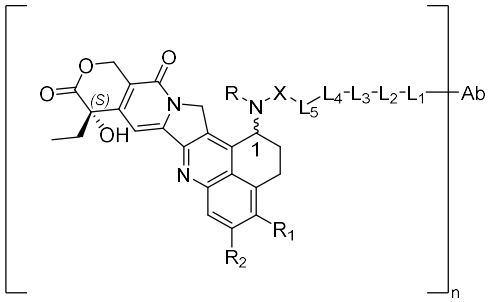
METHODS AND COMPOSITIONS FOR TREATING TUMORS USING ANTIBODY CAMPTOTHECIN DRUG CONJUGATES

CLAIMS

WHAT IS CLAIMED IS:

1. Use of a ligand-camptothecin conjugate of Formula I in the manufacture of a medicament for treating cancer or a tumor, wherein the ligand-camptothecin conjugate of Formula I, or a pharmaceutically acceptable salt or solvate thereof, is to be administered to a subject in need thereof, wherein the medicament is to be administered to the subject at a treatment dose per administration from about 0.1 mg/kg to 15.0 mg/kg,

wherein the Formula I has the following structure:

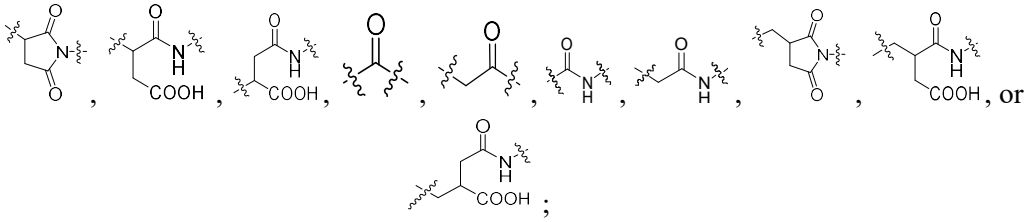


Formula I

wherein:

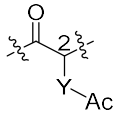
Ab is a bispecific antibody or antigen-binding fragment thereof having a binding affinity to EGFR and HER3;

L_1 is:



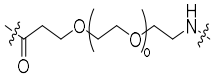
;

L_2 has the structure shown in Formula A,



Formula A

wherein Y is a scaffold selected from C1-C6 alkyl, substituted C1-C6 alkyl, or C3-C8 cycloalkyl; Ac is a hydrophilic structural unit; and the carbon 2 attached to Y is absolutely chiral in either the R configuration or the S configuration;

L_3 is present or absent, and when present, L_3 is selected from PEG hydrophilic units: , o is selected from an integer of 1-10;

L_4 is an enzymatically cleavable unit;

L_5 is a connection unit;

the chiral carbon atom No. 1 attached to N in Formula I has absolute chirality in either the R configuration or the S configuration;

R is selected from hydrogen atom, deuterium atom, halogen, C1-C6 alkyl, substituted C1-C6 alkyl, deuterated C1-C6 alkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl;

R_1 is selected from hydrogen atom, deuterium atom, halogen, C1-C6 alkyl, substituted C1-C6 alkyl, deuterated C1-C6 alkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, carboxyl, 3-7 heterocyclic, substituted 3-7 heterocyclic, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl;

R_2 is selected from hydrogen atom, deuterium atom, halogen, C1-C6 alkyl, substituted C1-C6 alkyl, deuterated C1-C6 alkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, carboxyl, 3-7 heterocyclic, substituted 3-7 heterocyclic, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl;

X selected from $-C(O)-CR_aR_b-(CR_3R_4)_m-O-$, $-C(O)-CR_aR_b-(CR_3R_4)_m-NH-$ or $-C(O)-CR_aR_b-(CR_3R_4)_m-S-$;

R_a and R_b are each independently selected from hydrogen atoms, deuterium atom, halogens, C1-C6 alkyl, deuterated C1-C6 alkyl, halogenated C1-C6 alkyl, C3-C8 cycloalkyl, C3-C8 cycloalkyl C1-C6 alkyl, C6-C10 aryl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, 3-7 heterocyclic group, substituted 3-7 heterocyclic group, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl;

R_3, R_4 are the same or different and are independently hydrogen atoms, deuterium atoms, halogens, C1-C6 alkyl, halogenated C1-C6 alkyl, deuterated C1-C6 alkyl, C1-C6 alkoxy, hydroxyl, amino, cyano, nitro, hydroxy C1-C6 alkyl, C3-C8 cycloalkyl, 3-7 heterocyclic, substituted 3-7 heterocyclic, respectively;

m is selected from integers 0-4; n is selected from integers 1-10.

2. The use of Claim 1, wherein the treatment comprises:

(a) a treatment cycle comprising a 4-week period with weekly dosing, wherein the treatment dose per administration is from about 0.25 mg/kg to about 10 mg/kg.

(b) a treatment cycle comprising a 4-weeks period with dosing on the first day of the first, second, and third weeks, and no dosing in the fourth week, wherein the treatment dose per administration is from about 1.5 mg/kg to about 15 mg/kg.

(c) a treatment cycle comprising a 4-week period with biweekly dosing, wherein the treatment dose per administration from about 2.0mg/kg to about 15mg/kg,

(d) a treatment cycle comprising 3-week period with weekly dosing, wherein the treatment dose per administration from about 0.25mg/kg to about 10mg/kg,

(e) a treatment cycle comprising a 3-week period with dosing on the first day of the first week and no dosing in the second and third weeks, wherein the treatment dose per administration from about 1.5mg/kg to about 6mg/kg,

(f) a treatment cycle comprising a 3-week period with dosing on the first day of the first and second weeks and no dosing in the third week, wherein the treatment dose per administration from about 2.0mg/kg to about 4.5mg/kg,

or a combination thereof.

3. The use of Claim 1-2, wherein the treatment dose per administration is from about 1.5 mg/kg to 5 mg/kg.

4. The use of Claim 1-3, wherein the treatment dose per administration is about 2.5mg/kg, 3 mg/kg or 3.5mg/kg.

5. The use of Claim 1-3, wherein the treatment dose per administration is about 2.0mg/kg, 2.2mg/mg, 2.5 mg/kg, or 2.75mg/kg.

6. The use of Claim 1-6, wherein the cancer or tumor comprises a cancer expressing EGFR, HER3, or a combination thereof.

7. The use of Claim 1-5, wherein the cancer or tumor comprises non-small cell lung cancer or small cell lung cancer, EGFR wild-type non-small cell lung cancer, EGFR mutant non-small cell lung cancer, head and neck squamous carcinoma, triple negative breast cancer, urothelial carcinoma (bladder cancer), esophageal squamous cell carcinoma (ESCC), or metastatic biliary track carcinoma (BTC).

8. The use of Claim 1, wherein the subject is a human.

9. The use of Claim 1-8, wherein the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvate thereof, is to be administered to the subject in the form of an injectable solution derived from a lyophilized powder injection formula, wherein the lyophilized powder injection formula comprises the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent compound thereof, and a pharmaceutical carrier composition.

10. The use of Claim 9, wherein the pharmaceutical carrier composition consists essentially of histidine, histidine hydrochloride, mannitol, sucrose, and polysorbate 80.

11. The use of Claim 9, the injectable solution is to be given to the subject intravenously.

12. The use of Claim 1-11, wherein a second treatment is to be administered to the subject before, after, or concurrently with the administration of the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent compound thereof, wherein the second treatment comprises hormonal treatment, chemotherapy, immune checkpoint inhibitor therapy, EGFR-TKI (epidermal growth factor receptor-lysine kinase inhibitor) therapy, immunotherapy, a targeted therapy, or a combination thereof.

13. The use of Claim 12, wherein for the immune checkpoint inhibitor therapy, an immune checkpoint inhibitor is to be administered, wherein the immune checkpoint inhibitor comprises anti-PD-1 mAb, anti-PD-L1 mAb, a combination of anti-PD-1 mAb and anti-PD-L1 mAb, anti-CTLA-4 mAb, anti-LAG3 mAb, anti-TIGIT mAb, or a combination thereof, and wherein for the chemotherapy, platinum-containing or non-platinum-containing chemotherapeutic agents are to be administered.

14. The use of Claim 13, wherein the subject is a patient with EGFR wild-type non-small cell lung cancer, a patient with small cell lung cancer, a patient with nasopharyngeal cancer, or a patient with head and neck cancer, and wherein the second treatment comprises the chemotherapy, the immune checkpoint inhibitor therapy, or a combination thereof.

15. The use of Claim 13, wherein the subject is a patient with EGFR-mutant non-small cell lung cancer, and wherein the second treatment comprises the EGFR-TKI therapy, the chemotherapy, the immune checkpoint inhibitor therapy, or a combination thereof.

16. The use of Claim 1, wherein the Ab comprises two IgG1 heavy chains, two κ light chains, and two scFv domains, wherein each scFv domain is connected to each of the IgG1 heavy chain or κ light chain through a linker, wherein the linker comprises an amino acid sequence of $(gly\text{-}gly\text{-}gly\text{-}gly\text{-}ser)_n$, and wherein n is an integer from 1 to 10.

17. The use of Claim 1, wherein Ab comprises,

an IgG1 heavy chain (HC), a, and a single-chain Fv (scFv) domain,

the IgG1 HC and κ LC form a Fab domain having a binding specificity for EGFR, and

the scFv domain has a binding specificity for HER3, wherein the scFv domain is connected to the IgG1 HC or the κ light chain (LC) through a linker to provide an IgG1 HC-linker-scFv or a κ LC-linker-scFv, wherein the linker is attached to the C-terminus or the N-terminus of the IgG1 HC or the C-terminus or the N-terminus of the κ LC, and wherein the scFv domain has a structural order of N-terminus-HC variable region-joint-LC variable region-C-terminus, or N-terminus-LC variable region-joint-HC variable region-C-terminus.

18. The use of Claim 17, wherein the linker comprises an amino acid sequence of $(gly\text{-}gly\text{-}gly\text{-}gly\text{-}ser)_n$, and wherein n is an integer from 1 to 10.

19. The use of Claim 17, wherein

the κ LC comprises a CDR as shown in SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,

the IgG1 HC comprises a CDR as shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, and

the scFv domains comprises HC variable region CDRs as shown in SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, and LC variable region CDRs as shown in SEQ ID NO: 12, SEQ ID NO: 13, SEQ

ID NO: 14.

20. The use of Claim 17, wherein the Ab comprises

the κ LC variable region as shown in SEQ ID NO: 2,

the IgG1 HC comprises a variable region as shown in SEQ ID NO: 7, and

the scFv domain contains a HC variable region as shown in SEQ ID NO: 15 and a LC variable region as shown in SEQ ID NO: 11.

21. The use of Claim 17, wherein

the κ LC comprises CDRs as shown in SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31,

the IgG1 HC comprises CDRs as shown in SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36 shown, and

the scFv domain contains the HC variable region CDRs as shown in SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, as the LC variable region CDRs as shown in SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14.

22. The use of Claim 17, wherein

the κ LC comprises a variable region as shown in SEQ ID NO: 28,

the IgG1 HC comprises a variable region as shown in SEQ ID NO: 33, and

the scFv domain comprising a HC variable region as shown in SEQ ID NO: 15 and a LC variable region as shown in SEQ ID NO: 11.

23. The use of Claim 17, wherein the Ab comprises,

the κ LC having a variable region as shown in SEQ ID NO: 20,

the IgG1 HC having a variable region as shown in SEQ ID NO: 24, and

the scFv domain comprising a HC variable region as shown in SEQ ID NO: 22 and a LC variable region as shown in SEQ ID NO: 21.

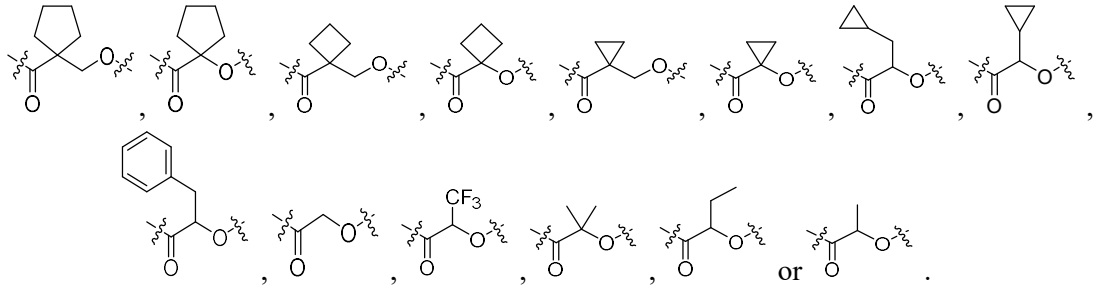
24. The use of Claim 17, wherein the Ab comprises,

a variable region as shown in SEQ ID NO: 40,

the IgG1 HC comprising a variable region as shown in SEQ ID NO: 42, and

the scFv domain comprising a HC variable region as shown in SEQ ID NO: 50 and a LC variable region as shown in SEQ ID NO: 21.

25. The use of Claim 1, wherein X comprises the following structures or isomers thereof:



where the left wavy line is connected to the camptothecin derivative, and the right wavy line is connected to L_5.

26. The use of Claim 1, wherein L_4 is selected from peptide residues comprising glycine (G) -glycine (G) -phenylalanine (F) -glycine (G).

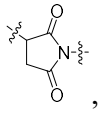
27. The use of Claim 1, wherein,

L_5 is selected from $-NR_5(CR_6R_7)_q-$ or a chemical bond, and q is selected from integers 0-6; and

R_5, R_6 and R_7 are the same or different and are each independently selected from hydrogen atoms, deuterium atoms, halogens, C1-C6 alkyl group, substituted C1-C6 alkyl group, deuterated C1-C6 alkyl group, C3-C8 cycloalkyl group, C3-C8 cycloalkyl C1-C6 alkyl group, C1-C6 alkoxy C1-C6 alkyl group, 3-7 heterocycloheteroaryl group, substituted 3-7 heterocycloheteroaryl group, C6-C10 aryl group, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl, or a combination thereof.

28. The use of Claim 26, wherein R_5, R_6 and R_7 are each independently selected from hydrogen atoms or C1-C6 alkyl group.

29. The use of Claim 1-15, wherein:

L_1 is ,

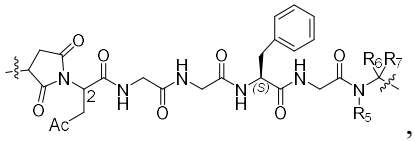
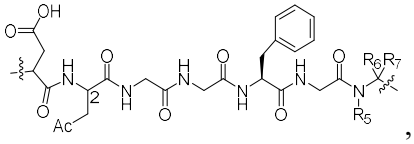
Y is C1-C6 alkyl, and the carbon 2 attached to Y is absolutely chiral in the S configuration,

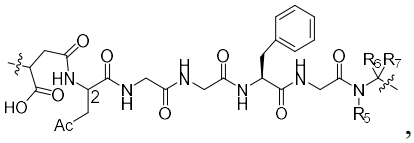
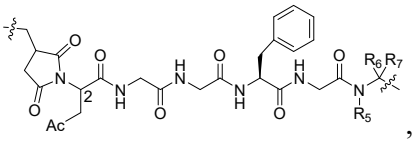
R is hydrogen, R_1 is C1-C6 alkyl, R_2 is halogen, and

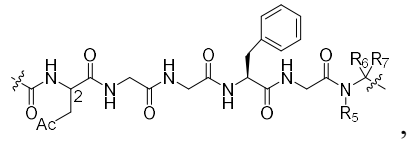
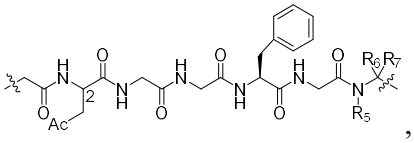
X selected from $-C(O)-CR_aR_b-(CR_3R_4)_m-O-$, wherein R_a and R_b are each independently selected from hydrogen and C1-C6 alkyl, and wherein m is 0.

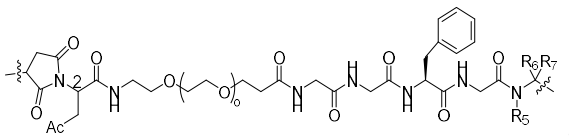
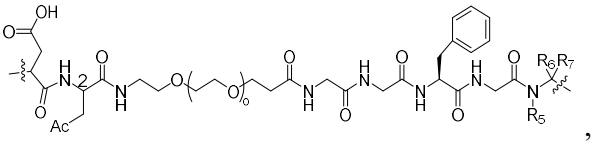
30. The use of Claim 28, wherein R_1 is methyl, R_2 is F, R_a and R_b are H and methyl.

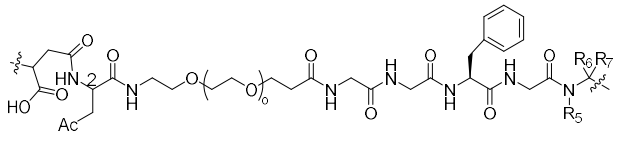
31. The use of Claim 1-15, wherein the linking unit $-L_1-L_2-L_3-L_4-L_5-$ comprises,

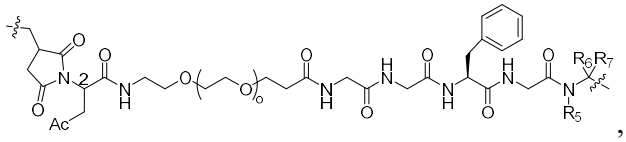
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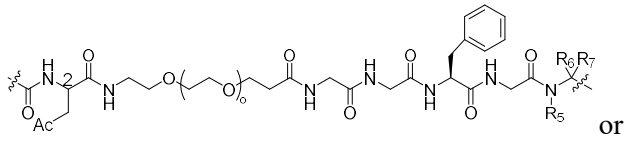
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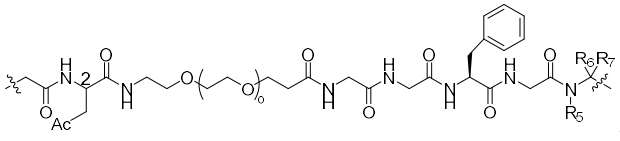
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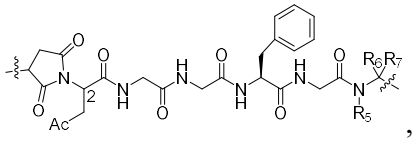
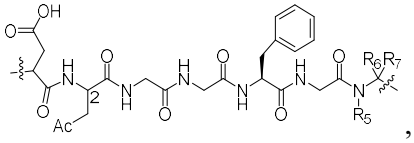
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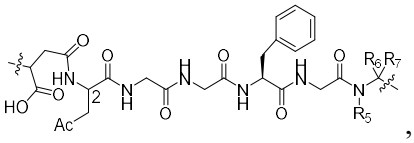
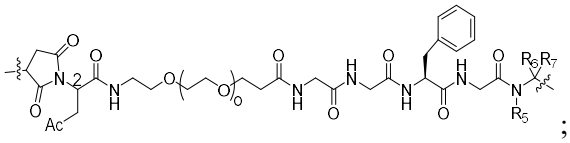
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or

.

32. The use of Claim 1-15, wherein the linking unit $-L_1-L_2-L_3-L_4-L_5-$ comprises,

, ,


, or 
;

wherein:

Ac is a hydrophilic structural unit,

R_5, R_6 and R_7 are the same or different and are each independently selected from hydrogen atom, deuterium atom, halogen, C1-C6 alkyl, substituted C1-C6 alkyl, deuterated C1-C6 alkyl, C3-C8 cycloalkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, 3-7 heterocyclic, substituted 3-7 heterocyclic, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl,

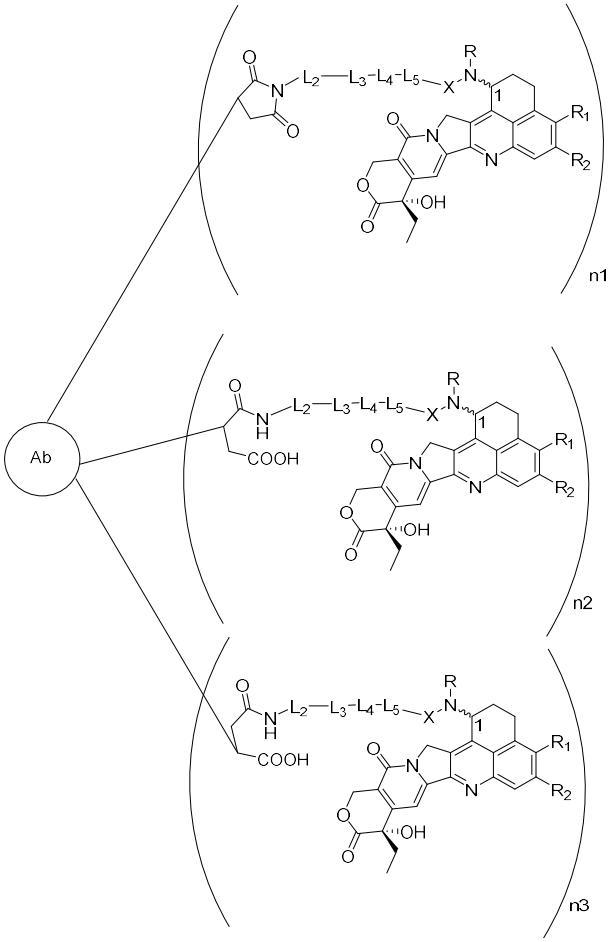
the carbon atom #2 attached to N has absolute chirality in either the R configuration or the S configuration,

the left wavy line is connected to the antibody or its antigen-binding fragment portion, and the right wavy line is connected to the X; and

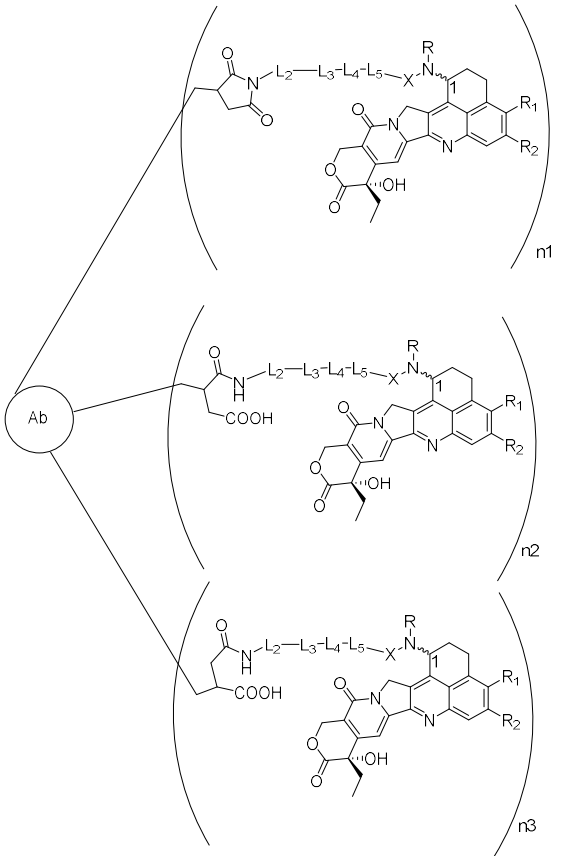
o is selected from integers 1-10.

33. The use of Claim 32, wherein R_5, R_6 and R_7 are each independently selected from a hydrogen atom or a C1-C6 alkyl group.

34. The use of Claim 1-15, wherein the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent compound thereof, has a structure as shown in Formula I-1 or I-2.



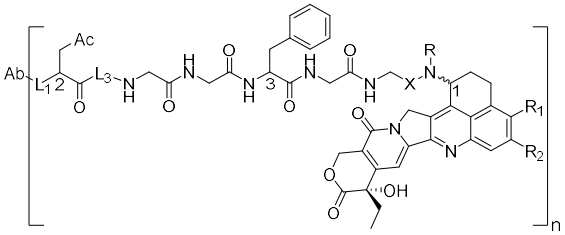
Formula I-1



Formula I-2

wherein n1, n2, n3 are each independently selected from any integer or any decimal number from 0-10, n1, n2, n3 are not simultaneously 0, and $1 \leq n1 + n2 + n3 \leq 10$.

