRWL A		11
SEQ ID NO: 131	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 131		
AASSLQS		7
SEQ ID NO: 132	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 132		

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QQAHTFPYT

9

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SEQ ID NO: 133      moltype = AA length = 121
FEATURE
source
1..121
mol_type = protein
organism = synthetic construct

SEQUENCE: 133
QVQLQESGPG LVKPSQTL SL TCTVSGGSIS SGYYYWSWIR QHPGKGLEWI GNIYYSGSTY 60
YNPSLKS RVT ISVDTSKNQF SLKLSSVTAA DTAVYYCARE SSTISADFDL WGRGTLVTVS 120
S                                         121

SEQ ID NO: 134      moltype = AA length = 107
FEATURE
source
1..107
mol_type = protein
organism = synthetic construct

SEQUENCE: 134
DIQMTQSPSS VSASVGDRVT ITCRASQGIS RWLAWYQQKP GKAPKLLIYA ASSLQSGVPS 60
RFGSGSGSTD PTLTSSLQP EDFATYYCQQ AHTFPYTFGG GTKVEIK 107

SEQ ID NO: 135      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct

SEQUENCE: 135
GSISHGGYW S 11

SEQ ID NO: 136      moltype = AA length = 16
FEATURE
source
1..16
mol_type = protein
organism = synthetic construct

SEQUENCE: 136
NIYYSGSTYY NPSLKS 16

SEQ ID NO: 137      moltype = AA length = 13
FEATURE
source
1..13
mol_type = protein
organism = synthetic construct

SEQUENCE: 137
ARESSTISAD FDL 13

SEQ ID NO: 138      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct

SEQUENCE: 138
RASQGISRWL A 11

SEQ ID NO: 139      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 139
AASSLQS 7

SEQ ID NO: 140      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 140
QQAHTFPYT 9

SEQ ID NO: 141      moltype = AA length = 121
FEATURE
source
1..121
mol_type = protein
organism = synthetic construct

SEQUENCE: 141
QLQLQESGPG LVKPSQTL SL TCTASGGGSIS HGGYYWSWIR QHPGKGLEWI GNIYYSGSTY 60

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YNPSSLKSRVT	MSVDTSKNQF	SLKLSSVTAA	DTAVYYCARE	SSTISADFDL	WGRGTLVTVS	120
S						121
SEQ ID NO: 142			moltype = AA length = 107			
FEATURE			Location/Qualifiers			
source			1..107			
			mol_type = protein			
			organism = synthetic construct			
SEQUENCE: 142						
DIQMTQSPSS	VSASVGDRVT	ITCRASQGIS	RWLAWYQQKP	GKAPKLLIYA	ASSLQSGVPS	60
RGSGSGSGTD	FTLTISQLP	EDFATYYCQQ	AHTFPYTFGG	GTKVEIK		107
SEQ ID NO: 143			moltype = AA length = 11			
FEATURE			Location/Qualifiers			
source			1..11			
			mol_type = protein			
			organism = synthetic construct			
SEQUENCE: 143						
GSISGGYYW S						11
SEQ ID NO: 144			moltype = AA length = 16			
FEATURE			Location/Qualifiers			
source			1..16			
			mol_type = protein			
			organism = synthetic construct			
SEQUENCE: 144						
NIYYSGSTYY NPSLKS						16
SEQ ID NO: 145			moltype = AA length = 13			
FEATURE			Location/Qualifiers			
source			1..13			
			mol_type = protein			
			organism = synthetic construct			
SEQUENCE: 145						
ARGLSTIDEA PDP						13
SEQ ID NO: 146			moltype = AA length = 11			
FEATURE			Location/Qualifiers			
source			1..11			
			mol_type = protein			
			organism = synthetic construct			
SEQUENCE: 146						
RASQSISSWL A						11
SEQ ID NO: 147			moltype = AA length = 7			
FEATURE			Location/Qualifiers			
source			1..7			
			mol_type = protein			
			organism = synthetic construct			
SEQUENCE: 147						
KASSLES						7
SEQ ID NO: 148			moltype = AA length = 9			
FEATURE			Location/Qualifiers			
source			1..9			
			mol_type = protein			
			organism = synthetic construct			
SEQUENCE: 148						
QQDNSYPYT						9
SEQ ID NO: 149			moltype = AA length = 121			
FEATURE			Location/Qualifiers			
source			1..121			
			mol_type = protein			
			organism = synthetic construct			
SEQUENCE: 149						
QVQLQESPGV	LVKPSQTLNL	TCTVSGGSIS	SGGYYWSWIR	QHPGKGLEWI	GNIYYSGSTY	60
YNPSSLKSRVT	ISVDTSKNQF	SLKLSSVTAA	DTAVYYCARG	LSTIDEAFDP	WGQGTLVTVS	120
S						121
SEQ ID NO: 150			moltype = AA length = 107			
FEATURE			Location/Qualifiers			
source			1..107			
			mol_type = protein			
			organism = synthetic construct			
SEQUENCE: 150						

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DIQMTQSPST LSASVGDRVT ITCRASQSI S SWLAWYQQKP GKAPKLLIYK ASSLESGVPS	60
RFSGSGSGTE FTLTISSLQP DDFATYYCQQ DNSYPYTFGG GTKVEIK	107
SEQ ID NO: 151	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 151	
GSISDGSYW S	11
SEQ ID NO: 152	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 152	
NIYYSGSTYY NPSLR S	16
SEQ ID NO: 153	moltype = AA length = 13
FEATURE	Location/Qualifiers
source	1..13
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 153	
ARGLSTIDEA FDP	13
SEQ ID NO: 154	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 154	
RASQSISSWL A	11
SEQ ID NO: 155	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 155	
KASSLES	7
SEQ ID NO: 156	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 156	
QQDNSYPYT	9
SEQ ID NO: 157	moltype = AA length = 121
FEATURE	Location/Qualifiers
source	1..121
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 157	
QLQLQESGPG LVKPSETLSL TCTVSGGSIS DGSYWWSIR QHPGKGLEWI GNIYYSGSTY	60
YNPSLRSRVT MSVDTSKNQF SLKLSSVTA DTAVYYCARG LSTIDEAFDP WGQGTLTVS	120
S	121
SEQ ID NO: 158	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 158	
DIQMTQSPST LSASVGDRVT ITCRASQSI S SWLAWYQQKP GKAPKLLIYK ASSLESGVPS	60
RFSGSGSGTE FTLTISSLQP DDFATYYCQQ DNSYPYTFGG GTKVEIK	107
SEQ ID NO: 159	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 159	

-continued

GSISDGSSYW S		11
SEQ ID NO: 160	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
source	1..16	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 160		
NIYYSGSTYY NPSLRS		16
SEQ ID NO: 161	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 161		
ARGLSTIDEA FDP		13
SEQ ID NO: 162	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 162		
RASKSISSWL A		11
SEQ ID NO: 163	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 163		
EASSLHS		7
SEQ ID NO: 164	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 164		
QQDNSYPYT		9
SEQ ID NO: 165	moltype = AA length = 121	
FEATURE	Location/Qualifiers	
source	1..121	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 165		
QVQLQESPGV LVKPSQTLSL TCTVSGGSIS DGSYYWSWIR QHPGKGLEWI GNIYYSGSTY 60		
YNPDSLRSRVT MSVDTSKNQF SLKLSSVTA DTAVYYCARG LSTIDEAFDP WGQGTLVTVS 120		
S		121
SEQ ID NO: 166	moltype = AA length = 107	
FEATURE	Location/Qualifiers	
source	1..107	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 166		
DIGMTQSPST LSASVGDRVT ITCRASKSIS SWLAWYQQKP GKAPKLLIYE ASSLHSGVPS 60		
RFSGSGSGTE FTLTISSSLQP DDFATYYCQQ DNSYPYTFGG GTKVEIK		107
SEQ ID NO: 167	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 167		
GSISSYYWS		9
SEQ ID NO: 168	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
source	1..16	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 168		
YIYSSGSGTNY NPSLKS		16

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SEQ ID NO: 169	moltype = AA length = 15
FEATURE	Location/Qualifiers
source	1..15
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 169	
ARGSGQYAAP DYGMD	15
SEQ ID NO: 170	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 170	
RASQSISSWL A	11
SEQ ID NO: 171	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 171	
KASSLES	7
SEQ ID NO: 172	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 172	
QQDNSFPPT	9
SEQ ID NO: 173	moltype = AA length = 122
FEATURE	Location/Qualifiers
source	1..122
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 173	
QVQLQESGPQ LVKPSETLSL TCTVSGGSIS SYYWSWIROQ PGKGLEWIGY IYSSGSTNYN	60
PSLKSRTS VDTSKNQFSL KLSSVTAADT AVYYCARGSG QYAAPDYGMD VWGQGTTVT	120
SS	122
SEQ ID NO: 174	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 174	
DIQMKTQSPST LSASVGDRVT ITCRASQHSIS SWLAWYQQKP GKAPKLLIYK ASSLEGVPS	60
RFSGSGSGTE FTLTISSLQP DDFATYYCQQ DNSFPFTFGG GTKVEIK	107
SEQ ID NO: 175	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 175	
GSIISYYWG	9
SEQ ID NO: 176	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 176	
YIYSSGSTATSY NPSLKS	16
SEQ ID NO: 177	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 177	
ARGSGLYAAP DYGLDV	16

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SEQ ID NO: 178	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 178	
RASQSISSWLA	11
SEQ ID NO: 179	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 179	
KASSLES	7
SEQ ID NO: 180	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 180	
QQDNSFPFT	9
SEQ ID NO: 181	moltype = AA length = 122
FEATURE	Location/Qualifiers
source	1..122
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 181	
QVQLQESGPG LVKPSETLSL TCTVSGGSII SYYWGWIROQ PGKGLEWIGY IYSSGSTS	60
PSLKSRTVTIS VDTSKNQFSL KLSSVTAADT AVYYCARGSG LYAAPDYGLD VWGQTTTV	120
SS	122
SEQ ID NO: 182	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 182	
DIQMTQSPST LSASVGDRVT ITCRASQSIIS SWLAWYQQKP GKAPKLLIYK ASSLEGVPS	60
RFSGSGSGTE FTLTSSLQP DDFATYYCQQ DNSFPFTFGG GTKVEIK	107
SEQ ID NO: 183	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 183	
FTFSSYAMS	9
SEQ ID NO: 184	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 184	
TISGGGGSTY YADSVKG	17
SEQ ID NO: 185	moltype = AA length = 13
FEATURE	Location/Qualifiers
source	1..13
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 185	
ARGAGHYDLV GRY	13
SEQ ID NO: 186	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 186	
RASQSISSYLN	11
SEQ ID NO: 187	moltype = AA length = 7

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FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 187	
AASSLQS	7
SEQ ID NO: 188	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 188	
QQLYSLPPT	9
SEQ ID NO: 189	moltype = AA length = 120
FEATURE	Location/Qualifiers
source	1..120
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 189	
EVQLLSEGGG LVQPGGSSLRL SCAASGFTFS SYAMMSVRQA PGKGLEWVST ISGGGGSTYY 60	
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARGA GHYDLVGRYW GQGTLVTVSS 120	
SEQ ID NO: 190	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 190	
DIQMTQSPSS LSASVGDRVT ITCRASQSIS SYLNWYQQKP GKAPKLLIYA ASSLQSGVPS 60	
RFGSGSGSTD FTLTISSLQP EDFATYYCQQ LYSLPPTFGG GTKVEIK 107	
SEQ ID NO: 191	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 191	
FTFSSYAMS	9
SEQ ID NO: 192	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 192	
AISGGGGSTY YADSVKG	17
SEQ ID NO: 193	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 193	
ARVGFRALNY	10
SEQ ID NO: 194	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 194	
RASQDISSWL A	11
SEQ ID NO: 195	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 195	
AASSLQS	7
SEQ ID NO: 196	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10

-continued

SEQUENCE: 196	mol_type = protein organism = synthetic construct	
QQATSYPPWT		10
SEQ ID NO: 197	moltype = AA length = 117	
FEATURE	Location/Qualifiers	
source	1..117	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 197		
EVOLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSA ISGSGGSTYY	60	
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARVG FRALNYWGQG TTDTVSS	117	
SEQ ID NO: 198	moltype = AA length = 108	
FEATURE	Location/Qualifiers	
source	1..108	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 198		
DIQLTQSPSS VSASVGDRTV ITCRASQDIS SWLAWYQQKP GKAPKLLIYA ASSLQSGVPS	60	
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ ATSYPPWTFG GGTKVEIK	108	
SEQ ID NO: 199	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 199		
GTFSSSYAIS		9
SEQ ID NO: 200	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 200		
GIIPIFGTAS YAQKFQG		17
SEQ ID NO: 201	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 201		
ARQQYDGRRY FGL		13
SEQ ID NO: 202	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 202		
RASQSVSSNL A		11
SEQ ID NO: 203	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 203		
SASTRAT		7
SEQ ID NO: 204	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 204		
QQVNVPPT		9
SEQ ID NO: 205	moltype = AA length = 120	
FEATURE	Location/Qualifiers	
source	1..120	
	mol_type = protein	
	organism = synthetic construct	

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SEQUENCE: 205
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPIPGTASY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARQQ YDGRRYFGLW GRGTLTVSS 120

SEQ ID NO: 206      moltype = AA length = 107
FEATURE           Location/Qualifiers
source            1..107
mol_type = protein
organism = synthetic construct

SEQUENCE: 206
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKP GQAPRLLIYS ASTRATGIPA 60
RFGSGSGSTE FTLTISSLQS EDFAVYYCQQ VNVWPPTFGG GTKVEIK 107

SEQ ID NO: 207      moltype = AA length = 9
FEATURE           Location/Qualifiers
source            1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 207
GTFSSSYAIS 9

SEQ ID NO: 208      moltype = AA length = 17
FEATURE           Location/Qualifiers
source            1..17
mol_type = protein
organism = synthetic construct

SEQUENCE: 208
GIIPIFGTAN YAQKFQG 17

SEQ ID NO: 209      moltype = AA length = 9
FEATURE           Location/Qualifiers
source            1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 209
ARGGPWFDP 9

SEQ ID NO: 210      moltype = AA length = 11
FEATURE           Location/Qualifiers
source            1..11
mol_type = protein
organism = synthetic construct

SEQUENCE: 210
RASQSISSSWL A 11

SEQ ID NO: 211      moltype = AA length = 7
FEATURE           Location/Qualifiers
source            1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 211
KASSLES 7

SEQ ID NO: 212      moltype = AA length = 10
FEATURE           Location/Qualifiers
source            1..10
mol_type = protein
organism = synthetic construct

SEQUENCE: 212
QQYNNSYPFPFT 10

SEQ ID NO: 213      moltype = AA length = 116
FEATURE           Location/Qualifiers
source            1..116
mol_type = protein
organism = synthetic construct

SEQUENCE: 213
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPIPGTANY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARGG PWFDPWGQGT LTVSS 116

SEQ ID NO: 214      moltype = AA length = 108
FEATURE           Location/Qualifiers
source            1..108
mol_type = protein
organism = synthetic construct

SEQUENCE: 214

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DIQMTQSPST LSASVGDRVT ITCRASQSIIS SWLAWYQQKP GKAPKLLIYK ASSLESGVPS	60
RFSGSGSGTE FTLTSSLQP DDFATYYCQQ YNSYPPFTFG GTKVEIK	108
SEQ ID NO: 215	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 215	
FTFSSYAMS	9
SEQ ID NO: 216	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 216	
AISGSGGSTS YADSVKG	17
SEQ ID NO: 217	moltype = AA length = 13
FEATURE	Location/Qualifiers
source	1..13
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 217	
AKPSLATMLA PDI	13
SEQ ID NO: 218	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 218	
RASQSISSWLA A	11
SEQ ID NO: 219	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 219	
DASSLES	7
SEQ ID NO: 220	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 220	
QQSKSYPR	9
SEQ ID NO: 221	moltype = AA length = 120
FEATURE	Location/Qualifiers
source	1..120
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 221	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVA ISGSGGSTSY	60
ADSVKGRFTI SRDNSKNLTY LQMNSLRAED TAVYYCAKPS LATMLAFDIW GQGTMVTVSS	120
SEQ ID NO: 222	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 222	
DIQMTQSPST LSASVGDRVT ITCRASQSIIS SWLAWYQQKP GKAPKLLIYD ASSLESGVPS	60
RFSGSGSGTE FTLTSSLQP DDFATYYCQQ SKSYPRFTFG GTKVEIK	107
SEQ ID NO: 223	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 223	
GSISSSVYYW S	11

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SEQ ID NO: 224      moltype = AA  length = 16
FEATURE
source
1..16
mol_type = protein
organism = synthetic construct
SEQUENCE: 224
SILVSGSTYY NPSLKS                                         16

SEQ ID NO: 225      moltype = AA  length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 225
ARAVSFSLDV                                         9

SEQ ID NO: 226      moltype = AA  length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 226
RASQSISSYLN                                         11

SEQ ID NO: 227      moltype = AA  length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 227
GASSLQS                                         7

SEQ ID NO: 228      moltype = AA  length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 228
QQSYDPPWT                                         9

SEQ ID NO: 229      moltype = AA  length = 117
FEATURE
source
1..117
mol_type = protein
organism = synthetic construct
SEQUENCE: 229
QLQLQESCPG LVKPSETLSL TCTVSGGSIS SSVYYWSWIR QPPGKGLEWI GSILVSGSTY 60
YNPSLKSRTV ISVDTSKNQF SLKLSSVTAA DTAVYYCARA VSFLDVWGQG TMVIVSS 117

SEQ ID NO: 230      moltype = AA  length = 107
FEATURE
source
1..107
mol_type = protein
organism = synthetic construct
SEQUENCE: 230
DIQMTQSPSS LSASVGDRVT ITCRASQSIIS SYLNWYQQKP GKAPKLLIYG ASSLQSGVPS 60
RFGSGSGSTD FTLTISSSLQP EDFATYYCQQ SYDPPWTFGG GTKVEIK 107

SEQ ID NO: 231      moltype = AA  length = 450
FEATURE
source
1..450
mol_type = protein
organism = synthetic construct
SEQUENCE: 231
QLQLQESCPG LVKPSETLSL TCTVSGGSIS SSSYYWGWR QPPGKGLEWI GNIYYSGSTY 60
YNPSLKSRTV ISVDTSKNQF SLKLSSVTAA DTAVYYCARE GSYPNWFPDW GQGTLTVSS 120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYPPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELGG 240
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNM YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGE EYKCKVSNKA LPAPIEKTS KAKGQPREPQ VYTLPSSRDE 360
LTKNQVSLTC LVKGFYPSDI AVEWESENQGP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW 420
QQGNVFSCSV MHEALHNHYT QKSLSLSPGK                                         450

SEQ ID NO: 232      moltype = AA  length = 214
FEATURE
Location/Qualifiers

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source          1..214
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 232
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKP GQAPRLLIYG ASTRATGIPA 60
RFSGSGSGTE FTLTISSLQS EDFAVYYCQQ YHSFPFTFGG GTKVEIKRTV AAPSVFIFPP 120
SDEQLKSGTA SVVCLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSLT 180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGECA 214

SEQ ID NO: 233      moltype = AA length = 450
FEATURE          Location/Qualifiers
source           1..450
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 233
QLQLQESGPV LVKPSETLSL TCTVSGGSIK SGSHYWGIR QPPGKGLEWI GNIYYSGSTY 60
YNPSLRSRVT ISVDTSKNQF SLKLSSVTAA DTAVYYCARE GSYPNWDPW GQGTLTVVSS 120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG 240
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTS KAKGQPREPQ VYTLPPSRDE 360
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW 420
QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450

SEQ ID NO: 234      moltype = AA length = 214
FEATURE          Location/Qualifiers
source           1..214
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 234
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKP GQAPRLLIYG ASTRATGIPA 60
RFSGSGSGTE FTLTISSLQS EDFAVYYCQQ YHSFPFTFGG GTKVEIKRTV AAPSVFIFPP 120
SDEQLKSGTA SVVCLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSLT 180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGECA 214

SEQ ID NO: 235      moltype = AA length = 450
FEATURE          Location/Qualifiers
source           1..450
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 235
QLQLQESGPV LVKPSETLSL TCTVSGGSIK SGSHYWGIR QPPGKGLEWI GNIYYSGSTY 60
YNPSLRSRVT ISVDTSKNQF SLKLSSVTAA DTAVYYCARE GSYPNWDPW GQGTLTVVSS 120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG 240
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTS KAKGQPREPQ VYTLPPSRDE 360
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW 420
QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450

SEQ ID NO: 236      moltype = AA length = 214
FEATURE          Location/Qualifiers
source           1..214
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 236
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKP GQAPRLLIYG ASTRATGIPA 60
RFSGSGSGTE FTLTISSLQS EDFAVYYCQQ YHSFPFTFGG GTKVEIKRTV AAPSVFIFPP 120
SDEQLKSGTA SVVCLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSLT 180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGECA 214

SEQ ID NO: 237      moltype = AA length = 450
FEATURE          Location/Qualifiers
source           1..450
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 237
QLQLQESGPV LVKPSETLSL TCTVSGGSIK SGSHYWGIR QPPGKGLEWI GNIYYSGSTY 60
YNPSLRSRVT ISVDTSKNQF SLKLSSVTAA DTAVYYCARE GSYPNWDPW GQGILTVVSS 120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG 240
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTS KAKGQPREPQ VYTLPPSRDE 360
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW 420
QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450

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SEQ ID NO: 238	moltype = AA length = 214
FEATURE	Location/Qualifiers
source	1..214
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 238	
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKG QGAPRLLIYG ASTRATGIPA	60
RFSGSGSGTE FTLTISLQS EDFAVYYCQQ YHSPFPFTGG GTKVEIKRTV AAPSVFIFPP	120
SDEQLKSGTA SVVCLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSTLT	180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEC	214
SEQ ID NO: 239	moltype = AA length = 450
FEATURE	Location/Qualifiers
source	1..450
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 239	
QLQLQESPGV LVKPSETLSL TCTVSGGSIK SGSHYWGWR QPPGKGLEWI GNIYYSGSTY	60
YNPSLKSRTV MSVDTSKNQF SLKLSSVTA DTAVYYCARE GSYPNWFDPW GQGTLTVVSS	120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS	180
GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG	240
PSVFLFPPK P DTLMSIRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN	300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIIS KAKGQPREPQ VYTLPPSRDE	360
LTKNQVSLTC LVKGFYPSDI AVEWESENQGP ENNYKTTTPV LDSDGSFFLY SKLTVDKSRW	420
QQGNVFSCSV MHEALHNHYT QKSLSLSPGK	450
SEQ ID NO: 240	moltype = AA length = 214
FEATURE	Location/Qualifiers
source	1..214
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 240	
EIVMTQSPAT LSVSPGERAT LSCRASQSVS TNLAWYQQKG QGAPRLLIYD ASARVTGIPA	60
RFSGSGSGTE FTLTISLQS EDFAVYYCQQ YHSPFPFTGG GTKVEIKRTV AAPSVFIFPP	120
SDEQLKSGTA SVVCLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSTLT	180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEC	214
SEQ ID NO: 241	moltype = AA length = 450
FEATURE	Location/Qualifiers
source	1..450
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 241	
QLQLQESPGV LVKPSETLSL TCTVSGGSIS SSSYYWGWR QPPGKGLEWI GNIYYSGSTY	60
YNPSLKSRTV ISVDTSKNQF SLKLSSVTA DTAVYYCARE GSYTTLVNVW GQGTMVTVSS	120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS	180
GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG	240
PSVFLFPPK P DTLMSIRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN	300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIIS KAKGQPREPQ VYTLPPSRDE	360
LTKNQVSLTC LVKGFYPSDI AVEWESENQGP ENNYKTTTPV LDSDGSFFLY SKLTVDKSRW	420
QQGNVFSCSV MHEALHNHYT QKSLSLSPGK	450
SEQ ID NO: 242	moltype = AA length = 215
FEATURE	Location/Qualifiers
source	1..215
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 242	
EIVLTQSPGT LSLSPGERAT LSCRASQSVS SSYLAWSYQOK PGQAPRLLIY GASSRATGIP	60
DRFGSGSGSGT DFTLTISRLF PEDAVYYCQ QAASYPLTFG GGTKVEIKRT VAAPSVFIFPP	120
PSDEQLKSGT ASVVCLNNFY YPREAKVQWKV DNALQSGNSQ QESVTEQDSK DSTYSLSSTL	180
TLSKADYEKH KVYACEVTHQ GLSSPVTKSF NRGE	215
SEQ ID NO: 243	moltype = AA length = 450
FEATURE	Location/Qualifiers
source	1..450
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 243	
QLQLQESPGV LVKPSETLSL TCTVSGGSIG RGSYYWGWR QPPGKGLEWI GNIYYSGSTY	60
YNPSLKSRTV ISVDTSKNQF SLKLSSVTA DTAVYYCARE GSYTTLVNVW GQGTMVTVSS	120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS	180
GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG	240
PSVFLFPPK P DTLMSIRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN	300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIIS KAKGQPREPQ VYTLPPSRDE	360
LTKNQVSLTC LVKGFYPSDI AVEWESENQGP ENNYKTTTPV LDSDGSFFLY SKLTVDKSRW	420

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QQGNVFSCSV MHEALHNHYT QKSLSLSPGK	450
SEQ ID NO: 244	
FEATURE	moltype = AA length = 215
source	Location/Qualifiers
	1..215
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 244	
EIVLTQSPGT LSLSPGERAT LSCRASQSV A SSHLAWYQQK PGQAPRLLIY DAVSRATGIP	60
DRFSGSGSGT DFTLTISRLR PEDFAVYYCQ QAASYPLTFG GGTKEIKRT VAAPSVFIFP	120
PSDEQLKSGT ASVVCLNNF YPREAKVQWK VDNALQSGNS QESVTEQDSK DSTYLSSTL	180
TLSKADYEKH K VYACEVTHQ GLSSPVTKSF NRGE C	215
SEQ ID NO: 245	
FEATURE	moltype = AA length = 451
source	Location/Qualifiers
	1..451
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 245	
QVQLQESPGV LVKPSQTL SL TCTVSGGSIS SGGYYWSWIR QHPGKGLEWI GNIYYSGSTY	60
YNPSLKSRTV ISVDTSKNQF SLKLSVTAA DTAVYYCARE SSTISADFDL WGRGLTVTS	120
SASTKGPSVF PLAPSSKSTS GGTAALGCLV KDYFPEPVTV SWNSGALTSG VHTFPAVLQS	180
SGLYSLSSVV TVPSSLGQT TYICNVNHKP SNTKVDKKVE PKSCDKTHTC PPCPAPELLG	240
GPSVFLFPK PKDTLMISRT PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTPREEQY	300
NSTYRVVSVL TVLHQDWLNG KEYCKVVSNK ALPAPIEKTI SKAKGQREP QVYTLPPSRD	360
ELTKNQVSLT CLVKGFYPSD IAEWESENQG PENNYKTTTP VLSDDGSSFL YSKLTVDKSR	420
WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K	451
SEQ ID NO: 246	
FEATURE	moltype = AA length = 214
source	Location/Qualifiers
	1..214
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 246	
DIQMTQSPSS VSASVGDRVT ITCRASQGIS RWLAWYQQKP GKAPKLLIYA ASSLQSGVPS	60
RFSGSGSGTD FTLSISSLQ EDFATYYCQ AHTFPYTFGG GTKVEIKRTV AAPSVFIFPP	120
SDEQLKSGTA SVVCLNNFY PREAKVQWK DNALQSGNSQ ESVTEQDSKD STYLSSTLT	180
LSKADYEKH K VYACEVTHQ GLSSPVTKSFN RGE C	214
SEQ ID NO: 247	
FEATURE	moltype = AA length = 451
source	Location/Qualifiers
	1..451
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 247	
QLQLQESPGV LVKPSQTL SL TCTASGGGSIS HGGYYWSWIR QHPGKGLEWI GNIYYSGSTY	60
YNPSLKSRTV MSVDTSKNQF SLKLSVTAA DTAVYYCARE SSTISADFDL WGRGLTVTS	120
SASTKGPSVF PLAPSSKSTS GGTAALGCLV KDYFPEPVTV SWNSGALTSG VHTFPAVLQS	180
SGLYSLSSVV TVPSSLGQT TYICNVNHKP SNTKVDKKVE PKSCDKTHTC PPCPAPELLG	240
GPSVFLFPK PKDTLMISRT PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTPREEQY	300
NSTYRVVSVL TVLHQDWLNG KEYCKVVSNK ALPAPIEKTI SKAKGQREP QVYTLPPSRD	360
ELTKNQVSLT CLVKGFYPSD IAEWESENQG PENNYKTTTP VLSDDGSSFL YSKLTVDKSR	420
WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K	451
SEQ ID NO: 248	
FEATURE	moltype = AA length = 214
source	Location/Qualifiers
	1..214
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 248	
DIQMTQSPSS VSASVGDRVT ITCRASQGIS RWLAWYQQKP GKAPKLLIYA ASSLQSGVPS	60
RFSGSGSGTD FTLSISSLQ EDFATYYCQ AHTFPYTFGG GTKVEIKRTV AAPSVFIFPP	120
SDEQLKSGTA SVVCLNNFY PREAKVQWK DNALQSGNSQ ESVTEQDSKD STYLSSTLT	180
LSKADYEKH K VYACEVTHQ GLSSPVTKSFN RGE C	214
SEQ ID NO: 249	
FEATURE	moltype = AA length = 451
source	Location/Qualifiers
	1..451
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 249	
QVQLQESPGV LVKPSQTL SL TCTVSGGSIS SGGYYWSWIR QHPGKGLEWI GNIYYSGSTY	60
YNPSLKSRTV ISVDTSKNQF SLKLSVTAA DTAVYYCARG LSTIDEAFDP WGQGLTVTS	120
SASTKGPSVF PLAPSSKSTS GGTAALGCLV KDYFPEPVTV SWNSGALTSG VHTFPAVLQS	180
SGLYSLSSVV TVPSSLGQT TYICNVNHKP SNTKVDKKVE PKSCDKTHTC PPCPAPELLG	240
GPSVFLFPK PKDTLMISRT PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTPREEQY	300