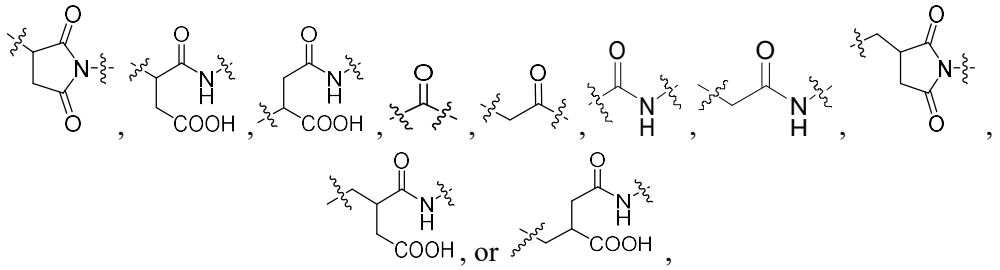
35. The use of Claim 1-15, wherein the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent compound thereof, has a structure as shown in Formula II:

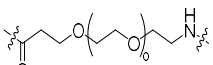


Formula II

wherein:

L_1 is a connection unit connected to Ab, comprising:



L_3 is present or absent, and when L3 is present, L_3 is selected from , o is selected

from an integer from 1-10,

Ac is a hydrophilic structural unit,

the 1-position, 2-position and 3-position chiral carbon atoms have two chiral configurations, the R-absolute configuration or the S-absolute configuration,

R is selected from hydrogen atoms, deuterium atoms, halogens, C1-C6 alkyl, substituted C1-C6 alkyl, deuterated C1-C6 alkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl,

R_1 is selected from hydrogen atoms, deuterium atoms, halogens, C1-C6 alkyl, substituted C1-C6 alkyl, deuterated C1-C6 alkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, carboxyl, 3-7 heterocyclic, substituted 3-7 heterocyclic, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl,

R_2 is selected from hydrogen atoms, deuterium atoms, halogens, C1-C6 alkyl, substituted C1-C6 alkyl, deuterated C1-C6 alkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, carboxyl, 3-7 heterocyclic, substituted 3-7 heterocyclic, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl,

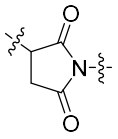
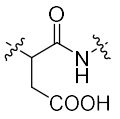
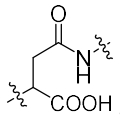
X selected from $-C(O)-CR_aR_b-(CR_3R_4)_m-O-$, $-C(O)-CR_aR_b-(CR_3R_4)_m-NH-$ or $-C(O)-CR_aR_b-(CR_3R_4)_m-S-$,

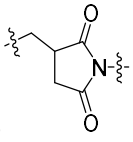
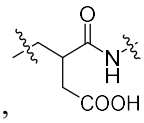
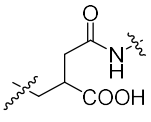
R_a and R_b are each independently selected from a hydrogen atom, a deuterium atom, a halogen, a C1-C6 alkyl, a deuterated C1-C6 alkyl, a halogenated C1-C6 alkyl, a C3-C8 cycloalkyl, a C3-C8 cycloalkyl C1-C6 alkyl, a C1-C6 alkoxy C1-C6 alkyl, a 3-7 heterocyclic group, a substituted 3-7 heterocyclic group, a C6-C10 aryl, a substituted C6-C10 aryl, a 5-10 heteroaryl, substituted 5-10 heteroaryl,

R_3, R_4 are the same or different and are independently hydrogen atoms, deuterium atoms, halogens, C1-C6 alkyl, halogenated C1-C6 alkyl, deuterated C1-C6 alkyl, C1-C6 alkoxy, hydroxyl, amino, cyano, nitro, hydroxy C1-C6 alkyl, C3-C8 cycloalkyl, 3-7 heterocyclic, substituted 3-7 heterocyclic, respectively,

m is selected from the integers 0-4, and

n is chosen from the integers 1-10.

36. The use of Claim 35, wherein L_1 is  ,  , or  .

37. The use of Claim 35, wherein L_1 is  ,  or  .

38. The use of Claim 35, wherein

R is hydrogen or C1-C6 alkyl.

R_1 is hydrogen or C1-C6 alkyl.

R_2 is hydrogen, halogen, or C1-C6 alkyl.

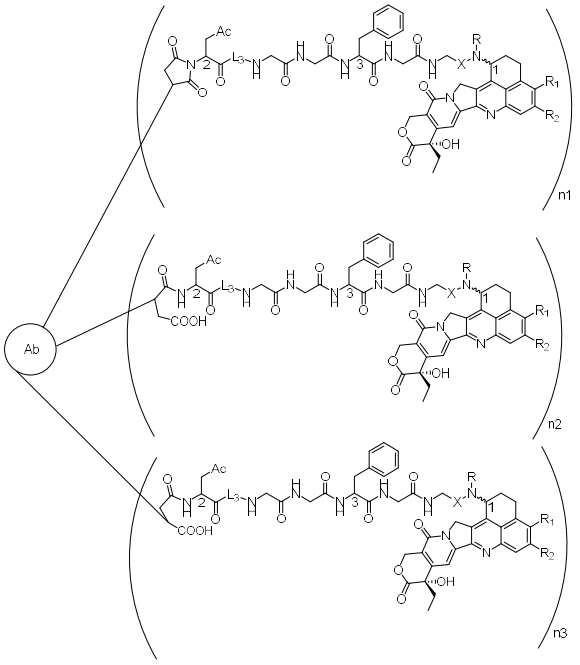
X is $-C(O)-CR_aR_b-(CR_3R_4)_m-O-$,

wherein R_a and R_b are each independently selected from a hydrogen atom, a C1-C6 alkyl, a halo-C1-C6 alkyl, a C3-C8 cycloalkyl C1-C6 alkyl or a C6-C10 aryl C1-C6 alkyl, or wherein R_a, R_b and the carbon atoms to which they are attached constitute C3-C8 cycloalkyl group, C3-C8 cycloalkyl C1-C6 alkyl group, 3-7 heterocycloalkyl group, substituted 3-7 heterocycloalkyl group, and

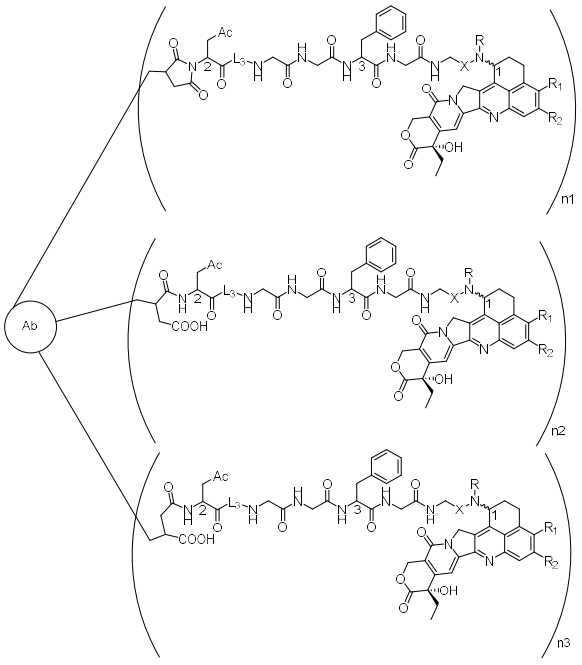
wherein R_3, R_4 are independently hydrogen or C1-C6 alkyl, or wherein R_3, R_4 and the carbon atoms attached thereto constitute a C3-C8 cycloalkyl group, a C3-C8 cycloalkyl C1-C6 alkyl group, a 3-7 heterocyclic group, a substituted 3-7 heterocyclic group.

39. The use of Claim 35, wherein R_a, R_b and the carbon atoms to which they are attached constitute C3-C8 cycloalkyl group.

40. The use of Claim 35, wherein the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent compound thereof, has a structure as shown in Formula II-1 or II-2:



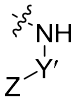
Formula II-1



Formula II-2

wherein n1, n2, and n3 are each independently selected from any integer or any decimal number from 0 to 10, n1, n2, and n3 are not simultaneously 0, and $1 \leq n1 + n2 + n3 \leq 10$.

41. The use of Claim 1, wherein the Ac has the structure shown in Formula B below.



Formula B

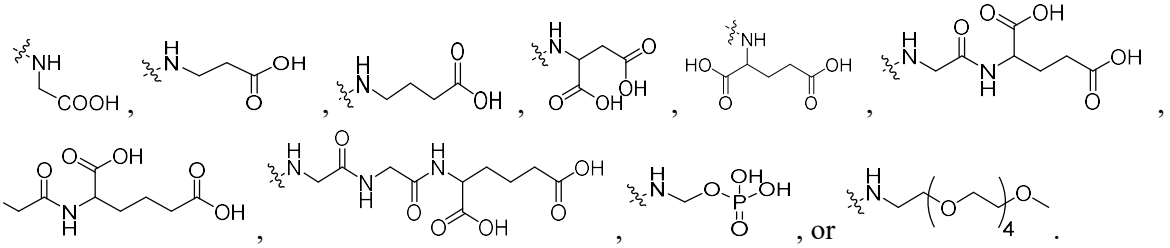
wherein:

Z comprises one or more of hydrophilic structural carboxyl group, phosphoric acid, polyphosphoric acid, phosphite, sulfonic acid, sulfinic acid, or polyethylene glycol (PEG),

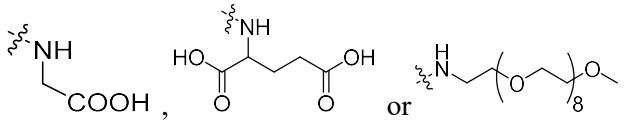
Y' is optionally a scaffold connecting the amino group to Z, wherein Y' is C1-C6 alkyl and Z is selected from hydrophilic structural carboxylates and phosphoric acid or polyethylene glycol (PEG), and

Ac is connected to the 2-position carbon that has been labeled in structural formula I by means of a bracket Y.

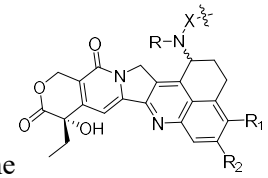
42. The use of Claim 1-15, wherein the Ac comprises glycine, (*D/L*) alanine, (*D/L*) leucine, (*D/L*) isoleucine, (*D/L*) valine, (*D/L*) phenylalanine, (*D/L*) proline, (*D/L*) tryptophan, (*D/L*) serine, (*D/L*) tyrosine, (*D/L*) cysteine, (D/L) cystine, (*D/L*) arginine, (*D/L*) histidine, (*D/L*) methionine, (*D/L*) asparagine, (D/L) glutamine, (*D/L*) threonine, (*D/L*) aspartic acid, (D/L*)* glutamic acid, natural or non-natural amino acid derivatives, or the following structures or isomers thereof:

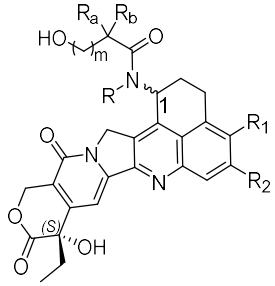


43. The use of Claim 42, wherein the Ac comprises



44. The use of Claim 1, wherein the Ac comprises a glycine, phosphoric acid, (*D/L*) glutamic acid, or polyethylene glycol hydrophilic structure.

45. The use of Claim 1-15, wherein the  has the structure shown in Formula D below:



Formula D

wherein:

R is selected from hydrogen atom, deuterium atom, halogen, C1-C6 alkyl, substituted C1-C6 alkyl, deuterated C1-C6 alkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl,

R_1 is selected from hydrogen atoms, deuterium atoms, halogens, C1-C6 alkyl, substituted C1-C6 alkyl, deuterated C1-C6 alkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, carboxyl, 3-7 heterocyclic, substituted 3-7 heterocyclic, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl,

R_2 is selected from hydrogen atoms, deuterium atoms, halogens, C1-C6 alkyl, substituted C1-C6 alkyl, deuterated C1-C6 alkyl, C3-C8 cycloalkyl C1-C6 alkyl, C1-C6 alkoxy C1-C6 alkyl, carboxyl, 3-7 heterocyclic, substituted 3-7 heterocyclic, C6-C10 aryl, substituted C6-C10 aryl, 5-10 heteroaryl, substituted 5-10 heteroaryl,

R_a and R_b are each independently selected from a hydrogen atom, a deuterium atom, a halogen, a C1-C6 alkyl, a deuterated C1-C6 alkyl, a halogenated C1-C6 alkyl, a C3-C8 cycloalkyl, a C3-C8 cycloalkyl C1-C6 alkyl, a C1-C6 alkoxy C1-C6 alkyl, a 3-7 heterocyclic group, a substituted 3-7 heterocyclic group, a C6-C10 aryl, a substituted C6-C10 aryl, a 5-10 heteroaryl, substituted 5-10 heteroaryl,

the 1-position chiral carbon atom has two chiral configurations, the R absolute configuration or the S absolute configuration, and

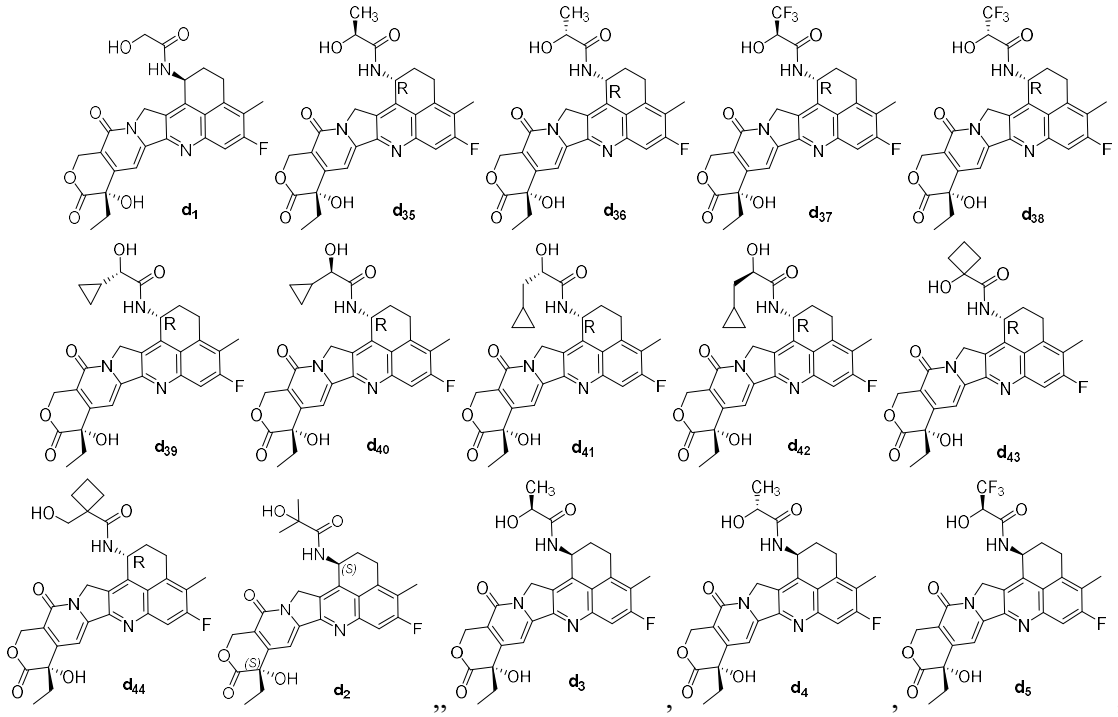
m is selected from 0 or 1.

46. The use of Claim 45, wherein R is hydrogen atom or C1-C6 alkyl, R_1 is C1-C6 alkyl, R_2 is halogen.

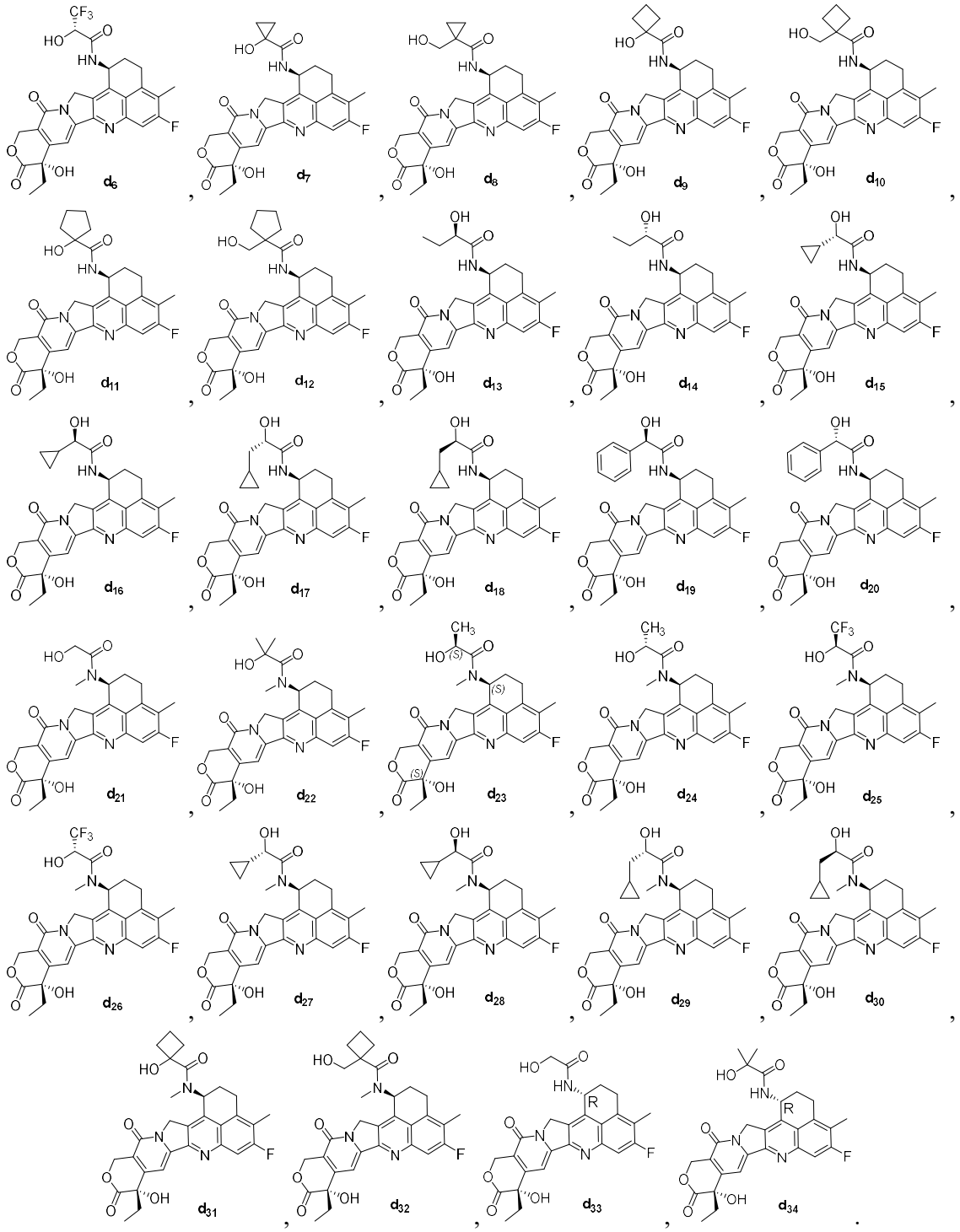
47. The use of Claim 45, wherein R_a and R_b are each independently selected from hydrogen, C1-C6 alkyl, halo-C1-C6 alkyl, C3-C8 cycloalkyl, C1-C6 alkyl, C6-C10 aryl, or wherein R_a, R_b and the carbon atoms to which they are attached constitute C3-C8 cycloalkyl, C3-C8 cycloalkyl, C1-C6 alkyl, 3-7 heterocycloalkyl, substituted 3-7 heterocycloalkyl;

48. The use of Claim 45, wherein R_a, R_b and the carbon atoms to which they are attached constitute a C3-C8 cycloalkyl group.

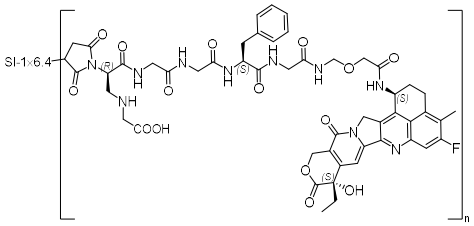
49. The use of Claim 45, wherein the Formula D comprises the following:



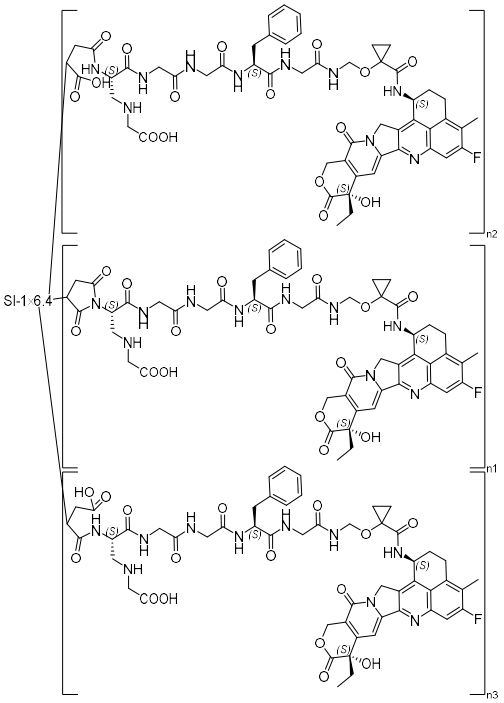
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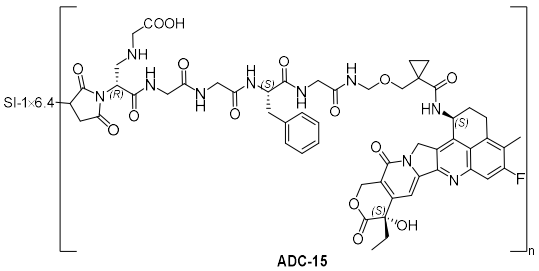
50. The use of Claim 1-15, wherein the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent compound thereof, comprises the following structure or a butanediimide ring-opening structure thereof or an isomer thereof:



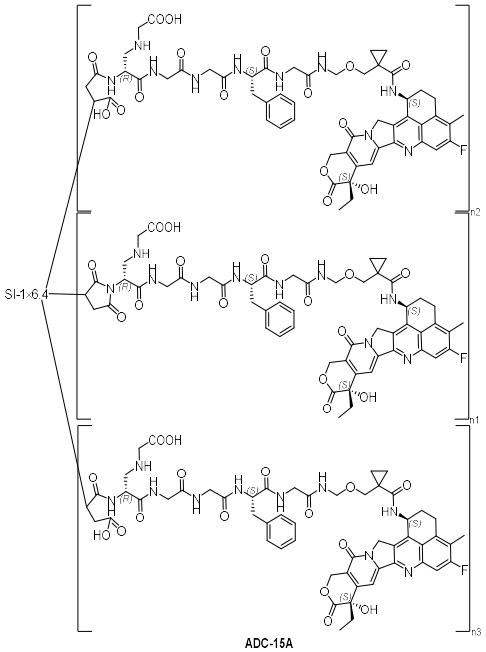
ADC-1



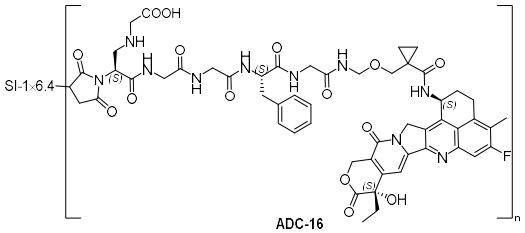
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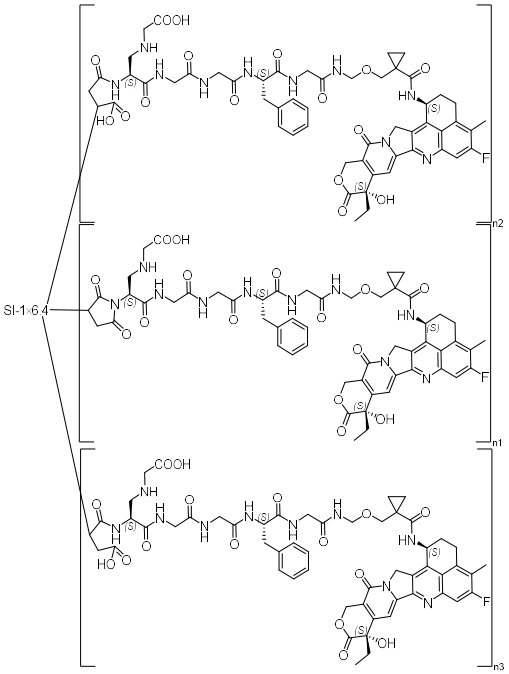
ADC-15