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NSTYRVVSVL	TVLHQDWLNG	KEYCKVSNK	ALPAPIEKTI	SKAKGQPREP	QVYTLPPSRD	360
ELTKNQVSLT	CLVKGFYPSD	IAVEWESNQQ	PENNYKTPPP	VLDSDGSFFL	YSKLTVDKSR	420
WQQGNVFSCS	VMHEALHNHY	TQKSLSLSPG K				451
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SEQ ID NO: 250	moltype = AA	length = 214				
FEATURE	Location/Qualifiers					
source	1..214					
	mol_type = protein					
	organism = synthetic construct					
SEQUENCE: 250						
DIQMTQSPST	LSASVGDRVT	ITCRASQSI	SWLAWYQQKP	GKAPKLLIYK	ASSLESGVPS	60
RFSGSGSGTE	FTLTISLQP	DDFATYYCQQ	DNSYPYTFGG	GTKVEIKRTV	AAPSVFIFPP	120
SDEQLKSGTA	SVVCLNNFY	PREAKVQWKV	DNALQSGNSQ	ESVTEQDSKD	STYSLSSTLT	180
LSKADYEKHK	VYACEVTHQG	LSSPVTKSFN	RGEC			214
<hr/>						
SEQ ID NO: 251	moltype = AA	length = 451				
FEATURE	Location/Qualifiers					
source	1..451					
	mol_type = protein					
	organism = synthetic construct					
SEQUENCE: 251						
QLQLQESPG	LVKPSETSL	TCTVSGGSIS	DGSYYWSWIR	QHPGKGLEWI	GNIYYSGSTY	60
YNPSLRSRVT	MSVDTSKNQF	SLKLSSVTAA	DTAVYYCARG	LSTIDEAFDP	WGQGTLVTVS	120
SASTKGPSV	PLAPSSKSTS	GGTAALGCLV	KDYFPEPVTV	SWNSGALTSG	VHTFPAAVLQS	180
SGLYSLSSVV	TVPSSSLGTQ	TYICNVNHKP	SNTKVDKKVE	PKSCDKTHTC	PPCPAPELLG	240
GPSVFLPPK	PKDTLMISRT	PEVTCVVVDV	SHEDPEVKFN	WYVDGVEVHN	AKTKPREEQY	300
NSTYRVVSVL	TVLHQDWLNG	KEYCKVSNK	ALPAPIEKTI	SKAKGQPREP	QVYTLPPSRD	360
ELTKNQVSLT	CLVKGFYPSD	IAVEWESNQQ	PENNYKTPPP	VLDSDGSFFL	YSKLTVDKSR	420
WQQGNVFSCS	VMHEALHNHY	TQKSLSLSPG K				451
<hr/>						
SEQ ID NO: 252	moltype = AA	length = 214				
FEATURE	Location/Qualifiers					
source	1..214					
	mol_type = protein					
	organism = synthetic construct					
SEQUENCE: 252						
DIQMTQSPST	LSASVGDRVT	ITCRASQSI	SWLAWYQQKP	GKAPKLLIYK	ASSLESGVPS	60
RFSGSGSGTE	FTLTISLQP	DDFATYYCQQ	DNSYPYTFGG	GTKVEIKRTV	AAPSVFIFPP	120
SDEQLKSGTA	SVVCLNNFY	PREAKVQWKV	DNALQSGNSQ	ESVTEQDSKD	STYSLSSTLT	180
LSKADYEKHK	VYACEVTHQG	LSSPVTKSFN	RGEC			214
<hr/>						
SEQ ID NO: 253	moltype = AA	length = 451				
FEATURE	Location/Qualifiers					
source	1..451					
	mol_type = protein					
	organism = synthetic construct					
SEQUENCE: 253						
QVQLQESPG	LVKPSQTSL	TCTVSGGSIS	DGSYYWSWIR	QHPGKGLEWI	GNIYYSGSTY	60
YNPSLRSRVT	MSVDTSKNQF	SLKLSSVTAA	DTAVYYCARG	LSTIDEAFDP	WGQGTLVTVS	120
SASTKGPSV	PLAPSSKSTS	GGTAALGCLV	KDYFPEPVTV	SWNSGALTSG	VHTFPAAVLQS	180
SGLYSLSSVV	TVPSSSLGTQ	TYICNVNHKP	SNTKVDKKVE	PKSCDKTHTC	PPCPAPELLG	240
GPSVFLPPK	PKDTLMISRT	PEVTCVVVDV	SHEDPEVKFN	WYVDGVEVHN	AKTKPREEQY	300
NSTYRVVSVL	TVLHQDWLNG	KEYCKVSNK	ALPAPIEKTI	SKAKGQPREP	QVYTLPPSRD	360
ELTKNQVSLT	CLVKGFYPSD	IAVEWESNQQ	PENNYKTPPP	VLDSDGSFFL	YSKLTVDKSR	420
WQQGNVFSCS	VMHEALHNHY	TQKSLSLSPG K				451
<hr/>						
SEQ ID NO: 254	moltype = AA	length = 214				
FEATURE	Location/Qualifiers					
source	1..214					
	mol_type = protein					
	organism = synthetic construct					
SEQUENCE: 254						
DIQMTQSPST	LSASVGDRVT	ITCRASKSI	SWLAWYQQKP	GKAPKLLIYE	ASSLHSGVPS	60
RFSGSGSGTE	FTLTISLQP	DDFATYYCQQ	DNSYPYTFGG	GTKVEIKRTV	AAPSVFIFPP	120
SDEQLKSGTA	SVVCLNNFY	PREAKVQWKV	DNALQSGNSQ	ESVTEQDSKD	STYSLSSTLT	180
LSKADYEKHK	VYACEVTHQG	LSSPVTKSFN	RGEC			214
<hr/>						
SEQ ID NO: 255	moltype = AA	length = 452				
FEATURE	Location/Qualifiers					
source	1..452					
	mol_type = protein					
	organism = synthetic construct					
SEQUENCE: 255						
QVQLQESPG	LVKPSETSL	TCTVSGGSIS	SYYWSWIROP	PGKGLEWIGY	IYSSGSTYN	60
PSLKSRTIS	VDTSKNQFSL	KLSSVTAADT	AVYYCARGSG	QYAAPDYGMD	VWGQGTTVTV	120
SSASTKGPSV	FPLAPSSKST	SGGTAALGCL	KDYFPEPVTV	VSWNSGALT	GVHTFPAAVLQ	180

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SSGLYSLSSV VTVPSLSSGT QTYICNVNHK PSNTKVDKV EPKSCDKHT CPPCPAPELL	240
GGPSVFLPPP KPKDTLMISR TPEVTCVVVD VSHEDEPEVKF NWYVDGVEVH NAKTKPREEQ	300
YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR	360
DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSDGSFF LYSKLTVDKS	420
RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GK	452
 SEQ ID NO: 256 moltype = AA length = 214	
FEATURE Location/Qualifiers	
source 1..214	
mol_type = protein	
organism = synthetic construct	
 SEQUENCE: 256	
DIQMTQSPST LSASVGDRVT ITCRASQSI S WLAQYQQKP GKAPKLLIYK ASSLEGVPS	60
RFGSGSGSTE FTLTISSLQP DDFATYYCQQ DNSFPFTFGG GTKVEIKRTV AAPSVFIFPP	120
SDEQLKSGTA SVVCLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSTLT	180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGE	214
 SEQ ID NO: 257 moltype = AA length = 452	
FEATURE Location/Qualifiers	
source 1..452	
mol_type = protein	
organism = synthetic construct	
 SEQUENCE: 257	
QVQLQESGPG LVKPSETLSL TCTVSGGSII SYYWGWIRQP PGKGLEWIGY IYSSGSTSYN	60
PSLKSRTVIS VDTSKNQFSL KLSSVTAADT AVYYCARGSG LYAAPDYGLD VWGQGTTTV	120
SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALT GVHTPPAVLQ	180
SSGLYSLSSGT QTYICNVNHK PSNTKVDKV EPKSCDKHTT CPPCPAPELL	240
GGPSVFLPPP KPKDTLMISR TPEVTCVVVD VSHEDEPEVKF NWYVDGVEVH NAKTKPREEQ	300
YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR	360
DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSDGSFF LYSKLTVDKS	420
RWQQGNVFSC SVMHEALHNH YTQKSLSLSP GK	452
 SEQ ID NO: 258 moltype = AA length = 214	
FEATURE Location/Qualifiers	
source 1..214	
mol_type = protein	
organism = synthetic construct	
 SEQUENCE: 258	
DIQMTQSPST LSASVGDRVT ITCRASQSI S WLAQYQQKP GKAPKLLIYK ASSLEGVPS	60
RFGSGSGSTE FTLTISSLQP DDFATYYCQQ DNSFPFTFGG GTKVEIKRTV AAPSVFIFPP	120
SDEQLKSGTA SVVCLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSTLT	180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGE	214
 SEQ ID NO: 259 moltype = AA length = 450	
FEATURE Location/Qualifiers	
source 1..450	
mol_type = protein	
organism = synthetic construct	
 SEQUENCE: 259	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVST ISGSGGSTYY	60
ADSVKGRFTI SRDNKNTLY LQMSNLRAED TAVYYCARGA GHYDLVGRYWW GQGTLVTVSS	120
ASTKGPSV LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS	180
GLYSLSSVVT VPSSSLGQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG	240
PSVFLFPKPK KDTLMISRTP EVTCVVVDVS HEDPEVKFWN YVDGVEVHNA KTKPREEQYN	300
STYRVSVS VLT VHODWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VYTLPSPRDE	360
LTKNQVSLTC LVKGKFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW	420
QQGNVNCSV MHEALHNHYT QKSLSLSPGK	450
 SEQ ID NO: 260 moltype = AA length = 214	
FEATURE Location/Qualifiers	
source 1..214	
mol_type = protein	
organism = synthetic construct	
 SEQUENCE: 260	
DIQMTQSPSS LSASVGDRVT ITCRASQSI SYLNWYQQKP GKAPKLLIYA ASSLQSGVPS	60
RFGSGSGSTD FTLTISSLQP EDFATYYCQQ LYSLPPTFGG GTKVEIKRTV AAPSVFIFPP	120
SDEQLKSGTA SVVCLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSTLT	180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGE	214
 SEQ ID NO: 261 moltype = AA length = 447	
FEATURE Location/Qualifiers	
source 1..447	
mol_type = protein	
organism = synthetic construct	
 SEQUENCE: 261	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSA ISGSGGSTYY	60

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ADSVKGRFTI	SRDNSKNTLY	LQMNSSLRAED	TAVYYCARVG	FRALNYWGQG	TTVTVSSAST	120
KGPSPFLAP	SSKSTGGTA	ALGCLVKDVF	PEPVTWSWNS	GALTSGVHTF	PAVLQSSGLY	180
SLSSVVTVP	SSLGTQTYIC	VNVHKPSNTK	VDKKVEPKSC	DKTHTCPPCP	APELLGGPSV	240
FLFPPPKD	LMISRTPEV	CVVVDVSHED	PEVKFNWYVD	GVEVHNAKTK	PREEQYNSTY	300
RVVSVLTVLH	QDWLNGKEYK	CKVSNKALPA	PIEKTISKAK	GQPREPQVYT	LPPSRDELTK	360
NQVSLTCLVK	GFYPSDIAVE	WESNGOPENN	YKTPPVLDLS	DGSFFFLYSKL	TVDKSRWQQG	420
NVFSCSVMHE	ALHNHYTQKS	LSLSPGK				447

SEQ ID NO: 262	moltype = AA	length = 215				
FEATURE	Location/Qualifiers					
source	1..215					
	mol_type = protein					
	organism = synthetic construct					
SEQUENCE: 262						
DIQLTQSPSS	VSASVGDRVT	ITCRASQDIS	SWLAWYQQKP	GKAPKLLIYA	ASSLQSGVPS	60
RFSGSGSGTD	FTLTISSSLQ	EDFATYYCQQ	ATSYPPWTFG	GGTKVEIKRT	VAAPSVFIFP	120
PSDEQLKSGT	ASVVCLLN	YPREAKVQWK	VDNALQSGNS	QESVTEQDSK	DSTYSLSSL	180
TL SKADYEKH	KVYACEVTHQ	GLSSPVTKSF	NRGEC			215

SEQ ID NO: 263	moltype = AA	length = 450				
FEATURE	Location/Qualifiers					
source	1..450					
	mol_type = protein					
	organism = synthetic construct					
SEQUENCE: 263						
QVQLVQSGAE	VKKPGSSVKV	SCKASGGTFS	SYAISWVRQA	PQGGLEWMGG	IIPIPGTASY	60
AQKFQGRVTI	TADESTSTAY	MELSSLRSED	TAVYYCARQQ	YDGRRYFGLW	GRGTLTVVSS	120
ASTKGPSVFP	LAPSSKSTSG	GTAALGCLVK	DYPPEPVTVS	WNSGALTSGV	HTFPAVLQSS	180
GLYSLSSVVT	VPSSSLGTQT	YICCNVNHKP	NTKVDDKKVEP	KSCDKTHTCP	PCPAPELLGG	240
PSVFLFPKPK	KDTLMISRTP	EVTCVVVDWS	HEDPEVKPNW	YVDGVEVHNA	KTKPREEQYN	300
STYRVVSVT	VLHQDWLNGK	EYKCKVSNKA	LPAPIEKTI	KAKGQPREPQ	VYTLPPSRDE	360
LTKNQVSLTC	LVKGFYPSDI	AVEWESNGQP	ENNYKTTTPV	LSDGSFFLY	SKLTVDKSRW	420
QQGNVFCSV	MHEALHNHYT	QKSLSLSPGK				450

SEQ ID NO: 264	moltype = AA	length = 214				
FEATURE	Location/Qualifiers					
source	1..214					
	mol_type = protein					
	organism = synthetic construct					
SEQUENCE: 264						
EIVMTQSPAT	LSVSPGERAT	LSCRASQSVS	SNLAWYQQKP	GQAPRLLIYS	ASTRATGIPA	60
RFSGSGSGTE	FTLTISSSLQS	EDFAVYYCQQ	VNVWPPFTFG	GTKVEIKRTV	AAPSVFIFP	120
SD EQLKSGTA	SVVCLLN	YPREAKVQWK	DNALQSGNSQ	QESVTEQDSK	DSTYSLSSL	180
LSKADYEKH K	VYACEVTHQ	GLSSPVTKSFN	RGEC			214

SEQ ID NO: 265	moltype = AA	length = 446				
FEATURE	Location/Qualifiers					
source	1..446					
	mol_type = protein					
	organism = synthetic construct					
SEQUENCE: 265						
QVQLVQSGAE	VKKPGSSVKV	SCKASGGTFS	SYAISWVRQA	PQGGLEWMGG	IIPIFGTANY	60
AQKFQGRVTI	TADESTSTAY	MELSSLRSED	TAVYYCARGG	PWFDPWGQGT	LVTVSSASTK	120
GPSVFPPLAPS	SKSTSGGTA	LGCLVKDVF	EPVTWSWN	ALTSGVHTFP	AVLQSSGLYS	180
LSSVTVTPSS	SLGTQTYICN	VNVHKPSNTK	DKKVEPKSCD	DKTHTCPPCPA	PELLGGPSVF	240
LFPPPKD	MISRTPEVTC	VVVDPVSHED	EVKFNWYVDG	VEVHNAKTKP	REEQYNSTYR	300
VVSVTVLHQ	DWLN	NGKEYKC	KVSNKALPA	IEKTISKAKG	QPREPQVYT	360
QVSLTCLVKG	FYPSDIAVEW	ESNGOPEN	YKTPPVLDLS	GSFFFLYSKL	VDKSRWQQGN	420
NVFSCSVMHEA	LHNHYTQKS	LSLSPGK				446

SEQ ID NO: 266	moltype = AA	length = 215				
FEATURE	Location/Qualifiers					
source	1..215					
	mol_type = protein					
	organism = synthetic construct					
SEQUENCE: 266						
DIQMTQSPST	LSASVGDRVT	ITCRASQSI	SWLAWYQQKP	GKAPKLLIYK	ASSLESGVPS	60
RFSGSGSGTE	FTLTISSSLQ	DDFATYYCQQ	YN SYPPFTFG	GGTKVEIKRT	VAAPSVFIFP	120
PSDEQLKSGT	ASVVCLLN	YPREAKVQWK	VDNALQSGNS	QESVTEQDSK	DSTYSLSSL	180
LSKADYEKH K	VYACEVTHQ	GLSSPVTKSF	NRGEC			215

SEQ ID NO: 267	moltype = AA	length = 450
FEATURE	Location/Qualifiers	
source	1..450	
	mol_type = protein	
	organism = synthetic construct	

-continued

SEQUENCE: 267

```
LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSA ISGSGGSTSY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKPS LATMLAFDIW GQGTMVTVSS 120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYPPEPVTVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSSVT VPSSSLGTQT YICCNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG 240
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNV YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIK KAKGQPREPQ VYTLPPSRDE 360
LTKNQVSLTC LVKGFPSPDI AVEWESENQGP ENNYKTTTPV LDSDGSFFLY SKLTVDKSRW 420
QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450
```

SEQ ID NO: 268 moltype = AA length = 214
FEATURE Location/Qualifiers
source 1..214
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 268

```
DIQMTQSPST LSASVGDRVT ITCRASQHSIS SWLAWYQQKP GKAPKLLIYD ASSLESGVPS 60
RFSGSGSGTE FTLTISSLQP DDFATYYCQQ SKSYPRTFGG GTKVEIKRTV AAPSVFIFPP 120
SDEQLKSGTA SVVCLLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSTLT 180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEc 214
```

SEQ ID NO: 269 moltype = AA length = 447
FEATURE Location/Qualifiers
source 1..447
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 269

```
QLQLQESPGV LVKPSETLSL TCTVSGGSIS SSVYYWSWIR QPPGKGLEWI GSILVSGSTY 60
YNPLSLKSRVT ISVDTSKNQF SLKLSSVTA DTAVYYCARA VSFLDWVGQG TMVIVSSAST 120
KGPSVFLAP SSKSTSGGT A ALGCLVKDYP PEPVTWSWNS GALTSGVHTF PAVLQSSGLY 180
SLLGTVTPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKTHTCPPCP APELLGGPSV 240
FLPPPDKT LMISRTPEVT C C VVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPEENN YKTTPPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVMHE ALHNHYTQKS LSLSPGK 447
```

SEQ ID NO: 270 moltype = AA length = 214
FEATURE Location/Qualifiers
source 1..214
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 270

```
DIQMTQSPSS LSASVGDRVT ITCRASQHSIS SYLNWYQQKP GKAPKLLIYG ASSLQSGVPS 60
RFSGSGSGTD FTLTISSLQP EDFATYYCQQ SYDPFWTFGG GTKVEIKRTV AAPSVFIFPP 120
SDEQLKSGTA SVVCLLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSTLT 180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEc 214
```

SEQ ID NO: 271 moltype = AA length = 5
FEATURE Location/Qualifiers
source 1..5
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 271

```
TAAIS 5
```

SEQ ID NO: 272 moltype = AA length = 17
FEATURE Location/Qualifiers
source 1..17
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 272

```
GIIPIFGKAYAQKFQG 17
```

SEQ ID NO: 273 moltype = AA length = 14
FEATURE Location/Qualifiers
source 1..14
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 273

```
KFHGVSGSPF GMDV 14
```

SEQ ID NO: 274 moltype = AA length = 11
FEATURE Location/Qualifiers
source 1..11
 mol_type = protein
 organism = synthetic construct

-continued

SEQUENCE: 274	RASQSVSSYL A	11
SEQ ID NO: 275	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 275	DASN RAT	7
SEQ ID NO: 276	moltype = AA length = 8	
FEATURE	Location/Qualifiers	
source	1..8	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 276	QQRSNWP T	8
SEQ ID NO: 277	moltype = AA length = 123	
FEATURE	Location/Qualifiers	
source	1..123	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 277	QVQLVQSGAE VKKPGSSVKV SCKTSGDTPS TAAISWVRQA PGQGLEWMGG IIPIPGKAHY	60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYFCARKF HFVSGSPFGM DVWGQQGTTVT	120	
VSS	123	
SEQ ID NO: 278	moltype = AA length = 106	
FEATURE	Location/Qualifiers	
source	1..106	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 278	EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD ASN RATGIPA	60
RFSGSGSGTD FTLTISSELP EDFAVYYCQQ RSNWPTFGQG TKVEIK	106	
SEQ ID NO: 279	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 279	NYGMN	5
SEQ ID NO: 280	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 280	WINTYTGEPT YADAFKG	17
SEQ ID NO: 281	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 281	DYGDYGMDY	9
SEQ ID NO: 282	moltype = AA length = 15	
FEATURE	Location/Qualifiers	
source	1..15	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 282	RASKSVSTSG YSFMH	15
SEQ ID NO: 283	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 283		

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LASNLES

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SEQ ID NO: 284      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 284
QHSREVPWT

SEQ ID NO: 285      moltype = AA length = 118
FEATURE
source
1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 285
QVQLVQSGAE VKKPGASVKV SCKASGYTFT NYGMNWVRQA PGQGLKWMGW INTYTGEPTY 60
ADAFKGRVTM TRDTSISTAY MELSLRSDD TAVYYCARDY GDYGMWDWQ GTTVTVSS 118

SEQ ID NO: 286      moltype = AA length = 111
FEATURE
source
1..111
mol_type = protein
organism = synthetic construct
SEQUENCE: 286
DIVMTQSPDS LAVSLGERAT INCRASKSVS TSGYSFMHWY QQKPGQPPKL LIYLASNLES 60
GVPDRFSGSG SGTDFTLTIS SLQAEDVAVY YCQHSREVPW TFGQGTKEI K 111

SEQ ID NO: 287      moltype = AA length = 448
FEATURE
source
1..448
mol_type = protein
organism = synthetic construct
SEQUENCE: 287
QVQLVQSGAE VKKPGASVKV SCKASGYTFT NYGMNWVRQA PGQGLKWMGW INTYTGEPTY 60
ADAFKGRVTM TRDTSISTAY MELSLRSDD TAVYYCARDY GDYGMWDWQ GTTVTVSSAS 120
TKGSPVPLA PSSKSTSGGT AALGCLVKDY FPEPPTVSWN SGALTSGVHT FPAVLQSSGL 180
YSLSSVVTVP SSSLGTQTYI CNVNHKPSNT KVDKKVEPKS CDKTHTCPG PAPELLGGPS 240
VFLFPKPKD TLMSRTPEV TCVVVDSHE DPEVKFNWYV DGVEVHNAAKT KPREEQYNST 300
YRVVSVLTVL KHDWLNGKEY KCKVSNKALP APIEKTISKA KGQPREPQVY TLPPSRDELT 360
KNQVSLTCLV KGFYPSDIAV EWESNGQOPEN NYKTPPPVLD SDGSFFLYSK LTVDKSRWQQ 420
GNVFSCSVMH EALHNHYTQK SLSLSPKG 448

SEQ ID NO: 288      moltype = AA length = 218
FEATURE
source
1..218
mol_type = protein
organism = synthetic construct
SEQUENCE: 288
DIVMTQSPDS LAVSLGERAT INCRASKSVS TSGYSFMHWY QQKPGQPPKL LIYLASNLES 60
GVPDRFSGSG SGTDFTLTIS SLQAEDVAVY YCQHSREVPW TFGQGTKEI KRTVAAPSVF 120
IFPPSDEQLK SGTAWSVCLL NNFYPREAKV QWKVDNALQGS GNSQESVTEQ DSKDSTYSL 180
STLTLKADY EKKHVYACEV THQGLSSPVK KSFNRGEC 218

SEQ ID NO: 289      moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 289
NYGMN

SEQ ID NO: 290      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 290
WINTYTGEPT YTDDFKG 17

SEQ ID NO: 291      moltype = AA length = 12
FEATURE
source
1..12
mol_type = protein
organism = synthetic construct
SEQUENCE: 291

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GGFGSSYWYF DV	12
SEQ ID NO: 292 FEATURE source	moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct
SEQUENCE: 292 KASQDVSIAV A	11
SEQ ID NO: 293 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct
SEQUENCE: 293 SASYRYT	7
SEQ ID NO: 294 FEATURE source	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct
SEQUENCE: 294 QQHYITPLT	9
SEQ ID NO: 295 FEATURE source	moltype = AA length = 121 Location/Qualifiers 1..121 mol_type = protein organism = synthetic construct
SEQUENCE: 295 QVQLQQSGSE LKKPGASVKV SCKASGYTFT NYGMNWKQKA PGQGLKWMGW INTYTGEPTY TDDFKGRFAF SLDTSVSTAY LQISSLKADD TAVYFCARGG FGSSYWFDV WGQGSLVTVS S	60 120 121
SEQ ID NO: 296 FEATURE source	moltype = AA length = 107 Location/Qualifiers 1..107 mol_type = protein organism = synthetic construct
SEQUENCE: 296 DIQLTQSPSS LSASVGDRVS ITCKASQDVS IAVAWYQQKP GKAPKLLIYS ASYRYTGVPD RFSGSGSGSTD FTLTISSLQP EDFAVYYCQQ HYITPLTFGA GTKVEIK	60 107
SEQ ID NO: 297 FEATURE source	moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct
SEQUENCE: 297 TAGMQ	5
SEQ ID NO: 298 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct
SEQUENCE: 298 WINTHSGVPK YAEDFKG	17
SEQ ID NO: 299 FEATURE source	moltype = AA length = 12 Location/Qualifiers 1..12 mol_type = protein organism = synthetic construct
SEQUENCE: 299 SGFGSSYWYF DV	12
SEQ ID NO: 300 FEATURE source	moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct
SEQUENCE: 300 KASQDVSTAV A	11

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SEQ ID NO: 301	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 301	
SASRYRT	7
SEQ ID NO: 302	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 302	
QQHYITPLT	9
SEQ ID NO: 303	moltype = AA length = 121
FEATURE	Location/Qualifiers
source	1..121
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 303	
QVQLVQSGAE VKKPGASVKV SCKASGYTFT TAGMQWVRQA PGQGLEWMGW INTHSGVPKY 60	
AEDFKGRVTI SADTSTSTAY LQLSSLKSED TAVYYCARSQ FGSSYWFDV WGQGTLVTVS 120	
S	121
SEQ ID NO: 304	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 304	
DIQMTQSPSS LSASVGDRVT ITCKASQDVS TAVAQYQQKP GKAPKLLIYS ASYRYTGVP 60	
RFSGSGSGTD FTLTISLQP EDFAVYYCQQ HYITPLTFQG GTKLEIK 107	
SEQ ID NO: 305	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 305	
SQNIY	5
SEQ ID NO: 306	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 306	
YIEPYNVVPM YNPKFKG	17
SEQ ID NO: 307	moltype = AA length = 8
FEATURE	Location/Qualifiers
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 307	
SGSSNFDY	8
SEQ ID NO: 308	moltype = AA length = 12
FEATURE	Location/Qualifiers
source	1..12
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 308	
SASSSISSHY LH	12
SEQ ID NO: 309	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 309	
RTSNLAS	7

-continued

SEQ ID NO: 310	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 310	
QQGSSLPLT	9
SEQ ID NO: 311	moltype = AA length = 117
FEATURE	Location/Qualifiers
source	1..117
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 311	
EIQLVQSGAE VKKPGASVKV SCKASGYAFT SQNIYWVRQA PGQGLEWIGY IEPYNVVPMY	60
NPKFKGRATL TVDKSTSTAY LELESSLRSED TAVYYCARSQ SSNFDYWQG TLVTVSS	117
SEQ ID NO: 312	moltype = AA length = 108
FEATURE	Location/Qualifiers
source	1..108
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 312	
DIQLTQSPSS LSASVGDRVT ITCSASSIS SHYLHWYQQK PGKSPKLLIY RTSNLASGVP	60
SRFSGSGSGT DYTLTISSLQ PEDFATYYCQ QGSSLPLTFG QGTKVEIK	108
SEQ ID NO: 313	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 313	
NYAMH	5
SEQ ID NO: 314	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 314	
LIWYDGSNKF YGDGVKG	17
SEQ ID NO: 315	moltype = AA length = 6
FEATURE	Location/Qualifiers
source	1..6
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 315	
EGSGHY	6
SEQ ID NO: 316	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 316	
RASQGISSAL A	11
SEQ ID NO: 317	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 317	
DASSLES	7
SEQ ID NO: 318	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 318	
QQFNSYPIT	9
SEQ ID NO: 319	moltype = AA length = 115
FEATURE	Location/Qualifiers

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source          1..115
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 319
QVQLVESGGG VVQPGRSLRL SCAASGFTFS NYAMHWVRQA PGEGLEWVAL IWYDGSNKFY 60
GDSVKGRFTI SRDNSKNTLY LQMNSLSAED TAVYYCAREG SGHYWGQGTL VTVSS      115

SEQ ID NO: 320      moltype = AA length = 107
FEATURE           Location/Qualifiers
source            1..107
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 320
AQLTQSPSS LSASVGDRVT ITCRASQGIS SALAWYQQKP GKVPKSLIYD ASSLESGVPS 60
RFGSGSGSTD FTLTISLQP EDFATYYCQQ FNSYPITFGQ GTRLEIK                107

SEQ ID NO: 321      moltype = AA length = 5
FEATURE           Location/Qualifiers
source            1..5
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 321
NYAMS                                         5

SEQ ID NO: 322      moltype = AA length = 17
FEATURE           Location/Qualifiers
source            1..17
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 322
YISPGGDYIY YADSVKG                                         17

SEQ ID NO: 323      moltype = AA length = 12
FEATURE           Location/Qualifiers
source            1..12
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 323
DRRHGYSYAM DY                                         12

SEQ ID NO: 324      moltype = AA length = 16
FEATURE           Location/Qualifiers
source            1..16
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 324
RSSKSLLHSN LNTYLY                                         16

SEQ ID NO: 325      moltype = AA length = 7
FEATURE           Location/Qualifiers
source            1..7
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 325
RMSNLAS                                         7

SEQ ID NO: 326      moltype = AA length = 9
FEATURE           Location/Qualifiers
source            1..9
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 326
MQHLEYPFT                                         9

SEQ ID NO: 327      moltype = AA length = 121
FEATURE           Location/Qualifiers
source            1..121
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 327
QVQLVESGGG LVKPGGSLRL SCAASGFTFS NYAMSWIRQA PGKGLEWVSY ISPGGDYIYY 60
ADSVKGRFTI SRDNNAKNSLY LQMNSLRAED TAVYYCTTDR RHYGYSYAMDY WGQGTLVTVS 120
S                                         121

SEQ ID NO: 328      moltype = AA length = 112
FEATURE           Location/Qualifiers

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source          1..112
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 328
DIVMTQSPLS LPVTPGEPAS ISCRSSKSLL HSNLNNTLYW FLQKPGQSPQ ILIYRMSNLA 60
SGVPDRFSGS GSGTAAFTLKI SRVEAEDVGV YYCMQHLEYP FTFGPGTKLE IK           112

SEQ ID NO: 329      moltype = AA length = 5
FEATURE
source          1..5
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 329
TYAFH                                         5

SEQ ID NO: 330      moltype = AA length = 17
FEATURE
source          1..17
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 330
GIVPIFGTLK YAQKFQD                                         17

SEQ ID NO: 331      moltype = AA length = 11
FEATURE
source          1..11
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 331
AIQLEGRPF D H                                         11

SEQ ID NO: 332      moltype = AA length = 11
FEATURE
source          1..11
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 332
RASQGITSYL A                                         11

SEQ ID NO: 333      moltype = AA length = 7
FEATURE
source          1..7
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 333
AASALQS                                         7

SEQ ID NO: 334      moltype = AA length = 10
FEATURE
source          1..10
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 334
QQVNRGAAIT                                         10

SEQ ID NO: 335      moltype = AA length = 120
FEATURE
source          1..120
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 335
QVQLVQSGAE VKKPGSSVRV SCRASGGSST TYAFHWRQQA PGQGLEWMGG IVPIFGTLKY 60
AQKFQDRVT L TADKSTGTAY MELNSLRDD TAVYYCARAI QLEGGRPF DHW GQGTQVTVSA 120

SEQ ID NO: 336      moltype = AA length = 108
FEATURE
source          1..108
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 336
DIQLTQSPSF LSASAVGDRVT ITCRASQGIT SYLAWYQQKP GKAPKLLIYA ASALQSGVPS 60
RFSGRGSGTE FTLTISLQP EDFATYYCQQ VNRGAAITFG HGTRLDIK           108

SEQ ID NO: 337      moltype = AA length = 5
FEATURE
source          1..5
               mol_type = protein
               organism = synthetic construct

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-continued

SEQUENCE: 337 RYTMH	mol_type = protein organism = synthetic construct	
		5
SEQ ID NO: 338 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17	
SEQUENCE: 338 VISFDGSNKY YVDSVKKG	mol_type = protein organism = synthetic construct	
		17
SEQ ID NO: 339 FEATURE source	moltype = AA length = 10 Location/Qualifiers 1..10	
SEQUENCE: 339 EARGSYAFDI	mol_type = protein organism = synthetic construct	
		10
SEQ ID NO: 340 FEATURE source	moltype = AA length = 11 Location/Qualifiers 1..11	
SEQUENCE: 340 RASQSVSSYL A	mol_type = protein organism = synthetic construct	
		11
SEQ ID NO: 341 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7	
SEQUENCE: 341 DASN RAT	mol_type = protein organism = synthetic construct	
		7
SEQ ID NO: 342 FEATURE source	moltype = AA length = 10 Location/Qualifiers 1..10	
SEQUENCE: 342 QQRSNWPPFT	mol_type = protein organism = synthetic construct	
		10
SEQ ID NO: 343 FEATURE source	moltype = AA length = 119 Location/Qualifiers 1..119	
SEQUENCE: 343 QVQLVESGG VVQPGRSRL SCAASGFTFS RYTMHWVRQA PGKGLEWAV IFSDGSNKYY 60 VDSVKGRFTI SRDNSENTLY LQVNILRAED TAVYYCAREA RGSYAFDIWG QGTMVTVSS 119	mol_type = protein organism = synthetic construct	
SEQ ID NO: 344 FEATURE source	moltype = AA length = 108 Location/Qualifiers 1..108	
SEQUENCE: 344 EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD ASN RATGIPA 60 RFSGSGSGTD FTLTISLEP EDFAVYYCQQ RSNWPPFTFG PGTKVDIK 108	mol_type = protein organism = synthetic construct	
SEQ ID NO: 345 FEATURE source	moltype = AA length = 5 Location/Qualifiers 1..5	
SEQUENCE: 345 SFWMH	mol_type = protein organism = synthetic construct	
		5
SEQ ID NO: 346 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17	
SEQUENCE: 346 SFWMH	mol_type = protein organism = synthetic construct	

-continued

SEQUENCE: 346 YINPRSGYTE YNEIFRD	17
SEQ ID NO: 347 FEATURE source moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 347 FLGRGAMDY	9
SEQ ID NO: 348 FEATURE source moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct	
SEQUENCE: 348 RASQDISNLY A	11
SEQ ID NO: 349 FEATURE source moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 349 YTISKIHS	7
SEQ ID NO: 350 FEATURE source moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 350 QQGNTFPYPT	9
SEQ ID NO: 351 FEATURE source moltype = AA length = 118 Location/Qualifiers 1..118 mol_type = protein organism = synthetic construct	
SEQUENCE: 351 QVQLQQSGGE LAKPGASVKV SCKASGYTFS SFWMHWVRQA PGQGLEWIGY INPRSGYTEY NEIFRDKATM TTDSTSTAY MELSSLRSED TAVYYCASFL GRGAMDYWGQ GTTVTVSS	60 118
SEQ ID NO: 352 FEATURE source moltype = AA length = 107 Location/Qualifiers 1..107 mol_type = protein organism = synthetic construct	
SEQUENCE: 352 DIQMTQSPSS LSASVGDRVT ITCRASQDIS NYLAWYQQKP GKAPKLLIYY TSKIHSGVPS RFGSGSGSTD YTFTISSLQP EDIATYYCQQ GNTFPYTFGQ GTKVEIK	60 107
SEQ ID NO: 353 FEATURE source moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 353 TSSYYWG	7
SEQ ID NO: 354 FEATURE source moltype = AA length = 16 Location/Qualifiers 1..16 mol_type = protein organism = synthetic construct	
SEQUENCE: 354 TIYYNGSTYY SPSLKs	16
SEQ ID NO: 355 FEATURE source moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct	
SEQUENCE: 355 QGYDIKINID V	11

-continued

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SEQ ID NO: 356      moltype = AA  length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 356
RASQSVSSYL A                                11

SEQ ID NO: 357      moltype = AA  length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 357
VASNRAT                                         7

SEQ ID NO: 358      moltype = AA  length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 358
QQRSNWPLT                                9

SEQ ID NO: 359      moltype = AA  length = 121
FEATURE
source
1..121
mol_type = protein
organism = synthetic construct
SEQUENCE: 359
QLQLQESCPG LVKPSETLSL TCTVSGGSIS TSSYYWGIR QPPGKGLEWI GTIYNGSTY 60
YSPSLKSRVS ISVDTSKNQF SLKLSSVTA DTSVYYCARQ GYDIKINIDV WGQGTTVVS 120
S                                         121

SEQ ID NO: 360      moltype = AA  length = 107
FEATURE
source
1..107
mol_type = protein
organism = synthetic construct
SEQUENCE: 360
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYV ASN RATGIPA 60
RFSGSGSGTD FTLTISSLP EDFAVYYCQQ RSNWPLTFGG GTKVEIK                107

SEQ ID NO: 361      moltype = AA  length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 361
SSWMN                                         5

SEQ ID NO: 362      moltype = AA  length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 362
RIYPGDGNTH YAQKFQG                                17

SEQ ID NO: 363      moltype = AA  length = 8
FEATURE
source
1..8
mol_type = protein
organism = synthetic construct
SEQUENCE: 363
GYLDPMDY                                         8

SEQ ID NO: 364      moltype = AA  length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 364
QASQGINNYL N                                11

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-continued

SEQ ID NO: 365	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 365	
YTSGLHA	7
SEQ ID NO: 366	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 366	
QQYSILPWT	9
SEQ ID NO: 367	moltype = AA length = 117
FEATURE	Location/Qualifiers
source	1..117
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 367	
QVQLVQSGAE VKKPGSSVKV SCKASGYAFT SSWMNWVRQA PGQGLEWMGR IYPGDGNTHY 60	
AQKFQGRVTL TADKSTSTAY MELSSLRSED TAVYYCGEGY LDPMDYWGQG TLTVSS	117
SEQ ID NO: 368	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 368	
DIQMTQSPSS LSASVGDRVT ITCQASQGIN NYLNWYQQP GKAPKLLIHY TSGLHAGVPS 60	
RFSGSGSGTD YTTLTISSLEP EDVATYYCQQ YSILPWTFGG GTKVEIK	107
SEQ ID NO: 369	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 369	
SYGMH	5
SEQ ID NO: 370	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 370	
VISYDGDSNKY YADSVKG	17
SEQ ID NO: 371	moltype = AA length = 18
FEATURE	Location/Qualifiers
source	1..18
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 371	
DMGWGSGWRP YYYYGMDV	18
SEQ ID NO: 372	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 372	
RTSQSISSSYL N	11
SEQ ID NO: 373	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 373	
WASTRES	7
SEQ ID NO: 374	moltype = AA length = 9
FEATURE	Location/Qualifiers

-continued

source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 374		
QQSYDIPYT		9
SEQ ID NO: 375	moltype = AA length = 127	
FEATURE	Location/Qualifiers	
source	1..127	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 375		
EVQLLESGGG VVQPGRLSLRL SCAASGFTFS SYGMHWVRQA PGKGLEWVAV ISYDGSNKYY 60		
ADSVKGRFTI SRDNSKNLTY LQMNSLRAED TAVYYCAKDM GWGSGWRPYY YYGMDVWGQG 120		
TTTVVSS		127
SEQ ID NO: 376	moltype = AA length = 107	
FEATURE	Location/Qualifiers	
source	1..107	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 376		
ELQMTQSPSS LSASVGDRVT ITCRTSQSIS SYLNWYQQKP GQPPKLLIYW ASTRESGVPD 60		
RFSGSGSGTD FTLTISSSLQP EDSATYYCQQ SYDIPYTFGQ GTKLEIK		107
SEQ ID NO: 377	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 377		
NYWMS		5
SEQ ID NO: 378	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 378		
NIKQDGSEKF YADSVKG		17
SEQ ID NO: 379	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 379		
VGPSWEQDY		9
SEQ ID NO: 380	moltype = AA length = 14	
FEATURE	Location/Qualifiers	
source	1..14	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 380		
TGSSSNIGSY YGVH		14
SEQ ID NO: 381	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 381		
SDTNRPS		7
SEQ ID NO: 382	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 382		
QSYDKGFGHR V		11
SEQ ID NO: 383	moltype = AA length = 118	
FEATURE	Location/Qualifiers	
source	1..118	

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mol_type = protein
organism = synthetic construct
SEQUENCE: 383
EVOLVESGGG LVQPGGSLRL SCAASGFTFS NYWMSWVRQA PGKGLEWVAN IKQDGSEKFY 60
ADSVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCARVG PSWEQDYWGQ GTLTVSA 118

SEQ ID NO: 384      moltype = AA length = 111
FEATURE
source
1..111
mol_type = protein
organism = synthetic construct
SEQUENCE: 384
QSVLTQPPSV SGAPGQRVTI SCTGSSSNIG SYYGVHWYQQ LPGTAPKLLI YSDTNRPSGV 60
PDRFSGSKSG TSASLAITGL QAEDEADYYC QSYDKGFGHR VFGGGTKLTV L 111

SEQ ID NO: 385      moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 385
SYAIS 5

SEQ ID NO: 386      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 386
GIIPIFGTAN YAQKFQG 17

SEQ ID NO: 387      moltype = AA length = 6
FEATURE
source
1..6
mol_type = protein
organism = synthetic construct
SEQUENCE: 387
GLLWNY 6

SEQ ID NO: 388      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 388
RASQSVSSNL A 11

SEQ ID NO: 389      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 389
GASTTAS 7

SEQ ID NO: 390      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 390
QQYNNWPPAY T 11

SEQ ID NO: 391      moltype = AA length = 115
FEATURE
source
1..115
mol_type = protein
organism = synthetic construct
SEQUENCE: 391
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPIFGTANY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARGL LWNYWGGTTL VTVSS 115

SEQ ID NO: 392      moltype = AA length = 109
FEATURE
source
1..109
mol_type = protein

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SEQUENCE: 392          organism = synthetic construct
EIVMTQSPAT LSVSPGERAT LSCRASQSVS SNLAWYQQKQ GQAPRLIIYG ASTTASGIPA 60
RFSASGSGTD FTLTISSLQS EDFAVYYCQQ YNNWPPAYTF QQGTTKLEIK           109

SEQ ID NO: 393          moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct

SEQUENCE: 393
NYGMN                                         5

SEQ ID NO: 394          moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct

SEQUENCE: 394
WINTYTGEPT YGEDFKG                                         17

SEQ ID NO: 395          moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 395
FGNYVDY                                         7

SEQ ID NO: 396          moltype = AA length = 16
FEATURE
source
1..16
mol_type = protein
organism = synthetic construct

SEQUENCE: 396
RSSKNLLHSN GITLY                                         16

SEQ ID NO: 397          moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 397
QMSNLAS                                         7

SEQ ID NO: 398          moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 398
AQNLLEIPRT                                         9

SEQ ID NO: 399          moltype = AA length = 116
FEATURE
source
1..116
mol_type = protein
organism = synthetic construct

SEQUENCE: 399
QVQLVQSGPE VKKPGASVKV SCKASGYTFT NYGMNWVRQA PGQGLEWMGW INTYTGEPTY 60
GEDFKGRFAF SLDTSASTAY MELSSLRSED TAVYFCARFG NYVDYWGQGS LVTVSS           116

SEQ ID NO: 400          moltype = AA length = 112
FEATURE
source
1..112
mol_type = protein
organism = synthetic construct

SEQUENCE: 400
DIVMTQSPPLS LPVTPGEPAS ISCRSSKNLL HSNGITYLYW YLQKPGQSPQ LLIYQMSNLA 60
SGVPDRFSSS GSGTDFTLKI SRVEAEDVGV YYCAQNLLEIP RTFGQGTTKVE IK           112

SEQ ID NO: 401          moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct

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-continued

SEQUENCE: 401	KYGMN	5
SEQ ID NO: 402	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 402	WINTYTEEPT YGDDFKG	17
SEQ ID NO: 403	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 403	FGSAVDY	7
SEQ ID NO: 404	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
source	1..16	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 404	RSSKSLLHSN GITYLY	16
SEQ ID NO: 405	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 405	QMSNRAS	7
SEQ ID NO: 406	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 406	AQNLELPRT	9
SEQ ID NO: 407	moltype = AA length = 116	
FEATURE	Location/Qualifiers	
source	1..116	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 407	QIQLVQSGPE VKKPGESVKI SCKASGYTFT KYGMNWVKQA PGQGLKWMGW INTYTEEPTY	60
	GDDFKGRFTF TLDTSTSTAY LEISSLRSED TATYFCARFG SAVDYWGQGT LVTVSS	116
SEQ ID NO: 408	moltype = AA length = 113	
FEATURE	Location/Qualifiers	
source	1..113	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 408	DIVMTQALS NPVTLGESGS ISCRSSKSLL HSNHGITYLYW YLQKPGQSPQ LLIYQMSNRA	60
	SGVPDRFSSS GSGTDFTLKI SRVEAEDVGV YYCAQNLLELP RTFGQQGKLE MKR	113
SEQ ID NO: 409	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 409	DYSMH	5
SEQ ID NO: 410	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 410	WINTETGEPT YADDFKG	17

-continued

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SEQ ID NO: 411      moltype = AA  length = 4
FEATURE
source
1..4
mol_type = protein
organism = synthetic construct
SEQUENCE: 411
TAVY                                         4

SEQ ID NO: 412      moltype = AA  length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 412
RASQEISVSL S                                         11

SEQ ID NO: 413      moltype = AA  length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 413
ATSTLDS                                         7

SEQ ID NO: 414      moltype = AA  length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 414
LQYASYPWT                                         9

SEQ ID NO: 415      moltype = AA  length = 113
FEATURE
source
1..113
mol_type = protein
organism = synthetic construct
SEQUENCE: 415
QVKLQESGPE LKKPGETVKI SCKASGYTFT DYSMHWVKQA PGKGLKWMGW INTETGEPTY  60
ADDFKGRFAF SLETSASTAY LQINNLKNED TATYFCARTA VYWGQGTTVT VSS          113

SEQ ID NO: 416      moltype = AA  length = 108
FEATURE
source
1..108
mol_type = protein
organism = synthetic construct
SEQUENCE: 416
DIQMTQSPSS LSASLGERVS LTCRASQEIS VSLSWLQQEP DGTIKRLIYA TSTLDGVPK  60
RFGSGSRSGSD YSLTISSLES EDFVVDYYCLQ YASYPWTFGG GTKLEIKR          108

SEQ ID NO: 417      moltype = AA  length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 417
NYGMN                                         5

SEQ ID NO: 418      moltype = AA  length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 418
WINTYSGEPR YADDFKG                                         17

SEQ ID NO: 419      moltype = AA  length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 419
DYGRWYFDV                                         9

SEQ ID NO: 420      moltype = AA  length = 10

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-continued

FEATURE source	Location/Qualifiers 1..10 mol_type = protein organism = synthetic construct	
SEQUENCE: 420 RASSSVSHMH		10
SEQ ID NO: 421	moltype = AA length = 7	
FEATURE source	Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 421 ATSNLAS		7
SEQ ID NO: 422	moltype = AA length = 9	
FEATURE source	Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 422 QQWSSTPRT		9
SEQ ID NO: 423	moltype = AA length = 118	
FEATURE source	Location/Qualifiers 1..118 mol_type = protein organism = synthetic construct	
SEQUENCE: 423 QIQLVQSGSE LKKPGASVKV SCKASGYTFT NYGMNWWVRQA PGQDLKWMGW INTYSGEPRY 60 ADDFKGRFVF SLDKSVNTAY LQISSLKAED TAVYYCARDY GRWYFDVWGQ GTTVTVSS 118		
SEQ ID NO: 424	moltype = AA length = 107	
FEATURE source	Location/Qualifiers 1..107 mol_type = protein organism = synthetic construct	
SEQUENCE: 424 QIVLSQSPAT LSLSPGERAT MSCRASSSVS HMHWYQQKPG QAPRPWIYAT SNLASGVPAR 60 FSGSGSGTDY TLTISSLEPE DFAVYYCQW SSTPRTFGGG TKVEIKR 107		
SEQ ID NO: 425	moltype = AA length = 5	
FEATURE source	Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct	
SEQUENCE: 425 RYWMS		5
SEQ ID NO: 426	moltype = AA length = 17	
FEATURE source	Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 426 EINPDSSTIN YAPSLKD		17
SEQ ID NO: 427	moltype = AA length = 10	
FEATURE source	Location/Qualifiers 1..10 mol_type = protein organism = synthetic construct	
SEQUENCE: 427 PDGNWYFDV		10
SEQ ID NO: 428	moltype = AA length = 11	
FEATURE source	Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct	
SEQUENCE: 428 KASQDVGIAV A		11
SEQ ID NO: 429	moltype = AA length = 7	
FEATURE source	Location/Qualifiers 1..7	

-continued

SEQUENCE: 429 WASTRHT	mol_type = protein organism = synthetic construct	
		7
SEQ ID NO: 430 FEATURE source	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 430 QQYSSYPYT		9
SEQ ID NO: 431 FEATURE source	moltype = AA length = 119 Location/Qualifiers 1..119 mol_type = protein organism = synthetic construct	
SEQUENCE: 431 EVOLVESGGG LVQPGGSLRL SCAASGFDFS RYWMSWVRQA PGKGLEWIGE INPDSSTINY 60 APSLKDKFII SRDNAKNSLY LQMNSLRAED TAVYYCARPD GNYWYFDVWG QGTLTVSS 119		
SEQ ID NO: 432 FEATURE source	moltype = AA length = 108 Location/Qualifiers 1..108 mol_type = protein organism = synthetic construct	
SEQUENCE: 432 DIQMTQSPSS LSASVGDRVT ITCKASQDVG IAVAWYQQKPK GKVPKLLIYW ASTRHTGVPD 60 RFGSGSGSTD FTLTISSSLQP EDVATYYCQQ YSSYPYTFGQ GTKVEIKR 108		
SEQ ID NO: 433 FEATURE source	moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct	
SEQUENCE: 433 SFAMS		5
SEQ ID NO: 434 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 434 AISGSGGGTY YADSVKG		17
SEQ ID NO: 435 FEATURE source	moltype = AA length = 13 Location/Qualifiers 1..13 mol_type = protein organism = synthetic construct	
SEQUENCE: 435 DKILWFGEPV FDY		13
SEQ ID NO: 436 FEATURE source	moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct	
SEQUENCE: 436 RASQSVSSYL A		11
SEQ ID NO: 437 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 437 DASN RAT		7
SEQ ID NO: 438 FEATURE source	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	

-continued

SEQUENCE: 438		
QQRSNWPPT		9
SEQ ID NO: 439	moltype = AA length = 122	
FEATURE	Location/Qualifiers	
source	1..122	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 439		
EVOLLESGGG LVQPGGSSLRL SCAVSGFTFN SFAMSWVRQA PGKGLEWVSA ISGSGGGTYY 60		
ADSVKGRTI SRDNSKNLTY LQMNSLRAED TAVYFCAKDK ILWFGEPVFD YWGQGTLVTV 120		
SS	122	
SEQ ID NO: 440	moltype = AA length = 108	
FEATURE	Location/Qualifiers	
source	1..108	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 440		
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD ASN RATGIPA 60		
RFSGSGSGTD FTLTISSLP EDFAVYYCQQ RSNWPPTFGQ GTKVEIKR		108
SEQ ID NO: 441	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 441		
SYRMH		5
SEQ ID NO: 442	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 442		
YINPSTGYTE YNQKFKD		17
SEQ ID NO: 443	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 443		
GGGVFDY		7
SEQ ID NO: 444	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 444		
SASSSISYMH		10
SEQ ID NO: 445	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 445		
TTSNLAS		7
SEQ ID NO: 446	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 446		
HQRSTYPLT		9
SEQ ID NO: 447	moltype = AA length = 116	
FEATURE	Location/Qualifiers	
source	1..116	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 447		

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QVQLVQSGAE VKPGSSVKV SCKASGYTFT SYRMHWVRQA PGQGLEWIGY INPSTGYTEY NQKFKDKATI TADESTNTAY MELSSLRSED TAVYYCARGG GVFDYWGQGT LTVSS	60 116
<hr/>	
SEQ ID NO: 448 FEATURE source SEQUENCE: 448 DIQMTQSPST LSASVGDRVT ITCSASSSIS YMHWYQQKPG KAPKLLIYTT SNLASGVPAR FSGSGSGTEF TLTISSLQPD DFATYYCHQR STYPLTFGQG TKVEVK	moltype = AA length = 106 Location/Qualifiers 1..106 mol_type = protein organism = synthetic construct moltype = AA length = 106 Location/Qualifiers 1..106
<hr/>	
SEQ ID NO: 449 FEATURE source SEQUENCE: 449 SYWMH	moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct moltype = AA length = 5 Location/Qualifiers 1..5
<hr/>	
SEQ ID NO: 450 FEATURE source SEQUENCE: 450 EIIPINGHTN YNEKFKS	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct moltype = AA length = 17 Location/Qualifiers 1..17
<hr/>	
SEQ ID NO: 451 FEATURE source SEQUENCE: 451 GGYYYYGSRD YFDY	moltype = AA length = 14 Location/Qualifiers 1..14 mol_type = protein organism = synthetic construct moltype = AA length = 14 Location/Qualifiers 1..14
<hr/>	
SEQ ID NO: 452 FEATURE source SEQUENCE: 452 KASQSVDYDG DSYMN	moltype = AA length = 15 Location/Qualifiers 1..15 mol_type = protein organism = synthetic construct moltype = AA length = 15 Location/Qualifiers 1..15
<hr/>	
SEQ ID NO: 453 FEATURE source SEQUENCE: 453 AASDLES	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct moltype = AA length = 7 Location/Qualifiers 1..7
<hr/>	
SEQ ID NO: 454 FEATURE source SEQUENCE: 454 QQSHEDPFT	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct moltype = AA length = 9 Location/Qualifiers 1..9
<hr/>	
SEQ ID NO: 455 FEATURE source SEQUENCE: 455 QVQLQQGAE LVKGASVKL SCKASGYTFT SYWMHWVKQR PGQGLEWIGE IIPINGHTNY NEKFKSKATL TLDKSSSTAY MQLSSLASED SAVYYCARGG YYYYGSRDYF DYWGQGTTLT VSS	60 120 123 moltype = AA length = 123 Location/Qualifiers 1..123 mol_type = protein organism = synthetic construct moltype = AA length = 123 Location/Qualifiers 1..123
<hr/>	
SEQ ID NO: 456 FEATURE source SEQUENCE: 456	moltype = AA length = 111 Location/Qualifiers 1..111 mol_type = protein organism = synthetic construct

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DIVLTQSPAS	LAVSLGQRAT	ISCKASQSVD	YDGDSYMNWY	QQIPGQPPKL	LIYAASDLES	60
GIPARFSGSG	SGTDFTLNIH	PVEEDAATY	YCQQSHEDPF	TFGGGTKLEI	K	111
SEQ ID NO: 457		moltype = AA	length = 5			
FEATURE		Location/Qualifiers				
source		1..5				
		mol_type = protein				
		organism = synthetic construct				
SEQUENCE: 457						
SWMH						5
SEQ ID NO: 458		moltype = AA	length = 17			
FEATURE		Location/Qualifiers				
source		1..17				
		mol_type = protein				
		organism = synthetic construct				
SEQUENCE: 458						
EIIPIFGHTN	YNEKFKS					17
SEQ ID NO: 459		moltype = AA	length = 14			
FEATURE		Location/Qualifiers				
source		1..14				
		mol_type = protein				
		organism = synthetic construct				
SEQUENCE: 459						
GGYYYYPRQG	FLDY					14
SEQ ID NO: 460		moltype = AA	length = 15			
FEATURE		Location/Qualifiers				
source		1..15				
		mol_type = protein				
		organism = synthetic construct				
SEQUENCE: 460						
KASQSVVDYSG	DSYMN					15
SEQ ID NO: 461		moltype = AA	length = 7			
FEATURE		Location/Qualifiers				
source		1..7				
		mol_type = protein				
		organism = synthetic construct				
SEQUENCE: 461						
AASDLES						7
SEQ ID NO: 462		moltype = AA	length = 9			
FEATURE		Location/Qualifiers				
source		1..9				
		mol_type = protein				
		organism = synthetic construct				
SEQUENCE: 462						
QQSHEDPFT						9
SEQ ID NO: 463		moltype = AA	length = 123			
FEATURE		Location/Qualifiers				
source		1..123				
		mol_type = protein				
		organism = synthetic construct				
SEQUENCE: 463						
EVQLVESGGG	LVKPGGSLRL	SCAASGFTFS	SYWMHWVRQA	PGKGLEWVGE	IIPIFGHTNY	60
NEKFKSRFTI	SLDNSKNLTY	LQMGSLRAED	TAVYYCARGG	YYYYPRQGFL	DYWGQGTTVT	120
VSS						123
SEQ ID NO: 464		moltype = AA	length = 111			
FEATURE		Location/Qualifiers				
source		1..111				
		mol_type = protein				
		organism = synthetic construct				
SEQUENCE: 464						
DIVMTQSPDS	LAVSLGERAT	ISCKASQSVD	YSGDSYMNWY	QQKPGQPPKL	LIYAASDLES	60
GIPARFSGSG	SGTDFTLTIS	SLEPEDFATY	YCQQSHEDPF	TFGQGTTVT	K	111
SEQ ID NO: 465		moltype = AA	length = 5			
FEATURE		Location/Qualifiers				
source		1..5				
		mol_type = protein				
		organism = synthetic construct				
SEQUENCE: 465						

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SYGMN	5
SEQ ID NO: 466 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct
SEQUENCE: 466 YISSLSSSTIY YADSVKG	17
SEQ ID NO: 467 FEATURE source	moltype = AA length = 6 Location/Qualifiers 1..6 mol_type = protein organism = synthetic construct
SEQUENCE: 467 GPGMDV	6
SEQ ID NO: 468 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct
SEQUENCE: 468 KSSQSVLYY NNKNYLA	17
SEQ ID NO: 469 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct
SEQUENCE: 469 WASTRES	7
SEQ ID NO: 470 FEATURE source	moltype = AA length = 10 Location/Qualifiers 1..10 mol_type = protein organism = synthetic construct
SEQUENCE: 470 QQYYSTPQLT	10
SEQ ID NO: 471 FEATURE source	moltype = AA length = 114 Location/Qualifiers 1..114 mol_type = protein organism = synthetic construct
SEQUENCE: 471 QVOLQQSGGG VVQPGRSLGL SCAASGFTFS SYGMNNWVRQA PGKGLEWVSY ISSSSSTIYY 60 ADSVVKGRFTI SRDNSKNLTY LQMNSLRAED TAVYYCARGP GMDVWGQGTT VTVS 114	
SEQ ID NO: 472 FEATURE source	moltype = AA length = 114 Location/Qualifiers 1..114 mol_type = protein organism = synthetic construct
SEQUENCE: 472 DIVLTQSPDS LAVSLGERAT INCKSSQSVL YSSNNKNYLA WYQQKPGQPP KLLIYWASTR 60 ESGVPDRFSG SGSGTDFTPA ISSLQAEDVA VYYCQQYYST PQLTFGGGTK VDIK 114	
SEQ ID NO: 473 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct
SEQUENCE: 473 TSGMGVG	7
SEQ ID NO: 474 FEATURE source	moltype = AA length = 16 Location/Qualifiers 1..16 mol_type = protein organism = synthetic construct
SEQUENCE: 474 HIWWDDDKRY NPALKS	16