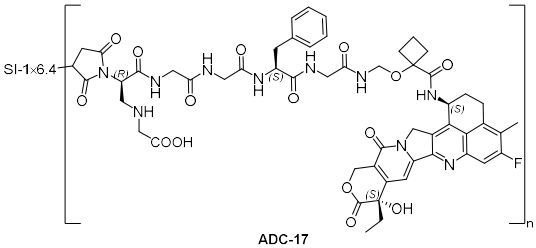
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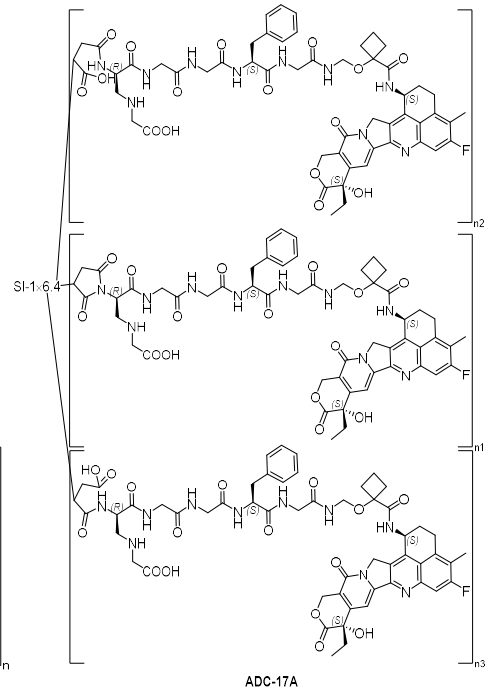
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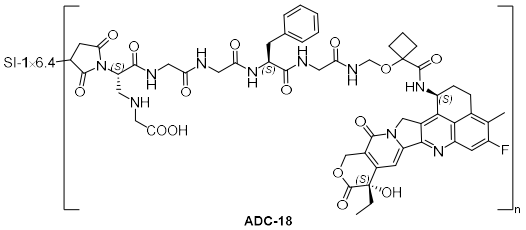
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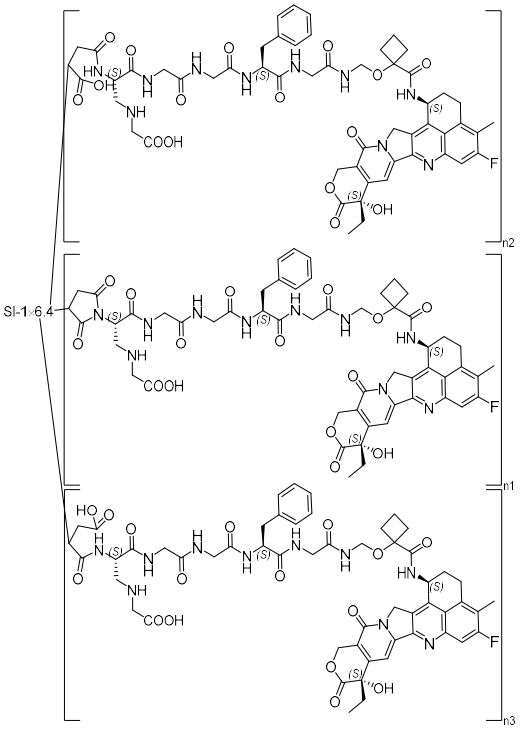
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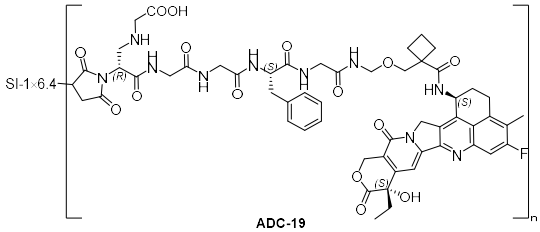
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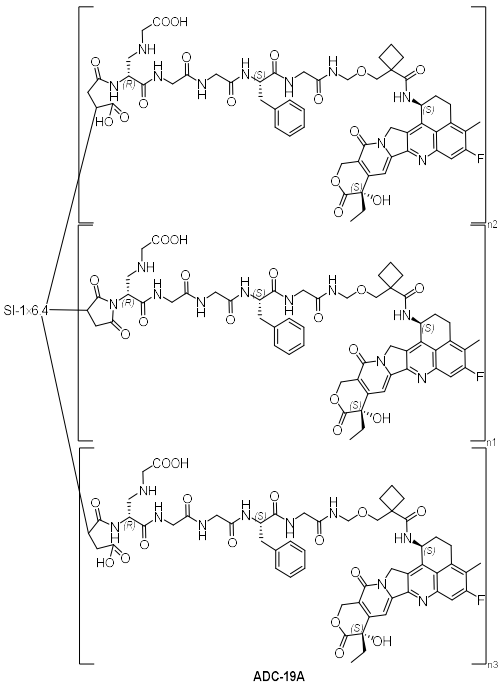
ADC-18



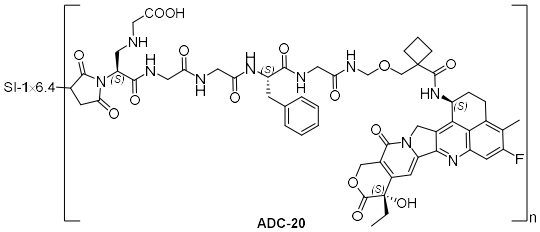
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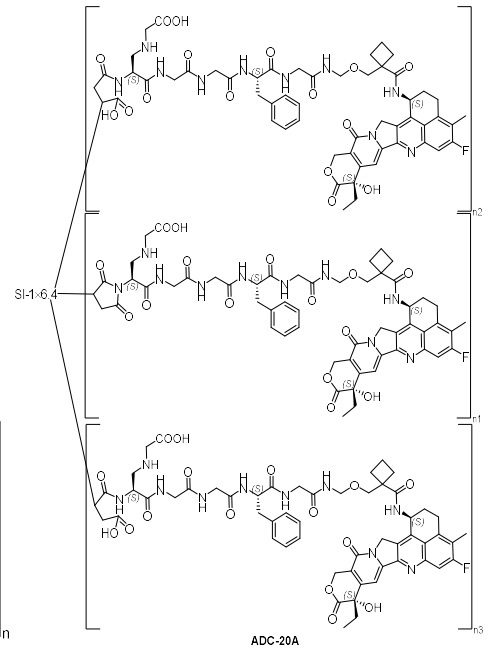
ADC-19



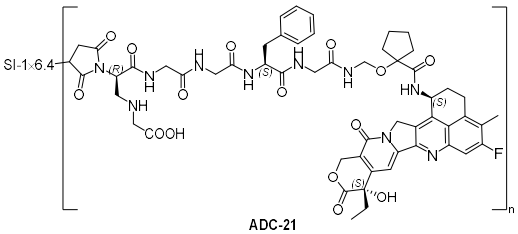
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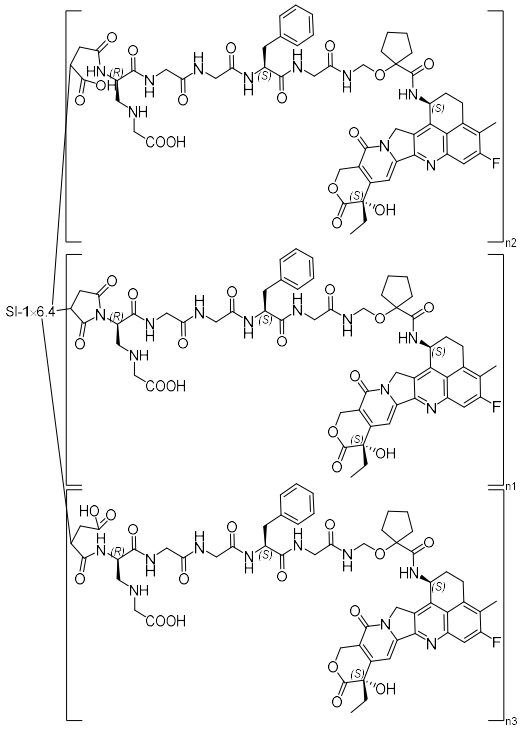
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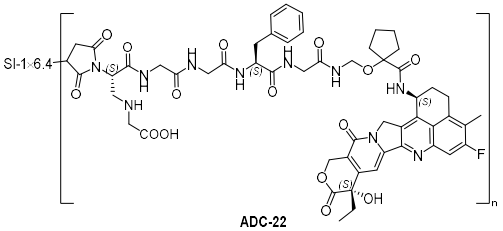
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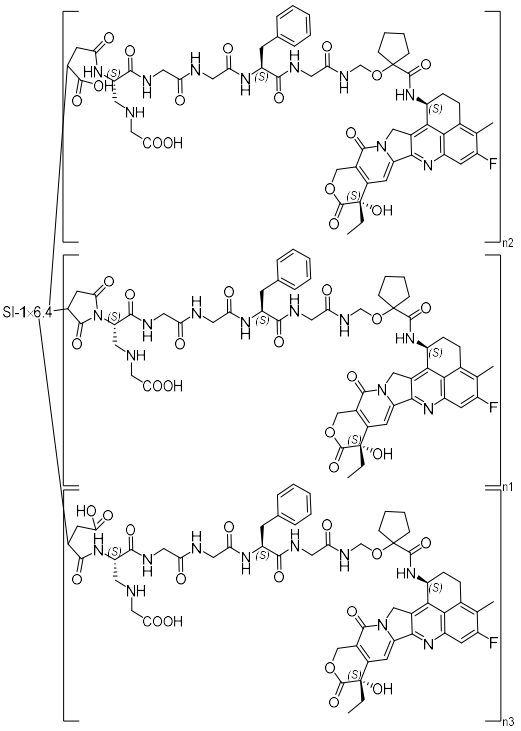
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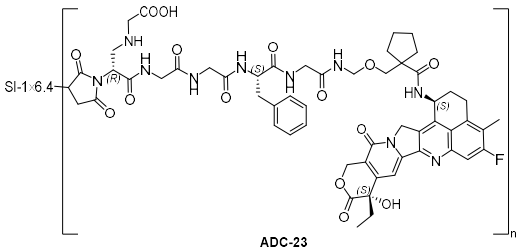
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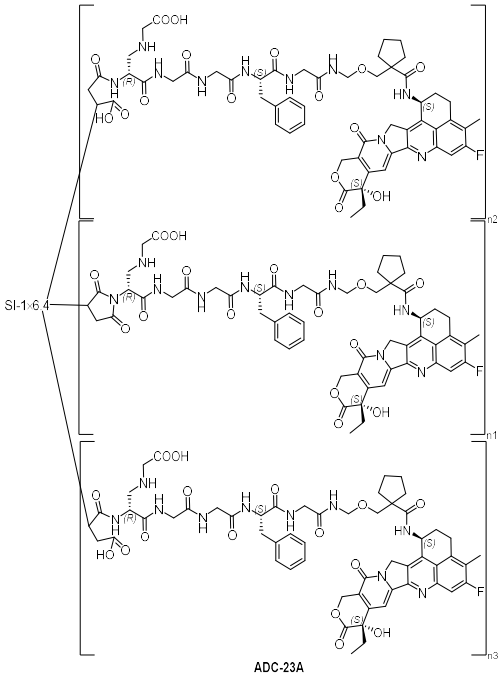
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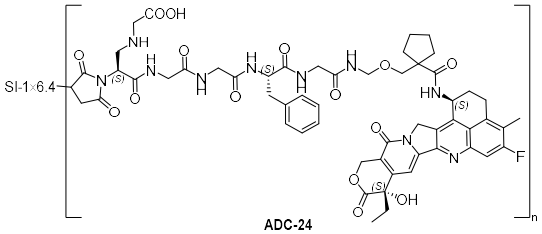
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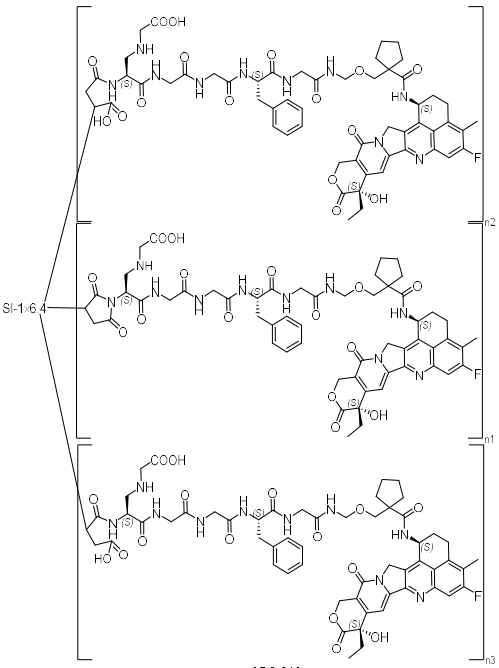
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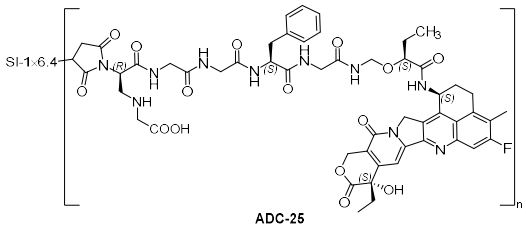
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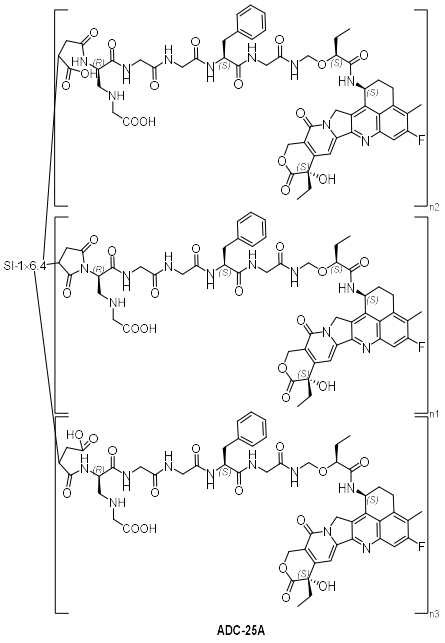
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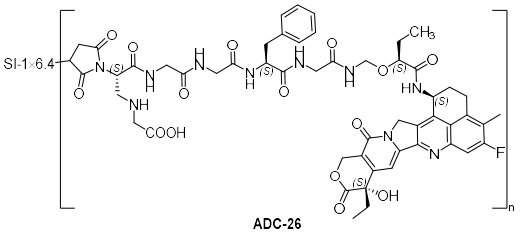
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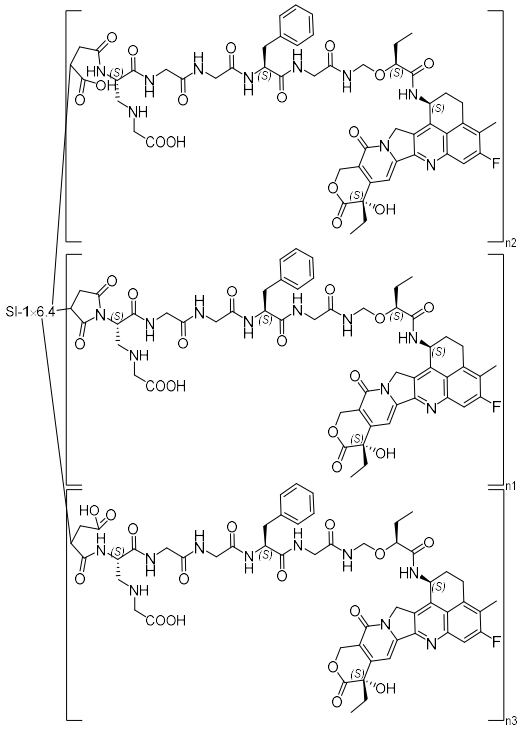
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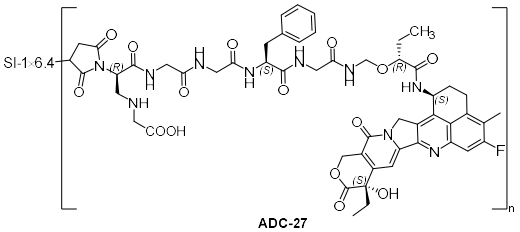
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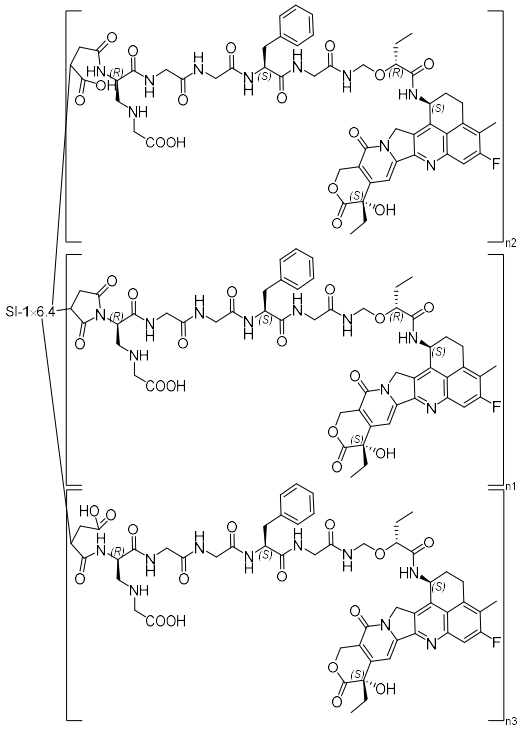
ADC-26



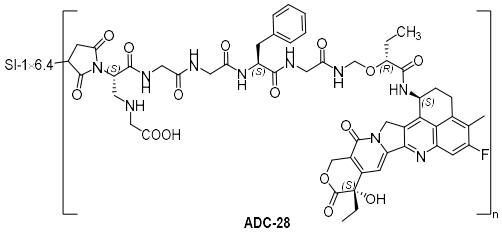
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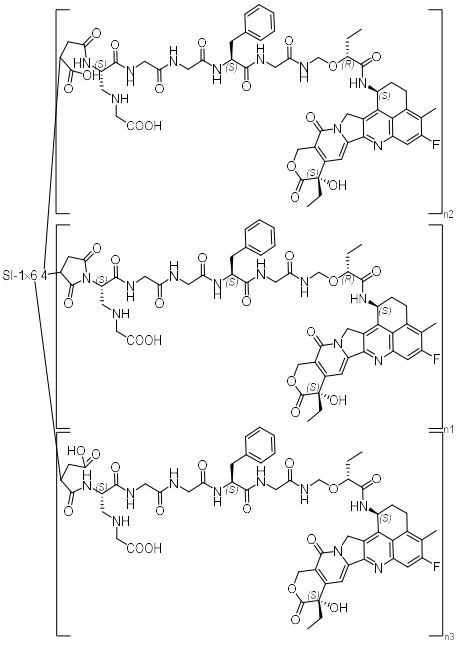
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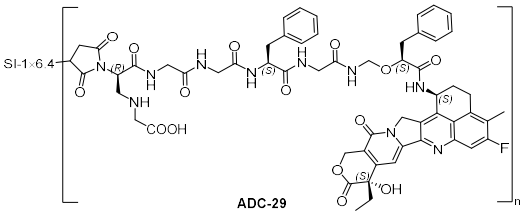
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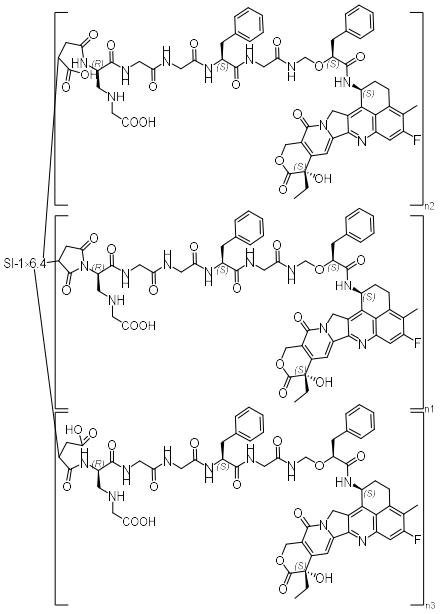
ADC-28



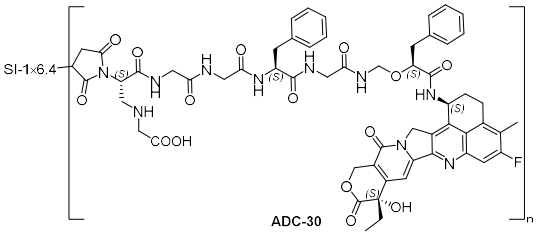
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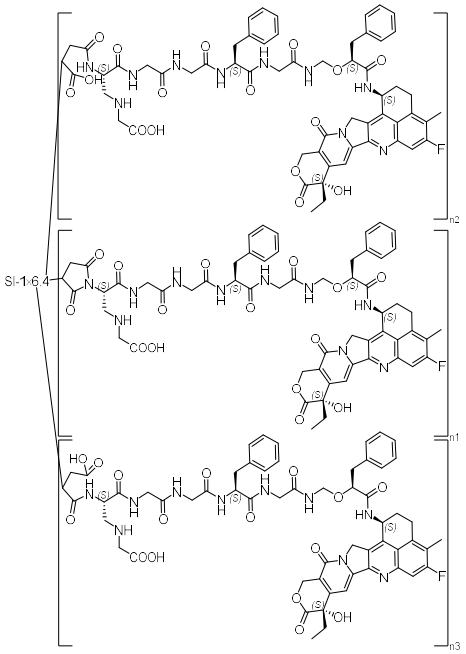
ADC-29



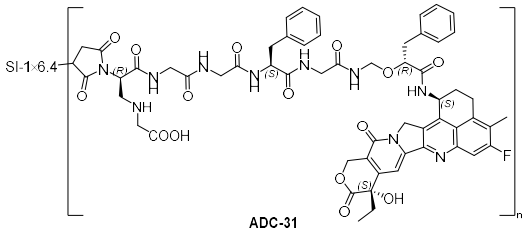
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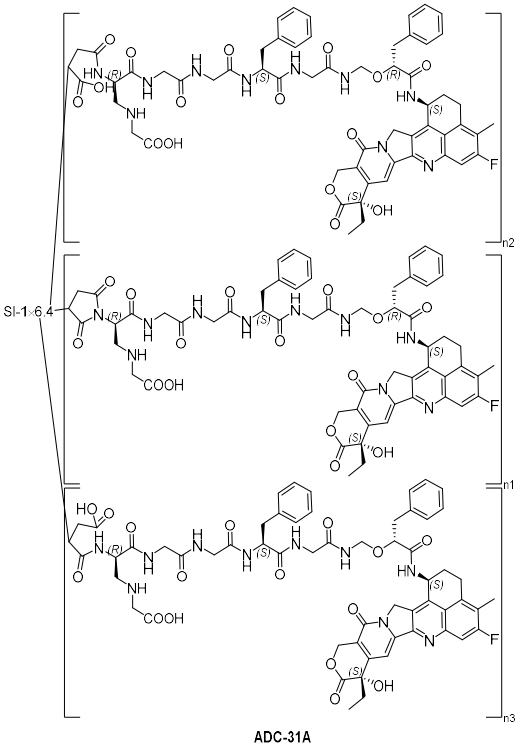
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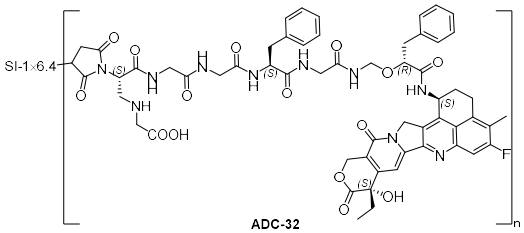
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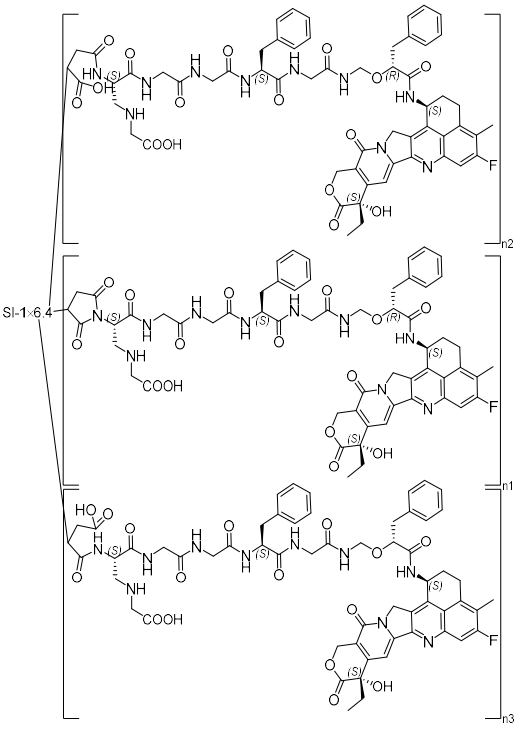
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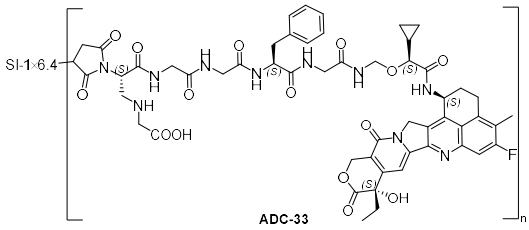
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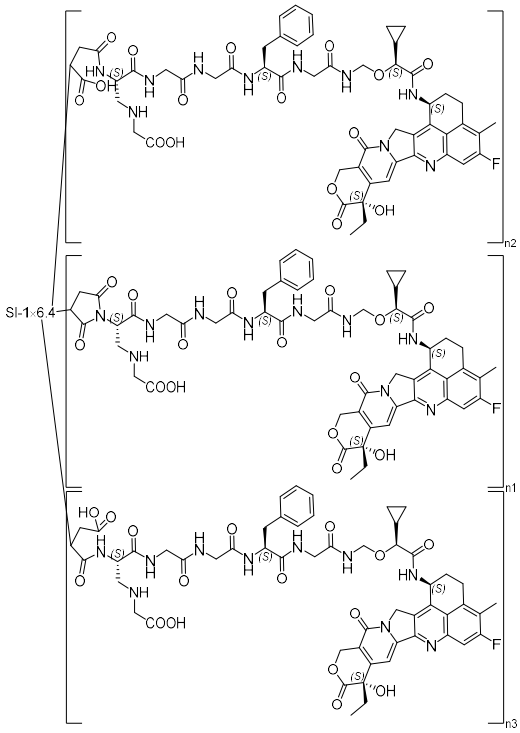
ADC-32