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SEQ ID NO: 475	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 475	
MELWSYYFDY	10
SEQ ID NO: 476	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 476	
SASSSVSYMH	10
SEQ ID NO: 477	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 477	
DTSKLAS	7
SEQ ID NO: 478	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 478	
FQGSVYPFT	9
SEQ ID NO: 479	moltype = AA length = 120
FEATURE	Location/Qualifiers
source	1..120
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 479	
QVQLQESGPG LVKPSQTL SL TCTVSGGSIS TSGMGVGWIR QHPGKGLEWI GHIWWDDDKR 60	
YNPALKSRVT ISVDTSKNQF SLKLSSVTAA DTAVYYCARM ELWSYYFDYW GQGTLTVSS 120	
SEQ ID NO: 480	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 480	
EIVLTQSPAT LSLSPGERAT LSCSASSSVS YMHWYQQKPG QAPRLLIYDT SKLASGIPAR 60	
FSGSGSGTDF TLTIISSLEPE DVAVYYCFQG SVYPFTFCQG TKLEIKRVA 107	
SEQ ID NO: 481	moltype = AA length = 450
FEATURE	Location/Qualifiers
source	1..450
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 481	
QVQLQESGPG LVKPSQTL SL TCTVSGGSIS TSGMGVGWIR QHPGKGLEWI GHIWWDDDKR 60	
YNPALKSRVT ISVDTSKNQF SLKLSSVTAA DTAVYYCARM ELWSYYFDYW GQGTLTVSS 120	
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYPPEPVTVS WNSGALTSGV HTFPAVLQSS 180	
GLYSLSSVVT VPSSSLGTQT YICCNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG 240	
PSVFLFPPKP KDTLMISRTP EVTCVVVVDVS HEDPEVKFNM VYDGVDEVHNA KTKPREEQYN 300	
STYRWSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIIS KAKGQPREPQ VYTLPPSDE 360	
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSSFLY SKLTVDKSRW 420	
QQGNVFSCSV MHEALHNHYT QKSLSLSPGK 450	
SEQ ID NO: 482	moltype = AA length = 213
FEATURE	Location/Qualifiers
source	1..213
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 482	
EIVLTQSPAT LSLSPGERAT LSCSASSSVS YMHWYQQKPG QAPRLLIYDT SKLASGIPAR 60	
FSGSGSGTDF TLTIISSLEPE DVAVYYCFQG SVYPFTFCQG TKLEIKRVA APSVIFPPS 120	
DEQLKSGTAS VVCLLNNFYP REAKVQWKVD NALQSGNSQE SVTEQDSKDS TYSLSTLTL 180	
SKADYEKHVK YACEVTHQGL SSPVTKSFNR GEC 213	

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SEQ ID NO: 483	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 483	
NYWIE	5
SEQ ID NO: 484	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 484	
EILPGTGRTI YNEKFKG	17
SEQ ID NO: 485	moltype = AA length = 13
FEATURE	Location/Qualifiers
source	1..13
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 485	
RDYYGNFYAA MDY	13
SEQ ID NO: 486	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 486	
SASQGINNYL N	11
SEQ ID NO: 487	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 487	
YTSTLQS	7
SEQ ID NO: 488	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 488	
QQYSKLPRT	9
SEQ ID NO: 489	moltype = AA length = 122
FEATURE	Location/Qualifiers
source	1..122
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 489	
QVQLQQSGSE LMMPGASVKI SCKATGYTFS NYWIEWVKQR PGHGLEWIGE ILPGTGRTIY	60
NEKFKGKATF TADISSNTVQ MQLSSLTSED SAVYYCARRD YYGNFYAMD YWGQGTSVT	120
SS	122
SEQ ID NO: 490	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 490	
DIQMTQSTSS LSASLGDRVT ISCSASQGIN NYLNWYQQKP DGTVELLIYY TSTLQSGVPS	60
RFSGSGSGTD YSLTISNLEP EDIGTYYCQQ YSKLPRTFGG GTKLEIK	107
SEQ ID NO: 491	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 491	
TYGMGVG	7
SEQ ID NO: 492	moltype = AA length = 16

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FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 492	
NIWWSEDKHY SPSLKS	16
SEQ ID NO: 493	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 493	
IDYGNDYAFY Y	11
SEQ ID NO: 494	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 494	
RSSKSLLHSN GITYLY	16
SEQ ID NO: 495	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 495	
QMSNLAS	7
SEQ ID NO: 496	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 496	
AQNLELPYT	9
SEQ ID NO: 497	moltype = AA length = 121
FEATURE	Location/Qualifiers
source	1..121
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 497	
QITLKESGPT LVKPTQTLTL TCTFSGFSLS TYGMGVGWR QPPGKALEWL ANIWWSEDKH 60	
YSPSLKSRLT ITKDTSKNQV VLTITNVDPV DTATYYCVQI DYGNDYAFTY WGQQLTVVS 120	
S	121
SEQ ID NO: 498	moltype = AA length = 112
FEATURE	Location/Qualifiers
source	1..112
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 498	
DIVMTQSPLS LPVTPGEPAS ISCRSSKSLL HSNGITYLYW YLQKPGQSQPQ LLIYQMSNLA 60	
SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCAQNLELP YTFGQQGKLE IK 112	
SEQ ID NO: 499	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 499	
SFGMH	5
SEQ ID NO: 500	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 500	
YISSGGSFTIY YADSVKG	17
SEQ ID NO: 501	moltype = AA length = 9
FEATURE	Location/Qualifiers

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source	1..9		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 501			
MRKGYAMDY		9	
SEQ ID NO: 502	moltype = AA length = 16		
FEATURE	Location/Qualifiers		
source	1..16		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 502			
RSSQIIIHSD GNTYLE		16	
SEQ ID NO: 503	moltype = AA length = 7		
FEATURE	Location/Qualifiers		
source	1..7		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 503			
KVSNRFS		7	
SEQ ID NO: 504	moltype = AA length = 9		
FEATURE	Location/Qualifiers		
source	1..9		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 504			
FQGSHVPHT		9	
SEQ ID NO: 505	moltype = AA length = 118		
FEATURE	Location/Qualifiers		
source	1..118		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 505			
QVQLVESGGG VVQPGRSLRL SCAASGFTFS SFGMHWVRQA PGKGLEWVAY ISSGSFTIYY	60		
ADSVKGRTI SRDNSKNLTY LQMNSLRAED TAVYYCARMR KGYAMDYWGQ GTLTVSS	118		
SEQ ID NO: 506	moltype = AA length = 112		
FEATURE	Location/Qualifiers		
source	1..112		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 506			
DVVMTQSPLS LPVTLGQPAS ISCRSSQIII HSDGNTYLEW FQQRPGQSPR RLIYKVSNRF	60		
SGVPDRFSGS GSGTDFTLKI SRVEAEDEVGV YYCFQGSHVP HTFGQQTKVE IK	112		
SEQ ID NO: 507	moltype = AA length = 5		
FEATURE	Location/Qualifiers		
source	1..5		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 507			
NYGVN		5	
SEQ ID NO: 508	moltype = AA length = 17		
FEATURE	Location/Qualifiers		
source	1..17		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 508			
WINPNTGEPT FDDDFKG		17	
SEQ ID NO: 509	moltype = AA length = 11		
FEATURE	Location/Qualifiers		
source	1..11		
	mol_type = protein		
	organism = synthetic construct		
SEQUENCE: 509			
SRGKNEAWFA Y		11	
SEQ ID NO: 510	moltype = AA length = 16		
FEATURE	Location/Qualifiers		
source	1..16		
	mol_type = protein		

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SEQUENCE: 510 RSSQSLVHRN GNTYLN	organism = synthetic construct	
		16
SEQ ID NO: 511 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 511 TVSNRFS		7
SEQ ID NO: 512 FEATURE source	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 512 SQSSHVPPT		9
SEQ ID NO: 513 FEATURE source	moltype = AA length = 120 Location/Qualifiers 1..120 mol_type = protein organism = synthetic construct	
SEQUENCE: 513 QVQLQQSGSE LKKPGASVKV SCKASGYTFT NYGVNWIQQA PGQGLQWMGW INPNPNTGEPTF DIDDFKGRFAF SLDTSVSTAY LQISSLKADD TAVYFCRSR GKNEAWFAYW GQGTLVTVSS	60	120
SEQ ID NO: 514 FEATURE source	moltype = AA length = 112 Location/Qualifiers 1..112 mol_type = protein organism = synthetic construct	
SEQUENCE: 514 DIQLTQSPLS LPVTLGQPAS ISCRSSQSLV HRNGNTYLHW FQQRPGQSPR LLIYTVDNR SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YFCSSQSHVP PTFGAGTRLE IK	60	112
SEQ ID NO: 515 FEATURE source	moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct	
SEQUENCE: 515 TYWMS		5
SEQ ID NO: 516 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 516 EIHPDSTIN YAPSLKD		17
SEQ ID NO: 517 FEATURE source	moltype = AA length = 10 Location/Qualifiers 1..10 mol_type = protein organism = synthetic construct	
SEQUENCE: 517 LYFGFPWFAY		10
SEQ ID NO: 518 FEATURE source	moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct	
SEQUENCE: 518 KASQDVGTsv A		11
SEQ ID NO: 519 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 519		

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WTSTRHT	7
SEQ ID NO: 520	moltype = AA length = 8
FEATURE	Location/Qualifiers
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 520	
QQYSLYRS	8
SEQ ID NO: 521	moltype = AA length = 119
FEATURE	Location/Qualifiers
source	1..119
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 521	
EVQLVESGGG VVQPGRSLRL SCSASGFDFT TYWMSWVRQA PGKGLEWIGE IHPDSSTINY 60	
APSLKDRFTI SRDNAKNTLF LQMDSLRPED TGVYFCASLY FGFPWFAYWG QGTPVTVSS 119	
SEQ ID NO: 522	moltype = AA length = 106
FEATURE	Location/Qualifiers
source	1..106
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 522	
DIQLTQSPSS LSASVGDRVT ITCKASQDVG TSVAWYQQKP GKAPKLLIYW TSTRHTGVPS 60	
RGSGSGSGTD FTFTISSLQP EDIATYYCQQ YSLYRSFGQG TKVEIK 106	
SEQ ID NO: 523	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 523	
YYGMN	5
SEQ ID NO: 524	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 524	
WIDTTTGEPT YAQKFQG	17
SEQ ID NO: 525	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 525	
RGPYWNWYFDV	10
SEQ ID NO: 526	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 526	
RSSKSLLHSN GNTYLY	16
SEQ ID NO: 527	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 527	
RMSNLVS	7
SEQ ID NO: 528	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 528	
LQHLEYPFT	9

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SEQ ID NO: 529	moltype = AA length = 119
FEATURE	Location/Qualifiers
source	1..119
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 529	
QVQLVQSGAE VKKPGETVKI	SCKASDYTFT YYGMNWWVKQA PGQGLKWMGW IDTTTGEPTY 60
AQKFQGRIAF SLETSASTAY	LQIKSLKSED TATYFCARRG PYNWYFDVWG QGTTTVSS 119
SEQ ID NO: 530	moltype = AA length = 112
FEATURE	Location/Qualifiers
source	1..112
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 530	
DIVMTQSPLS VPVTPGEPVS	ISCRSSKSLL HSNGNTLYIW FLQRPGQSPQ LLIYRMSNLV 60
SGVPDRFSGS GSGTAFTLRI	SRVEAEDVGV YYCLQHLEYP FTFGPGTKLE LK 112
SEQ ID NO: 531	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 531	
NYGMN	5
SEQ ID NO: 532	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 532	
WINTYTGEPT YADDFKG	17
SEQ ID NO: 533	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 533	
IGDSSPSDY	9
SEQ ID NO: 534	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 534	
KASQSVSNNDV V	11
SEQ ID NO: 535	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 535	
YASNRYT	7
SEQ ID NO: 536	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 536	
QQDYTSPWT	9
SEQ ID NO: 537	moltype = AA length = 118
FEATURE	Location/Qualifiers
source	1..118
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 537	
QVQLVQSGAE VKKPGASVKV	SCKASGYTFT NYGMNWWVRQA PGQGLEWMGW INTYTGEPTY 60
ADDFKGRVTM TTDTSTSTAY	MELRSLSRSD TAVYYCARIG DSSPSDYWGQ GTLVTVSS 118
SEQ ID NO: 538	moltype = AA length = 107

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FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 538	
EIVMTQSPAT LSVSPGERAT LSCKASQSVS NDVWYQQKP GQAPRLLIYY ASNRYTGIPA	60
RFSGSGSGTE FTLTSSLQS EDFAVYYCQQ DYTSPWTFQG GTKLEIK	107
SEQ ID NO: 539	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 539	
SYWIE	5
SEQ ID NO: 540	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 540	
EILPGSGNTY YNERFKD	17
SEQ ID NO: 541	moltype = AA length = 14
FEATURE	Location/Qualifiers
source	1..14
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 541	
RAAAAYYSNPE WFAY	14
SEQ ID NO: 542	moltype = AA length = 12
FEATURE	Location/Qualifiers
source	1..12
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 542	
TASSSVNSFY LH	12
SEQ ID NO: 543	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 543	
STSNLAS	7
SEQ ID NO: 544	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 544	
HQYHRSPYT	9
SEQ ID NO: 545	moltype = AA length = 123
FEATURE	Location/Qualifiers
source	1..123
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 545	
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYWIEWVRQA PGQGLEWMGE ILPGSGNTYY	60
NERFKDRVTI TADESTSTAY MELSSLRSED TAVYYCARA AAYYSNPEWF AYWGQQTLVT	120
VSS	123
SEQ ID NO: 546	moltype = AA length = 108
FEATURE	Location/Qualifiers
source	1..108
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 546	
EIVLTQSPAT LSLSPGERAT LSCTASSSVN SFYLHWYQQK PGLAPRLLIY STSNLASGIP	60
DRFSGSGSGT DFTLTISRLE PEDFAVYYCH QYHRSPYTGF QGTKLEIK	108
SEQ ID NO: 547	moltype = AA length = 5

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FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 547	
SYWMQ	5
SEQ ID NO: 548	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 548	
TIYPGDDTT YTQKRFQG	17
SEQ ID NO: 549	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 549	
YDAPGYAMDY	10
SEQ ID NO: 550	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 550	
RASQDINNYL A	11
SEQ ID NO: 551	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 551	
YTSTLHP	7
SEQ ID NO: 552	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 552	
LQYDNLLYT	9
SEQ ID NO: 553	moltype = AA length = 119
FEATURE	Location/Qualifiers
source	1..119
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 553	
QVQLVQSGAE VAKPGASVKL SCKASGYTFT SYWMQWVKQR PGQGLECIGT IYPGDGDTTY	60
TQKFQGKATL TADKSSSTAY MQLSSLRSED SAVYYCARYD APGYAMDYWG QGTLVTVSS	119
SEQ ID NO: 554	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 554	
DIGMTQSPSS LSASVGDRVT ITCRASQDIN NYLAWYQHKP GKGPKLLIHY TSTLHPGIPS	60
RFSGSGSGRD YSFSISSLEP EDIATYYCLQ YDNLLYTFGQ GTKLEIK	107
SEQ ID NO: 555	moltype = AA length = 6
FEATURE	Location/Qualifiers
source	1..6
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 555	
RDFAWN	6
SEQ ID NO: 556	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16

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SEQUENCE: 556	mol_type = protein organism = synthetic construct	
YISYNGNTRY QPSLKS		16
SEQ ID NO: 557	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 557		
ASRGFPY		7
SEQ ID NO: 558	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 558		
HSSQDINSNI G		11
SEQ ID NO: 559	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 559		
HGTNLDD		7
SEQ ID NO: 560	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 560		
VQYAQFPWT		9
SEQ ID NO: 561	moltype = AA length = 116	
FEATURE	Location/Qualifiers	
source	1..116	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 561		
EVQLQESGPG LVKPSQTLSL TCTVSGYSIS R DFAWNWIRQ PPGKGLEWMG YISYNGNTRY	60	
QPSLKSRTI SRDTSKNQFF LKLNSVTAAD TATYYCVTAS RGFPYWGQGT LVTVSS		116
SEQ ID NO: 562	moltype = AA length = 107	
FEATURE	Location/Qualifiers	
source	1..107	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 562		
DIQMTQSPSS MSVSVGDRVT ITC HSSQDIN SNIGWLQQKP GKSFKGLIYH GTNLDDGVPS	60	
RFSGSGSGTD YTTLTISSLQP EDFATYYCVQ YAQFPWTFGG GTKLEIK		107
SEQ ID NO: 563	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 563		
NYGVH		5
SEQ ID NO: 564	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
source	1..16	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 564		
VIWGGGNTDY NTPFTS		16
SEQ ID NO: 565	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	

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SEQUENCE: 565 ALTYDYEFA Y	11
SEQ ID NO: 566 FEATURE source moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct	
SEQUENCE: 566 RASQSIGTNI H	11
SEQ ID NO: 567 FEATURE source moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 567 YASESIS	7
SEQ ID NO: 568 FEATURE source moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 568 QQQNNNWPTT	9
SEQ ID NO: 569 FEATURE source moltype = AA length = 119 Location/Qualifiers 1..119 mol_type = protein organism = synthetic construct	
SEQUENCE: 569 QVQLKQSPGQ LVQPSQSLSI TCTVSGFSLT NYGVHWRQG PGKGLEWLGV IWSGGNTDYN 60 TPFTTSRLSIN KDNNSKSQVFF KMNSLQSNDT AIYYCARALT YYDYEFAWQG QGTLTVSA 119	
SEQ ID NO: 570 FEATURE source moltype = AA length = 107 Location/Qualifiers 1..107 mol_type = protein organism = synthetic construct	
SEQUENCE: 570 DILLTQSPVI LSVSPGERVS FSCRASQSIG TNIHWYQORT NGSPRLLIKY ASE SIS GIPS 60 RFSGSGSGTD FTLSINSVES EDIADYYCQQ NNNWPTTFGA GTKLELK 107	
SEQ ID NO: 571 FEATURE source moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct	
SEQUENCE: 571 GYFMN	5
SEQ ID NO: 572 FEATURE source moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 572 RIHPYDGDTF YNQKFQG	17
SEQ ID NO: 573 FEATURE source moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 573 YDGSRAMDY	9
SEQ ID NO: 574 FEATURE source moltype = AA length = 15 Location/Qualifiers 1..15 mol_type = protein organism = synthetic construct	
SEQUENCE: 574 KASQSVSFAG TSLMH	15

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SEQ ID NO: 575      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 575
RASNLEA

SEQ ID NO: 576      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 576
QQSREYPYT

SEQ ID NO: 577      moltype = AA length = 118
FEATURE
source
1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 577
QVQLVQSGAE VVKPGASVKI SCKASGYTFT GYPMNWKQS PGQSLEWIGR IHPYDGTFY 60
NQKFQGKATL TVDKSSNTAH MELLSLTSED FAVYYCTRYD GSRAMDYWGQ GTTVTVSS 118

SEQ ID NO: 578      moltype = AA length = 111
FEATURE
source
1..111
mol_type = protein
organism = synthetic construct
SEQUENCE: 578
DIVLTQSPLS LAVSLGQPAI ISCKASQSVS FAGTSLMHWY HQKPGQQPRL LIYRASNLEA 60
GVPDGRFSGSG SKTDFTLTIS PVEAEDAATY YCQQSREYPY TFGGGTKLEI K 111

SEQ ID NO: 579      moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 579
GYGLS

SEQ ID NO: 580      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 580
MISSGGSYTY YADSVKG

SEQ ID NO: 581      moltype = AA length = 10
FEATURE
source
1..10
mol_type = protein
organism = synthetic construct
SEQUENCE: 581
HGDDPAWFAY

SEQ ID NO: 582      moltype = AA length = 12
FEATURE
source
1..12
mol_type = protein
organism = synthetic construct
SEQUENCE: 582
SVSSSISSNN LH

SEQ ID NO: 583      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 583
GTSNLAS

SEQ ID NO: 584      moltype = AA length = 11

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FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 584	
QQWSSYPYMY T	11
SEQ ID NO: 585	moltype = AA length = 119
FEATURE	Location/Qualifiers
source	1..119
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 585	
EVLVLESGGG VVQPGRSLRL SCSASGFTFS GYGLSWVRQA PGKGLEWVAM ISSGGSYTYY 60	
ADSVKGKFAI SRDNNAKNTLF LQMDSLRPED TGVYFCARHG DDPWFAYWG QGTPVTVSS 119	
SEQ ID NO: 586	moltype = AA length = 110
FEATURE	Location/Qualifiers
source	1..110
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 586	
DQLTQSPSS LSASVGDRVT ITCSVSSIS SNNLHWHYQQK PGKAPKPWIY GTSNLASGVP 60	
SRFSGSGSGT DYTFTISSLQ PEDIATYYCQ QWSSYPYMYT FGQGTKVEIK 110	
SEQ ID NO: 587	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 587	
NYWMN	5
SEQ ID NO: 588	moltype = AA length = 19
FEATURE	Location/Qualifiers
source	1..19
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 588	
EIRLKSNNYT THYAESVKG	19
SEQ ID NO: 589	moltype = AA length = 6
FEATURE	Location/Qualifiers
source	1..6
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 589	
HYYFDY	6
SEQ ID NO: 590	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 590	
RSSKSLLHSN GITYFF	16
SEQ ID NO: 591	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 591	
QMSNLAS	7
SEQ ID NO: 592	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 592	
AQNLELPPT	9
SEQ ID NO: 593	moltype = AA length = 117
FEATURE	Location/Qualifiers
source	1..117

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mol_type = protein
organism = synthetic construct

SEQUENCE: 593
EVQLVESGGG LVQPGGSMRL SCVASGFPFS NYWMNWRQQA PGKGLEWVGE IRLKSNNYTT 60
HYAESVKGRF TISRDDSKNS LYLMQMSLKT EDTAVYYCTR HYYFDYWQGQ TLTVSS 117

SEQ ID NO: 594      moltype = AA length = 112
FEATURE
source
1..112
mol_type = protein
organism = synthetic construct

SEQUENCE: 594
DIVMTQSPLS NPVTGPGEPAS ISCRSSKSLL HSNGITYFFW YLQKPGQSPQ LLIYQMSNLA 60
SGVPDRFSGS GSGTDFTLRI SRVEAEDVGV YYCAQNLELP PTFGQQGTKE IK 112

SEQ ID NO: 595      moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct

SEQUENCE: 595
SYWIG 5

SEQ ID NO: 596      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct

SEQUENCE: 596
IIDPGDSRTR YSPSFQG 17

SEQ ID NO: 597      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct

SEQUENCE: 597
GQLYGGTYMD G 11

SEQ ID NO: 598      moltype = AA length = 14
FEATURE
source
1..14
mol_type = protein
organism = synthetic construct

SEQUENCE: 598
TGTSSDIGGY NSVS 14

SEQ ID NO: 599      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 599
GVNNRPS 7

SEQ ID NO: 600      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct

SEQUENCE: 600
SSYDIESATP V 11

SEQ ID NO: 601      moltype = AA length = 120
FEATURE
source
1..120
mol_type = protein
organism = synthetic construct

SEQUENCE: 601
QVELVQSGAE VKKPGEESLKI SCKGSGYSFT SYWIGWVRQQA PGKGLEWMGI IDPGDSRTRY 60
SPSFQGQVTI SADKSISTAY LQWSSLKASD TAMYYCARGQ LYGGTYMDGW GQGTLTVSS 120

SEQ ID NO: 602      moltype = AA length = 111
FEATURE
source
1..111
mol_type = protein

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SEQUENCE: 602          organism = synthetic construct
DIALTQPASV SGSPGQSITI SCTGTSSDIG GYNNSVSWYQQ HPGKAPKLMI YGVNNRPSGV 60
SNRFSGSKSG NTASLTISGL QAEDEADYYC SSYDIESATP VFGGGTKLTV L           111

SEQ ID NO: 603          moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 603
AYNIH
5

SEQ ID NO: 604          moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 604
SFDPYDGGS YNQKFKD
17

SEQ ID NO: 605          moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 605
GWYYFDY
7

SEQ ID NO: 606          moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 606
RASKSISKYL A
11

SEQ ID NO: 607          moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 607
SGSTLQS
7

SEQ ID NO: 608          moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 608
QQHDESPYT
9

SEQ ID NO: 609          moltype = AA length = 116
FEATURE
source
1..116
mol_type = protein
organism = synthetic construct
SEQUENCE: 609
QVQLQESGPG LVKPSQTLSL TCTVSGYAFT AYNIHWVRQA PGQGLEWMGS FDPYDGSSY 60
NQKFKDRLTI SKDTSKNQVV LTMTNMDPV TATYYCARGW YYFDYWGHGT LTVSS       116

SEQ ID NO: 610          moltype = AA length = 107
FEATURE
source
1..107
mol_type = protein
organism = synthetic construct
SEQUENCE: 610
DIVMTQTPLS LPVTPGEPAS ISCRASKSIS KYLAWYQQKP QQAPRLLIYS GSTLQSGIPP 60
RFSGSGYGTDF TLTIINNIES EDAAYYFCQQ HDESPYTFGE GTKVEIK             107

SEQ ID NO: 611          moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct

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SEQUENCE: 611		
SFGMH		5
SEQ ID NO: 612	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 612		
YISSLSSAIY YADTVKG		17
SEQ ID NO: 613	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 613		
GRENIYYGSR LDY		13
SEQ ID NO: 614	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 614		
KASQNVDTNV A		11
SEQ ID NO: 615	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 615		
SASYRYS		7
SEQ ID NO: 616	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 616		
QQYNNYPFT		9
SEQ ID NO: 617	moltype = AA length = 122	
FEATURE	Location/Qualifiers	
source	1..122	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 617		
DVQLVESGGG LVQPGGSRKSL SCAASGFTFS SFGMHWVRQA PEKGLEWVAY ISSDSSAIYY	60	
ADTVVKGRFTI SRDNPKNTLF LQMQLSLRSED TAMYYCGRGR ENIYYGSRLD YWGQGTTLV	120	
SS	122	
SEQ ID NO: 618	moltype = AA length = 107	
FEATURE	Location/Qualifiers	
source	1..107	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 618		
DIAMTQSQKF MSTSVGDRVS VTCKASQNVN TNVAWYQQKP GQSPKALIYS ASYRYSGVPD	60	
RFTGSGSGTD FTLTINNVQS EDLAEYFCQQ YNNYPFTFGS GTKLEIK	107	
SEQ ID NO: 619	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 619		
SYGMS		5
SEQ ID NO: 620	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 620		

-continued

TINSGGSNTY YPDSLKG	17
SEQ ID NO: 621	moltype = AA length = 8
FEATURE	Location/Qualifiers
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 621	
HDGGAMDY	8
SEQ ID NO: 622	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 622	
RASESIYSYL A	11
SEQ ID NO: 623	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 623	
NTKTLPE	7
SEQ ID NO: 624	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 624	
QHHYGTPPWT	10
SEQ ID NO: 625	moltype = AA length = 117
FEATURE	Location/Qualifiers
source	1..117
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 625	
EVOLVESGGG LVKPGGSLRL SCAASGFTFS SYGMSWVRQA PGKGLEWVAT INSGGSNTYY	60
PDSLKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCARHD GGAMDYWGQG TTVTVSS	117
SEQ ID NO: 626	moltype = AA length = 108
FEATURE	Location/Qualifiers
source	1..108
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 626	
DIQMTQSPSS LSASVGDRVT ITCRASESIY SYLAWYQQKP GKAPKLLVYN TKTLPEGVPS	60
RFSGSGSGTD FTLTISSLQP EDFATYYCQH HYGTPPWTFG QGTRLEIK	108
SEQ ID NO: 627	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 627	
SFGMH	5
SEQ ID NO: 628	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 628	
YISSSGSGTIY YADTVKG	17
SEQ ID NO: 629	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 629	
HGYRYEGFDY	10

-continued

SEQ ID NO: 630	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 630	
KASQNVDTNV A	11
SEQ ID NO: 631	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 631	
SASYRYS	7
SEQ ID NO: 632	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 632	
QQYNNYPFT	9
SEQ ID NO: 633	moltype = AA length = 119
FEATURE	Location/Qualifiers
source	1..119
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 633	
EVQLVESGGG LVQPGGSLRL SCAASGFTFS SFGMHWVRQAA PGKGLEWVAY ISSGSGTIYY 60	
ADTVKGRFTI SRDNNAKNSLY LQMNSLRAED TAVYYCARHG YRYEGFDYWG QGTTTVSS 119	
SEQ ID NO: 634	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 634	
DIQMTQSPF LSASVGDRVT ITCKASQNVTD TNVAWYQQKPG KAKPALKIYS ASYRYSGVPS 60	
RFGSGSGTDF FTLTISLQP EDFAEYFCQQ YNNYPFTFGQ GTKLEIK 107	
SEQ ID NO: 635	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 635	
NYVMH	5
SEQ ID NO: 636	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 636	
YINPYNDDVK YNEKFKG	17
SEQ ID NO: 637	moltype = AA length = 13
FEATURE	Location/Qualifiers
source	1..13
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 637	
WGYYGSPLYY FDY	13
SEQ ID NO: 638	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 638	
RASSRLIYMH	10
SEQ ID NO: 639	moltype = AA length = 7
FEATURE	Location/Qualifiers

-continued

source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 639		
ATSNLAS		7
SEQ ID NO: 640	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 640		
QQWNSNPPT		9
SEQ ID NO: 641	moltype = AA length = 122	
FEATURE	Location/Qualifiers	
source	1..122	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 641		
EVQLQQSGPE LVKPGASVKM SCKASGYTFT NYVMHWVKQK PGQGLEWIGY INPYNDDVKY	60	
NEKFKGKATQ TSDKSSSTAY MELSSLTSED SAVYYCARWG YYGSPLYYFD YWGQGTTLTV	120	
SS	122	
SEQ ID NO: 642	moltype = AA length = 106	
FEATURE	Location/Qualifiers	
source	1..106	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 642		
QIVLSQLSPTI LSASPGEKVT MTCRASSRLI YMHWYQQKPG SSPKPWIYAT SNLASGVPAR	60	
FSGSGSGTSY SLTISRVEAE DAATYYCQW NSNPPTFGTG TKLELK	106	
SEQ ID NO: 643	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 643		
NYVMH		5
SEQ ID NO: 644	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 644		
YINPYNDDVK YNEKFKG		17
SEQ ID NO: 645	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 645		
WGYYGSPLYY FDY		13
SEQ ID NO: 646	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 646		
RASSRLIYMH		10
SEQ ID NO: 647	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 647		
ATSNLAS		7
SEQ ID NO: 648	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	

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SEQUENCE: 648 QQWNSNPPT	mol_type = protein organism = synthetic construct	
		9
SEQ_ID NO: 649 FEATURE source	moltype = AA length = 122 Location/Qualifiers 1..122 mol_type = protein organism = synthetic construct	
SEQUENCE: 649 QVQLVQSGAE VKKPGSSVKV SCKASGYTFT NYVMHWVRQA PGQGLEWMGY INPYNDDVKY NEFKGKGRVTI TADESTSTAY MELSSLRSED TAVYYCARWG YYGSPLYYFD YWGQGTLVTV SS	60 120 122	
SEQ_ID NO: 650 FEATURE source	moltype = AA length = 106 Location/Qualifiers 1..106 mol_type = protein organism = synthetic construct	
SEQUENCE: 650 EIVLTQSPAT LSLSPGERAT LSCRASSRLI YMHWYQQKPG QAPRPLIYAT SNLASGIPAR FSGSGSGTDF TLTISSLPE DFAVYYCQW NSNPPTFGQG TKVEIK	60 106	
SEQ_ID NO: 651 FEATURE source	moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct	
SEQUENCE: 651 SYTIH		5
SEQ_ID NO: 652 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 652 YINPNSRNTD YAQKFQG		17
SEQ_ID NO: 653 FEATURE source	moltype = AA length = 12 Location/Qualifiers 1..12 mol_type = protein organism = synthetic construct	
SEQUENCE: 653 YSGSTPYWYF DV		12
SEQ_ID NO: 654 FEATURE source	moltype = AA length = 10 Location/Qualifiers 1..10 mol_type = protein organism = synthetic construct	
SEQUENCE: 654 RASSSVSYMN		10
SEQ_ID NO: 655 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 655 ATSNLAS		7
SEQ_ID NO: 656 FEATURE source	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 656 QQWSSNPLT		9
SEQ_ID NO: 657 FEATURE source	moltype = AA length = 121 Location/Qualifiers 1..121 mol_type = protein	

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SEQUENCE: 657 organism = synthetic construct
EVQLVQSGAE VKKPGSSVKV SCKASGYSFT SYTIHWVRQA PGQGLEWMGY INPNSRNTDY 60
AQKFQGRVTL TADKSTSTAY MELSSLRSED TAVYYCARYS GSTPYWYFDV WGQGTTVTVS 120
S 121

SEQ ID NO: 658 moltype = AA length = 106
FEATURE Location/Qualifiers
source 1..106
mol_type = protein
organism = synthetic construct

SEQUENCE: 658
DIQLTQSPSF LSASVGDRVT ITCRASSSVS YMNWYQQKPG KSPKPWIYAT SNLASGVPSR 60
FSVSVSGTEH TLTISSLQPE DFATYYCQQW SSNPLTFGQG TKLEIK 106

SEQ ID NO: 659 moltype = AA length = 5
FEATURE Location/Qualifiers
source 1..5
mol_type = protein
organism = synthetic construct

SEQUENCE: 659
SYWMH 5

SEQ ID NO: 660 moltype = AA length = 17
FEATURE Location/Qualifiers
source 1..17
mol_type = protein
organism = synthetic construct

SEQUENCE: 660
LIHPDSGSTN YNEMFKN 17

SEQ ID NO: 661 moltype = AA length = 8
FEATURE Location/Qualifiers
source 1..8
mol_type = protein
organism = synthetic construct

SEQUENCE: 661
GGRLYFDY 8

SEQ ID NO: 662 moltype = AA length = 16
FEATURE Location/Qualifiers
source 1..16
mol_type = protein
organism = synthetic construct

SEQUENCE: 662
RSSQSLVHSN GDTYLR 16

SEQ ID NO: 663 moltype = AA length = 7
FEATURE Location/Qualifiers
source 1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 663
KVSNRFS 7

SEQ ID NO: 664 moltype = AA length = 9
FEATURE Location/Qualifiers
source 1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 664
SQSTHVPYT 9

SEQ ID NO: 665 moltype = AA length = 117
FEATURE Location/Qualifiers
source 1..117
mol_type = protein
organism = synthetic construct

SEQUENCE: 665
EVQLVQSGAE VKKPGSSVKV SCKASGYTFS SYWMHWVRQA PGQGLEWIGL IHPDSGSTNY 60
NEMFKNRATL TVDRSTSTAY VELSSLRSED TAVYFCAGGG RLYFDYWGQG TTGTVSS 117

SEQ ID NO: 666 moltype = AA length = 112
FEATURE Location/Qualifiers
source 1..112
mol_type = protein

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SEQUENCE: 666          organism = synthetic construct
DVVMTQSPLS LPVTPGEPAS ISCRSSQSLV HSNGDTYLRW YLQKPGQSPQ LLIYKVSNRF 60
SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCSQSTHVP YTFGGGTKVE IK      112

SEQ ID NO: 667          moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 667
SYWMH
5

SEQ ID NO: 668          moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 668
LIHPESGSTN YNEMFKN
17

SEQ ID NO: 669          moltype = AA length = 8
FEATURE
source
1..8
mol_type = protein
organism = synthetic construct
SEQUENCE: 669
GGRLYFDY
8

SEQ ID NO: 670          moltype = AA length = 16
FEATURE
source
1..16
mol_type = protein
organism = synthetic construct
SEQUENCE: 670
RSSQSLVHSN QDTYLR
16

SEQ ID NO: 671          moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 671
KVSNRFS
7

SEQ ID NO: 672          moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 672
SQSTHVPYT
9

SEQ ID NO: 673          moltype = AA length = 117
FEATURE
source
1..117
mol_type = protein
organism = synthetic construct
SEQUENCE: 673
EVQLVQSGAE VKKPGSSVKV SCKASGYTFS SYWMHWVRQA PGQGLEWIGL IHPEGSTNY 60
NEMFKNRATL TVDRSTSTAY MELSSLRSED TAVYYCAGGG RLYFDYWGQG TTVTVSS      117

SEQ ID NO: 674          moltype = AA length = 112
FEATURE
source
1..112
mol_type = protein
organism = synthetic construct
SEQUENCE: 674
DIVMTQSPLS LPVTPGEPAS ISCRSSQSLV HSNQDTYLRW YLQKPGQSPQ LLIYKVSNRF 60
SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCSQSTHVP YTFGGGTKVE IK      112

SEQ ID NO: 675          moltype = AA length = 6
FEATURE
source
1..6
mol_type = protein
organism = synthetic construct

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SEQUENCE: 675	SGYSHW	6
SEQ ID NO: 676	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
source	1..16	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 676		
YIHSSGSTNY NPSLKS		16
SEQ ID NO: 677	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 677		
YDDYFEY		7
SEQ ID NO: 678	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 678		
KASQNVGPNV AW		12
SEQ ID NO: 679	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 679		
SASYRYS		7
SEQ ID NO: 680	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 680		
QQYNWYPFT		9
SEQ ID NO: 681	moltype = AA length = 116	
FEATURE	Location/Qualifiers	
source	1..116	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 681		
EVQLQESPGV LVKPSETLSL TCAVTGYSIT SGYSHWIRQ FPGNGLEWMG YIHSSGSTNY	60	
NPSLKSRI SI RDTSKNQFF LKLSSVTAAD TAVYYCAGYD DYFELYWGQGT TTVVSS	116	
SEQ ID NO: 682	moltype = AA length = 107	
FEATURE	Location/Qualifiers	
source	1..107	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 682		
DIGMTQSPSS LSASVGDRVT ITCKASQNVG FNVAWYQQKP GKSPKALIYS ASYRYSGVPS	60	
RFGSGSGTQ FTLTISSSLQP EDFAEYFCQQ YNWYPFTFGQ GTKLEIK	107	
SEQ ID NO: 683	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 683		
NYDIN		5
SEQ ID NO: 684	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 684		
WIFPGDDSTQ YNEKFKG		17

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SEQ ID NO: 685      moltype = AA  length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 685
QTTGTFWFAY                                     9

SEQ ID NO: 686      moltype = AA  length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 686
RASQSISDYL Y                                     11

SEQ ID NO: 687      moltype = AA  length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 687
YASQSIIS                                         7

SEQ ID NO: 688      moltype = AA  length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 688
QNQHHSFPLT                                     9

SEQ ID NO: 689      moltype = AA  length = 118
FEATURE
source
1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 689
QVQLVQSGAE VVKPGAVKLSCKTSGYTFT NYDINWVRQR PGQGLEWIGW IFPGDDSTQY 60
NEKFKGKATL TTDTSSTAY MELSSLRSED TAVYFCARQ TGTWFAYWGQ GTLVTVSS 118

SEQ ID NO: 690      moltype = AA  length = 107
FEATURE
source
1..107
mol_type = protein
organism = synthetic construct
SEQUENCE: 690
EIVMTQSPAT LSVSPGERVT LSCRASQSIIS DYLYWYQQKS HESPRLLIKY ASQSIISGIPA 60
RFSGSGSGSE FTLTINSVEP EDVGVYYCQN GHSFPLTFGQ GTKLELK 107

SEQ ID NO: 691      moltype = AA  length = 119
FEATURE
source
1..119
mol_type = protein
organism = synthetic construct
SEQUENCE: 691
QVQLQQGAE VVKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPILGIANY 60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARGG SGSYHMDVWG KGTTTVSS 119

SEQ ID NO: 692      moltype = AA  length = 109
FEATURE
source
1..109
mol_type = protein
organism = synthetic construct
SEQUENCE: 692
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD ASN RATGIPA 60
RFSGSGSGTD FTLTISSLEP EDFAVYYCQQ RSNWPPRITF GQGTRLEIK 109

SEQ ID NO: 693      moltype = AA  length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 693
IYNVH                                             5

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SEQ ID NO: 694      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 694
TIFPGNGDTS YNQKFKD                                17

SEQ ID NO: 695      moltype = AA length = 10
FEATURE
source
1..10
mol_type = protein
organism = synthetic construct
SEQUENCE: 695
WDDGNVGFH                                10

SEQ ID NO: 696      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 696
RASENINNNYL T                                11

SEQ ID NO: 697      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 697
HAKTLAE                                7

SEQ ID NO: 698      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 698
QHHYGTTPPT                                9

SEQ ID NO: 699      moltype = AA length = 119
FEATURE
source
1..119
mol_type = protein
organism = synthetic construct
SEQUENCE: 699
QVQLQQPGAE LVKPGASVKM SCKASGYTFT IYNVHWIKQT PGQGLEWMGT IFPGNGDTSY 60
NQKFKDKATL TTDKSSKTAY MQLNSLTSED SAVYYCARWD DGNVGFAHWG QGTLTVSA 119

SEQ ID NO: 700      moltype = AA length = 107
FEATURE
source
1..107
mol_type = protein
organism = synthetic construct
SEQUENCE: 700
DIQMTQSPAS LSASVGETVT ITCRASENIN NYLTWFQQKQ GKSPQLLVYH AKTLAEGVPS 60
RFSGSGSGTQ FSLKINSLQP EDFGSYYCQH HYGTPPTFGG GTKLEIK 107

SEQ ID NO: 701      moltype = AA length = 119
FEATURE
source
1..119
mol_type = protein
organism = synthetic construct
SEQUENCE: 701
EVOLVQSGAE VKKPGASVKV SCKASGYTFT IYNVHWVRQA PGQGLEWMGT IFPGNGDTSY 60
NQKFKDKVTM TTDTSTSTAY MELSSLRSED TAVYYCARWD DGNVGFAHWG QGTLTVSS 119

SEQ ID NO: 702      moltype = AA length = 107
FEATURE
source
1..107
mol_type = protein
organism = synthetic construct
SEQUENCE: 702
DIQMTQSPSS LSASVGDRVT ITCRASENIN NYLTWFQQKQ GKSPQLLIYH AKTLAEGVPS 60
RFSGSGSGTQ FTLTISSLQP EDFATYYCQH HYGTPPTFGG GTKVEIK 107

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SEQ ID NO: 703      moltype = AA length = 119
FEATURE          Location/Qualifiers
source           1..119
mol_type = protein
organism = synthetic construct

SEQUENCE: 703
EVOLVQSGAE VKKPGASVKV SCKASGYTFT IYNVHWIIRQA PGQGLEWMGT IFPGNGDTSY 60
NQKFKDRATL TTDKSTKTAY MELRSLSDD TAVYYCARWD DGNVGFAHWG QGTLTVSS 119

SEQ ID NO: 704      moltype = AA length = 107
FEATURE          Location/Qualifiers
source           1..107
mol_type = protein
organism = synthetic construct

SEQUENCE: 704
DIQMTQSPSS LSASVGDRVT ITCRASENIN NYLTWFQQKQ GKAPKLLVYH AKTLaEGVPS 60
RFGSGSGSGTQ FTLTISSSLQP EDFATYYCQH HYGTPPTFGQ GTKLEIK 107

SEQ ID NO: 705      moltype = AA length = 447
FEATURE          Location/Qualifiers
source           1..447
mol_type = protein
organism = synthetic construct

SEQUENCE: 705
QVOLQQWGAG LLKPSETLQL TCAVYGGSPS GYYWSWIROQ PGKGLEWIGE INHSGSTYN 60
PSLKSRVTIS VETSKNQFSL KLSVTAADT AVYYCARDKW TWYFDLWGRG TLTVSSAST 120
KGPSVFLAP SSKSTSGGTA ALGLCLVKDYF PEPPTVSWNS GALTSVGHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKRVEPKSC DKTHTCPPCP APELLGGPSV 240
FLPPPDKDT LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSREEMTK 360
NQVSCLCLVK GFYPSPDIAVE WESNGQOPENN YKTPPVLDs DGSSFLYSKL TVDKSRWQQG 420
NVSFCVMHE ALHNHYTQKS LSLSPGK 447

SEQ ID NO: 706      moltype = AA length = 220
FEATURE          Location/Qualifiers
source           1..220
mol_type = protein
organism = synthetic construct

SEQUENCE: 706
DIEMTQSPDS LAVSLGERAT INCRSSQSVL YSSSNRNYLA WYQQNPGQOPP KLLIYWASTR 60
ESGVVPDRFSG SGSGTDFTLT ISSLQAEDVA VYYCQQYYST PRTFGQGTKV EIKRTVAAPS 120
VFIFFPPSDEQ LKSGTASVVC LLNNFYYPREA KVQWKVDNAL QSGNSQESTV EQDSKDSTYS 180
LSSTLTLASKA DYEKHKVYAC EVTHQGLSSP VTKSFRNRGE 220

SEQ ID NO: 707      moltype = AA length = 445
FEATURE          Location/Qualifiers
source           1..445
mol_type = protein
organism = synthetic construct

SEQUENCE: 707
EVQLLESGGG LVQPGGSSLRL SCAASGFTFS HYVMAWVRQA PGKGLEWVSS ISSSGGWTL 60
ADSVVKGRFTI SRDN SKNNTLY LQMNLSRAED TAVYYCTRGL KMATIFDYWG QGTLTVSSA 120
STKGPSVFL APPCSRTSES TAALGCLVKD YFPEPVTVSW NSGALTSGVH TFPAVLQSSG 180
LYSLVVTVV PSSNFQTQTY TCNVHDHKPSN TKVDKTVRK CCVECPCCPA PPVAGPSVFL 240
FPPPKDFTLW QSRTPEVTCV VVDVSHEDVQ VQFNWYVDGV EVHNAKTKPR EEQFNSTFRV 300
VSVLTVVHQD WLNGKEYKCK VS NKGGLPAPI EKTI SKTKQG PREPVYVTLPS PSREEMTKNQ 360
VSLTCLVKGF YPSDIAVEWE SNGQPENNYK TTPPMULDSDG SFFLYSKLTV DKSRWQQGNV 420
FSCSVMHEAL HNHYTQKSLS LSPGK 445

SEQ ID NO: 708      moltype = AA length = 217
FEATURE          Location/Qualifiers
source           1..217
mol_type = protein
organism = synthetic construct

SEQUENCE: 708
QSALTQPAV SGSPGQSITI SCTGTSSDVG SYNVVSWYQQ HPGKAPKLIY YEVSQRPSGV 60
SNRFSGSKSG NTASLTISGL QTEDEADYYC CSYAGSSIFV IFGGGTKVTV LGQPKAAPSV 120
TLPFPPSSEEL QANKATLVCL VSDFYPGAVT VAWKADGSVQ KVGVETTKPS KQSNNKYAAS 180
SYLSLTPEQW KSHRSYSCRV THEGSTVEKT VAPAEC 217

SEQ ID NO: 709      moltype = AA length = 447
FEATURE          Location/Qualifiers
source           1..447
mol_type = protein
organism = synthetic construct

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SEQUENCE: 709				
EVOLLESGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSA INSQGKSTYY	60			
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARWG DEGFDIWGQG TLTVSSAST	120			
KGPSVFLAP SSKSTSGGTA ALGLCLVKDVF PEPVTWSWNS GALTSGVHTF PAVLQSSGLY	180			
SLSSSVTVPs SSLGTQTYIC NVNHKPSNTK VDKRVEPKSC DKTHTCPPCP APELLGGPSV	240			
FLFPPPKD T LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY	300			
RVVSVLTVLH QDWLNKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSREEMTK	360			
NQVSLTCLVK GFYPSPDI AVE WESNGOPENN YKTTPPVLDs DGSFFFLYSKL TVDKSRWQQG	420			
NVFSCSVMHE ALHNHYTQKS LSLSPGK	447			
 SEQ ID NO: 710	moltype = AA length = 214			
FEATURE	Location/Qualifiers			
source	1..214			
	mol_type = protein			
	organism = synthetic construct			
SEQUENCE: 710				
DIQMTQSPSS LSASVGDRVT ITCRASQGIS NWLAWYQQKP GKAPKLLIYG ASSLQSGVPS	60			
RFGSGSGSTD FTLTISSLQP EDFATYYCQQ YSSFPTTFPGQ GTKVEIKRTV AAPSVFIFPP	120			
SDEQLKSGTA SVVCLLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSTLT	180			
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEC	214			
 SEQ ID NO: 711	moltype = AA length = 449			
FEATURE	Location/Qualifiers			
source	1..449			
	mol_type = protein			
	organism = synthetic construct			
SEQUENCE: 711				
QVQLVQSGAE VKKPGAVKV SCKASGYTFR SSYISWVRQA PGQGLEWMW IYAGTGSPSY	60			
NQKLOGRVTM TTDTSTSTAY MELRSLRSDD TAVYYCARHR DYYSNSLTYW GQGTLVTVSS	120			
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYPPEPVTVS WNSGALTSGV HTFPAVLQSS	180			
GLYSLSSVVT PTKVDKKKVEP KSCDKTHTCP PCPAPELLGG	240			
PSVFLFPPKP KDTLMISRTP ETCVTVVDS HEDPEVKFWN VYDGVEVHNA KTKPREEQYN	300			
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTS KAKGQPREPQ VYTLPPSRDE	360			
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGFFFLY SKLTVDKSRW	420			
QQGNVFSCSV MHEALHNHYT QKSLSLSPG	449			
 SEQ ID NO: 712	moltype = AA length = 220			
FEATURE	Location/Qualifiers			
source	1..220			
	mol_type = protein			
	organism = synthetic construct			
SEQUENCE: 712				
DIVMTQSPDS DAVSLGERAT INCKSSQSVL NSGNQKNYLT WYQQKPGQPP KLLIYWASTR	60			
ESGPVPDRFSG SGSGTDFTLT ISSLQAEDVA VYYCQSDYST PYTFGQGTKL EIKRTVAAPS	120			
VFFFPPPSDEQ LKSGTASVVC LLNNFYPRERA KVQWKVDNAL QSGNSQESVT EQDSKDSTYS	180			
LSSTLTLASKA DYEKHKVYAC EVTHQGLSSP VTKSFRNRGEC	220			
 SEQ ID NO: 713	moltype = AA length = 7			
FEATURE	Location/Qualifiers			
source	1..7			
	mol_type = protein			
	organism = synthetic construct			
SEQUENCE: 713				
TSNMGVG		7		
 SEQ ID NO: 714	moltype = AA length = 16			
FEATURE	Location/Qualifiers			
source	1..16			
	mol_type = protein			
	organism = synthetic construct			
SEQUENCE: 714				
HIWWDDDKYY SPSLKS		16		
 SEQ ID NO: 715	moltype = AA length = 10			
FEATURE	Location/Qualifiers			
source	1..10			
	mol_type = protein			
	organism = synthetic construct			
SEQUENCE: 715				
SNYGYAWFAY		10		
 SEQ ID NO: 716	moltype = AA length = 11			
FEATURE	Location/Qualifiers			
source	1..11			
	mol_type = protein			
	organism = synthetic construct			

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SEQUENCE: 716 KASQDIYPYL N	11
SEQ ID NO: 717 FEATURE source moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 717 RTNRLLD	7
SEQ ID NO: 718 FEATURE source moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 718 LQYDEFPLT	9
SEQ ID NO: 719 FEATURE source moltype = AA length = 120 Location/Qualifiers 1..120 mol_type = protein organism = synthetic construct	
SEQUENCE: 719 QTILKESGPT LVKPTQTLTL TCTPSGFSL S TSNMGVGWIR QPPGKALEWL AHIWWDDDKY 60 YSPSLKSRLT ITKDTSKNQV VLTMTNMDPV DTATYYCVRS NYGYAWFAYW GQGTLTVSS 120	
SEQ ID NO: 720 FEATURE source moltype = AA length = 107 Location/Qualifiers 1..107 mol_type = protein organism = synthetic construct	
SEQUENCE: 720 DIQMTQSPSS LSASVGDRVT ITCKASQDIY PYLNWFQQKP GKAPKTLIYR TNRLLDGVPS 60 RFGSGSGSTD FTFTISSLQP EDIATYYCLQ YDEFPLTFGA GTKLEIK 107	
SEQ ID NO: 721 FEATURE source moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct	
SEQUENCE: 721 DYAVH	5
SEQ ID NO: 722 FEATURE source moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 722 VISTYNDYTY NNQDFKG	17
SEQ ID NO: 723 FEATURE source moltype = AA length = 10 Location/Qualifiers 1..10 mol_type = protein organism = synthetic construct	
SEQUENCE: 723 GNSYFYALDY	10
SEQ ID NO: 724 FEATURE source moltype = AA length = 15 Location/Qualifiers 1..15 mol_type = protein organism = synthetic construct	
SEQUENCE: 724 RASESVDSYG KSFMH	15
SEQ ID NO: 725 FEATURE source moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 725 RASNLES	7

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SEQ ID NO: 726      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 726
QQSNEDPWT

SEQ ID NO: 727      moltype = AA length = 119
FEATURE
source
1..119
mol_type = protein
organism = synthetic construct
SEQUENCE: 727
QVOLVQSGPE VKKPGASVKV SCKASGYTFT DYAVHWRQQA PGKRLEWIGV ISTYNDYTYN 60
NQDFKGRVTM TRDTSASTAY MELSLRLSED TAVYYCARGN SYFYALDYWG QGTSVTVSS 119

SEQ ID NO: 728      moltype = AA length = 111
FEATURE
source
1..111
mol_type = protein
organism = synthetic construct
SEQUENCE: 728
EIVLTQSPAT LSLSPGERAT LSCRASESVD SYGKSFMHWW QQKPGQAPRL LIYRASNLES 60
GIPARFSGSG SGTDFTLTIS SLEPEDFAVY YCQQSNEDPW TFGGGTKEI K 111

SEQ ID NO: 729      moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 729
RYWMS

SEQ ID NO: 730      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 730
DLNPDSSAIN YVDSVKG

SEQ ID NO: 731      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 731
ITTLVPYTMDF F

SEQ ID NO: 732      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 732
ITNTDIDDDMN

SEQ ID NO: 733      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 733
EGNGLRP

SEQ ID NO: 734      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 734
LQSDNLPLT

SEQ ID NO: 735      moltype = AA length = 120

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9

5

17

11

11

7

9

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FEATURE	Location/Qualifiers
source	1..120
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 735	
EVOLVESGGG LVQPGGSLRL SCAASGFDFS RYWMWSVRQA PGKGLEWIGD LNPDSAINY 60	
VDSVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCTLLT TLVPYTMDFW GQGTSVTVSS 120	
SEQ ID NO: 736	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 736	
ETTLTQSPAF MSATPGDKVN ISCITNTDID DDMNWYQQKP GEAAILLISE GNGLRPGIPP 60	
RFSGSGYGTDF TLTTINNIES EDAAYYFCLQ SDNLPLTPGS GTKLEIK 107	
SEQ ID NO: 737	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 737	
DYYMH	5
SEQ ID NO: 738	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 738	
WIDPENGDTE YGPKFQG	17
SEQ ID NO: 739	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 739	
HNAHYGTWFA Y	11
SEQ ID NO: 740	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 740	
RSSQSLLHSS GNTYLE	16
SEQ ID NO: 741	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 741	
KISTRFS	7
SEQ ID NO: 742	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 742	
FQGSHVPYT	9
SEQ ID NO: 743	moltype = AA length = 120
FEATURE	Location/Qualifiers
source	1..120
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 743	
QVQLVQSGAE VKKPGASVKV SCKASGLTIE DYYMHWVRQA PGQGLEWMGW IDPENGDEY 60	
GPKFQGRVTM TRDTSINTAY MELSLRSDD TAVYYCAVHN AHYGTWFAYW GQGTLTVSS 120	
SEQ ID NO: 744	moltype = AA length = 112
FEATURE	Location/Qualifiers

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source          1..112
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 744
DVVMTQSPLS LPVTLGQPAS ISCRSSQSLL HSSGNTYLEW YQQRPGQSPR PLIYKISTRF 60
SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCFQGSHPV YTFGGTKVE IK           112

SEQ ID NO: 745      moltype = AA  length = 449
FEATURE          Location/Qualifiers
source           1..449
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 745
QVQLVQSGAE VKKPGAVKV SCKASGLTIE DYMMHWVRQA PGQGLEWMGW IDPENGDEY 60
GPKFQGRVTM TRDTSINTAY MELSRLRSDD TAVYYCAVHN AHYGTWFAYW GQGTLTVSS 120
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYPPEPVITVS WNSGALTSGV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTQT YICCNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG 240
PSVFLFPKPK KDTLMISRTP EVTCVVVDVS HEDPEVKPFW YVDGVEVHNA KTKPREEQYN 300
STYRVVSVLT VLHQDWLNKG EYKCKVSNKA LPAPIEKTIIS KAKGQPREPQ VYTLPSSRDE 360
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTTPPV LDSDGSFFLY SKLTVDKSRW 420
QQGNVFSCSV MHEALHNHYT QKSLSLSPG                                449

SEQ ID NO: 746      moltype = AA  length = 219
FEATURE          Location/Qualifiers
source           1..219
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 746
DVVMTQSPLS LPVTLGQPAS ISCRSSQSLL HSSGNTYLEW YQQRPGQSPR PLIYKISTRF 60
SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCFQGSHPV YTFGGTKVE IKRTVAAPSV 120
FIFPPSDEQL KSGTASVVCL LNNFYPREAK VQWKVDNALQ SGNSQESVTE QDSKDSTYSL 180
STTLTLSKAD YEKHHKVYACE VTHQGLSSPV TKSFNRGEC                  219

SEQ ID NO: 747      moltype = AA  length = 5
FEATURE          Location/Qualifiers
source           1..5
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 747
GYFMN                                         5

SEQ ID NO: 748      moltype = AA  length = 17
FEATURE          Location/Qualifiers
source           1..17
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 748
LINPYNGDSF YNQKFKG                                         17

SEQ ID NO: 749      moltype = AA  length = 8
FEATURE          Location/Qualifiers
source           1..8
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 749
GLRRDFDY                                         8

SEQ ID NO: 750      moltype = AA  length = 16
FEATURE          Location/Qualifiers
source           1..16
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 750
KSSQSLLDSD GKTYLN                                         16

SEQ ID NO: 751      moltype = AA  length = 7
FEATURE          Location/Qualifiers
source           1..7
               mol_type = protein
               organism = synthetic construct
SEQUENCE: 751
LVSELDs                                         7

SEQ ID NO: 752      moltype = AA  length = 9
FEATURE          Location/Qualifiers
source           1..9

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	mol_type = protein
	organism = synthetic construct
SEQUENCE: 752 WQGTHFPRT	
	9
SEQ ID NO: 753 FEATURE source	moltype = AA length = 117 Location/Qualifiers 1..117 mol_type = protein organism = synthetic construct
SEQUENCE: 753 QVQLVQSGAE VKKPGASVKV SCKASGYSFS GYPMNWRQQA PGQGLEWMGL INPYNGDSFY 60 NQKFKGRVTM TRQTSTSTVY MELSSLRSED TAVYYCVRGL RRDFDYWGQG TLTVSS 117	
SEQ ID NO: 754 FEATURE source	moltype = AA length = 112 Location/Qualifiers 1..112 mol_type = protein organism = synthetic construct
SEQUENCE: 754 DVVMTQSPLS LPVTLGQPAS ISCKSSQSLL DSDGKTYLNW LFQRPGQSPR RLIYLVSLED 60 SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCWQGTHFP RTFGGGTKLE IK 112	
SEQ ID NO: 755 FEATURE source	moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct
SEQUENCE: 755 DFGMN	
	5
SEQ ID NO: 756 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct
SEQUENCE: 756 WINTFTGEPS YGNVFKG	
	17
SEQ ID NO: 757 FEATURE source	moltype = AA length = 10 Location/Qualifiers 1..10 mol_type = protein organism = synthetic construct
SEQUENCE: 757 RHGNGNVFDS	
	10
SEQ ID NO: 758 FEATURE source	moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct
SEQUENCE: 758 RASQSIGSNI H	
	11
SEQ ID NO: 759 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct
SEQUENCE: 759 YTSEISIS	
	7
SEQ ID NO: 760 FEATURE source	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct
SEQUENCE: 760 QQSNNSWPLT	
	9
SEQ ID NO: 761 FEATURE source	moltype = AA length = 119 Location/Qualifiers 1..119 mol_type = protein organism = synthetic construct