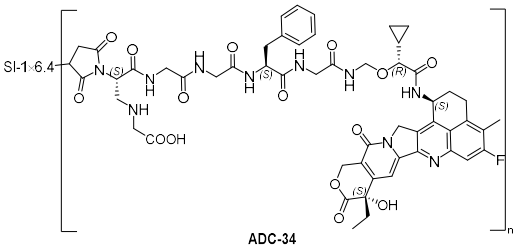
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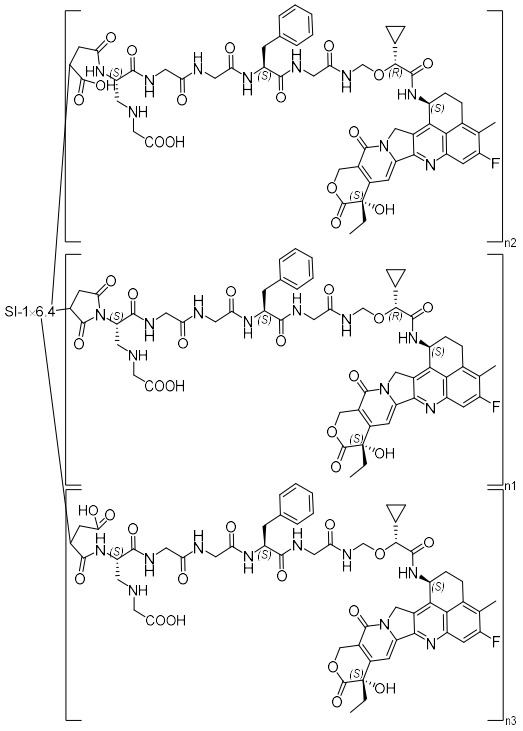
ADC-33



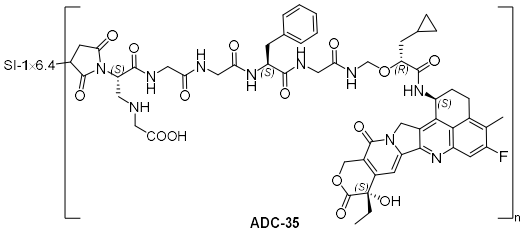
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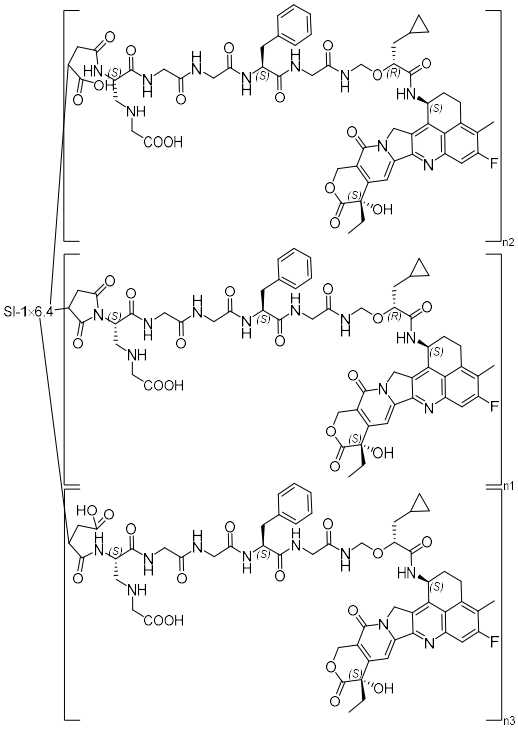
ADC-34



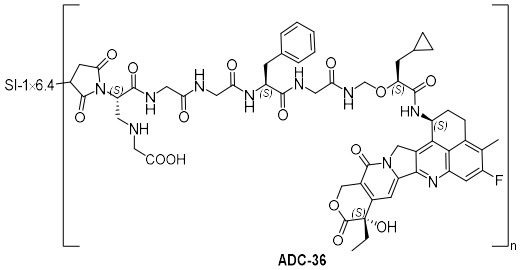
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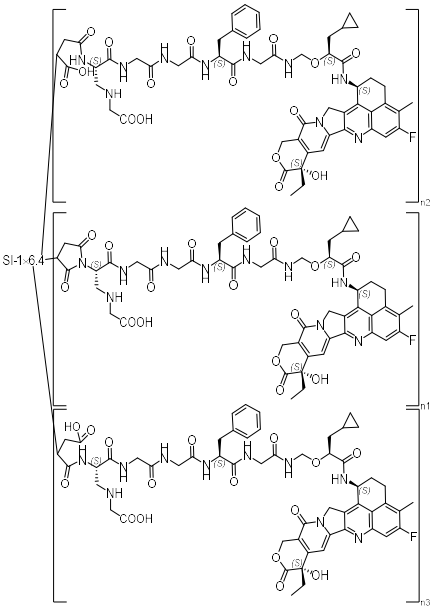
ADC-35



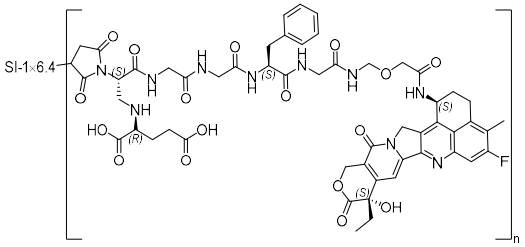
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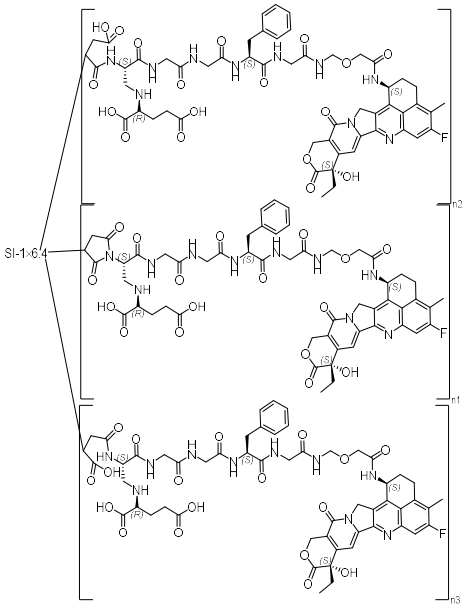
ADC-36



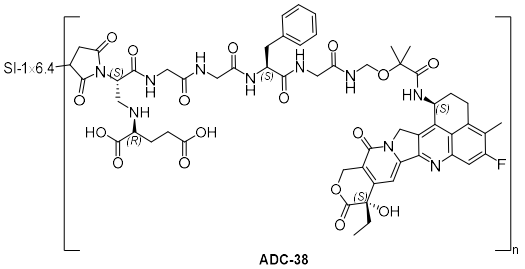
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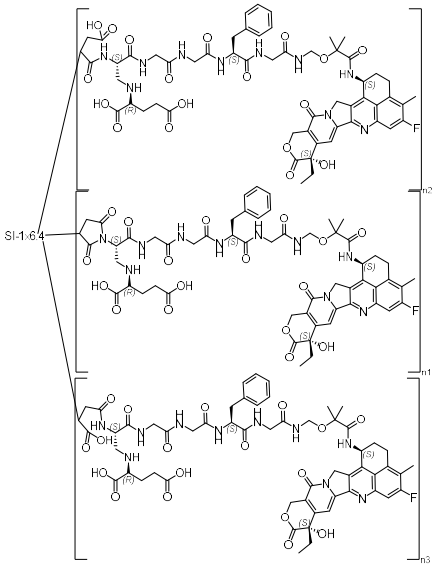
ADC-37



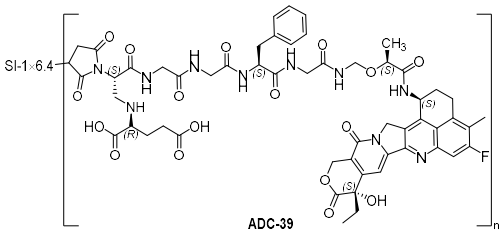
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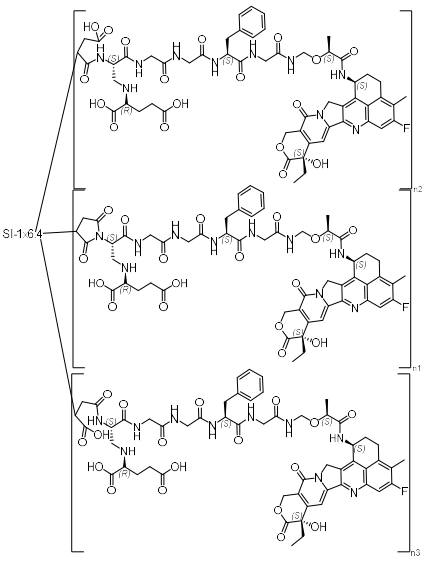
ADC-38



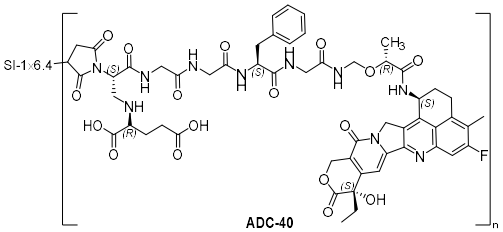
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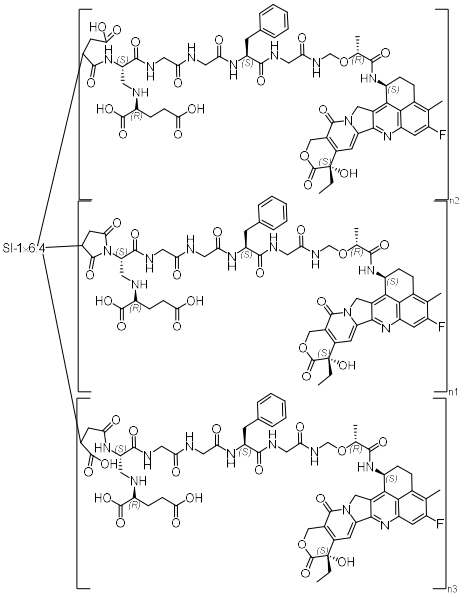
ADC-39



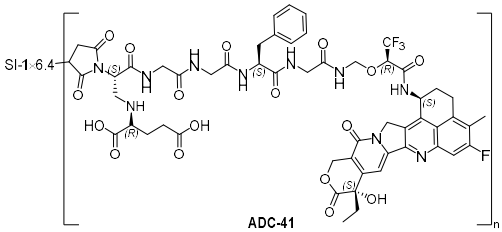
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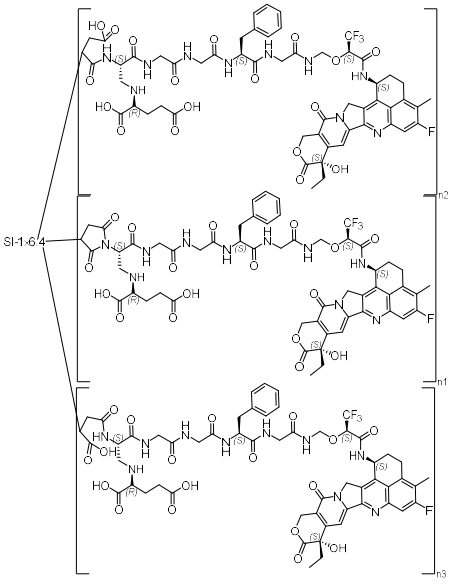
ADC-40



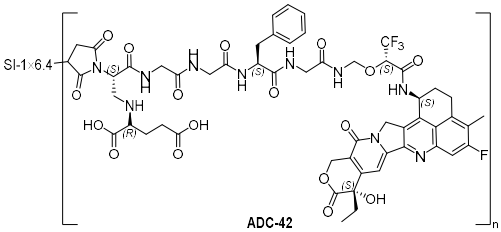
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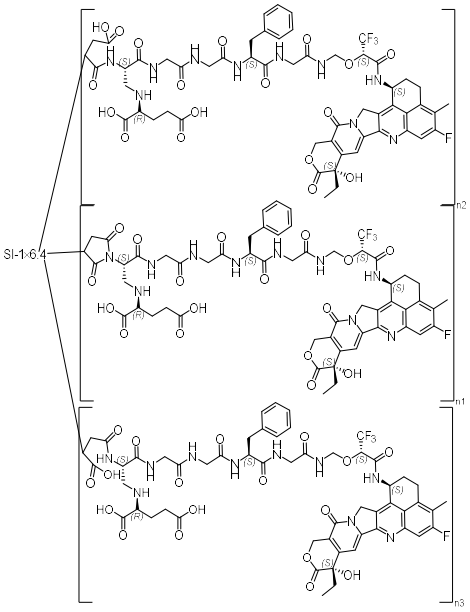
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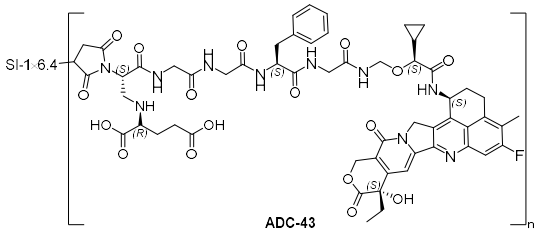
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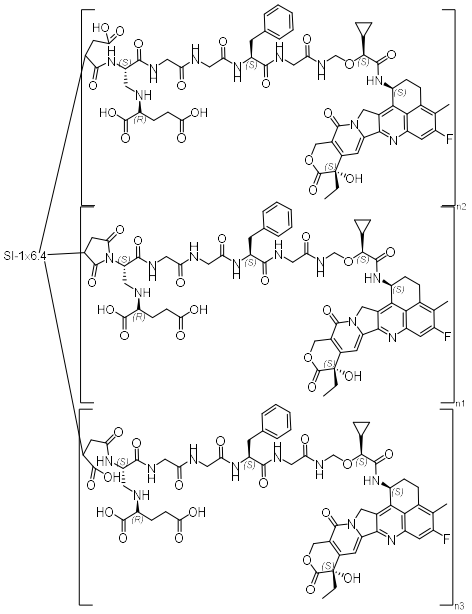
ADC-42



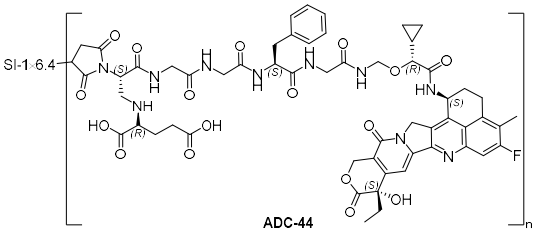
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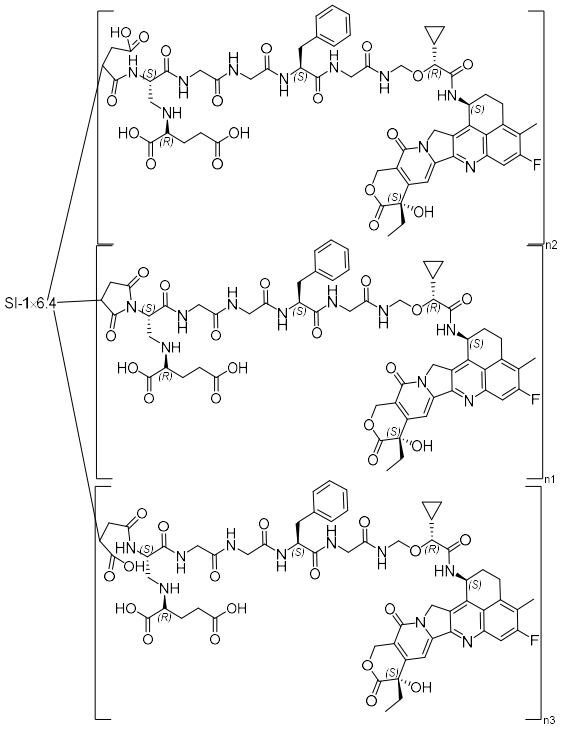
ADC-43



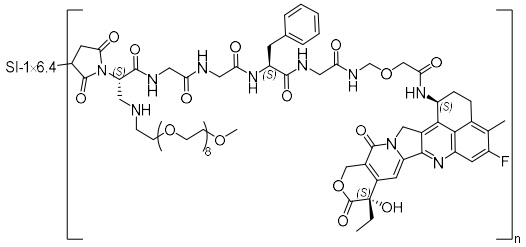
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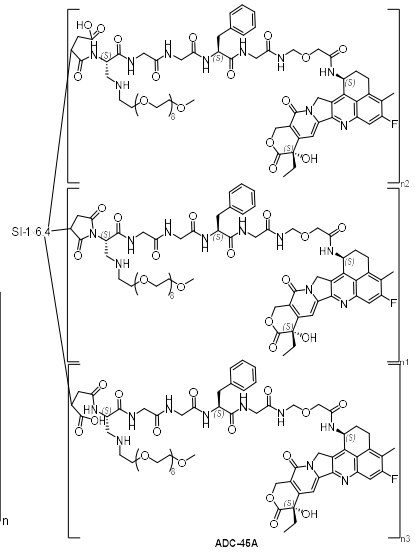
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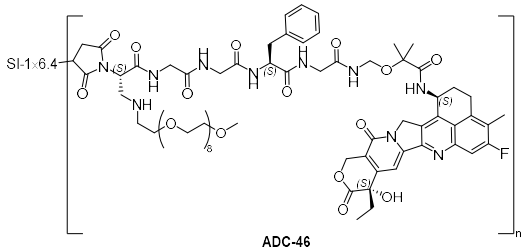
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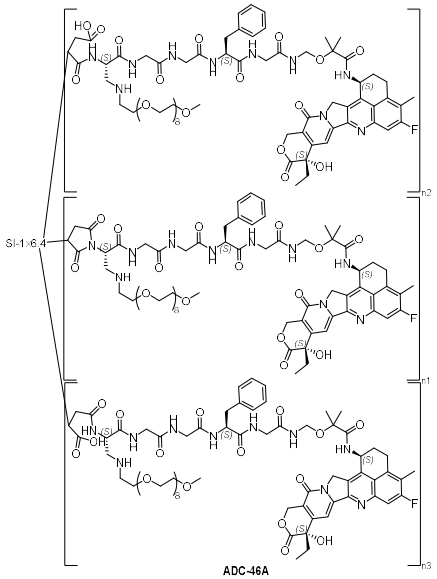
ADC-45



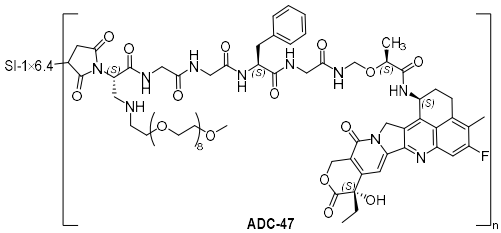
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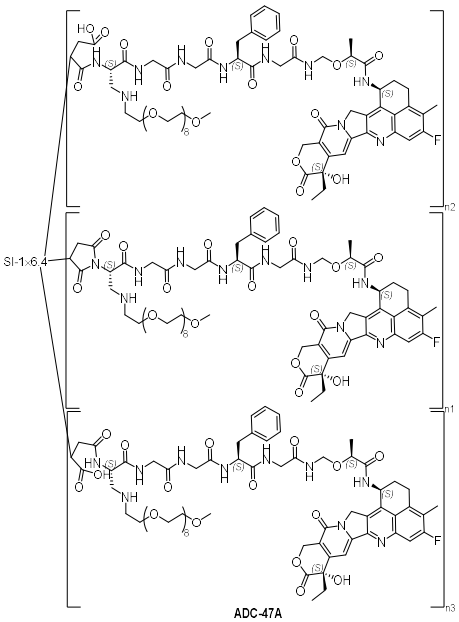
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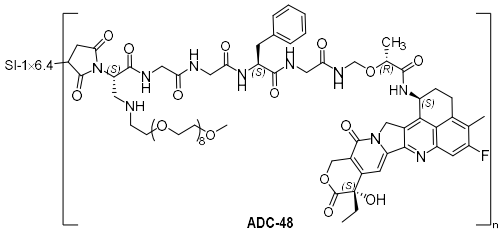
ADC-46A



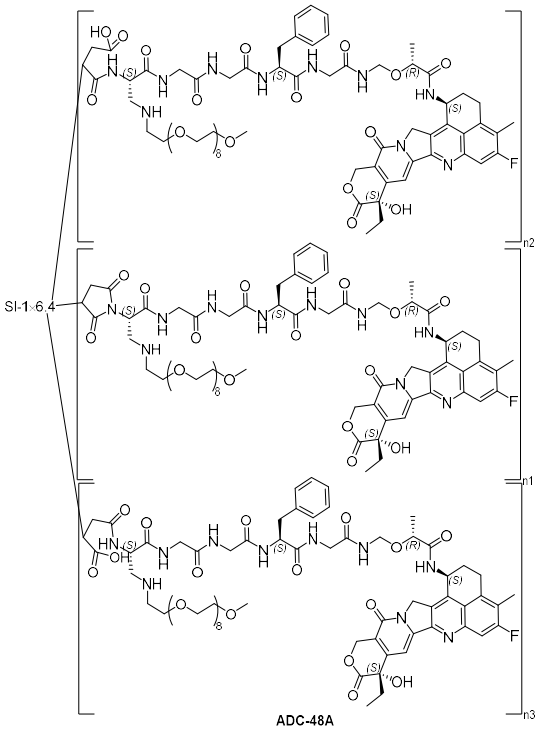
ADC-47



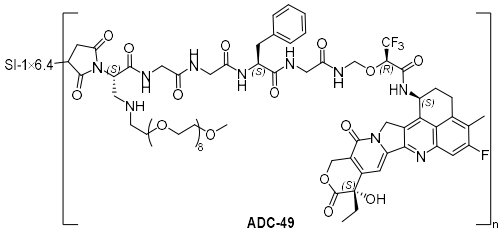
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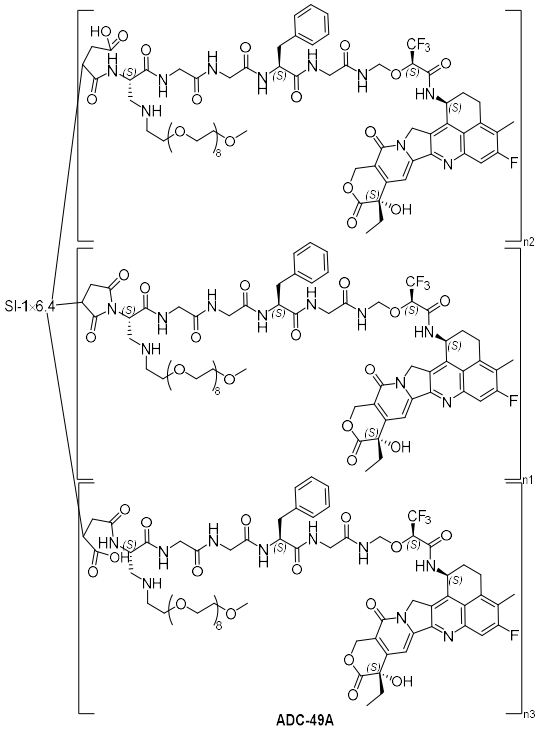
ADC-48