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SEQUENCE: 761
QVOLVQSGSE LKKPGASVKV SCKASGYTFT DFGMNWVRQA PGQGLEWMGW INTFTGEPSY 60
GNVFKGKGRFV SLDTSTVSTAY LQISSLKAED TAVYYCARRH GNGNVFDSWG QGTLVTVSS 119

SEQ ID NO: 762      moltype = AA length = 108
FEATURE
source
Location/Qualifiers
1..108
mol_type = protein
organism = synthetic construct
SEQUENCE: 762
EVILTQSPDF QSVPKEKVT ITCRASQSIG SNIHWYQQKP DQSPKLLIKY TSESISGVPS 60
RFSGSGSGTD FTLTINSLEA EDAATYYCQQ SNSWPLTFGG GTKVEIKR 108

SEQ ID NO: 763      moltype = AA length = 5
FEATURE
source
Location/Qualifiers
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 763
SYAIS 5

SEQ ID NO: 764      moltype = AA length = 17
FEATURE
source
Location/Qualifiers
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 764
GIIPIFGTAN YAQKFQG 17

SEQ ID NO: 765      moltype = AA length = 21
FEATURE
source
Location/Qualifiers
1..21
mol_type = protein
organism = synthetic construct
SEQUENCE: 765
APLRFLEWST QDHYYYYYYMD V 21

SEQ ID NO: 766      moltype = AA length = 11
FEATURE
source
Location/Qualifiers
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 766
QGDSLRSYYA T 11

SEQ ID NO: 767      moltype = AA length = 7
FEATURE
source
Location/Qualifiers
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 767
GENKRPS 7

SEQ ID NO: 768      moltype = AA length = 11
FEATURE
source
Location/Qualifiers
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 768
KS RDGSQHL V 11

SEQ ID NO: 769      moltype = AA length = 130
FEATURE
source
Location/Qualifiers
1..130
mol_type = protein
organism = synthetic construct
SEQUENCE: 769
EVOLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IIPIPGTANY 60
AQKFQGRVTI TADKSTSTAY MELSSLRSED TAVYYCARAP LRFLEWSTQD HYYYYYMDVW 120
GKGTTTVTSS 130

SEQ ID NO: 770      moltype = AA length = 108
FEATURE
source
Location/Qualifiers
1..108
mol_type = protein
organism = synthetic construct

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SEQUENCE: 770
SSELTLQDPAV SVALGQTVRI TCQGDLSRSY YATWYQQKPG QAPILVIYGE NKRPSGIPDR 60
FSGSSSGNTA SLTITGAQAE DEADYYCKSR DGSGQHLVFG GGTKLTVL 108

SEQ ID NO: 771      moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 771
SYWIN
5

SEQ ID NO: 772      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 772
NIYPSDSYTN YNQKFKD 17

SEQ ID NO: 773      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 773
SWRGNSFDY
9

SEQ ID NO: 774      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 774
KSSQSLLNSG NQKNYLT 17

SEQ ID NO: 775      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 775
WASTRES
7

SEQ ID NO: 776      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 776
QNDYSYPFT
9

SEQ ID NO: 777      moltype = AA length = 118
FEATURE
source
1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 777
QVOLQQGAE LVRPGASVKL SCKASGYPT SYWINWVKQR PGQGLEWIGN IYPSDSYTNY 60
NQKFKDKATL TVDKSSSTAY MQLSSPTSED SAVYYCTRSW RGNSFDYWQG GTTLTVSS 118

SEQ ID NO: 778      moltype = AA length = 113
FEATURE
source
1..113
mol_type = protein
organism = synthetic construct
SEQUENCE: 778
DIVMTQSPSS LTVTAGEKVT MSCKSSQSL NSGNQKNYLT WYQQKPGQPP KLLIYWASTR 60
ESGVVPDRFTG SGSGTDFTLT ISSVQAEDLA VYYCQNDYSY PFTFGSGTKL EIK 113

SEQ ID NO: 779      moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 779

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NYGMN

5

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SEQ ID NO: 780      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct

SEQUENCE: 780
WINTNTGEPT YAEEFKG                                         17

SEQ ID NO: 781      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 781
LGFGNAMDY                                         9

SEQ ID NO: 782      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct

SEQUENCE: 782
KSSQSLNLNG NQKNYLT                                         17

SEQ ID NO: 783      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 783
WASTRES                                         7

SEQ ID NO: 784      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 784
QNDYSYPLT                                         9

SEQ ID NO: 785      moltype = AA length = 118
FEATURE
source
1..118
mol_type = protein
organism = synthetic construct

SEQUENCE: 785
QIQLVQSGPE LKKPGETVKI SCKASGYTFT NYGMNWVKQA PGKGLKWMGW INTNTGEPTY 60
AEEFKGRFAF SLETSASTAY LQINNLKNED TATYFCARLG FGNAMDYWGQ GTSVTVSS 118

SEQ ID NO: 786      moltype = AA length = 113
FEATURE
source
1..113
mol_type = protein
organism = synthetic construct

SEQUENCE: 786
DIVMTQSPSS LTVTAGEKVT MSCKSSQSLL NSGNQKNYLT WYQQKPGQPP KLLIYWASTR 60
ESGVPDRFTG SGSGTDFTLT ISSVQAEDLA VYYCQNDYSY PLTFGAGTKL ELK           113

SEQ ID NO: 787      moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct

SEQUENCE: 787
SYNMN                                         5

SEQ ID NO: 788      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct

SEQUENCE: 788
YISSSSSTIY YADSVKG                                         17

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-continued

SEQ ID NO: 789	moltype = AA length = 8
FEATURE	Location/Qualifiers
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 789	
AYYYGMDV	8
SEQ ID NO: 790	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 790	
RASQGISGWL A	11
SEQ ID NO: 791	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 791	
AASTLQS	7
SEQ ID NO: 792	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 792	
QQANSFPPT	9
SEQ ID NO: 793	moltype = AA length = 117
FEATURE	Location/Qualifiers
source	1..117
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 793	
EVOLVESGGGVQPGGSLRL SCAASGFTFS SYNMNWRQAGPKGLEWVSY ISSSSSTIYV	60
ADSVKGRFTI SRDNNAKNSLS LQMNSLRDED TAVYYCARAY YYGMDVWGQG TTGTVSS	117
SEQ ID NO: 794	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 794	
DIQMTQSPSS VSASVGDRVT ITCRASQGIS GWLAWYQQKP GKAPKFLIYA ASTLQSGVPS	60
RFSGSGSGTD FTLTISLQP EDFATYYCQQ ANSFPPPTFGG GTKVEIK	107
SEQ ID NO: 795	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 795	
SYGMH	5
SEQ ID NO: 796	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 796	
VIWYDGSNQY YADSVKG	17
SEQ ID NO: 797	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 797	
GLTSGRYGMD V	11
SEQ ID NO: 798	moltype = AA length = 16
FEATURE	Location/Qualifiers

-continued

source	1..16	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 798		
RSSQSLLSH GFNYLD		16
SEQ ID NO: 799	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 799		
LGSSRAS		7
SEQ ID NO: 800	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 800		
MQPLQIPWT		9
SEQ ID NO: 801	moltype = AA length = 120	
FEATURE	Location/Qualifiers	
source	1..120	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 801		
QVQLVESGGG VVQPGRSLRL	SCAASGFTFS SYGMHWVRQA PGKGLEWVAV IWYDGSNQYY	60
ADSVKGRFTI SRDNSKNTLF	LQMHSLRAED TAVYYCARGL TSGRYGMDVW GQGTTTVSS	120
SEQ ID NO: 802	moltype = AA length = 112	
FEATURE	Location/Qualifiers	
source	1..112	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 802		
DIVMTQSPLS LPVTPGEPAS	ISCRSSQSL LSHGFNYLDW YLQKPGQSPQ LLIYLGSSRA	60
SGVPDRFSGS GSGTDFTLKI	SRVEAEDVGL YYCMQPLQIP WTFGQQGTKE IK	112
SEQ ID NO: 803	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 803		
NYAMS		5
SEQ ID NO: 804	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 804		
SISGSGDYTY YTDSVKG		17
SEQ ID NO: 805	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 805		
SPWGYYLDS		9
SEQ ID NO: 806	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 806		
RASQGISSRL A		11
SEQ ID NO: 807	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	

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SEQUENCE: 807 AASSLQS	organism = synthetic construct	
		7
SEQ ID NO: 808 FEATURE source	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 808 QQYNNSYPYT		9
SEQ ID NO: 809 FEATURE source	moltype = AA length = 118 Location/Qualifiers 1..118 mol_type = protein organism = synthetic construct	
SEQUENCE: 809 EVQLLESGGG LVQPGGSLRL SCAASGFTFS NYAMSWVRQA PGKGLEWVSS ISGSGDYTYY 60 TDSVKGRFTI SRDNSKNLTY LQMNSLRAED TAVYYCARSP WGYYLDSWGQ GTLTVSS 118		
SEQ ID NO: 810 FEATURE source	moltype = AA length = 107 Location/Qualifiers 1..107 mol_type = protein organism = synthetic construct	
SEQUENCE: 810 DIQMTQSPS LSASAGDRVVT ITCRASQGIS SRLAWYQQKP EKAPKSLIYA ASSLQSGVPS 60 RFGSGSGSGTD FTLTSSLQP EDFATYYCQQ YNSYPYTFGQ GTKLEIK 107		
SEQ ID NO: 811 FEATURE source	moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct	
SEQUENCE: 811 DHAIH		5
SEQ ID NO: 812 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 812 YFSPGNDDIK YNEKFRG		17
SEQ ID NO: 813 FEATURE source	moltype = AA length = 6 Location/Qualifiers 1..6 mol_type = protein organism = synthetic construct	
SEQUENCE: 813 SLSTPY		6
SEQ ID NO: 814 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 814 KSSQSLLNRG NHKNYLT		17
SEQ ID NO: 815 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 815 WASTRES		7
SEQ ID NO: 816 FEATURE source	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 816		

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QNDYTYPYT	9
SEQ ID NO: 817	moltype = AA length = 115
FEATURE	Location/Qualifiers
source	1..115
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 817	
EVQLVQSGAE VVKPGASVKV SCKASGYTFT DHAIHWVRQA PGQGLEWMGY FSPGNDDIKY	60
NEKFRGRVTM TADKSSTAY MELRSLRSDD TAVYFCKRSL STPYWGQGTL VTVSS	115
SEQ ID NO: 818	moltype = AA length = 113
FEATURE	Location/Qualifiers
source	1..113
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 818	
DIVMTQSPDS LAVSLGERAT INCKSSQSLL NRGNHKNYLT WYQQKPGQPP KLLIYWASTR	60
ESGVPDFSG SGSGTDFTLT ISSLQAEDVA VYYCQNDYTY PYTFGQGTKV EIK	113
SEQ ID NO: 819	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 819	
SYNMH	5
SEQ ID NO: 820	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 820	
AIYPGNGDTS YNQKFKG	17
SEQ ID NO: 821	moltype = AA length = 12
FEATURE	Location/Qualifiers
source	1..12
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 821	
STYYGGDWYF NV	12
SEQ ID NO: 822	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 822	
RASSSVSYIH	10
SEQ ID NO: 823	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 823	
ATSNLAS	7
SEQ ID NO: 824	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 824	
QQWTSNPPT	9
SEQ ID NO: 825	moltype = AA length = 121
FEATURE	Location/Qualifiers
source	1..121
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 825	
QVQLQQGAE LVKPGASVKM SCKASGYTFT SYNMHWVKQT PGRGLEWIGA IYPGNGDTSY	60
NQKFKGKATL TADKSSTAY MQLSSLTSED SAVYYCARST YYGGDWYFNV WGAGTTVVS	120

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A		121
SEQ ID NO: 826	moltype = AA length = 106	
FEATURE	Location/Qualifiers	
source	1..106	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 826		
QIVLSQSPAI LSASPGEKVT MTCRASSSVS YIHWFQQKPG SSPKPWIYAT SNLASGVPR	60	
FSGSGSGTSY SLTISRVEAE DAATYYCQW TSNPPTFGGG TKLEIK	106	
SEQ ID NO: 827	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 827		
DTYIH		5
SEQ ID NO: 828	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 828		
RIYPTNGYTR YADSVKG		17
SEQ ID NO: 829	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 829		
WGDDGFYAMD Y		11
SEQ ID NO: 830	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 830		
RASQDVNTAV A		11
SEQ ID NO: 831	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 831		
SASFLYS		7
SEQ ID NO: 832	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 832		
QQHYTTTPPT		9
SEQ ID NO: 833	moltype = AA length = 120	
FEATURE	Location/Qualifiers	
source	1..120	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 833		
EVOLVESCGGG LVQPGGSLRL SCAASGFNIK DTYIHWRQVA PGKGLEWVAR IYPTNGYTRY	60	
ADSVKGRFTI SADTSKNTAY LQMNSLRAED TAVYYCSRWG GDGFYAMDYW GQGTLTVSS	120	
SEQ ID NO: 834	moltype = AA length = 107	
FEATURE	Location/Qualifiers	
source	1..107	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 834		
DIQMTQSPSS LSASVGDRVT ITCRASQDVN TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS	60	
RFSGSRSGTD FTLTISSLQP EDFATYYCQW HYTPPTFGQ GTKVEIK	107	

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SEQ ID NO: 835	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 835	
SYWIE	5
SEQ ID NO: 836	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 836	
EILPGGGDTN YNEIFKG	17
SEQ ID NO: 837	moltype = AA length = 8
FEATURE	Location/Qualifiers
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 837	
RVPIRLDY	8
SEQ ID NO: 838	moltype = AA length = 15
FEATURE	Location/Qualifiers
source	1..15
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 838	
KASQSVDYEG DSFLN	15
SEQ ID NO: 839	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 839	
AASNLES	7
SEQ ID NO: 840	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 840	
QQSNEDPLT	9
SEQ ID NO: 841	moltype = AA length = 117
FEATURE	Location/Qualifiers
source	1..117
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 841	
EVQLVESGGG LVQPGGSLRL SCAASGYTFS SYWIEWVRQA PGKGLEWIGE ILPGGGDTNY 60	
NEIFKGRATF SADTSKNTAY LQMNSLRAED TAVYYCTRRV PIRLDYWQGQ TLTVSS	117
SEQ ID NO: 842	moltype = AA length = 111
FEATURE	Location/Qualifiers
source	1..111
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 842	
DIQLTQSPSS LSASVGDRVT ITCKASQSD YEGDSFLNWY QQKPGKAPKL LIYASNLES 60	
GVPSRFSGSG SGTDFTLTIS SLQPEDFATY YCQQSNEDPL TFGQGTKVEI K	111
SEQ ID NO: 843	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 843	
DFAMs	5
SEQ ID NO: 844	moltype = AA length = 17

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FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 844	
TIGRVAFHYY YPDMSMKG	17
SEQ ID NO: 845	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 845	
HRGFDVGHFD F	11
SEQ ID NO: 846	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 846	
RSSETLVHSS GNTYLE	16
SEQ ID NO: 847	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 847	
RVSNRFS	7
SEQ ID NO: 848	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 848	
FQGSFNPLT	9
SEQ ID NO: 849	moltype = AA length = 120
FEATURE	Location/Qualifiers
source	1..120
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 849	
EVQLVESGGG LVQPGGSLRL SCAASGFSFS DFAMSWVRQA PGKGLEWVAT IGRVAFHYY 60	
PDMSMKRTI SRDNSKNTLY LQMNSLRAED TAVYYCARHR GFDVGHDFW GQGTLTVSS 120	
SEQ ID NO: 850	moltype = AA length = 112
FEATURE	Location/Qualifiers
source	1..112
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 850	
DIGMTQSPSS LSASVGDRVT ITCRSSETLV HSSGNTYLEW YQQKPGKAPK LLIYRVSNRF 60	
SGVPSRSGS GSGTDFTLTI SSLQPEDFAT YYCFQGSFNP LTFGQGTKVE IK 112	
SEQ ID NO: 851	moltype = AA length = 6
FEATURE	Location/Qualifiers
source	1..6
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 851	
NDYAWN	6
SEQ ID NO: 852	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 852	
YISYSGYTTY NPSLKS	16
SEQ ID NO: 853	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7

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	mol_type = protein
	organism = synthetic construct
SEQUENCE: 853	
WTSGLDY	7
SEQ ID NO: 854	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 854	
KASDLIHNWL A	11
SEQ ID NO: 855	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 855	
GATSLET	7
SEQ ID NO: 856	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 856	
QQYWTTPFT	9
SEQ ID NO: 857	moltype = AA length = 116
FEATURE	Location/Qualifiers
source	1..116
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 857	
EVOLVESGGG LVQPGGSLRL SCAASGYSIT NDYAWNWRQ APGKGLEWVG YISYSGYTTY	60
NPSLKSRTFI SRDTSKNTLY LQMNSLRAED TAVYYCARWT SGLDYGQGT LTVSS	116
SEQ ID NO: 858	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 858	
DIQMTQSPSS LSASVGDRVT ITCKASDLIH NWLAWYQQKP GKAPKLLIYG ATSLETGVPS	60
RFSGSGSGTD FTLTISLQP EDFATYYCQQ YTTPFTFGQ GTKVEIK	107
SEQ ID NO: 859	moltype = AA length = 6
FEATURE	Location/Qualifiers
source	1..6
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 859	
SDYAWN	6
SEQ ID NO: 860	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 860	
YISNSGSTS YNPSLKS	16
SEQ ID NO: 861	moltype = AA length = 15
FEATURE	Location/Qualifiers
source	1..15
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 861	
ERNYDYDDYY YAMDY	15
SEQ ID NO: 862	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct

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SEQUENCE: 862 KSSQSLLYRS NQKNYLA	17
SEQ ID NO: 863 FEATURE source moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 863 WASTRES	7
SEQ ID NO: 864 FEATURE source moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 864 QQYNNPRT	9
SEQ ID NO: 865 FEATURE source moltype = AA length = 124 Location/Qualifiers 1..124 mol_type = protein organism = synthetic construct	
SEQUENCE: 865 EVOLVESGGG LVQPGGSLRL SCAVSGYSIT SDYAWNVRQ APGKGLEWVG YISNSGSTSY NPSLKSRTI SRDTSKNTLY LQMNSLRAED TAVYYCARER NYDYDDYYYA MDYWQGQTLV TVSS	60 120 124
SEQ ID NO: 866 FEATURE source moltype = AA length = 113 Location/Qualifiers 1..113 mol_type = protein organism = synthetic construct	
SEQUENCE: 866 DIQMTQSPSS LSASVGDRVT ITCKSSQSLL YRSNQKNYLA WYQQKPGKAP KLLIYWASTR ESGVPSRFSQ SGSGTDFTLT ISSLQPEDFA TYYCQQQYYN PRTFGQGTKV EIK	60 113
SEQ ID NO: 867 FEATURE source moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct	
SEQUENCE: 867 NYWMH	5
SEQ ID NO: 868 FEATURE source moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 868 ATYRGHSDTY YNQKFKG	17
SEQ ID NO: 869 FEATURE source moltype = AA length = 12 Location/Qualifiers 1..12 mol_type = protein organism = synthetic construct	
SEQUENCE: 869 GAIYDGYDVL DN	12
SEQ ID NO: 870 FEATURE source moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct	
SEQUENCE: 870 SASQDISNYL N	11
SEQ ID NO: 871 FEATURE source moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 871	

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YTSNLHS

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SEQ ID NO: 872      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 872
QQYRKLPWT

SEQ ID NO: 873      moltype = AA length = 121
FEATURE
source
1..121
mol_type = protein
organism = synthetic construct

SEQUENCE: 873
QVQLVQSGAE VKKPGSSVKV SCKASGGTFS NYWMHWVRQA PGQGLEWMGA TYRGHSDTYY 60
NQKFKGRVTI TADKSTSTAY MELSSLRSED TAVYYCARGA IYDGYDVLDN WGQGTLVTVS 120
S 121

SEQ ID NO: 874      moltype = AA length = 107
FEATURE
source
1..107
mol_type = protein
organism = synthetic construct

SEQUENCE: 874
DIQMTQSPSS LSASVGDRVT ITCSASQDIS NYLNWYQCKP GKAPKLLIYY TSNLHSGVPS 60
RFGSGSGSTD FTLTISSLQP EDFATYYCQQ YRKLPWTFGQ GTKLEIK 107

SEQ ID NO: 875      moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct

SEQUENCE: 875
AYTMH 5

SEQ ID NO: 876      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct

SEQUENCE: 876
WIKPNNGLAN YAQKFQG 17

SEQ ID NO: 877      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 877
SEITTEFDY 9

SEQ ID NO: 878      moltype = AA length = 15
FEATURE
source
1..15
mol_type = protein
organism = synthetic construct

SEQUENCE: 878
KSSESVDSYA NSFLH 15

SEQ ID NO: 879      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct

SEQUENCE: 879
RASTRES 7

SEQ ID NO: 880      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct

SEQUENCE: 880
QQSKEDPLT 9

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SEQ ID NO: 881      moltype = AA length = 118
FEATURE
source
1..118
mol_type = protein
organism = synthetic construct
SEQUENCE: 881
QVOLVQSGAE VKKPGASVKV SCKASGYIFT AYTMHWVRQA PGQGLEWMGW IKPNNGLANY 60
AQKFQGRVTM TRDTSISTAY MELSLRSDD TAVYYCARSE ITTEFDYWQG GTLTVSS 118

SEQ ID NO: 882      moltype = AA length = 111
FEATURE
source
1..111
mol_type = protein
organism = synthetic construct
SEQUENCE: 882
DIVMTQSPDS LAVSLGERAT INCKSSESVD SYANSFLHWY QQKPGQPPKL LIYRASTRES 60
GVPDFRFSGSG SGTDFTLTIS SLQAEDEVY YCQQSKEDPL TFGGGTKEI K 111

SEQ ID NO: 883      moltype = AA length = 6
FEATURE
source
1..6
mol_type = protein
organism = synthetic construct
SEQUENCE: 883
SDPAWN                                         6

SEQ ID NO: 884      moltype = AA length = 16
FEATURE
source
1..16
mol_type = protein
organism = synthetic construct
SEQUENCE: 884
YISYSGNTRY QPSLKS                                         16

SEQ ID NO: 885      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 885
AGRGFPY                                         7

SEQ ID NO: 886      moltype = AA length = 11
FEATURE
source
1..11
mol_type = protein
organism = synthetic construct
SEQUENCE: 886
HSSQDINSNI G                                         11

SEQ ID NO: 887      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 887
HGTNLDD                                         7

SEQ ID NO: 888      moltype = AA length = 9
FEATURE
source
1..9
mol_type = protein
organism = synthetic construct
SEQUENCE: 888
VQYAQFPWT                                         9

SEQ ID NO: 889      moltype = AA length = 116
FEATURE
source
1..116
mol_type = protein
organism = synthetic construct
SEQUENCE: 889
QVQLQESGPG LVKPSQTLSL TCTVSGYSIS SDPAWNWIRQ PPGKGLEWMG YISYSGNTRY 60
QPSLKSRSITI SRDTSKNQFF LKLNNSVTAAD TATYYCVTAG RGFPYWGQGT LVTVSS 116

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SEQ ID NO: 890	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 890	
DIQMTQSPSS MSMSVGDRVT ITCHSSQDIN SNIGWLQQKP GKSFKGLIYH GTNLDDGVPS	60
RFSGSGSGTD YTLTISSLQP EDFATYYCQV YAQFPWTFGG GTKLEIK	107
SEQ ID NO: 891	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 891	
DYMYA	5
SEQ ID NO: 892	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 892	
SINYDGGSSTY YVDHSVKG	17
SEQ ID NO: 893	moltype = AA length = 8
FEATURE	Location/Qualifiers
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 893	
DRGYYFDY	8
SEQ ID NO: 894	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 894	
RSSQSLVHSN GNTYLN	16
SEQ ID NO: 895	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 895	
KVSNRFS	7
SEQ ID NO: 896	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 896	
SQSTHVPPFT	10
SEQ ID NO: 897	moltype = AA length = 117
FEATURE	Location/Qualifiers
source	1..117
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 897	
EVQLVESGGG LVQPGGSLRL SCAASGFTPS DYMMAWRQA PGKGLEWVAS INYDGSSSTYY	60
VDSVKGRFTI SRDNAKNSLY LQMNSLRAED TAVYYCARDR YYFDFYWGQG TTIVTVSS	117
SEQ ID NO: 898	moltype = AA length = 113
FEATURE	Location/Qualifiers
source	1..113
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 898	
DVVMQTPLS LSVTPGQPAS ISCRSSQSLV HSNGNTYLHW YLQKPGQSPQ LLIYKVSNRF	60
SGVPDRFGS GSGTDFTLKI SRVEAEDVGV YFCSQSTHVP PFTFGGGTKV EIK	113
SEQ ID NO: 899	moltype = AA length = 5

-continued

FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 899	
NAWMS	5
SEQ ID NO: 900	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 900	
YISSLGGSTIY YADSVKKG	17
SEQ ID NO: 901	moltype = AA length = 8
FEATURE	Location/Qualifiers
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 901	
EGLWAFDY	8
SEQ ID NO: 902	moltype = AA length = 14
FEATURE	Location/Qualifiers
source	1..14
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 902	
TGSSSNIGAG YVWH	14
SEQ ID NO: 903	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 903	
DNNKRPS	7
SEQ ID NO: 904	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 904	
AAWDDRLNGP V	11
SEQ ID NO: 905	moltype = AA length = 117
FEATURE	Location/Qualifiers
source	1..117
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 905	
EVQLLESGGG LVQPGGSLRL SCAASGFTFS NAWMSWVRQA PGKGLEWVSY ISSSGSTIYY 60 ADSVVKGRFTI SRDNSKNLTY LQMNSLRAED TAVYYCAREG LWAFDYWGQG TLTVSS 117	
SEQ ID NO: 906	moltype = AA length = 111
FEATURE	Location/Qualifiers
source	1..111
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 906	
ESVLTQPPSV SGAPGQRVTI SCTGSSSNIG AGYVVHWWQQ LPGTAPKLII YDNNKRPSGV 60 PDRFSGSKSG TSASLAISGL RSEDEADYYC AAWDDRLNGP VFGGGTLTV L 111	
SEQ ID NO: 907	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 907	
GYWWS	5
SEQ ID NO: 908	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16

-continued

	mol_type = protein
	organism = synthetic construct
SEQUENCE: 908	
EINHRGNTND NPSLKS	16
SEQ ID NO: 909	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 909	
ERGYTYGNFD H	11
SEQ ID NO: 910	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 910	
RASQSVSRNL A	11
SEQ ID NO: 911	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 911	
GASTRAT	7
SEQ ID NO: 912	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 912	
QQYKTPWPRT	9
SEQ ID NO: 913	moltype = AA length = 119
FEATURE	Location/Qualifiers
source	1..119
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 913	
QVQLQQWGAG LLKPSETLSL TCAVFGGSFS GYYWSWIROQ PGKGLEWIGE INHRGNTNDN 60	
PSLKSRTVTIS VDTSKNQFAL KLSSVTAADT AVYYCARERG YTYGNFDHWG QGTLTVSS 119	
SEQ ID NO: 914	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 914	
EIVMTQSPAT LSVSPGERAT LSCRASQSVS RNLAQYQQKP QQAPRLLIYG ASTRATGIPA 60	
RFSGSGSGTE FTLTIGSLQS EDFAVYYCQQ YKTWPRTFGQ GTNVEIK 107	
SEQ ID NO: 915	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 915	
SYAMN	5
SEQ ID NO: 916	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 916	
TTSGSGASTY YADSVKG	17
SEQ ID NO: 917	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct

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SEQUENCE: 917 IWIAFDI	7
SEQ ID NO: 918 FEATURE source moltype = AA length = 12 Location/Qualifiers 1..12 mol_type = protein organism = synthetic construct	
SEQUENCE: 918 RASQSVSSY LA	12
SEQ ID NO: 919 FEATURE source moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 919 GASSRAT	7
SEQ ID NO: 920 FEATURE source moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 920 QQYGSSPYT	9
SEQ ID NO: 921 FEATURE source moltype = AA length = 116 Location/Qualifiers 1..116 mol_type = protein organism = synthetic construct	
SEQUENCE: 921 EVQLLESGGG LVQPGGSLRL SCAASGFTFS SYAMNWRQAA PGKGLEWVST TSGSGASTYY 60 ADSVVKGRFTI SRDNSKNLTY LQMNSLRAED TAVYYCAKIW IAFDIWGQGT MVTVSS 116	
SEQ ID NO: 922 FEATURE source moltype = AA length = 108 Location/Qualifiers 1..108 mol_type = protein organism = synthetic construct	
SEQUENCE: 922 EIVLTQSPGT LSLSPLGERAT LSCRASQSVS SSYLAWSQOK PQQAPRLLIY GASSRATGIP 60 DRFSGSGSGT DFTLTISRLK PEDFAVYYCQ QYGSSPYTFQ QGTKLEIK 108	
SEQ ID NO: 923 FEATURE source moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 923 SFNYYWS	7
SEQ ID NO: 924 FEATURE source moltype = AA length = 16 Location/Qualifiers 1..16 mol_type = protein organism = synthetic construct	
SEQUENCE: 924 YIYYSGSTYS NPSLKS	16
SEQ ID NO: 925 FEATURE source moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 925 GYNWNYPDY	9
SEQ ID NO: 926 FEATURE source moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct	
SEQUENCE: 926 RASQSVVDNNL V	11

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SEQ ID NO: 927      moltype = AA length = 7
FEATURE
source
1..7
mol_type = protein
organism = synthetic construct
SEQUENCE: 927
GASTRAT                                         7

SEQ ID NO: 928      moltype = AA length = 10
FEATURE
source
1..10
mol_type = protein
organism = synthetic construct
SEQUENCE: 928
QQYNNNWPWPT                                         10

SEQ ID NO: 929      moltype = AA length = 119
FEATURE
source
1..119
mol_type = protein
organism = synthetic construct
SEQUENCE: 929
QVQLQESPGV LVKPSQTLSL TCTVSGGSIS SFNYYWSWIR HHPGKGLEWI GYIYYSGGSTY 60
SNPSLKSRTV ISVDTSKNQF SLTLLSSVTAA DTAVYYCARG YNWNYFDYWG QGTLTVSSA 119