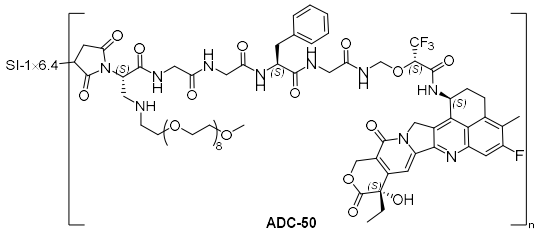
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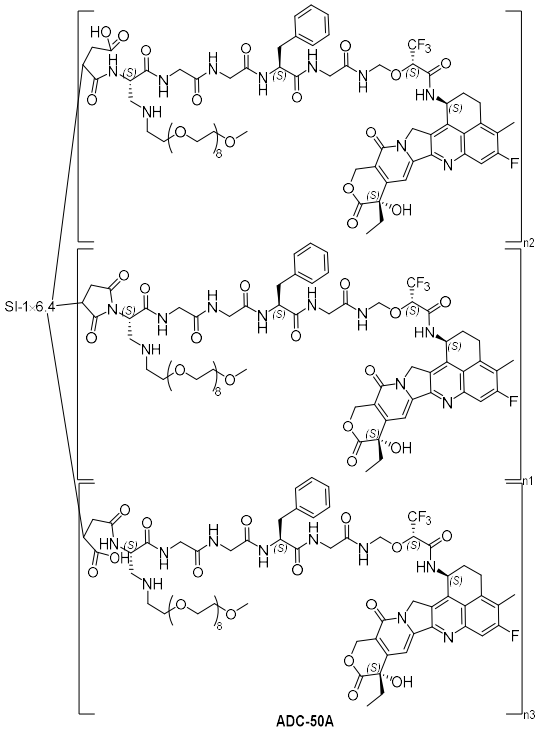
ADC-49



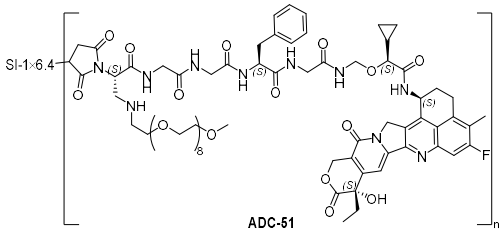
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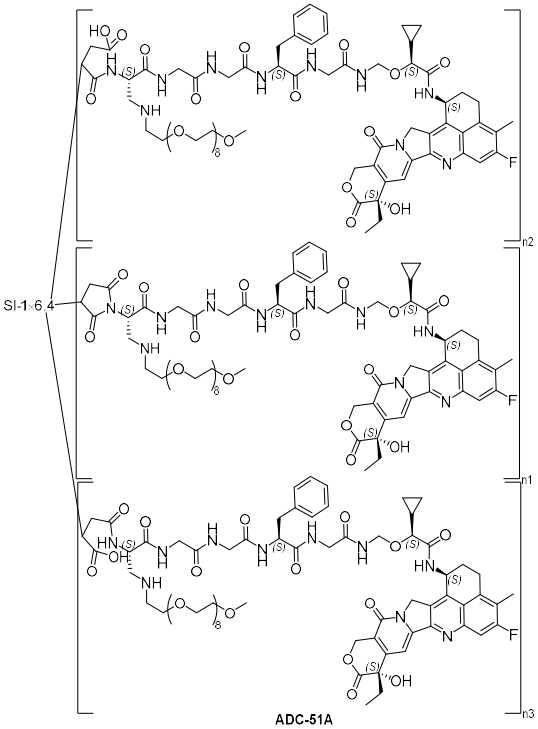
ADC-50



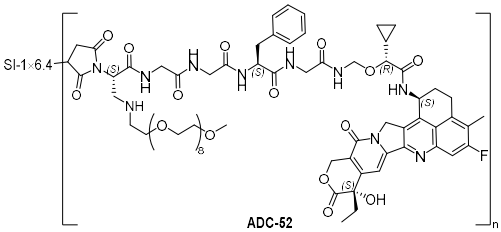
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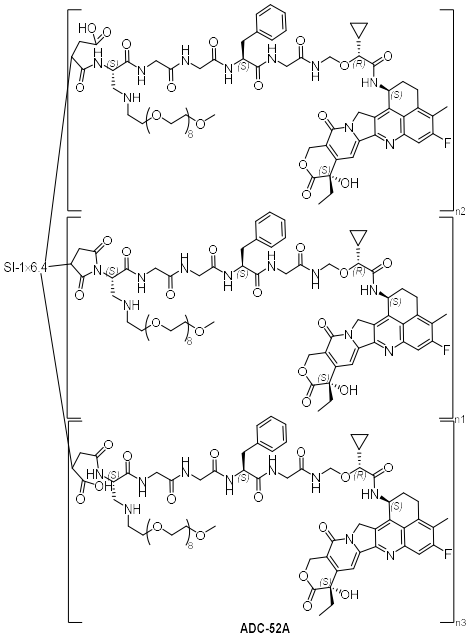
ADC-51



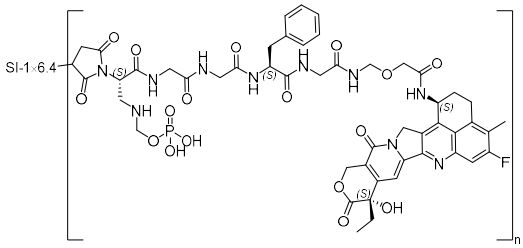
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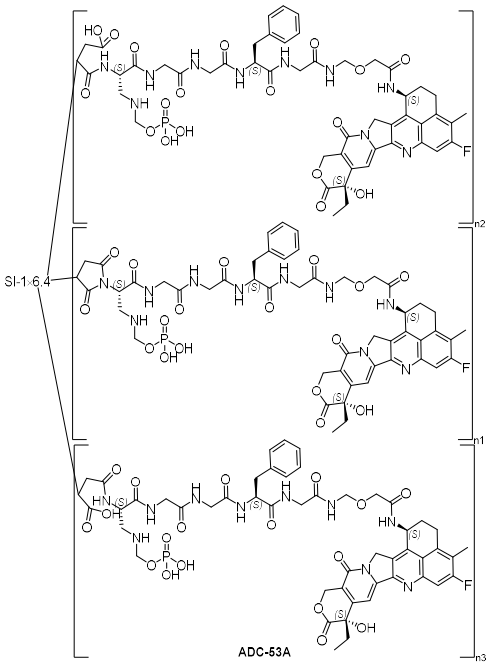
ADC-52



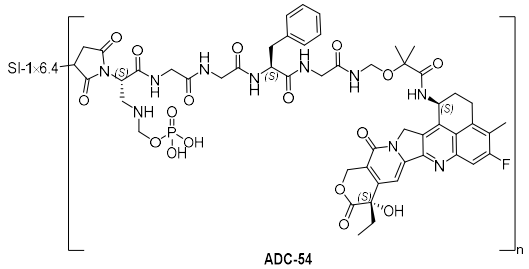
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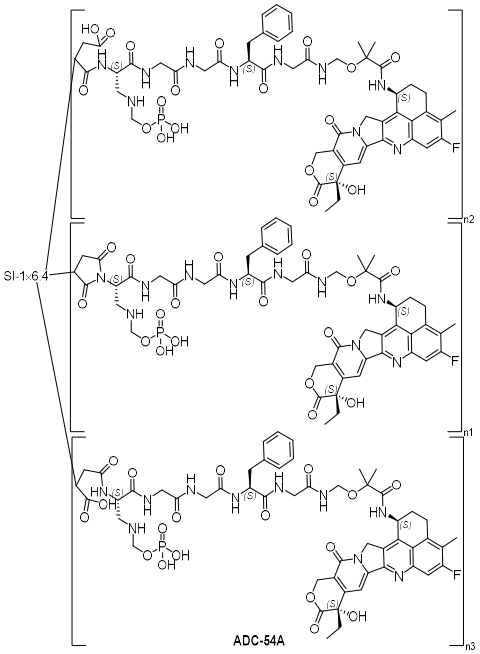
ADC-53



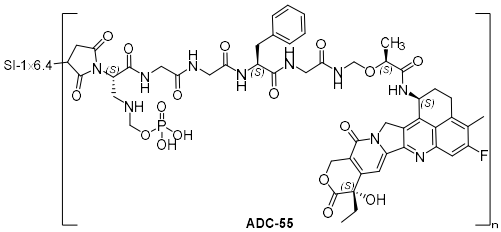
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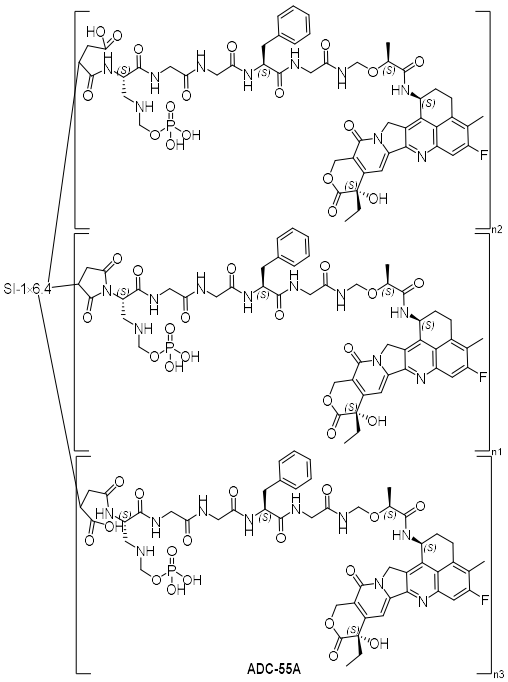
ADC-54



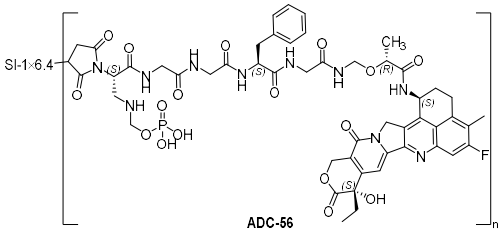
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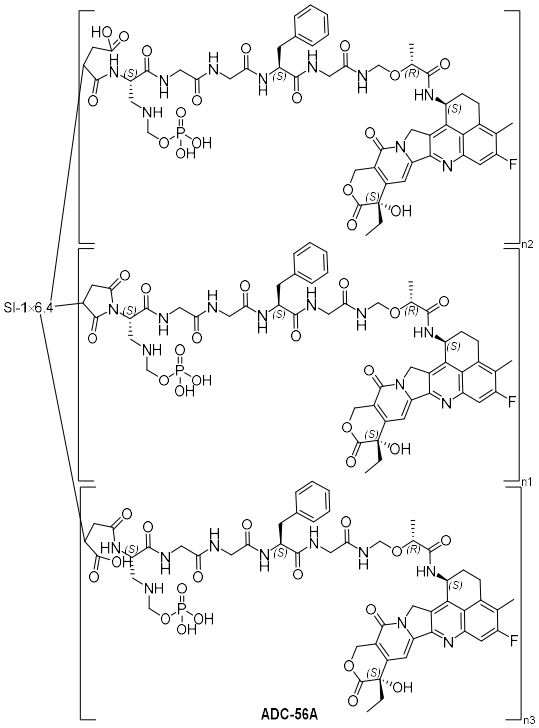
ADC-55



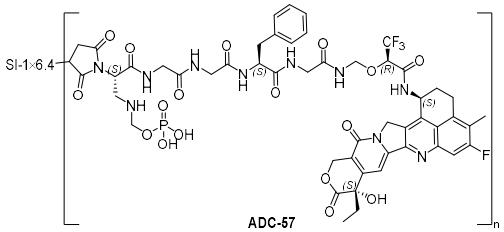
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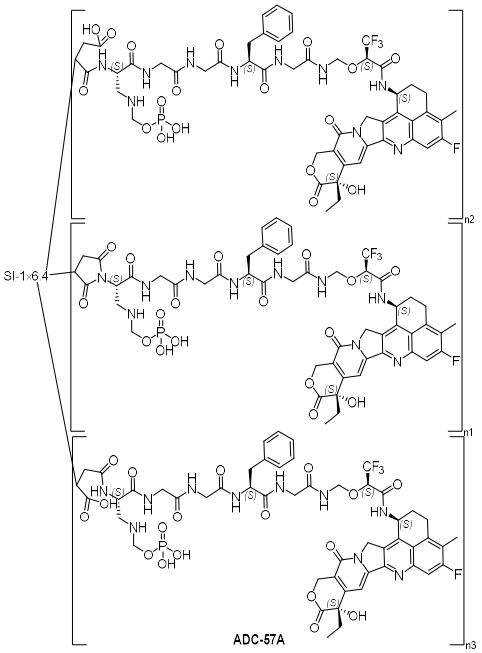
ADC-56



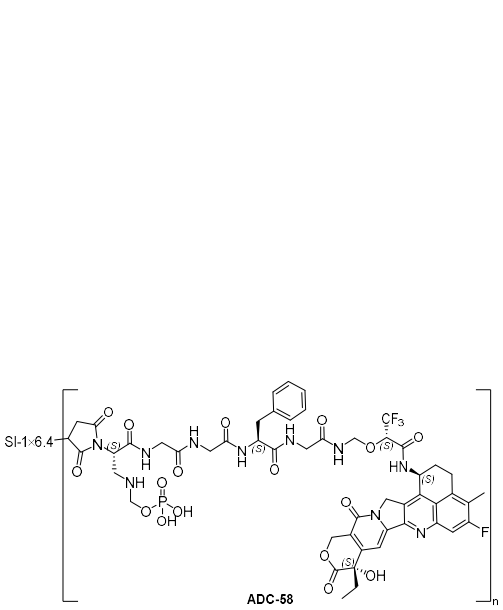
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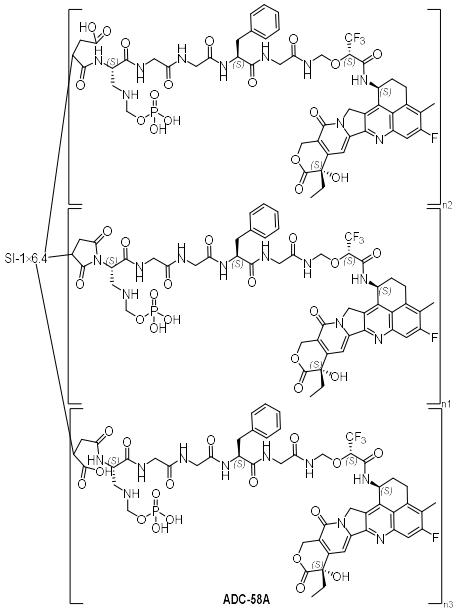


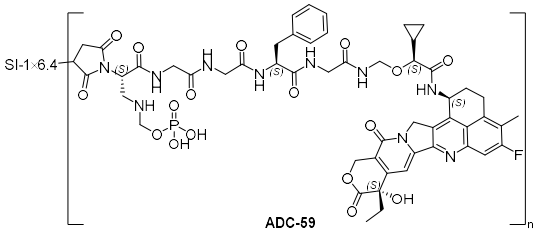
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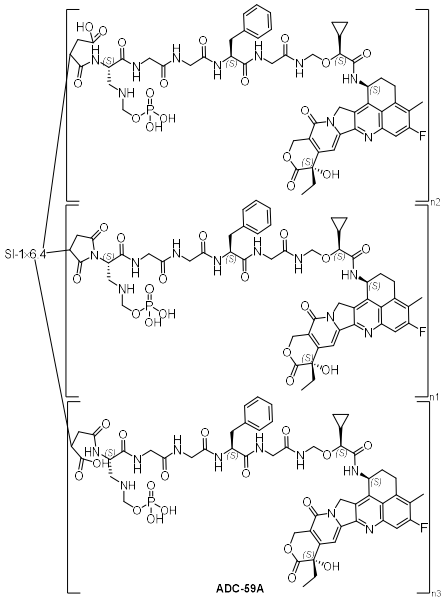


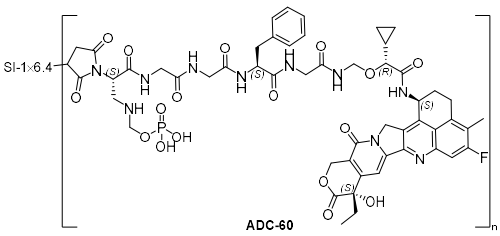
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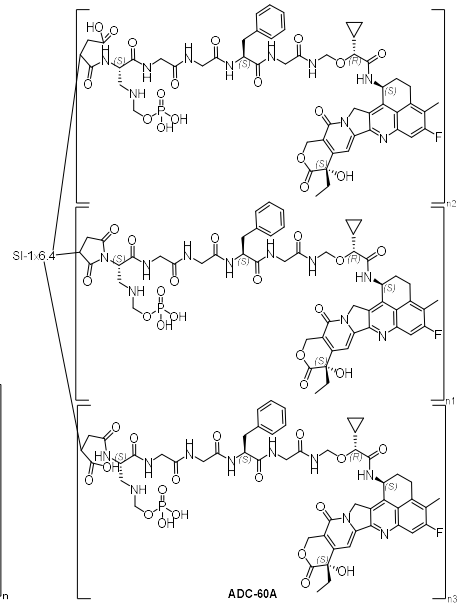

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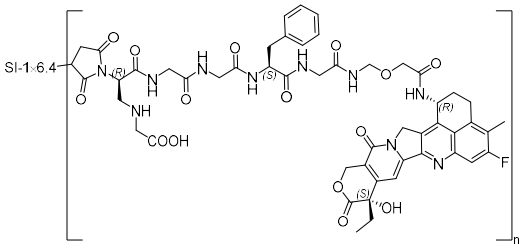

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ADC-58A


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ADC-59

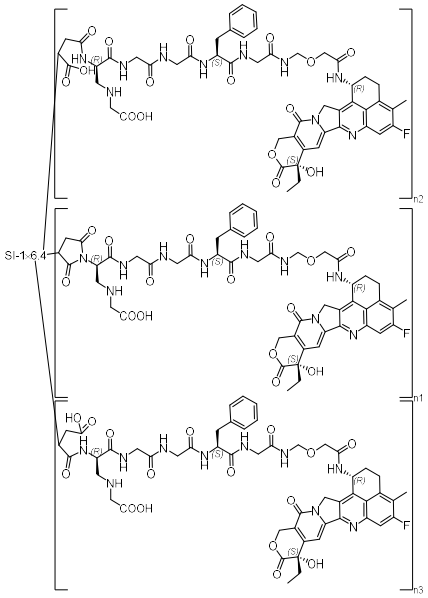

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ADC-60

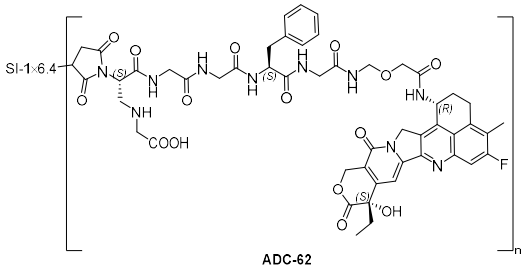

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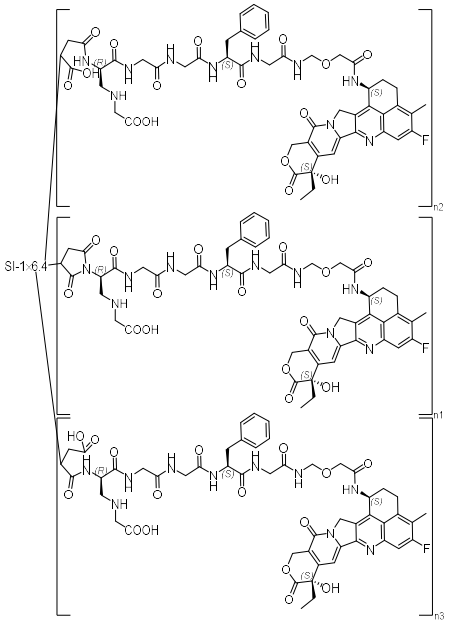
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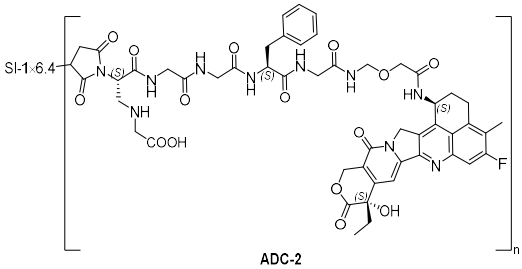
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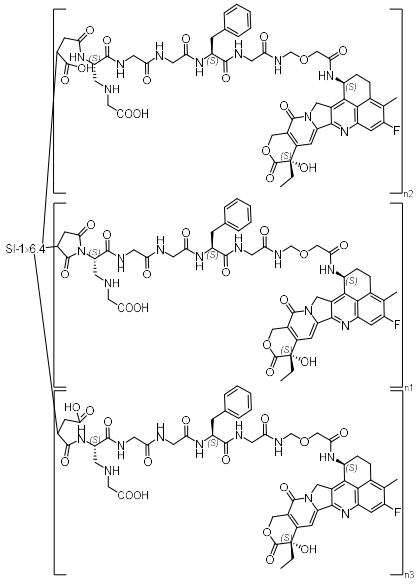
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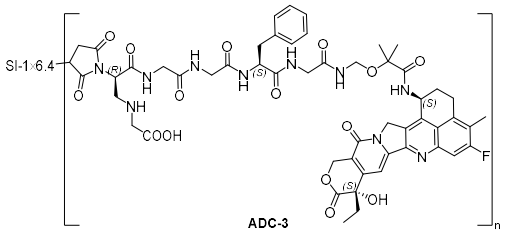
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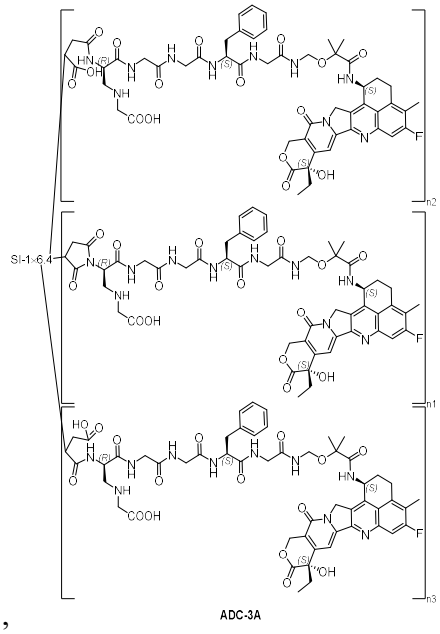
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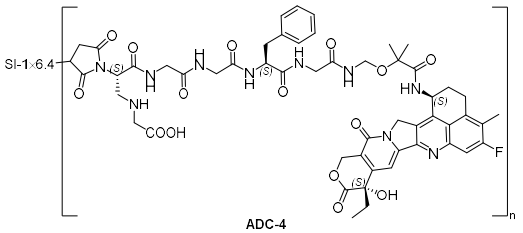
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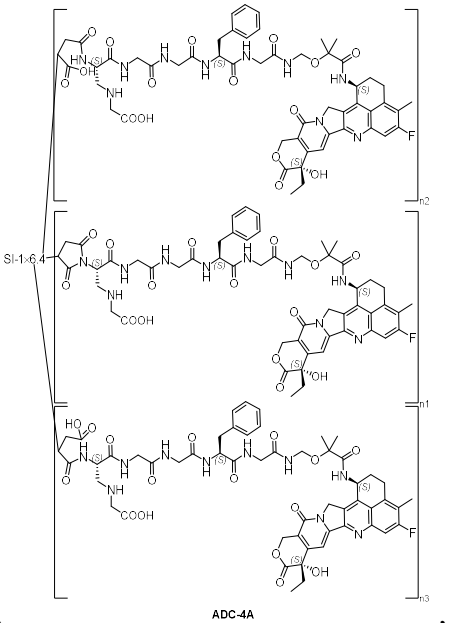
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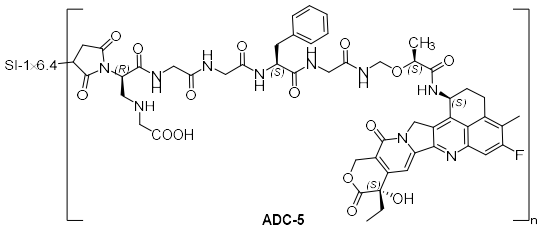
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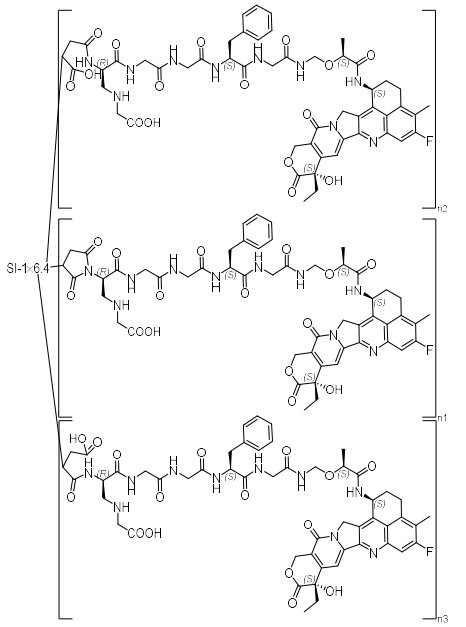
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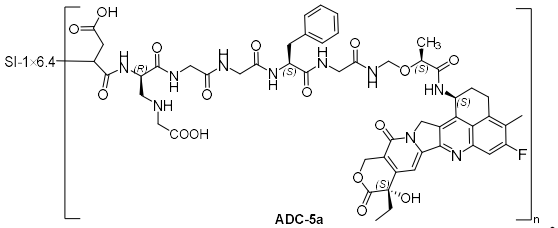
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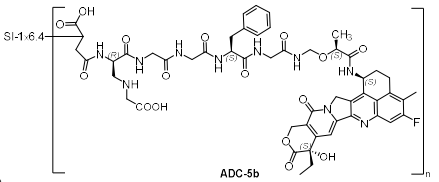
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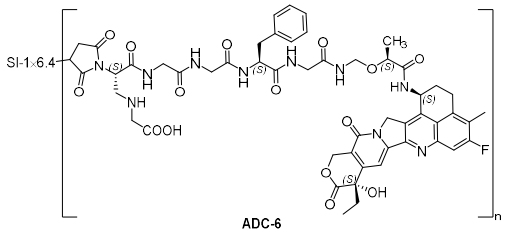
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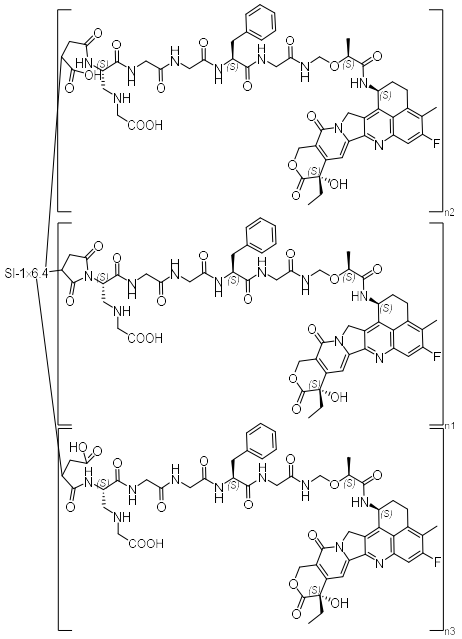
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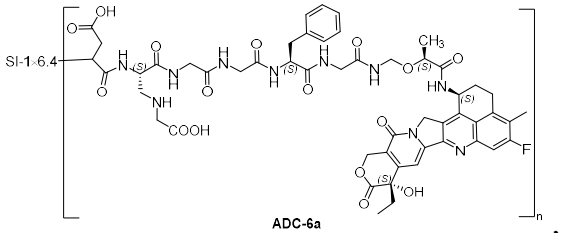
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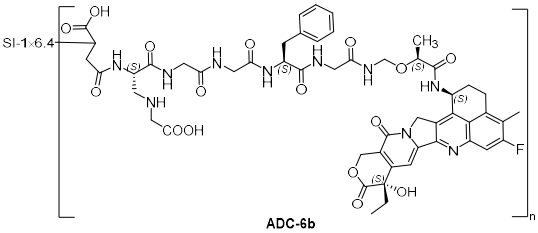
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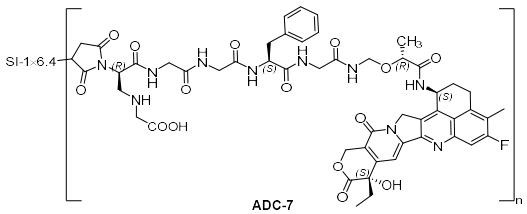
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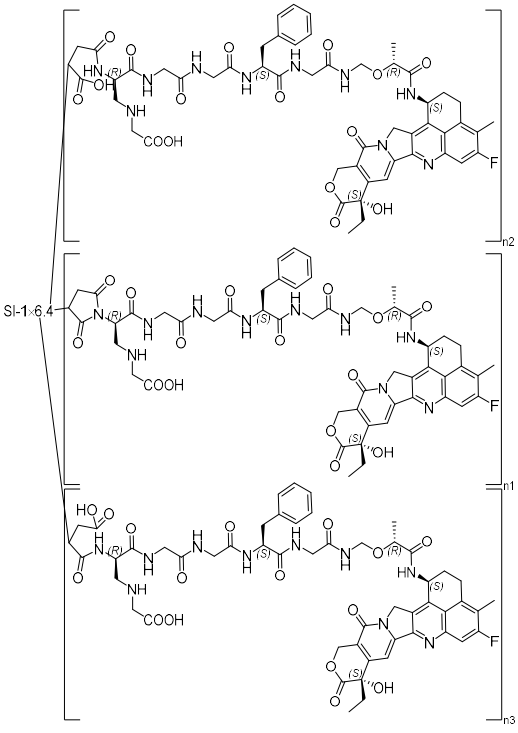
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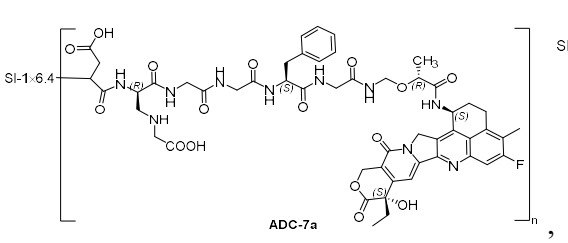
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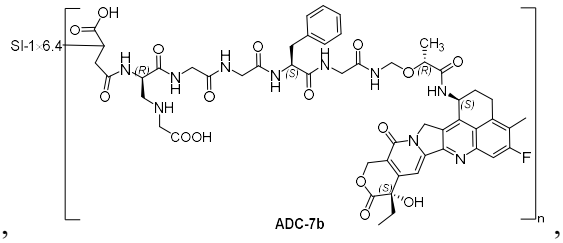
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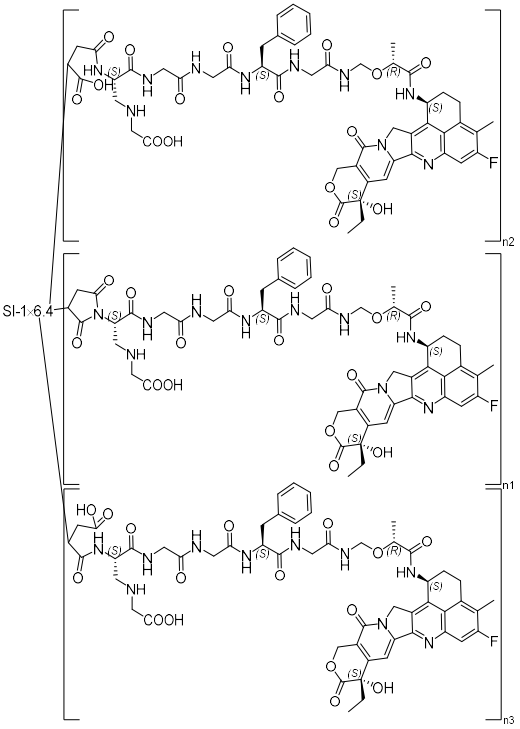
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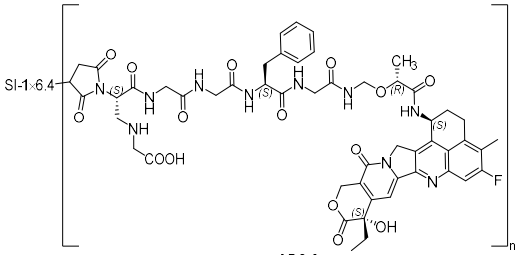
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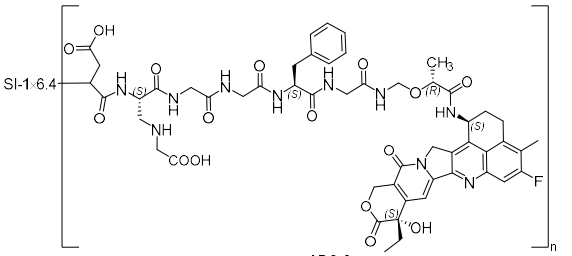
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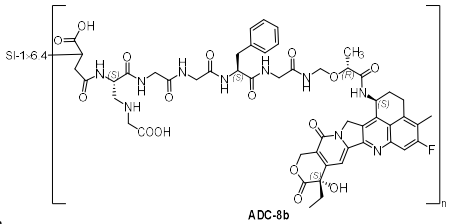
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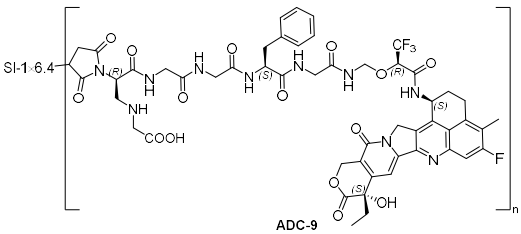
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ADC-8a ,

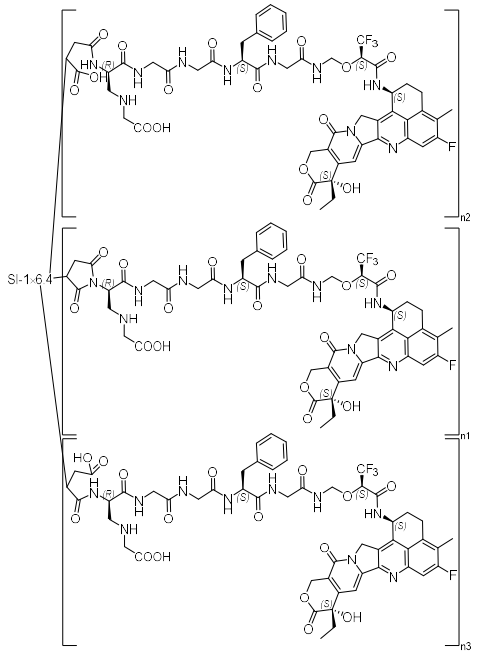


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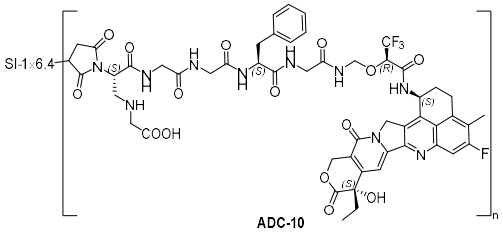
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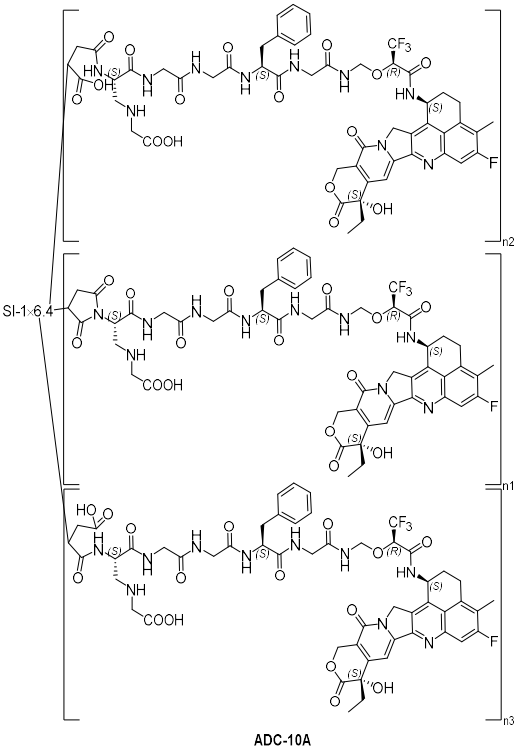
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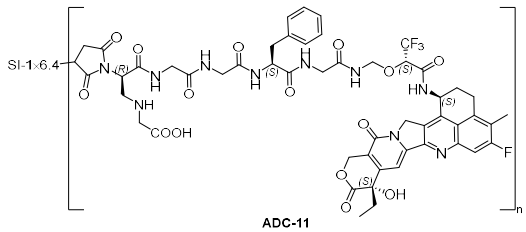
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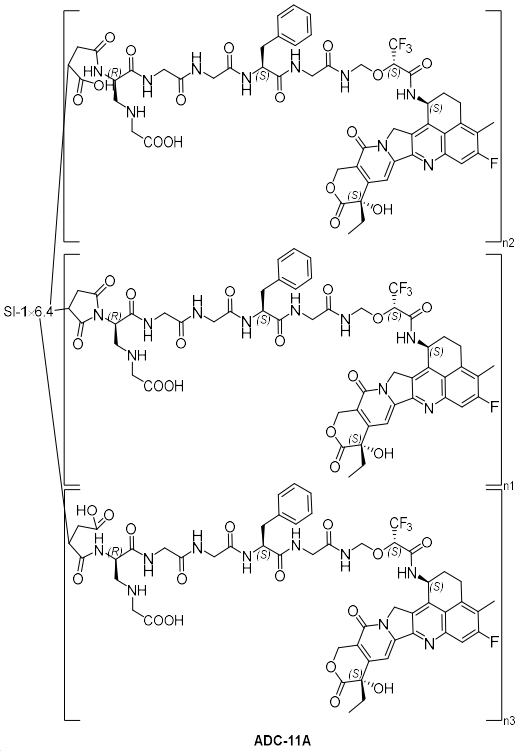
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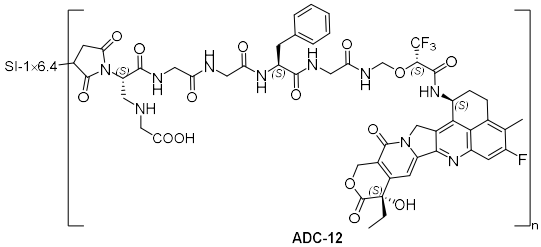
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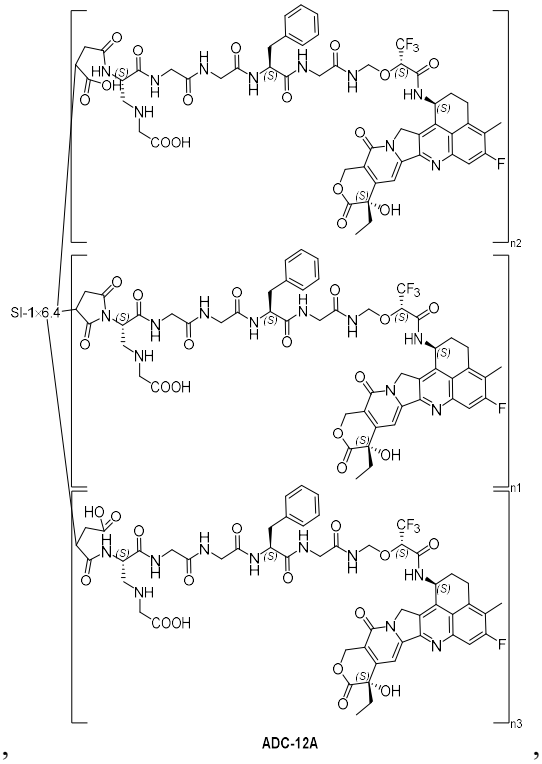
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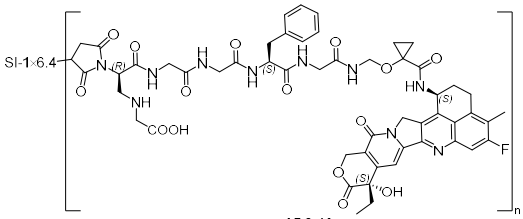
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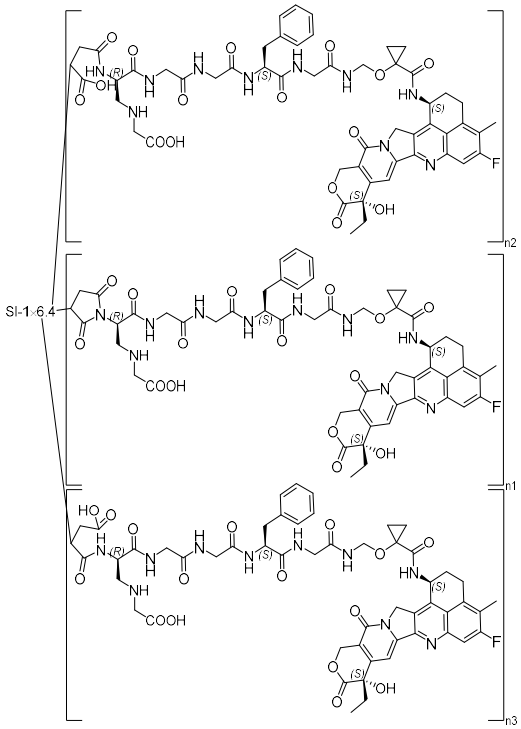
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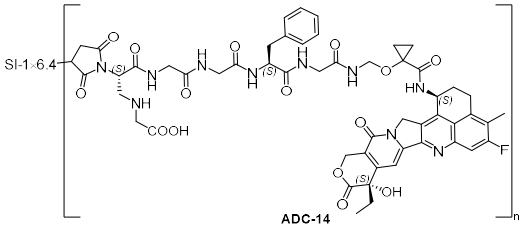
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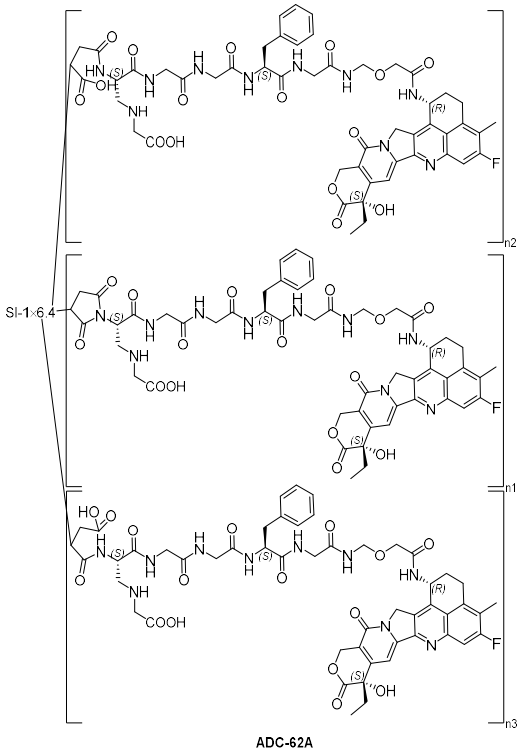


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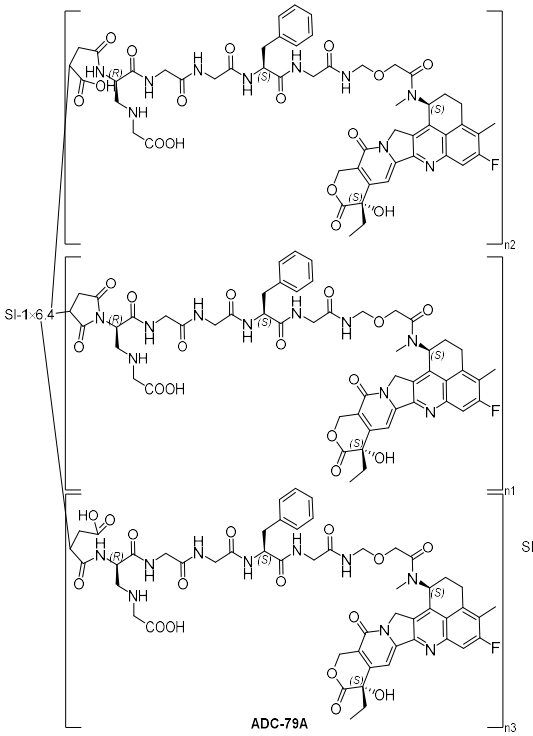
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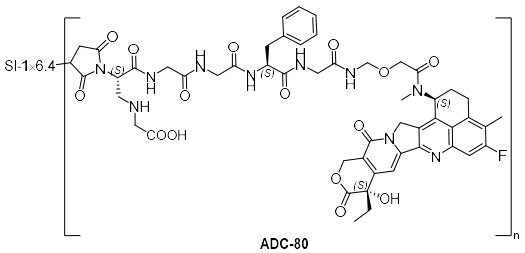
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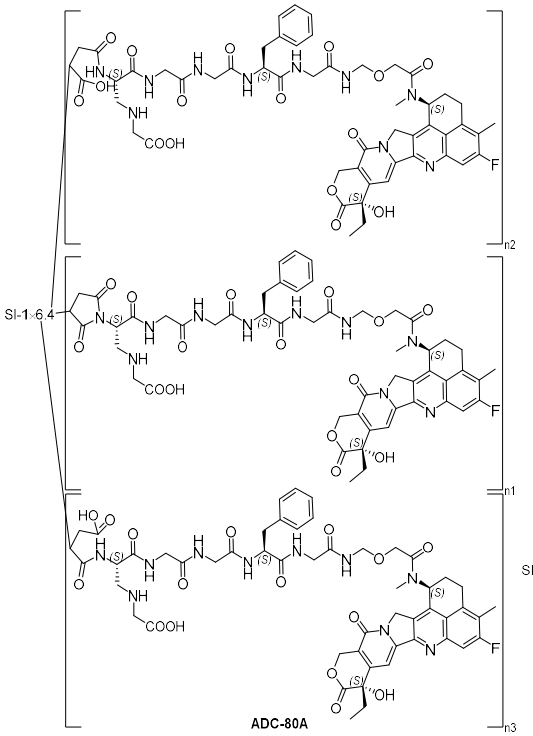
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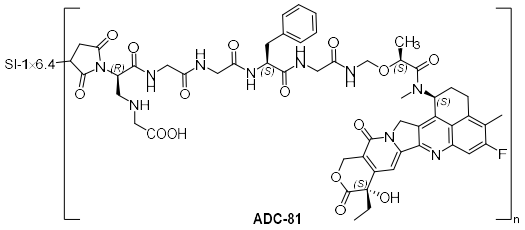
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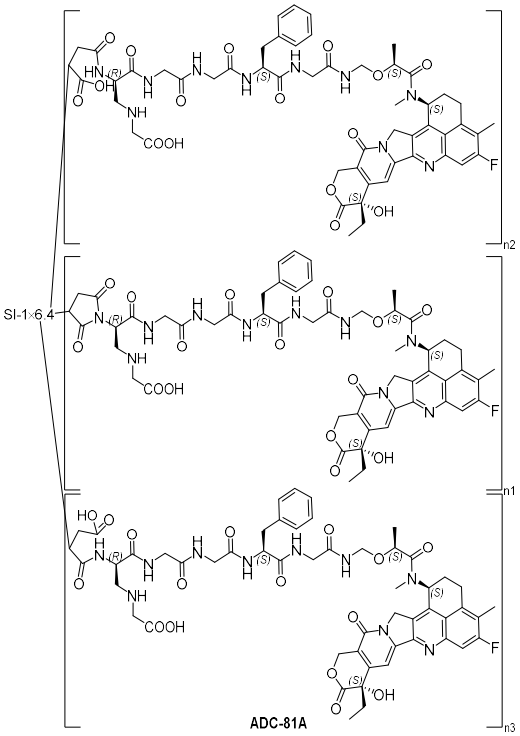
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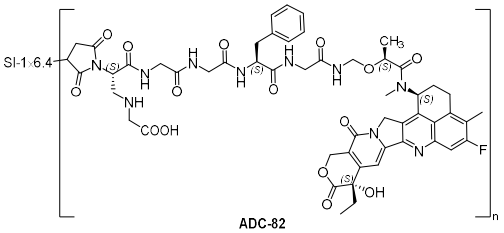
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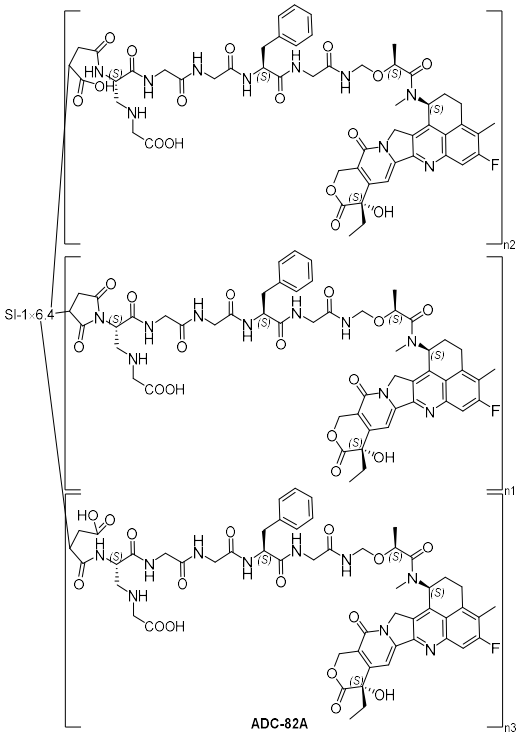
ADC-81