SEQ ID NO: 930      moltype = AA length = 108
FEATURE
source
1..108
mol_type = protein
organism = synthetic construct
SEQUENCE: 930
EIVMTQSPAT LSVSPGERAT LSCRASQSVD NNLLWYQQKP GQAPRLLIYG ASTRATGIPA 60
RFSGSGSGTE FTLTISLQS EDFAVYYCQQ YNNWPPWTFG QGKTVKEIK 108

SEQ ID NO: 931      moltype = AA length = 449
FEATURE
source
1..449
mol_type = protein
organism = synthetic construct
SEQUENCE: 931
QVQLQESPGV LVKPSQTLSL TCTVSGGSIS SFNYYWSWIR HHPGKGLEWI GYIYYSGGSTY 60
SNPSLKSRTV ISVDTSKNQF SLTLLSSVTAA DTAVYYCARG YNWNYFDYWG QGTLTVSSA 120
STKGPSVFPL APSSKSTSGG TAALGCLVKD YFPEPVTVSW NSGALTSGVH TFPAVLQSSG 180
LYSLSSVVTV PSSSLGTQTY ICNVNHHKPSN TKVDKKVEPK SCDAKTHCPP CPAPELLGGP 240
SVFLFPPKPK DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VGVEVHNAAK TKPREEQYNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTIKK AKGQPREPQV YTLPPSRDEL 360
TNQVQSLTCL VKGFYFSDIA VEWESENQPE NNYKTPPVLDSDGSFFLYS KLTVDKSRWQ 420
QGNVFSCSVM HEALHNHYTQ KSLSLSPGK                                         449

SEQ ID NO: 932      moltype = AA length = 215
FEATURE
source
1..215
mol_type = protein
organism = synthetic construct
SEQUENCE: 932
EIVMTQSPAT LSVSPGERAT LSCRASQSVD NNLLWYQQKP GQAPRLLIYG ASTRATGIPA 60
RFSGSGSGTE FTLTISLQS EDFAVYYCQQ YNNWPPWTFG QGKTVKEIKT VAAPSVFIFP 120
PSDEQLKSGT AVSVCLNNF YPREAKVQWK VDNALQSGNS QESVTEQDSK DSTYSLSSL 180
TLSKADYEKH KVYACEVTHQ GLSSPVTKSF NRGEQ                                         215

SEQ ID NO: 933      moltype = AA length = 5
FEATURE
source
1..5
mol_type = protein
organism = synthetic construct
SEQUENCE: 933
TYWMH                                         5

SEQ ID NO: 934      moltype = AA length = 17
FEATURE
source
1..17
mol_type = protein
organism = synthetic construct
SEQUENCE: 934
EIDPSDSYSN YNQKFKD                                         17

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SEQ ID NO: 935	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 935	
NGGLGPWAWS Y	11
SEQ ID NO: 936	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 936	
KASQYVGTAV A	11
SEQ ID NO: 937	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 937	
SASNRYT	7
SEQ ID NO: 938	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 938	
QQYSSYPWT	9
SEQ ID NO: 939	moltype = AA length = 120
FEATURE	Location/Qualifiers
source	1..120
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 939	
EVQLVQSGAE VKKPGSSVKV SCKASGYTFT TYWMHWVRQA PGQGLEWIGE IDPSDSYSNY 60	60
NQKFKDRATL TVDKSTSTAY MELSSLRSED TAVYYCARNG GLGPAWFSYW GQGTLTVSS 120	120
SEQ ID NO: 940	moltype = AA length = 107
FEATURE	Location/Qualifiers
source	1..107
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 940	
DIQMTQSPSS VSASVGDRVT ITCKASQYVG TAVAWYQQKP GKSPKLLIYS ASNRYTGVP 60	60
RFSDSGSGTD FTLTISLQP EDFATYFCQQ YSSYPWTFGG GTKVEIK 107	107
SEQ ID NO: 941	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 941	
SYAMS	5
SEQ ID NO: 942	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 942	
AISGSGTSTY YADSVKG	17
SEQ ID NO: 943	moltype = AA length = 13
FEATURE	Location/Qualifiers
source	1..13
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 943	
VRYNWNHGDW FDP	13
SEQ ID NO: 944	moltype = AA length = 13

-continued

FEATURE	Location/Qualifiers
source	1..13
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 944	
SGSSSNIGNN YVS	13
SEQ ID NO: 945	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 945	
ENYNRPA	7
SEQ ID NO: 946	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 946	
SSWDDSLNYW V	11
SEQ ID NO: 947	moltype = AA length = 122
FEATURE	Location/Qualifiers
source	1..122
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 947	
EVOLLESGGG LVQPGGSSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSA ISGSGTSTYY 60	
ADSVKGRTI SRDNSKNTLY LQMNSLRAED TAVYYCARVR YNWNHGDWFD PWGQGTLVTV 120	
SS	122
SEQ ID NO: 948	moltype = AA length = 110
FEATURE	Location/Qualifiers
source	1..110
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 948	
QSVLTQPPSA SGTPGQRVTI SCSSGSSSNIG NNYVSWYQQL PGTAPKLLIY ENYNRPAGVP 60	
DRFGSGSKSGT SASLAISGLR SEDEADYYCS SWDDSLNYWV FGGGTKLTVL 110	
SEQ ID NO: 949	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 949	
SYGMS	5
SEQ ID NO: 950	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 950	
TISSGGSYKY YVDHSVKG	17
SEQ ID NO: 951	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 951	
HPDYDGWFWA Y	11
SEQ ID NO: 952	moltype = AA length = 10
FEATURE	Location/Qualifiers
source	1..10
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 952	
SVSSSVFYVH	10
SEQ ID NO: 953	moltype = AA length = 7
FEATURE	Location/Qualifiers

-continued

source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 953		
DTSKLAS		7
SEQ ID NO: 954	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 954		
QQWNSNPPT		9
SEQ ID NO: 955	moltype = AA length = 120	
FEATURE	Location/Qualifiers	
source	1..120	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 955		
EVQLVESGGG LVQPGGSLRL SCAASGFTFN SYGMSWVRQA PGKGLEWVAT ISSGGSYKYY 60		
VDSVKGRFTI SRDANKNSLY LQMNSLRAED TAVYYCARHP DYDGFWFAYW GQGTLTVSS 120		
SEQ ID NO: 956	moltype = AA length = 106	
FEATURE	Location/Qualifiers	
source	1..106	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 956		
DIQMTQSPSS LSASVGDRVT ITCSVSSSVF YVHWYQQKPG KAPKLLIYDT SKLASGVPSR 60		
FSGSGSGTDF TFTISSLQPE DIATYYCQQW NSNPPTFGGG TKVEIK 106		
SEQ ID NO: 957	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 957		
SYGMS		5
SEQ ID NO: 958	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 958		
TISSGGSYTY YPDHSVKG		17
SEQ ID NO: 959	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 959		
HPDYDGVWFA Y		11
SEQ ID NO: 960	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 960		
SVSSSVFYVH		10
SEQ ID NO: 961	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 961		
DTSKLAS		7
SEQ ID NO: 962	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
source	1..9	
	mol_type = protein	

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SEQUENCE: 962	organism = synthetic construct	
QQWNNSNPPT		9
SEQ ID NO: 963	moltype = AA length = 120	
FEATURE	Location/Qualifiers	
source	1..120	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 963		
EVQLVESGGD LVKPGGSLKL SCAASGFTFN SYGMSWRQQT PDKRLEWVAT ISSGGSYTYY 60		
PSDSVKGRFTI SRDNNAKNTLY LQMSSLKSED TAMYYCARHP DYDGVWFAYW GQGTLTVSA 120		
SEQ ID NO: 964	moltype = AA length = 106	
FEATURE	Location/Qualifiers	
source	1..106	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 964		
QIVLTQSPAI MSASPGEKVT MTCCSVSSSVF YVHWYQQKSG TSPKRWIYDT SKLASGVPAR 60		
FSGSGSGTSY SLTISSMEAE DAATYYCQOW NSNPPTFGGG TKLEIK		106
SEQ ID NO: 965	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 965		
SYYMH		5
SEQ ID NO: 966	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 966		
IINPSGGSTS YAQKFQG		17
SEQ ID NO: 967	moltype = AA length = 19	
FEATURE	Location/Qualifiers	
source	1..19	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 967		
DGVLRYFDWL LDYYYYYMDV		19
SEQ ID NO: 968	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 968		
RASQSVGSYL A		11
SEQ ID NO: 969	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 969		
DASN RAT		7
SEQ ID NO: 970	moltype = AA length = 8	
FEATURE	Location/Qualifiers	
source	1..8	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 970		
QQRANVFT		8
SEQ ID NO: 971	moltype = AA length = 128	
FEATURE	Location/Qualifiers	
source	1..128	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 971		

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EVQLVQSGAE VKKPGASVKV SCKASGYTFT SYMMHWVRQA PGQGLEWMGI INPSGGSTS Y	60
AQKFQGRVTM TRDTSTSTVY MELSSLRSED TAVYYCARDG VLRYFDWL LD YYYYMDVWG K	120
GTTTVVSS	128
SEQ ID NO: 972	moltype = AA length = 106
FEATURE	Location/Qualifiers
source	1..106
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 972	
EIVLTQSPAT LSLSPGERAT LSCRASQSVG SYLAWYQQRP GQAPRLLIYD ASN RATGIPA	60
RFSGSGSGTD FTLTISSE P EDFAVYYCQQ RANVFTFCQ G TKVEIK	106
SEQ ID NO: 973	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 973	
SYYMH	5
SEQ ID NO: 974	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 974	
IINPSGGSTS YAQKFQG	17
SEQ ID NO: 975	moltype = AA length = 19
FEATURE	Location/Qualifiers
source	1..19
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 975	
DAELRHFDHL LDYHYYMDV	19
SEQ ID NO: 976	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 976	
RASQSVGSYLA	11
SEQ ID NO: 977	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 977	
DASN RAT	7
SEQ ID NO: 978	moltype = AA length = 8
FEATURE	Location/Qualifiers
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 978	
QQRQAQEF	8
SEQ ID NO: 979	moltype = AA length = 128
FEATURE	Location/Qualifiers
source	1..128
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 979	
EVQLVQSGAE VKKPGASVKV SCKASGYTFT SYMMHWVRQA PGQGLEWMGI INPSGGSTS Y	60
AQKFQGRVTM TRDTSTSTVY MELSSLRSED TAVYYCARDG ELRHFDHLLD YHYYMDVWG Q	120
GTTTVVSS	128
SEQ ID NO: 980	moltype = AA length = 106
FEATURE	Location/Qualifiers
source	1..106
	mol_type = protein
	organism = synthetic construct

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SEQUENCE: 980
EIVMTQSPAT LSLSPGERAT LSCRASQSVG SYLAWYQQKP GQAPRLLIYD ASN RATGIPA 60
RFSGSGSGTD FTLTISSSLQP EDFAVYYCQQ RAQEFTFGQG TKVEIK 106

SEQ ID NO: 981      moltype = AA length = 120
FEATURE           Location/Qualifiers
source            1..120
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 981
QVQLVQSGSE LKKPGAPVKV SCKASGYTFS TFGMSWVRQA PGQGLKWMGW IHTYAGVPIY 60
GDDFKGRFVF SLDTSVSTAY LQISSLKAED TAVYFCARRS DNYRYFFDYW GQGTTVTVSS 120

SEQ ID NO: 982      moltype = AA length = 107
FEATURE           Location/Qualifiers
source            1..107
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 982
DIQMTQSPSS LSASLGDRVVT ITCRASQDIR NYLNWYQQKP GKAPKLLIYY TSRLHSGVPS 60
RFSGSGSGTD YTLTISSSLQP EDFATYFCQQ GHTLPPTFGQ GTKLEIK 107

SEQ ID NO: 983      moltype = AA length = 120
FEATURE           Location/Qualifiers
source            1..120
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 983
QIQLVQSGPE LKKPGAPVKI SCKASGYTFT TFGMSWVKQA PGQGLKWMGW IHTYAGVPIY 60
GDDFKGRFVF SLDTSVSTAY LQISSVKAED TATYFCARRS DNYRYFFDYW GQGTTLTVSS 120

SEQ ID NO: 984      moltype = AA length = 107
FEATURE           Location/Qualifiers
source            1..107
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 984
DIQMTQSPSS LSASLGDRVVT ITCRASQDIR NYLNWYQQKP GKAPKLLIYY TSRLHSGVPS 60
RFSGSGSGTD YTLTISSSLQP EDFATYFCQQ GHTLPPTFGQ GTKLEIK 107

SEQ ID NO: 985      moltype = AA length = 5
FEATURE           Location/Qualifiers
source            1..5
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 985
NYYMA                                         5

SEQ ID NO: 986      moltype = AA length = 17
FEATURE           Location/Qualifiers
source            1..17
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 986
STKGGGNTY YRDSVKG                                         17

SEQ ID NO: 987      moltype = AA length = 14
FEATURE           Location/Qualifiers
source            1..14
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 987
QVTIAAVSTS YFDS                                         14

SEQ ID NO: 988      moltype = AA length = 15
FEATURE           Location/Qualifiers
source            1..15
                  mol_type = protein
                  organism = synthetic construct
SEQUENCE: 988
KTNQKVVDYYG NSYVY                                         15

SEQ ID NO: 989      moltype = AA length = 7
FEATURE           Location/Qualifiers
source            1..7
                  mol_type = protein

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SEQUENCE: 989 LASNLAS	organism = synthetic construct	
		7
SEQ ID NO: 990 FEATURE source	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 990 QQSRNLPYT		9
SEQ ID NO: 991 FEATURE source	moltype = AA length = 123 Location/Qualifiers 1..123 mol_type = protein organism = synthetic construct	
SEQUENCE: 991 EVQLVESGGG LVQSGRSIRL SCAASGFSFS NYYMAWVRQA PSKGLEWVAS ITKGGGNNTYY RDSVKGRFTF SRDNAKSTLY LQMDSLRSED TATYYCARQV TIAAVSTSYF DSWGQGVMVT VSS	60 120 123	
SEQ ID NO: 992 FEATURE source	moltype = AA length = 110 Location/Qualifiers 1..110 mol_type = protein organism = synthetic construct	
SEQUENCE: 992 DIVLTQSPAL AVSLGQRATI SCKTNQKVDY YGNSYVYWWQ QKPGQQPKLL IYLASNLSAG IPARFSGRGS GTDFTLTIDP VEADDTATYY CQQSRNLPYT FGAGTKLELK	60 110	
SEQ ID NO: 993 FEATURE source	moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct	
SEQUENCE: 993 DYYMK		5
SEQ ID NO: 994 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 994 DIIPSONGATF YNQKFKG		17
SEQ ID NO: 995 FEATURE source	moltype = AA length = 11 Location/Qualifiers 1..11 mol_type = protein organism = synthetic construct	
SEQUENCE: 995 SHLLRASWFA Y		11
SEQ ID NO: 996 FEATURE source	moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 996 KSSQSLLNSG NQKNYLT		17
SEQ ID NO: 997 FEATURE source	moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 997 WASTRES		7
SEQ ID NO: 998 FEATURE source	moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	

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SEQUENCE: 998 QNDYSYPYT	9
SEQ ID NO: 999 FEATURE source moltype = AA length = 120 Location/Qualifiers 1..120 mol_type = protein organism = synthetic construct	
SEQUENCE: 999 QVQLVQSGAE VKKPGASVKM SCKASGYTFT DYMMKWWVKQA PGQGLEWIGD IIPSNGATFY 60 NQKFKGKATL TVDRSISTAY MHLNRRLRSDD TAVYYCTRSH LLRASWFAYW GQGTLVTVSS 120	
SEQ ID NO: 1000 FEATURE source moltype = AA length = 113 Location/Qualifiers 1..113 mol_type = protein organism = synthetic construct	
SEQUENCE: 1000 DFVMTQSPDS LAVSLGERAT INCKSSQSL NSGNQKNYLT WYLQKPGQPP KLLIYWASTR 60 ESGPVPDRFSG SGSGQTDFTLT ISSLQAEDVA VYYCQNDSY PYTFGQGTKL EIK 113	
SEQ ID NO: 1001 FEATURE source moltype = AA length = 5 Location/Qualifiers 1..5 mol_type = protein organism = synthetic construct	
SEQUENCE: 1001 DYEMH	5
SEQ ID NO: 1002 FEATURE source moltype = AA length = 17 Location/Qualifiers 1..17 mol_type = protein organism = synthetic construct	
SEQUENCE: 1002 GIDPETGGTA YNQKFKG	17
SEQ ID NO: 1003 FEATURE source moltype = AA length = 6 Location/Qualifiers 1..6 mol_type = protein organism = synthetic construct	
SEQUENCE: 1003 YYSFAY	6
SEQ ID NO: 1004 FEATURE source moltype = AA length = 16 Location/Qualifiers 1..16 mol_type = protein organism = synthetic construct	
SEQUENCE: 1004 RSSQSIVHSN ANTYLQ	16
SEQ ID NO: 1005 FEATURE source moltype = AA length = 7 Location/Qualifiers 1..7 mol_type = protein organism = synthetic construct	
SEQUENCE: 1005 KVSNRFS	7
SEQ ID NO: 1006 FEATURE source moltype = AA length = 9 Location/Qualifiers 1..9 mol_type = protein organism = synthetic construct	
SEQUENCE: 1006 FQVSHVPYT	9
SEQ ID NO: 1007 FEATURE source moltype = AA length = 115 Location/Qualifiers 1..115 mol_type = protein organism = synthetic construct	
SEQUENCE: 1007 EVQLVQSGAE VKKPGATVKI SCKVSGYTFT DYEMHWVQQA PGKGLEWMGG IDPETGGTAY 60	

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NQKFGRVTL TADKSTDAY MELSSLRSED TAVYYCGRYY SFAYWGQGTL VTVSS	115
SEQ ID NO: 1008	moltype = AA length = 112
FEATURE	Location/Qualifiers
source	1..112
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1008	
DVVMTQSPLS LPVTLGQPAS ISCRSSQSIV HSNANTYLQW FQQRPGQSPR LLIYKVSNRF	60
SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCFQVSHVP YTFGQGTKLE IK	112
SEQ ID NO: 1009	moltype = AA length = 5
FEATURE	Location/Qualifiers
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1009	
SYAIS	5
SEQ ID NO: 1010	moltype = AA length = 17
FEATURE	Location/Qualifiers
source	1..17
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1010	
SIPIFGTAN YAQKFQG	17
SEQ ID NO: 1011	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1011	
GPSEVGAILG YVWFDP	16
SEQ ID NO: 1012	moltype = AA length = 16
FEATURE	Location/Qualifiers
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1012	
RSSQSLLHSN GNYLD	16
SEQ ID NO: 1013	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1013	
LGSNRAS	7
SEQ ID NO: 1014	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1014	
MQARRIPIT	9
SEQ ID NO: 1015	moltype = AA length = 125
FEATURE	Location/Qualifiers
source	1..125
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1015	
QQLVLQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGS IIPIFGTANY	60
AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCARGP SEVGAILGYV WFDPWGQGTL	120
VTVSS	125
SEQ ID NO: 1016	moltype = AA length = 112
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	mol_type = protein
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SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCMQARRIP ITFGGGTKVE IK	112
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	organism = synthetic construct
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SEQ ID NO: 1018	moltype = AA length = 17
FEATURE	Location/Qualifiers
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	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1018	
WIYPGDGSTK YNEKFKA	17
SEQ ID NO: 1019	moltype = AA length = 8
FEATURE	Location/Qualifiers
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1019	
GYEDAMDY	8
SEQ ID NO: 1020	moltype = AA length = 11
FEATURE	Location/Qualifiers
source	1..11
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1020	
KASQDINSYL S	11
SEQ ID NO: 1021	moltype = AA length = 7
FEATURE	Location/Qualifiers
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1021	
RANRLVD	7
SEQ ID NO: 1022	moltype = AA length = 9
FEATURE	Location/Qualifiers
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1022	
LQYDEFPLT	9
SEQ ID NO: 1023	moltype = AA length = 117
FEATURE	Location/Qualifiers
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	mol_type = protein
	organism = synthetic construct
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QVQLVQSGAE VKPGAVSKV SCKASGYTFT NYDINWVRQA PGQGLEWIGW IYPGDGSTKY NEKFAKATL TADTSTSTAY MELRSLRSDD TAVYYCASGY EDAMDYWGQG TTVTVSS	60 117
SEQ ID NO: 1024	moltype = AA length = 107
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	mol_type = protein
	organism = synthetic construct
SEQUENCE: 1024	
DIQMTQSPSS LSASVGDRVT INCKASQDIN SYLSWFQQKP GKAPKTLIYR ANRLVDGVPS RFGSGSGSQD YTTLTISSLQP EDFATYYCLQ YDEFPLTFGG GTKVEIK	60 107
SEQ ID NO: 1025	moltype = AA length = 5
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source	1..5
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DYYIH	5

-continued

SEQ ID NO: 1026	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
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SEQ ID NO: 1027	moltype = AA length = 12	
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	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 1027		
YMWERVTGFF DF		12
SEQ ID NO: 1028	moltype = AA length = 11	
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	mol_type = protein	
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SEQUENCE: 1028		
LASEDISDDL A		11
SEQ ID NO: 1029	moltype = AA length = 7	
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	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 1029		
TTSSLQS		7
SEQ ID NO: 1030	moltype = AA length = 9	
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	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 1030		
QQTYKFPPT		9
SEQ ID NO: 1031	moltype = AA length = 121	
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	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 1031		
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AQKFQGRATM TADKSINTAY VELSRLRSDD TAVYFCTRYM WERVTGFDF WGQGTMVTVS	120	
S	121	
SEQ ID NO: 1032	moltype = AA length = 107	
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source	1..107	
	mol_type = protein	
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RGSGSGSGTD FTLTISLQP EDFATYFCQQ TYKFPPTFGG GTKVEIK	107	
SEQ ID NO: 1033	moltype = AA length = 755	
FEATURE	Location/Qualifiers	
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	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 1033		
MARKLSVILI LTFALSVTNP LHELKAAAPP QTTEKISPWN ESGINVDLAI STROYHLQQL	60	
FYRYGENNSL SVEGFRKLLQ NIGIDKIKRI HIHHHDHHS DHEHHSDHER HSDHEHHSEH	120	
EHHSDHDHHS HHNHAASGKN KRKAICPDHD SDSSGKDPRN SQGKGahrpe HASGRRNVKD	180	
SVSASEVTST VYNTVSEGTH FLETIETPRP GKLFPKDVS STPPSVTSKS RVSRLAGRKT	240	
NESVSEPRKG PMYSRNTNEN PQECFNASKL LTSHGGMQIV PLNATEFNYL CPAIIHQIDA	300	
RSCLIHTSEK KAEIPPKTYS LQIAWVGGFI AISIISFLSL LGVILVPLMN RVFFKFLLSF	360	
LVALAVGTLS GDAFLHLLPH SHASHHHSHS HEEPAMEMKR GPLFSHLSSQ NIEESAYFDS	420	
TWKGLTALGG LYFMLVVEHV LTLIKQFKDK KKKNQKKPEN DDDVEIKQL SKYESQLSTN	480	
EEKVDTDDRT EGYLRADSQE PSHFDSQQPA VLEEEEVMIA HAHPQEVDNE YVPRGCKNKC	540	
HSHFHDTLGQ SDDLIHHHHY YHHILHHHH QNHHPHSHSQ RYSREELKDA GVATLAWMVI	600	
MGDGLHNFSN GLAIGAAFTE GLSSGLSTSV AVPCHELPHE LGDFAVLLKA GMTVKQAVLY	660	

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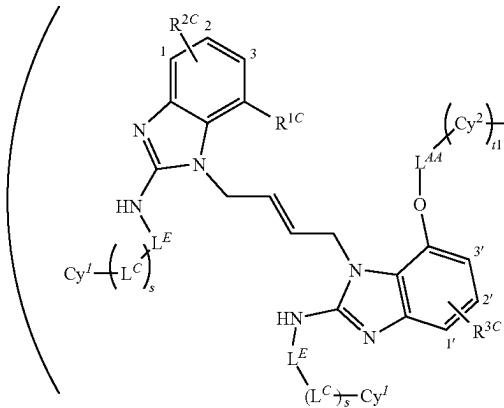
NALSAMMLAYL GMATGIFIGH YAENVSMWIF ALTAGLFMYV ALVDMVPEML HNDASDHGCS	720
RWGYFFLQNA GMLLGPGIML LISIFEHKIV FRINF	755

SEQ ID NO: 1034 moltype = AA length = 8
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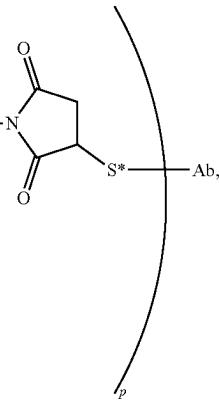
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1.-3. (canceled)

4. An antibody-drug conjugate comprising an antigen-binding protein or an antigen-binding fragment thereof that binds CD228, wherein the antibody-drug conjugate is represented by the structure:



each Cy¹ is independently a 4-6 membered heterocycle, a 5-6 membered heteroaryl, or a C₃₋₆ cycloalkyl, each optionally substituted with one or more R^K;
 each R^K is independently selected from the group consisting of: C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆



or a pharmaceutically acceptable salt thereof, wherein:

Ab is the antigen-binding protein or an antigen-binding fragment thereof;

each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;

subscript p is an integer from 2 to 8;

R^{1C} is hydrogen, hydroxyl, C₁₋₆ alkoxy, -(C₁₋₆ alkyl) C₁₋₆ alkoxy, -(CH₂)_n-NR^AR^B, or PEG2 to PEG4;

R^{2C} is -CO₂R^M, -(C=O)NR^CR^D, -S(O)₂NR^CR^D, -S(O)₂R^M, -(CH₂)_q-NR^ER^F, -(CH₂)_q-OR^M, -O(C=O)-NR^ER^F, or -NR^M(C=O)-NR^ER^F, wherein R^{2C} is attached at any one of positions labeled 1, 2, or 3;

R^{3C} is -CO₂R^M, -(C=O)NR^CR^D, -S(O)₂NR^CR^D, -S(O)₂R^M, -(CH₂)_q-NR^ER^F, -(CH₂)_q-OR^M, -O(C=O)-NR^ER^F, or -NR^M(C=O)-NR^ER^F, wherein R^{3C} is attached at any one of positions labeled 1', 2', or 3';

each R^A, R^B, R^C, R^D, R^E, R^F, and R^M are independently hydrogen or C₁₋₆ alkyl;

each subscript n is independently an integer from 0 to 6;

each subscript q is independently an integer from 0 to 6;

L^E is -(C=O)- or -S(O)₂-;

L^C is -(CR^IR^J)₁₋₃-

each R^I and R^J are independently hydrogen or C₁₋₃ alkyl; subscript s is 0 or 1;

haloalkoxy, halogen, -OH, =O, -NR^{d2}R^{e2}, -C(O)NR^{d2}R^{e2}, -C(O)(C₁₋₆ alkyl), and -C(O)O(C₁₋₆ alkyl);

each R^{d2} and R^{e2} are independently hydrogen or C₁₋₃ alkyl;

L^{AA} is -(CH₂)₁₋₆-, -C(O)(CH₂)₁₋₆-, -C(O)NR^L(CH₂)₁₋₆-, -(CH₂)₁₋₆O-, -C(O)(CH₂)₁₋₆O-, or -C(O)NR^L(CH₂)₁₋₆O-;

R^L is hydrogen or C₁₋₃ alkyl;

Cy² is C₃₋₆ cycloalkyl, 4-6 membered heterocycle, 5-6 membered heteroaryl, or phenyl,

each optionally substituted with one or more R^U;

each R^U is independently selected from the group consisting of -CO₂R^{J1}, -(C=O)NR^{d3}R^{e3}, -S(O)₂NR^{d3}R^{e3}, -(CH₂)_{q1}-NR^{g1}R^{h1}, -(CH₂)_{q1}-OR^{J1}, and -(CH₂)_{q1}-(OCH₂CH₂)₁₋₈OH;

each R^{d3}, R^{e3}, R^{g1}, R^{h1}, and R^{J1} are independently hydrogen or C₁₋₆ alkyl;

subscript q1 is an integer from 0 to 6;

subscripts t1 and t2 are independently 0 or 1, wherein at least one of t1 and t2 is 1;

L^D is -(CH₂)₁₋₆-;

subscript u is 0 or 1;

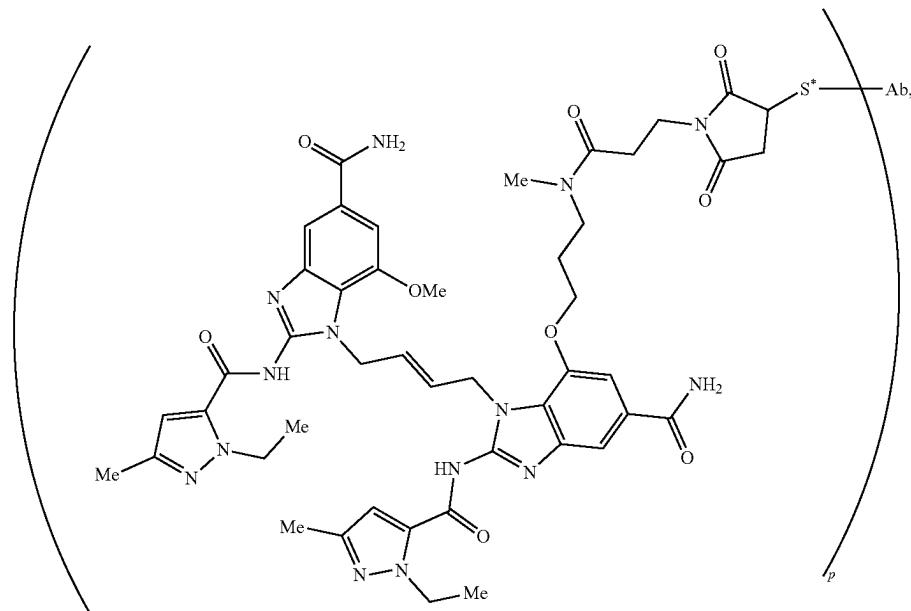
Z is -N(R^{HH})- or -N⁺(C₁₋₆ alkyl)(R^{HH})-;

R^{HH} is hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, $-(CH_2)_{1-3}C_3-$ cycloalkyl, $-(CH_2)_{1-3}C_{1-3}$ alkoxy, $-(CH_2)_{1-3}$ 4-6 membered heterocycle, or $-(CH_2)_{1-3}$ 5-6 membered heteroaryl;
 Y is a self-immolative moiety, a non-self-immolative releasable moiety, or a non-cleavable moiety;
 w subscript y is 0 or 1;

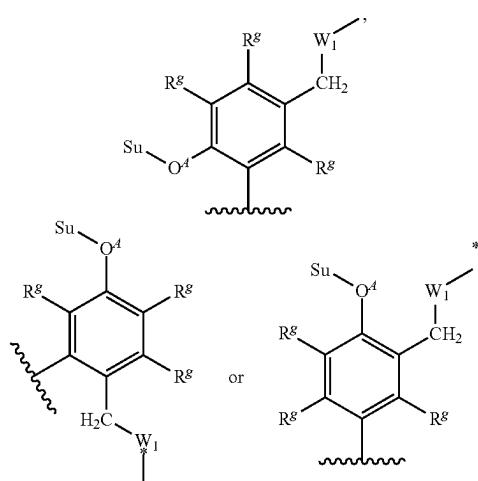
subscript w is 0 or 1;
 L^{BB} is $-(CH_2)_{1-6}-$, $-C(O)(CH_2)_{1-6}-$, or $-[NHC(O)(CH_2)_{1-4}]_{1-3}-$; and

each subscript b is independently an integer from 1 to 6.