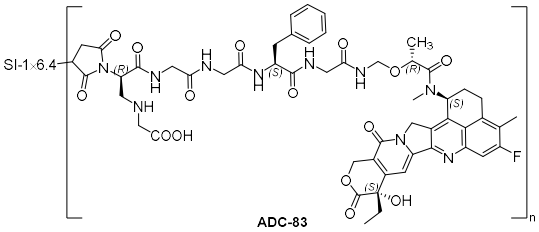
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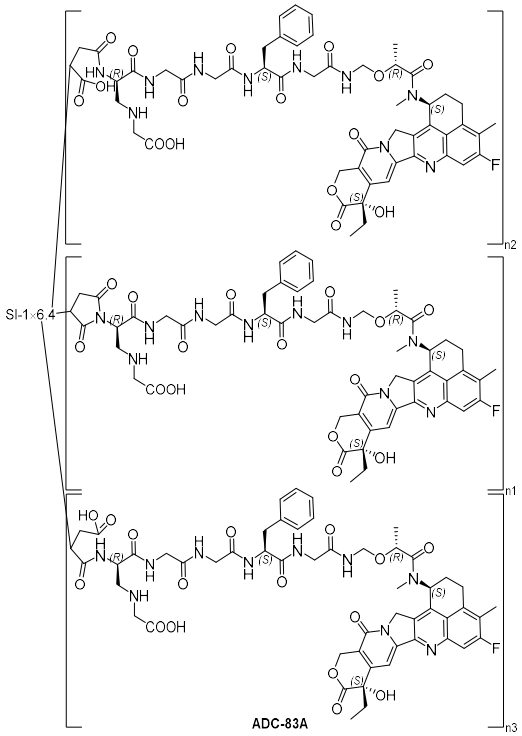
ADC-82



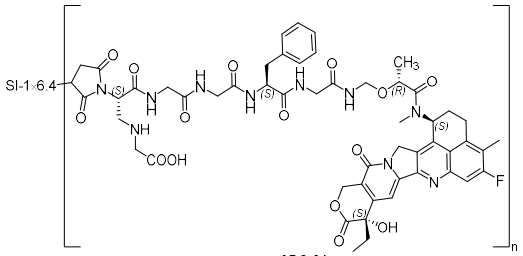
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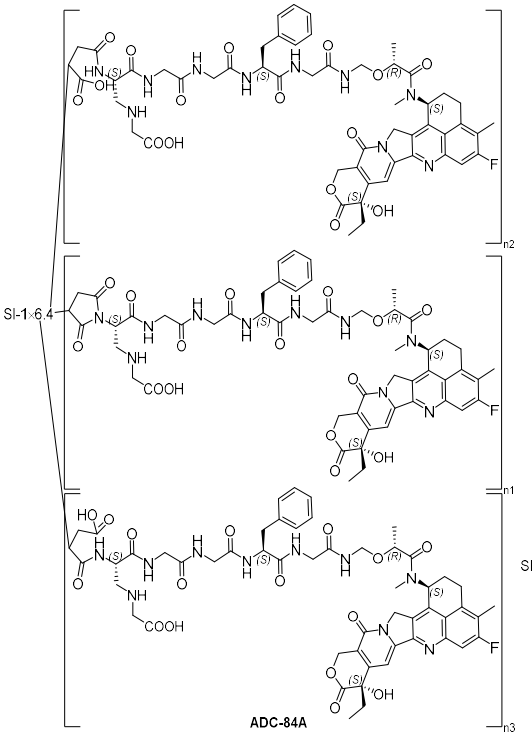
ADC-83



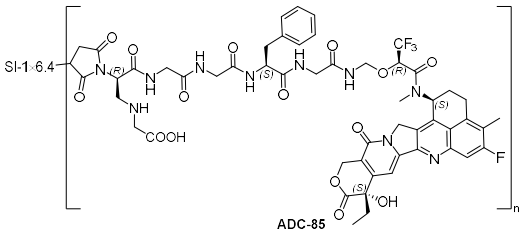
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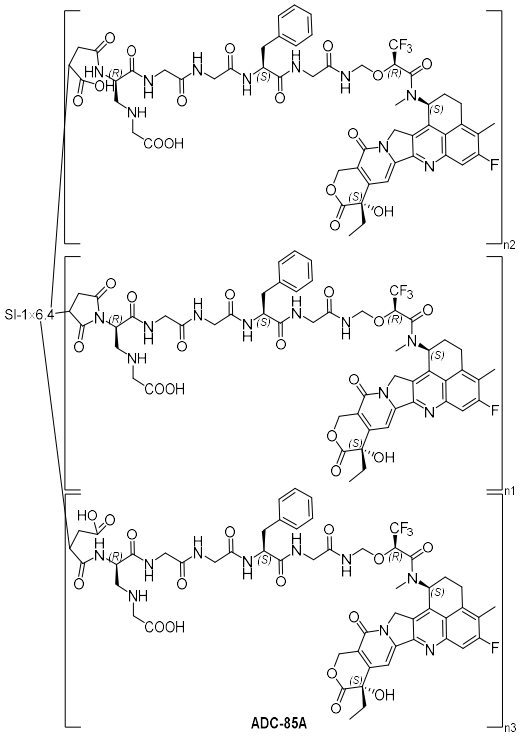
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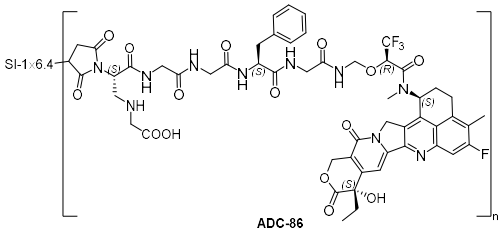
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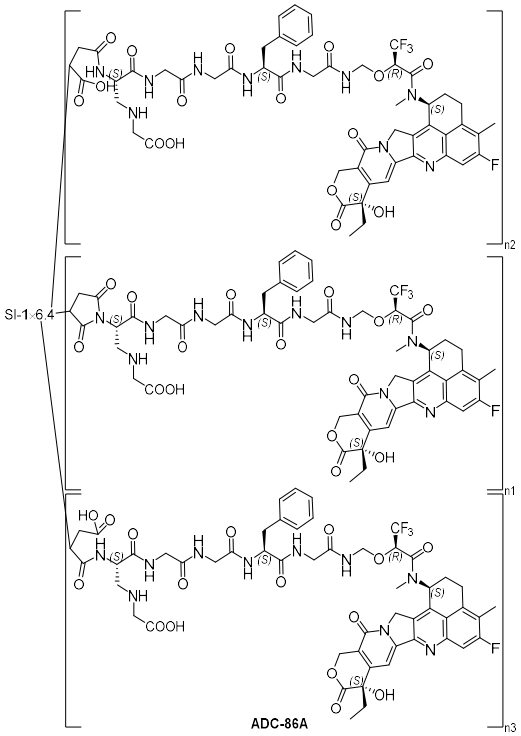
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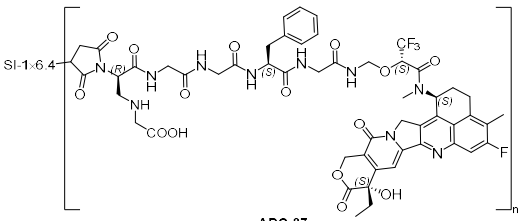
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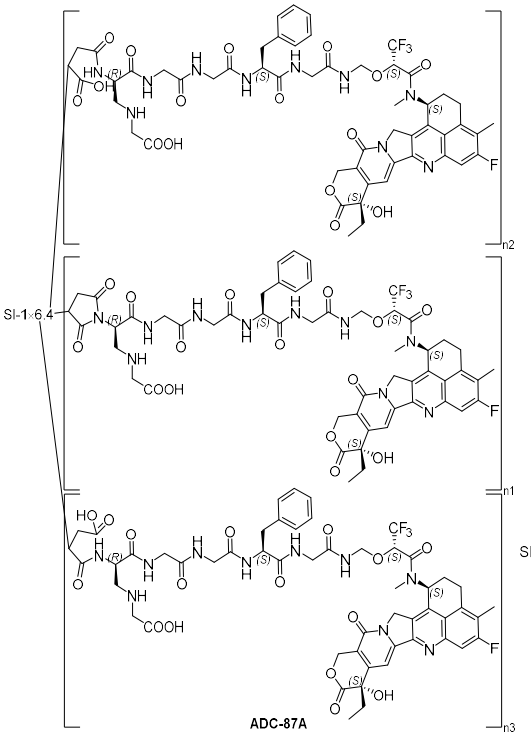
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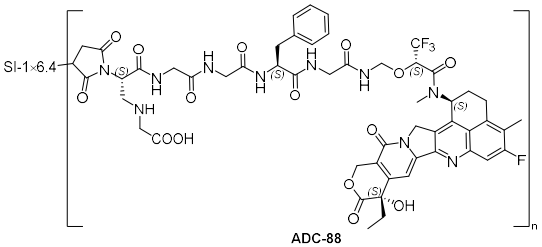
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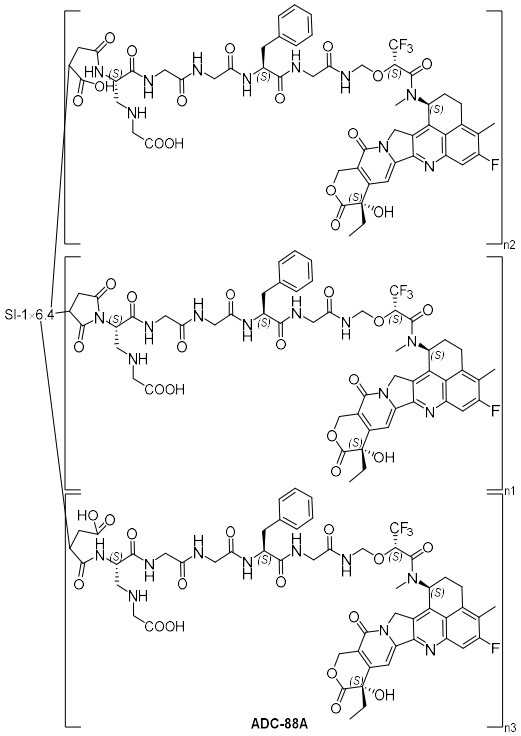
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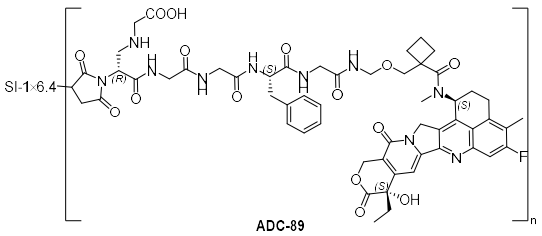
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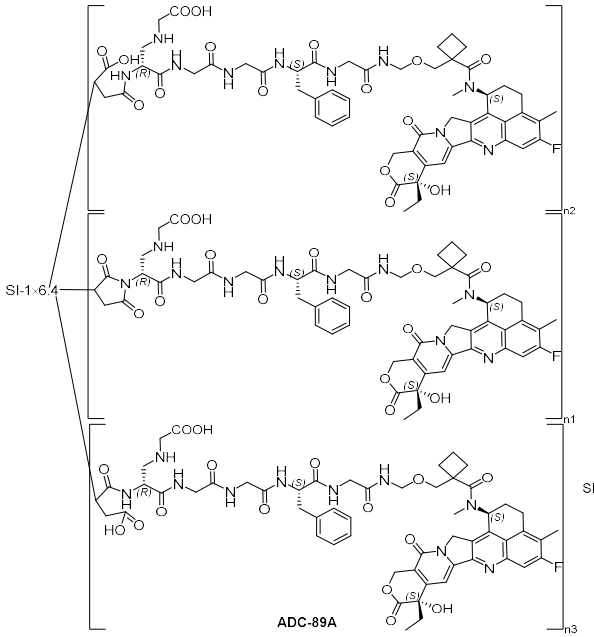
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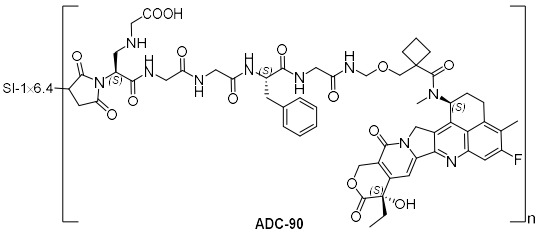
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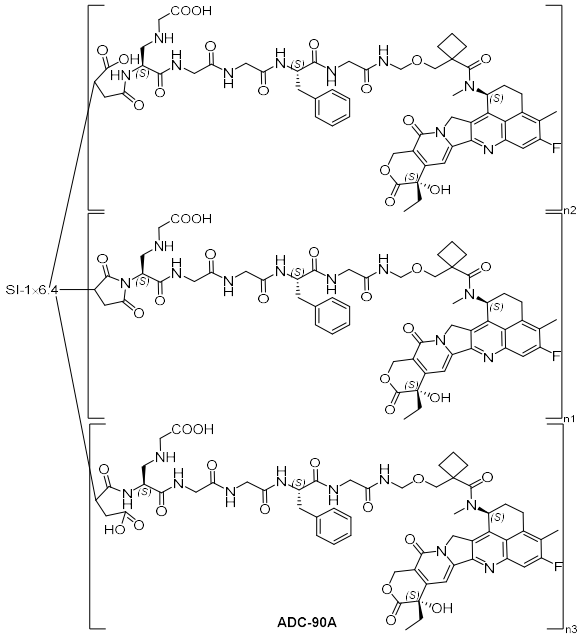
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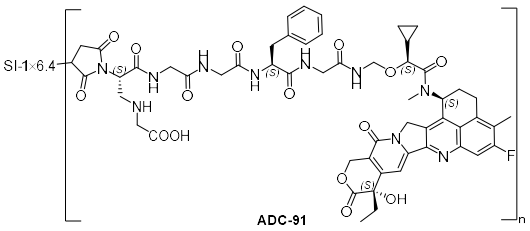
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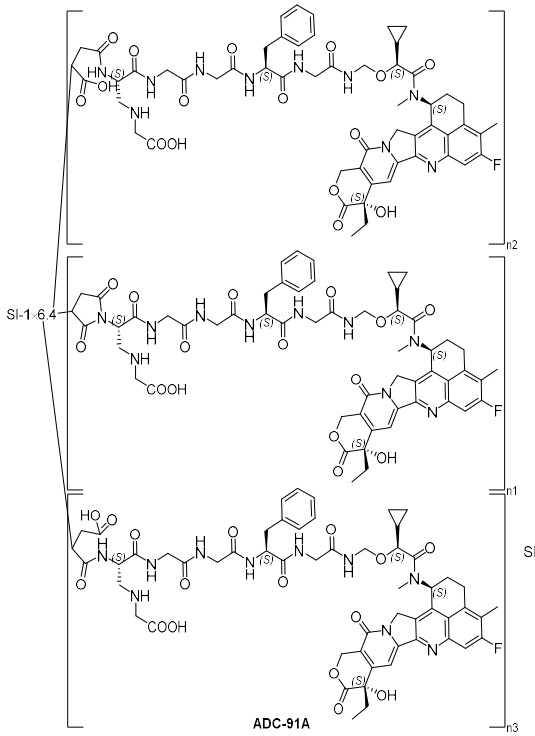
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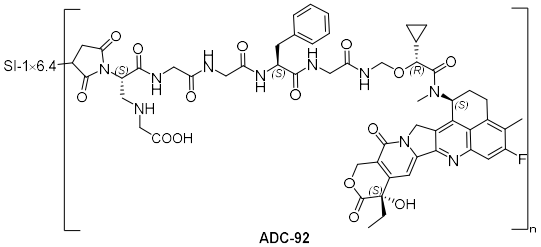
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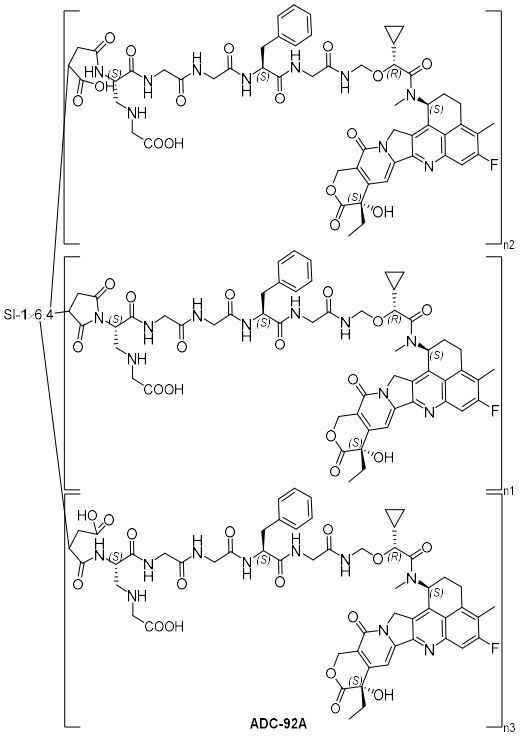
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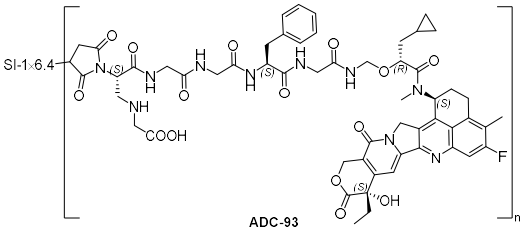
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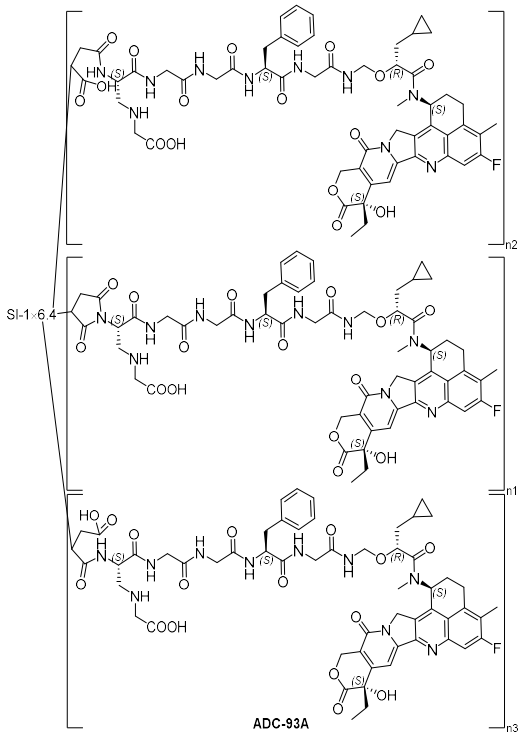
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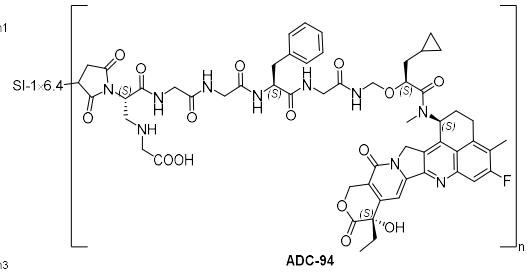
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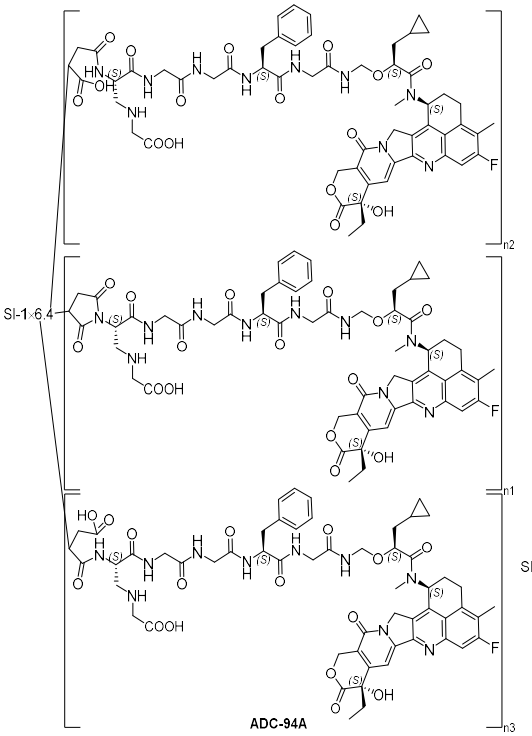
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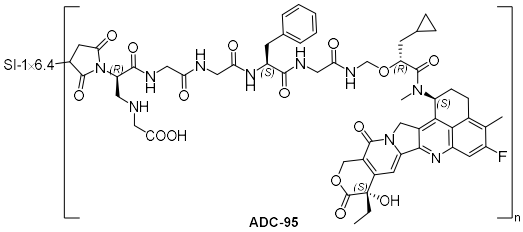
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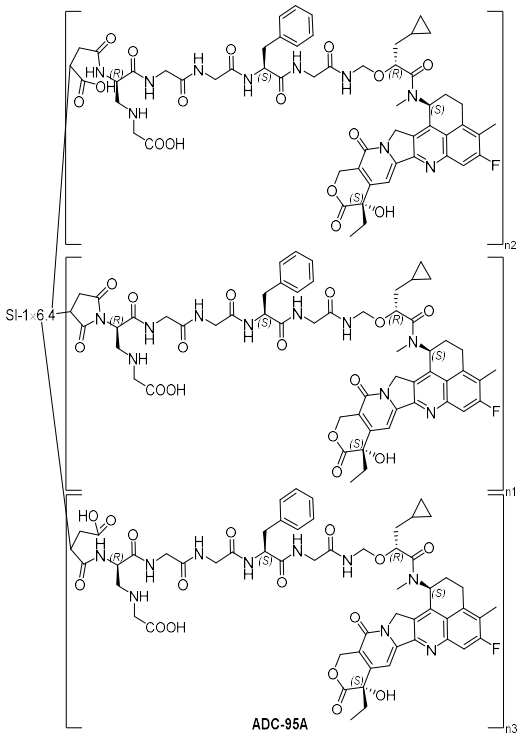
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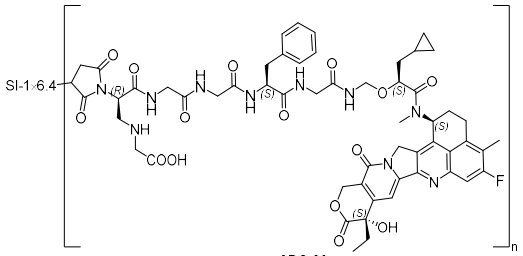
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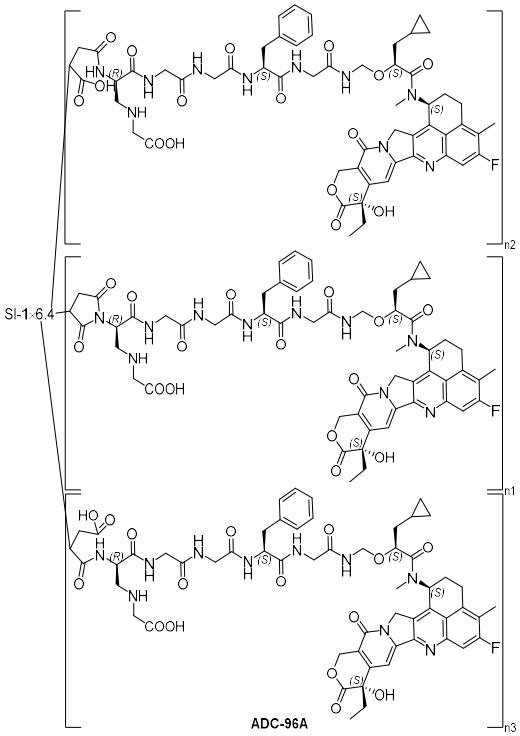
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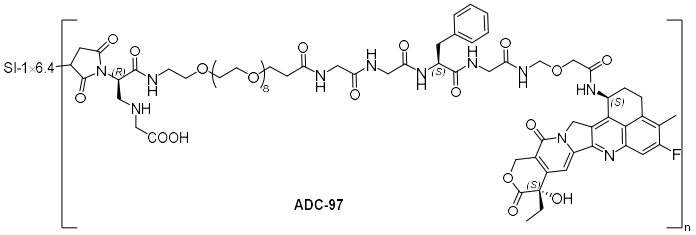
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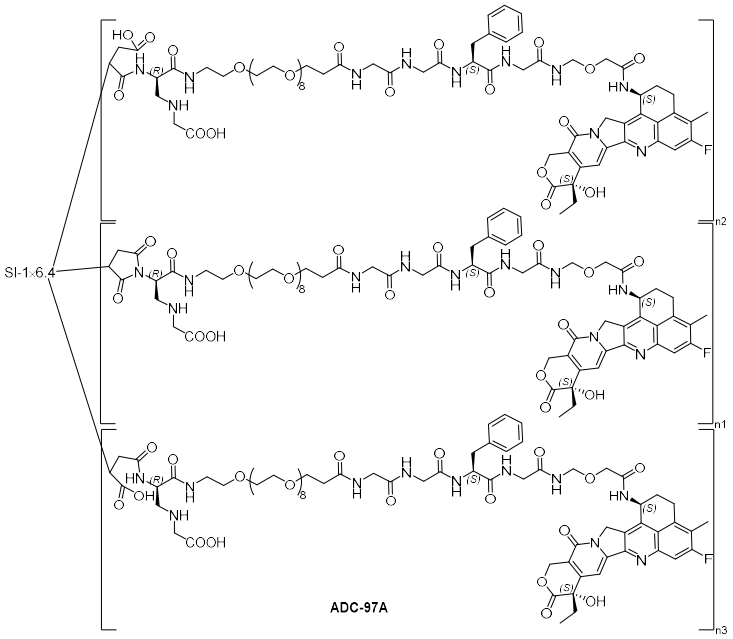
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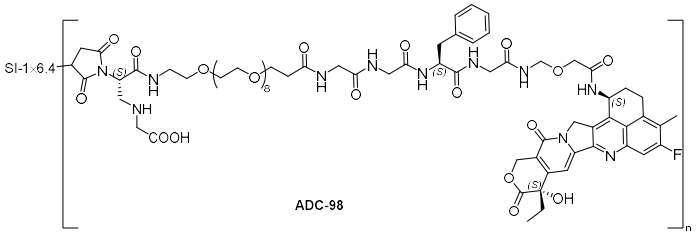
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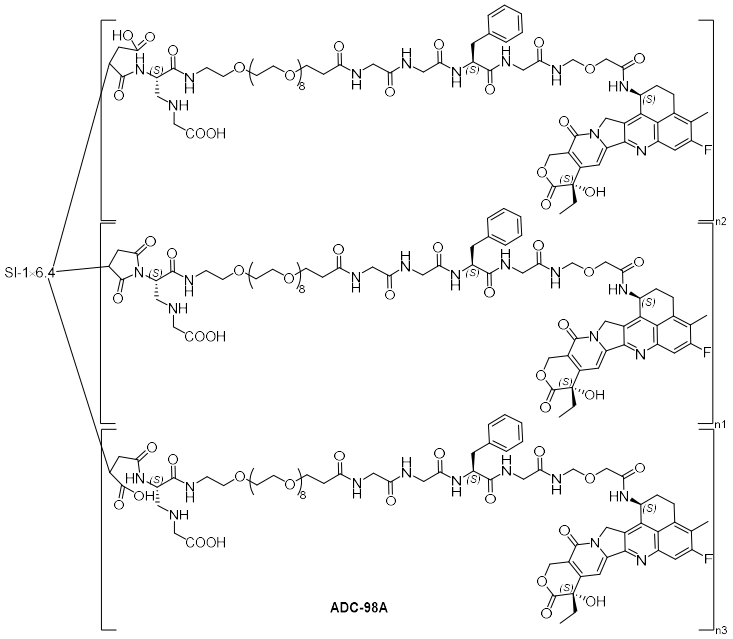
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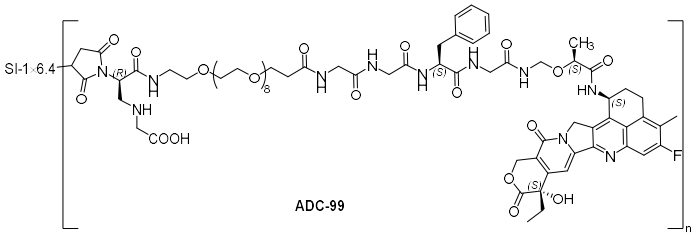
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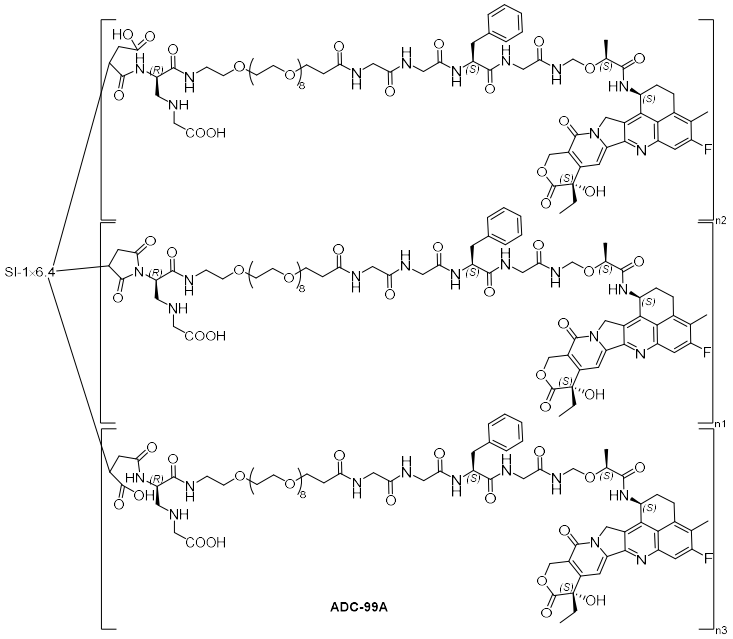
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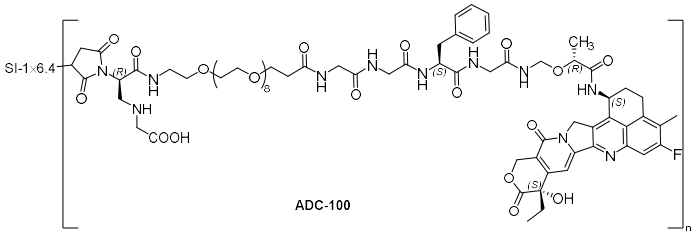
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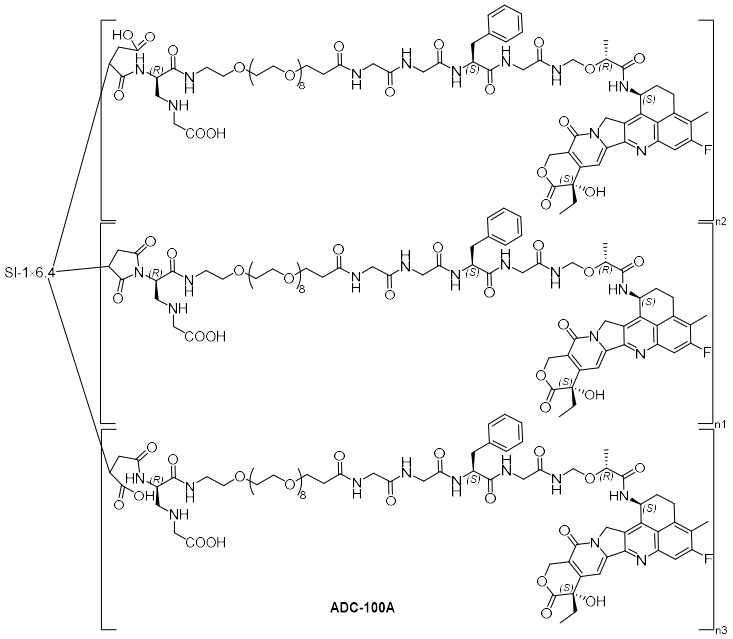
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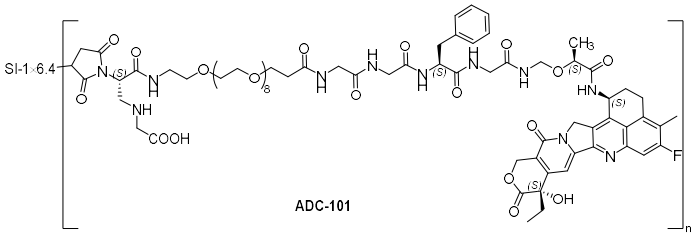
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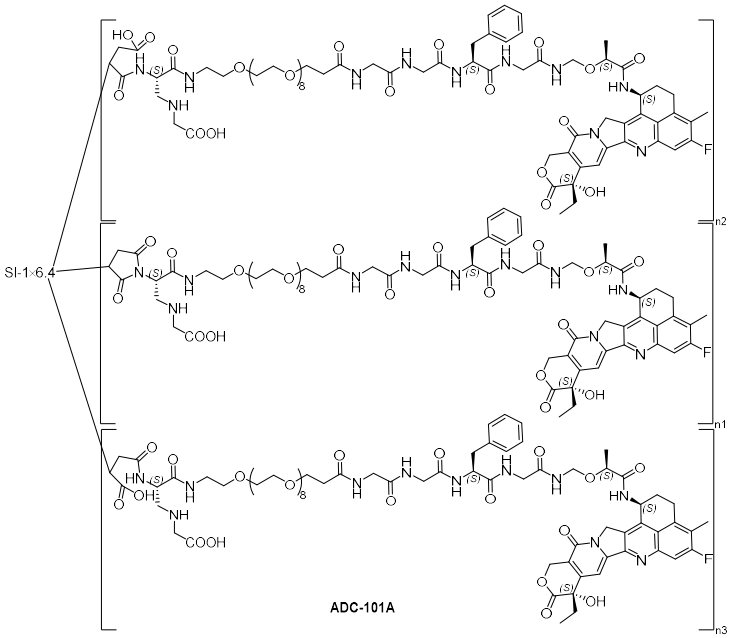
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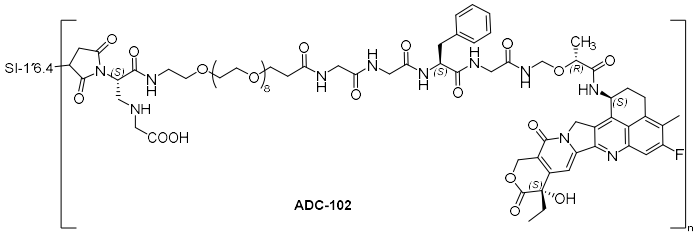
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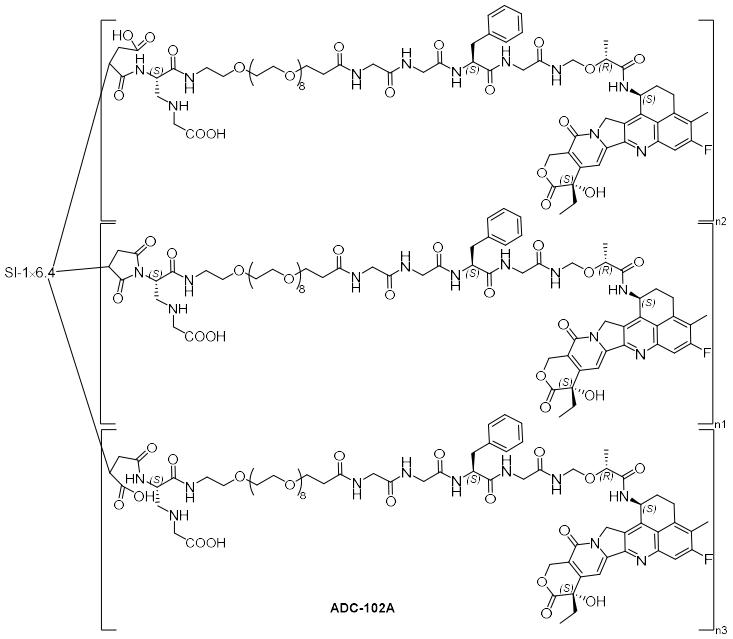
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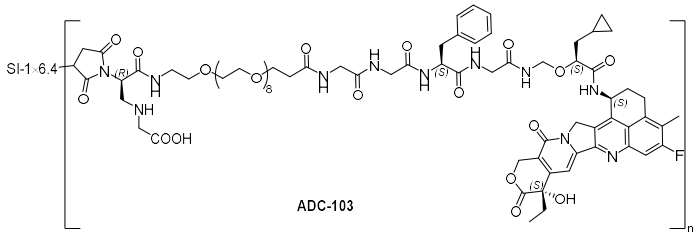
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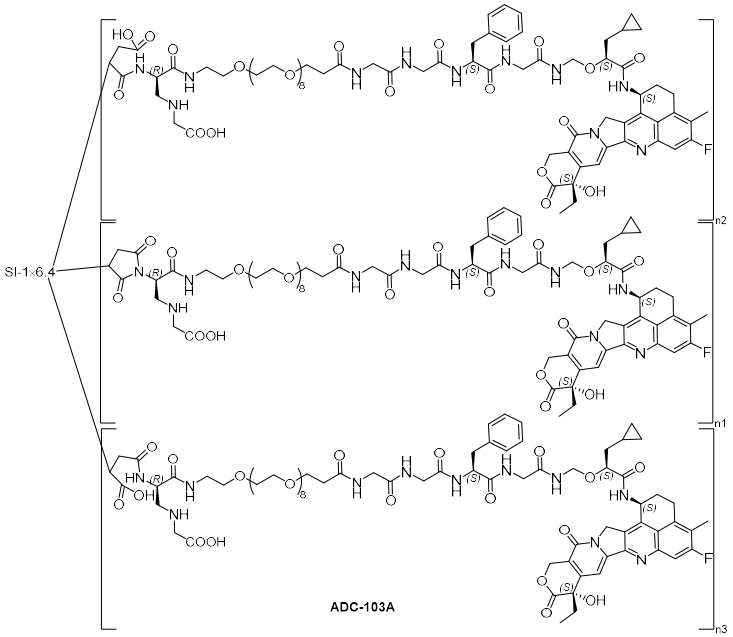
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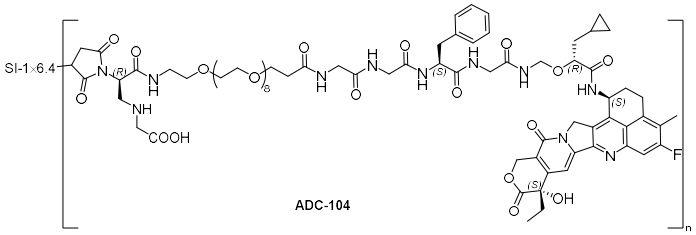
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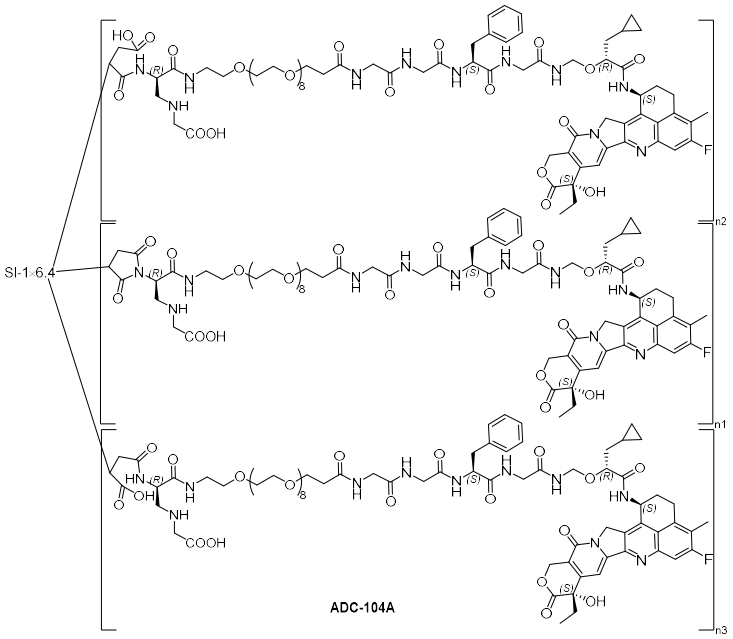
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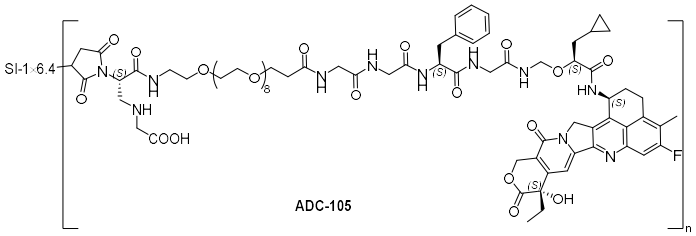
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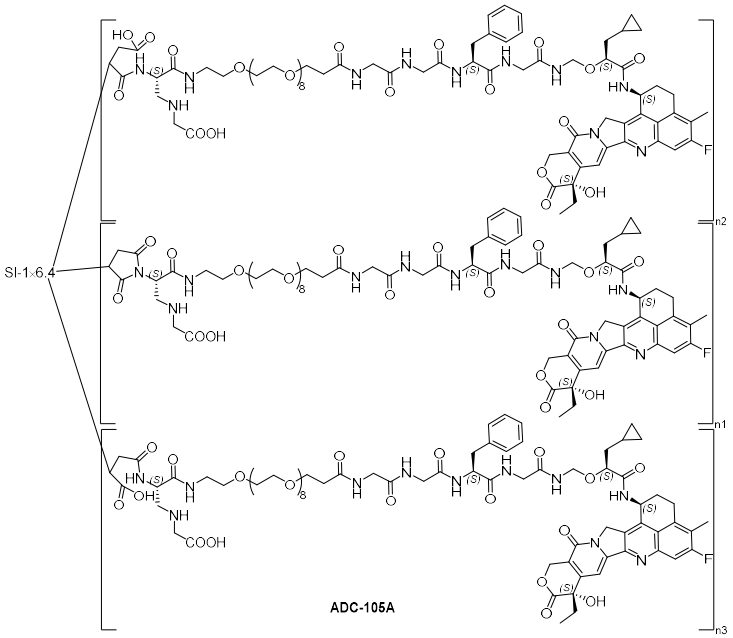
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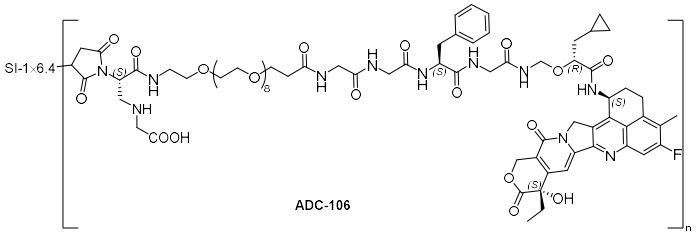
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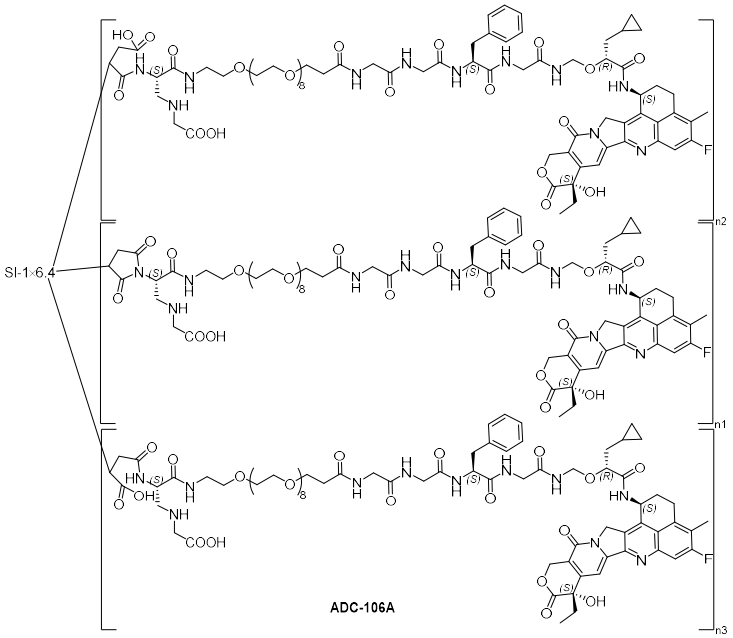
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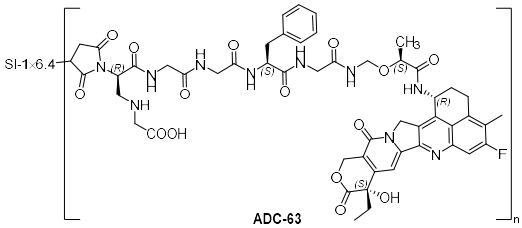
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ADC-106