5. The antibody-drug conjugate of claim 4, wherein the antibody-drug conjugate is represented by the structure:



W is a chain of 1-12 amino acids or has the structure:



wherein Su is a Sugar moiety;

$-O^4-$ represents a glycosidic bond;

each R^9 is independently hydrogen, halogen, $-CN$, or $-NO_2$;

W^1 is absent or $-O-C(=O)-$;

$\sim\sim\sim$ represents covalent attachment to L^{BB} ;

* represents covalent attachment to Y , L^D , NR^{HH} , or Cy^2 ;

or a pharmaceutically acceptable salt thereof.

6. The antibody-drug conjugate of claim 4, wherein the antigen-binding protein or antigen-binding fragment thereof is hL49 HALC IgG1.

7. The antibody-drug conjugate of claim 4, wherein the antigen-binding protein or antigen-binding fragment thereof comprises the following 6 CDRs:

an CDR-H1 comprising the amino acid sequence of SEQ ID NO: 29;

an CDR-H2 comprising the amino acid sequence of SEQ ID NO: 30;

an CDR-H3 comprising the amino acid sequence of SEQ ID NO: 31;

an CDR-L1 comprising the amino acid sequence of SEQ ID NO: 32;

an CDR-L2 comprising the amino acid sequence of SEQ ID NO: 33; and

an CDR-L3 comprising the amino acid sequence of SEQ ID NO: 34.

8. The antibody-drug conjugate of claim 4, wherein the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 35 and the VL has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 36.

9. The antibody-drug conjugate of claim 4, wherein the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH comprises the

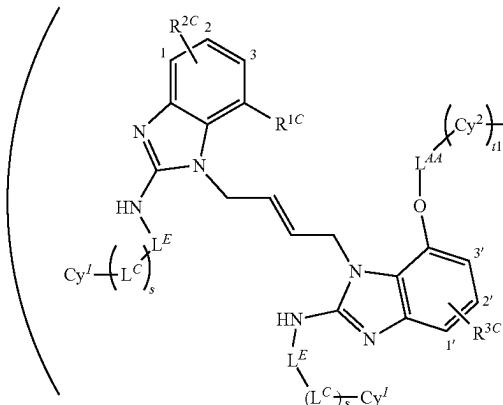
amino acid sequence of SEQ ID NO: 35 and the VL comprises the amino acid sequence of SEQ ID NO: 36.

10. The antibody-drug conjugate of claim 4, wherein the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 37 or SEQ ID NO: 38 and an LC comprising the amino acid sequence of SEQ ID NO: 39.

11. The antibody-drug conjugate of claim 4, wherein the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 40 or SEQ ID NO: 41 and an LC comprising the amino acid sequence of SEQ ID NO: 42.

12.-14. (canceled)

15. An antibody-drug conjugate comprising an antigen-binding protein or an antigen-binding fragment thereof that binds $\alpha\beta\beta 6$, wherein the antibody-drug conjugate is represented by the structure:



or a pharmaceutically acceptable salt thereof, wherein:

Ab is the antigen-binding protein or an antigen-binding fragment thereof;

each S* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;

subscript p is an integer from 2 to 8;

R^{1C} is hydrogen, hydroxyl, C₁₋₆ alkoxy, -(C₁₋₆ alkyl)C₁₋₆ alkoxy, -(CH₂)_n-NR⁴R^B, or PEG2 to PEG4; R^{2C} is -CO₂R^M, -(C=O)NR^CR^D, -S(O)₂NR^CR^D, -S(O)₂R^M, -(CH₂)_q-NR^ER^F, -(CH₂)_q-OR^M, -O(C=O)-NR^ER^F, or -NR^M(C=O)-NR^ER^F, wherein R^{2C} is attached at any one of positions labeled 1, 2, or 3;

R^{3C} is -CO₂R^M, -(C=O)NR^CR^D, -S(O)₂NR^CR^D, -S(O)₂R^M, -(CH₂)_q-NR^ER^F, -(CH₂)_q-OR^M, -O(C=O)-NR^ER^F, or -NR^M(C=O)-NR^ER^F, wherein R^{3C} is attached at any one of positions labeled 1', 2', or 3';

each R^A, R^B, R^C, R^D, R^E, R^F, and R^M are independently hydrogen or C₁₋₆ alkyl;

each subscript n is independently an integer from 0 to 6;

each subscript q is independently an integer from 0 to 6;

L^E is -(C=O)- or -S(O)₂-;

L^C is -(CR^IR^J)₁₋₃-

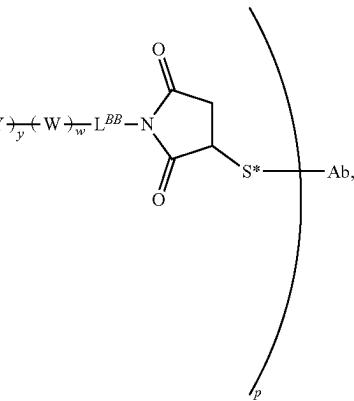
each R^I and R^J are independently hydrogen or C₁₋₃ alkyl; subscript s is 0 or 1;

each Cyⁱ is independently a 4-6 membered heterocycle, a 5-6 membered heteroaryl, or a C₃₋₆ cycloalkyl, each optionally substituted with one or more R^K;

each R^K is independently selected from the group consisting of: C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, halogen, -OH, =O, -NR^{d2}R^{e2}, -C(O)NR^{d2}R^{e2}, -C(O)(C₁₋₆ alkyl), and -C(O)O(C₁₋₆ alkyl);

each R^{d2} and R^{e2} are independently hydrogen or C₁₋₃ alkyl;

L^{A4} is -(CH₂)₁₋₆-, -C(O)(CH₂)₁₋₆-, -C(O)NR^L(CH₂)₁₋₆-, -(CH₂)₁₋₆O-, -C(O)(CH₂)₁₋₆O-, or -C(O)NR^L(CH₂)₁₋₆O-;



R^L is hydrogen or C₁₋₃ alkyl;

Cy² is C₃₋₆ cycloalkyl, 4-6 membered heterocycle, 5-6 membered heteroaryl, or phenyl, each optionally substituted with one or more R^U;

each R^U is independently selected from the group consisting of -CO₂R^I, -(C=O)NR^{d3}R^{e3}, -S(O)₂NR^{d3}R^{e3}, -(CH₂)_{q1}-NR^{g1}R^{h1}, -(CH₂)_{q1}-OR³¹, and -(CH₂)_{q1}-(OCH₂CH₂)₁₋₈OH;

each R^{d3}, R^{e3}, R^{g1}, R^{h1}, and R³¹ are independently hydrogen or C₁₋₆ alkyl;

subscript q1 is an integer from 0 to 6;

subscripts t1 and t2 are independently 0 or 1, wherein at least one of t1 and t2 is 1;

L^D is -(CH₂)₁₋₆-;

subscript u is 0 or 1;

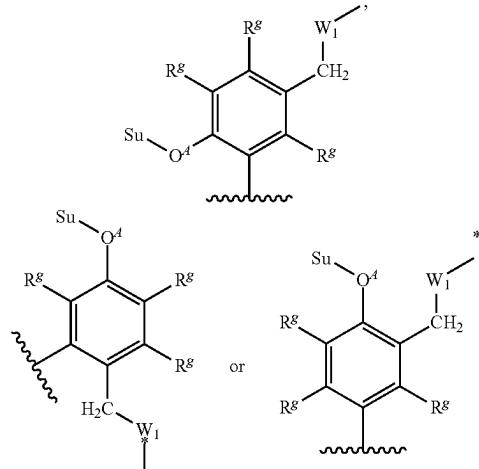
Z is -N(R^{HH})- or -N+(C₁₋₆ alkyl)(R^{HH})-;

R^{HH} is hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, -(CH₂)₁₋₃C₁₋₃ alkoxy, -(CH₂)₁₋₃ 4-6 membered heterocycle, or -(CH₂)₁₋₃ 5-6 membered heteroaryl;

Y is a self-immolative moiety, a non-self-immolative releasable moiety, or a non-cleavable moiety;

subscript y is 0 or 1;

W is a chain of 1-12 amino acids or has the structure:



wherein Su is a Sugar moiety;

—O^d— represents a glycosidic bond;

each R^g is independently hydrogen, halogen, —CN, or —NO₂;

W¹ is absent or —O—C(=O)—;

~~~~~ represents covalent attachment to L<sup>BB</sup>;

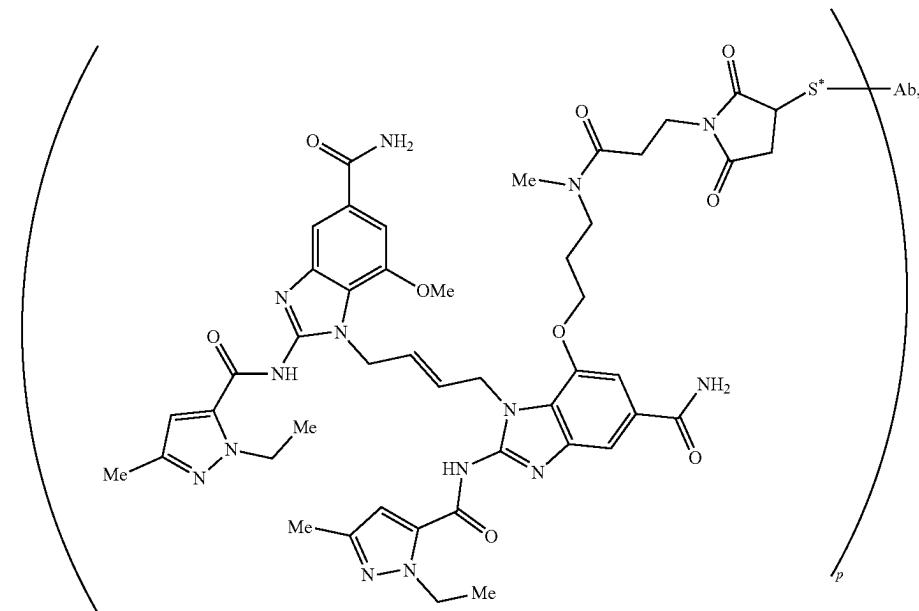
\* represents covalent attachment to Y, L<sup>D</sup>, NR<sup>HH</sup> or Cy<sup>2</sup>;

subscript w is 0 or 1;

L<sup>BB</sup> is —(CH<sub>2</sub>)<sub>1-6</sub>—, —C(O)(CH<sub>2</sub>)<sub>1-6</sub>—, or —[NHC(O)(CH<sub>2</sub>)<sub>1-4</sub>]<sub>1-3</sub>—; and

each subscript b is independently an integer from 1 to 6.

**16.** The antibody-drug conjugate of claim 15, wherein the antibody-drug conjugate is represented by the structure:



or a pharmaceutically acceptable salt thereof.

**17.** The antibody-drug conjugate of claim 15, wherein the antigen-binding protein or antigen-binding fragment thereof is h2A2 HCLG IgG1.

**18.** The antibody-drug conjugate of claim 15, wherein the antigen-binding protein or antigen-binding fragment thereof comprises the following 6 CDRs:

an CDR-H1 comprising the amino acid sequence of SEQ ID NO: 43;

an CDR-H2 comprising the amino acid sequence of SEQ ID NO: 44;

an CDR-H3 comprising the amino acid sequence of SEQ ID NO: 45;

an CDR-L1 comprising the amino acid sequence of SEQ ID NO: 46;

an CDR-L2 comprising the amino acid sequence of SEQ ID NO: 47; and

an CDR-L3 comprising the amino acid sequence of SEQ ID NO: 48.

**19.** The antibody-drug conjugate of claim **15**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 49 and the VL has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 50.

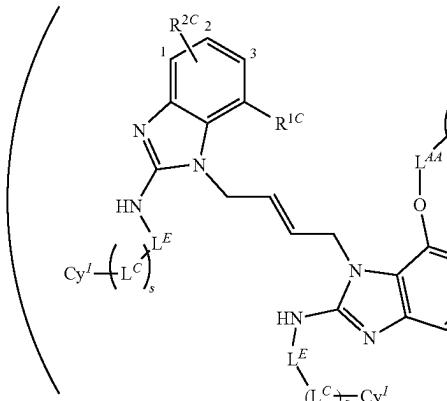
**20.** The antibody-drug conjugate of claim **15**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 49 and the VL comprises the amino acid sequence of SEQ ID NO: 50.

**21.** The antibody-drug conjugate of claim **15**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 51 or SEQ ID NO: 52 and an LC comprising the amino acid sequence of SEQ ID NO: 53.

**22.** The antibody-drug conjugate of claim **15**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 54 or SEQ ID NO: 55 and an LC comprising the amino acid sequence of SEQ ID NO: 56.

**23.-25.** (canceled)

**26.** An antibody-drug conjugate comprising an antigen-binding protein or an antigen-binding fragment thereof that binds B7-H4, wherein the antibody-drug conjugate is represented by the structure:



R<sup>3C</sup> is —CO<sub>2</sub>R<sup>M</sup>, —(C=O)NR<sup>C</sup>R<sup>D</sup>, —S(O)<sub>2</sub>NR<sup>C</sup>R<sup>D</sup>, —S(O)<sub>2</sub>R<sup>M</sup>, —(CH<sub>2</sub>)<sub>q</sub>—NR<sup>E</sup>R<sup>F</sup>, —(CH<sub>2</sub>)<sub>q</sub>—OR<sup>M</sup>, —O(C=O)—NR<sup>E</sup>R<sup>F</sup>, or —NR<sup>M</sup>(C=O)—NR<sup>E</sup>R<sup>F</sup>, wherein R<sup>3C</sup> is attached at any one of positions labeled 1', 2', or 3';

each R<sup>A</sup>, R<sup>B</sup>, R<sup>C</sup>, R<sup>D</sup>, R<sup>E</sup>, R<sup>F</sup>, and R<sup>M</sup> are independently hydrogen or C<sub>1-6</sub> alkyl;

each subscript n is independently an integer from 0 to 6;

each subscript q is independently an integer from 0 to 6;

L<sup>E</sup> is —(C=O)— or —S(O)<sub>2</sub>—;

L<sup>C</sup> is —(CR<sup>I</sup>R<sup>J</sup>)<sub>1-3</sub>—

each R<sup>I</sup> and R<sup>J</sup> are independently hydrogen or C<sub>1-3</sub> alkyl;

subscript s is 0 or 1;

each Cy<sup>1</sup> is independently a 4-6 membered heterocycle, a 5-6 membered heteroaryl, or a C<sub>3-6</sub> cycloalkyl, each optionally substituted with one or more R<sup>K</sup>;

each R<sup>K</sup> is independently selected from the group consisting of: C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkoxy, halogen, —OH, —O, —NR<sup>d2</sup>R<sup>e2</sup>, —C(O)NR<sup>d2</sup>R<sup>e2</sup>, —C(O)(C<sub>1-6</sub> alkyl), and —C(O)O(C<sub>1-6</sub> alkyl);

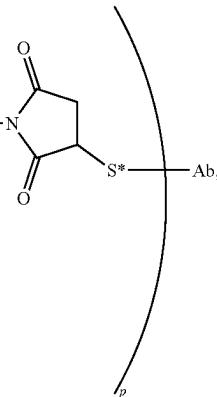
each R<sup>d2</sup> and R<sup>e2</sup> are independently hydrogen or C<sub>1-3</sub> alkyl;

L<sup>4A</sup> is —(CH<sub>2</sub>)<sub>1-6</sub>—, —C(O)(CH<sub>2</sub>)<sub>1-6</sub>—, —C(O)NR<sup>L</sup>(CH<sub>2</sub>)<sub>1-6</sub>—, —(CH<sub>2</sub>)<sub>1-6</sub>O—, —C(O)(CH<sub>2</sub>)<sub>1-6</sub>O—, or —C(O)NR<sup>L</sup>(CH<sub>2</sub>)<sub>1-6</sub>O—;

R<sup>L</sup> is hydrogen or C<sub>1-3</sub> alkyl;

Cy<sup>2</sup> is C<sub>3-6</sub> cycloalkyl, 4-6 membered heterocycle, 5-6 membered heteroaryl, or phenyl, each optionally substituted with one or more R<sup>U</sup>;

each R<sup>U</sup> is independently selected from the group consisting of —CO<sub>2</sub>R<sup>I</sup>, —(C=O)NR<sup>d3</sup>R<sup>e3</sup>, —S(O)<sub>2</sub>R<sup>d3</sup>R<sup>e3</sup>, —(CH<sub>2</sub>)<sub>q1</sub>—NR<sup>g1</sup>R<sup>h1</sup>, —(CH<sub>2</sub>)<sub>q1</sub>—OR<sup>I</sup>, and —(CH<sub>2</sub>)<sub>q1</sub>—(OCH<sub>2</sub>CH<sub>2</sub>)<sub>1-8</sub>OH;



or a pharmaceutically acceptable salt thereof, wherein:

Ab is the antigen-binding protein or an antigen-binding fragment thereof;

each S\* is a sulfur atom from a cysteine residue of the antigen-binding protein or an antigen-binding fragment thereof;

subscript p is an integer from 2 to 8;

R<sup>1C</sup> is hydrogen, hydroxyl, C<sub>1-6</sub> alkoxy, —(C<sub>1-6</sub> alkyl)

C<sub>1-6</sub> alkoxy, —(CH<sub>2</sub>)<sub>n</sub>—NR<sup>E</sup>R<sup>F</sup>, or PEG2 to PEG4;

R<sup>2C</sup> is —CO<sub>2</sub>R<sup>M</sup>, —(C=O)NR<sup>C</sup>R<sup>D</sup>, —S(O)<sub>2</sub>NR<sup>C</sup>R<sup>D</sup>,

—S(O)<sub>2</sub>R<sup>M</sup>, —(CH<sub>2</sub>)<sub>q</sub>—NR<sup>E</sup>R<sup>F</sup>, —(CH<sub>2</sub>)<sub>q</sub>—OR<sup>M</sup>,

—O(C=O)—NR<sup>E</sup>R<sup>F</sup>, or —NR<sup>M</sup>(C=O)—NR<sup>E</sup>R<sup>F</sup>, wherein R<sup>2C</sup> is attached at any one of positions labeled 1, 2, or 3;

each R<sup>d3</sup>, R<sup>e3</sup>, R<sup>g1</sup>, R<sup>h1</sup>, and R<sup>j1</sup> are independently hydrogen or C<sub>1-6</sub> alkyl;

subscript q1 is an integer from 0 to 6;

subscripts t1 and t2 are independently 0 or 1, wherein at least one of t1 and t2 is 1;

L<sup>D</sup> is —(CH<sub>2</sub>)<sub>1-6</sub>—;

subscript u is 0 or 1;

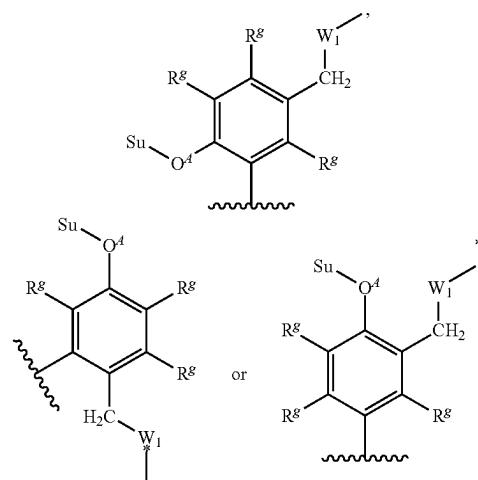
Z is —N(R<sup>HH</sup>)— or -N+(C<sub>1-6</sub> alkyl)(R<sup>HH</sup>)—;

R<sup>HH</sup> is hydrogen, C<sub>1-6</sub> alkyl, C<sub>3-6</sub> cycloalkyl, —(CH<sub>2</sub>)<sub>1-3</sub>C<sub>3-6</sub> cycloalkyl, —(CH<sub>2</sub>)<sub>1-3</sub>C<sub>1-3</sub> alkoxy, —(CH<sub>2</sub>)<sub>1-3</sub> 4-6 membered heterocycle, or —(CH<sub>2</sub>)<sub>1-3</sub> 5-6 membered heteroaryl;

Y is a self-immolative moiety, a non-self-immolative releasable moiety, or a non-cleavable moiety;

subscript y is 0 or 1;

W is a chain of 1-12 amino acids or has the structure:



wherein Su is a Sugar moiety;

$\text{—O}^4\text{—}$  represents a glycosidic bond;

each  $R^g$  is independently hydrogen, halogen,  $\text{—CN}$ , or

$\text{—NO}_2$ ;

$W^1$  is absent or  $\text{—O—C(=O)—}$ ;

$\text{~~~~~}$  represents covalent attachment to  $L^{BB}$ ;

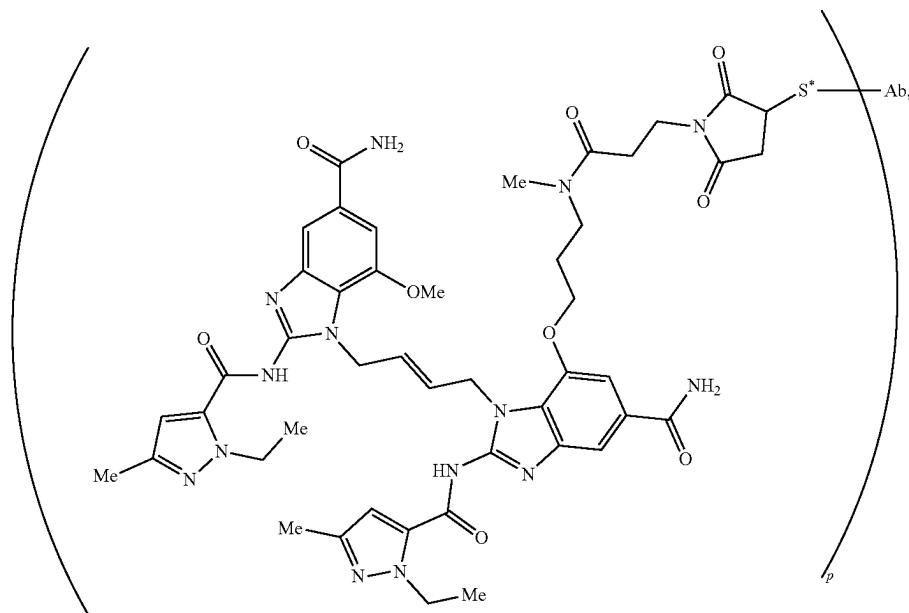
\* represents covalent attachment to Y,  $L^D$ ,  $NR^{HH}$  or  $Cy^2$ ;

subscript w is 0 or 1;

$L^{BB}$  is  $\text{—(CH}_2\text{)}_{1-6}\text{—}$ ,  $\text{—C(O)(CH}_2\text{)}_{1-6}\text{—}$ , or  $\text{—[NHC(O)}$   
 $\text{(CH}_2\text{)}_{1-4}\text{]}_{1-3}\text{—}$ ; and

each subscript b is independently an integer from 1 to 6.

**27.** The antibody-drug conjugate of claim **26**, wherein the antibody-drug conjugate is represented by the structure:



or a pharmaceutically acceptable salt thereof.

**28.** The antibody-drug conjugate of claim **26**, wherein the antigen-binding protein or antigen-binding fragment thereof is B7H41001 hIgG1.

**29.** The antibody-drug conjugate of claim **26**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises the following 6 CDRs:

- an CDR-H1 comprising the amino acid sequence of SEQ ID NO: 57;
- an CDR-H2 comprising the amino acid sequence of SEQ ID NO: 58;
- an CDR-H3 comprising the amino acid sequence of SEQ ID NO: 59;
- an CDR-L1 comprising the amino acid sequence of SEQ ID NO: 60;
- an CDR-L2 comprising the amino acid sequence of SEQ ID NO: 61; and
- an CDR-L3 comprising the amino acid sequence of SEQ ID NO: 62.

**30.** The antibody-drug conjugate of claim **26**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 63 and the VL has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 64.

**31.** The antibody-drug conjugate of claim **26**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 63 and the VL comprises the amino acid sequence of SEQ ID NO: 64.

**32.** The antibody-drug conjugate of claim **26**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 65 or SEQ ID NO: 66 and an LC comprising the amino acid sequence of SEQ ID NO: 67.

**33.** The antibody-drug conjugate of claim **26**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises an HC comprising the amino acid sequence of SEQ ID NO: 68 or SEQ ID NO: 69 and an LC comprising the amino acid sequence of SEQ ID NO: 70.

**34.** The antibody-drug conjugate of claim **26**, wherein the antigen-binding protein or antigen-binding fragment thereof is selected from the group consisting of B7H4-15461, B7H4-20500, B7H4-20501, B7H4-20502.1, B7H4-22208, B7H4-15462, B7H4-22213, B7H4-15465, B7H4-20506, B7H4-15483, B7H4-20513, B7H4-22216, B7H4-15489, B7H4-20516, B7H4-15472, B7H4-15503, B7H4-15495, B7H4-15478, B7H4-15441, and B7H4-20496.

**35.** The antibody-drug conjugate of claim **26**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises VH CDR1, VH CDR2, VH CDR3 and VL CDR1, VL CDR2, and VL CDR3 sequences selected from the group consisting of:

- (a) SEQ ID NOs: 71-76, respectively;
- (b) SEQ ID NOs: 79-84, respectively;
- (c) SEQ ID NOs: 87-92, respectively;
- (d) SEQ ID NOs: 95-100, respectively;
- (e) SEQ ID NOs: 103-108, respectively;
- (f) SEQ ID NOs: 111-116, respectively;
- (g) SEQ ID NOs: 119-124, respectively;
- (h) SEQ ID NOs: 127-132, respectively;
- (i) SEQ ID NOs: 135-140, respectively;
- (j) SEQ ID NOs: 143-148, respectively; F

(k) SEQ ID NOs: 151-156, respectively;

(l) SEQ ID NOs: 159-164, respectively;

(m) SEQ ID NOs: 167-172, respectively;

(n) SEQ ID NOs: 175-180, respectively;

(o) SEQ ID NOs: 183-188, respectively;

(p) SEQ ID NOs: 191-196, respectively;

(q) SEQ ID NOs: 199-204, respectively;

(r) SEQ ID NOs: 207-212, respectively;

(s) SEQ ID NOs: 215-220, respectively; and

(t) SEQ ID NOs: 223-228, respectively.

**36.** The antibody-drug conjugate of claim **26**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 77, 85, 93, 101, 109, 117, 125, 133, 141, 149, 157, 165, 173, 181, 189, 197, 205, 213, 221, and 229 and the VL has at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% amino acid sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 78, 86, 94, 102, 110, 118, 126, 134, 142, 150, 158, 166, 174, 182, 190, 198, 206, 214, 222, and 230, respectively.

**37.** The antibody-drug conjugate of claim **26**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises a VH and a VL, wherein the VH has an amino acid sequence selected from the group consisting of SEQ ID NOs: 77, 85, 93, 101, 109, 117, 125, 133, 141, 149, 157, 165, 173, 181, 189, 197, 205, 213, 221, and 229 and the VL has an amino acid sequence selected from the group consisting of SEQ ID NOs: 78, 86, 94, 102, 110, 118, 126, 134, 142, 150, 158, 166, 174, 182, 190, 198, 206, 214, 222, and 230, respectively.

**38.** The antibody-drug conjugate of claim **26**, wherein the antigen-binding protein or antigen-binding fragment thereof comprises an HC having an amino acid sequence selected from the group consisting of SEQ ID NOs: 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, and 269 and an LC having an amino acid sequence selected from the group consisting of SEQ ID NOs: 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, and 270, respectively.

**39-42.** (canceled)

**43.** A pharmaceutical composition comprising the antibody-drug conjugate of claim **4** and a pharmaceutically acceptable carrier.

**44.** A method of treating a CD228-expressing cancer in an individual comprising administering to an individual in need thereof an effective amount of the antibody-drug conjugate of claim **4**.

**45.** A method of treating  $\alpha\beta\delta$ -expressing cancer in an individual comprising administering to an individual in need thereof an effective amount of the antibody-drug conjugate of claim **15**.

**46.** A method of treating a B7-H4-expressing cancer in an individual comprising administering to an individual in need thereof an effective amount of the antibody-drug conjugate of claim **26**.

**47.** A pharmaceutical composition comprising the antibody-drug conjugate of claim **15** and a pharmaceutically acceptable carrier.

**48.** A pharmaceutical composition comprising the anti-body-drug conjugate of claim **26** and a pharmaceutically acceptable carrier.

\* \* \* \* \*