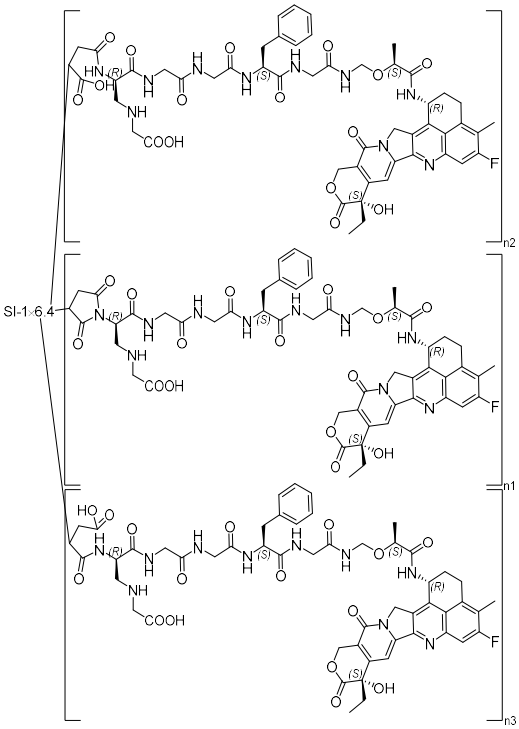


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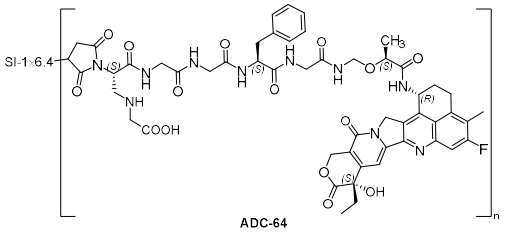
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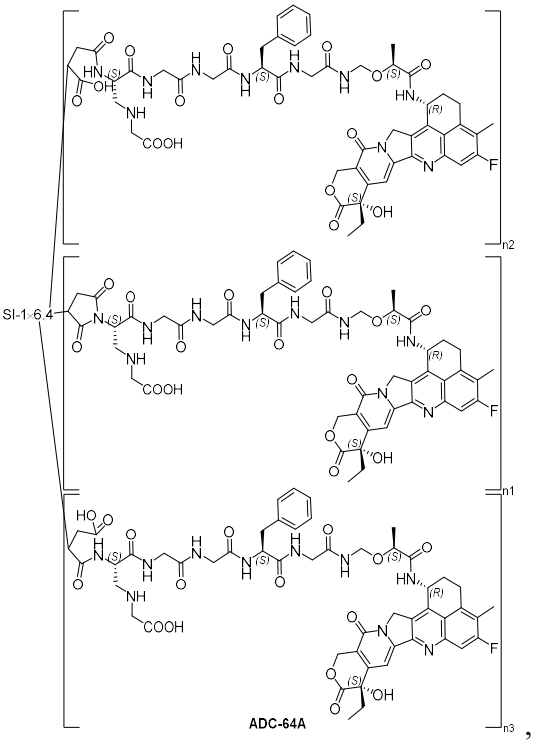
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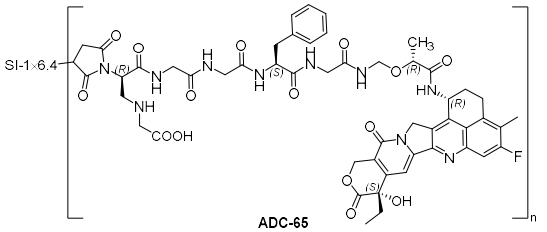
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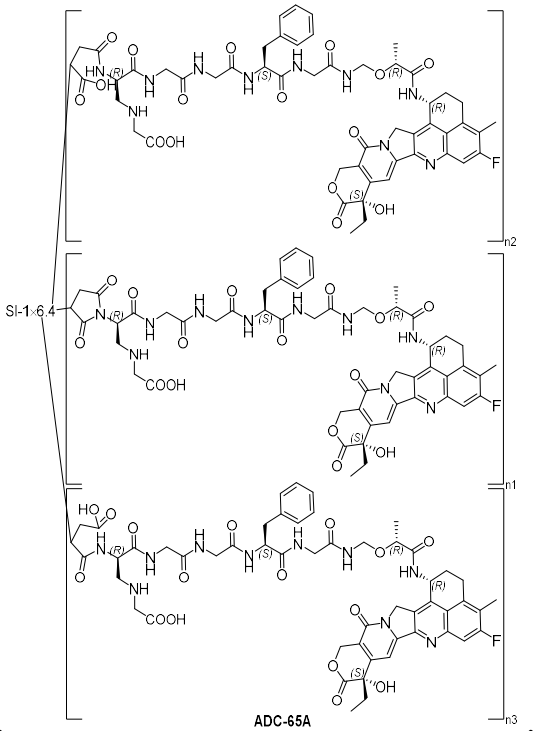


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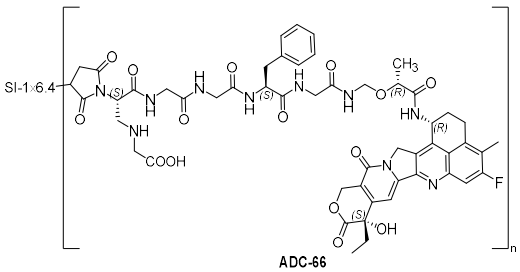
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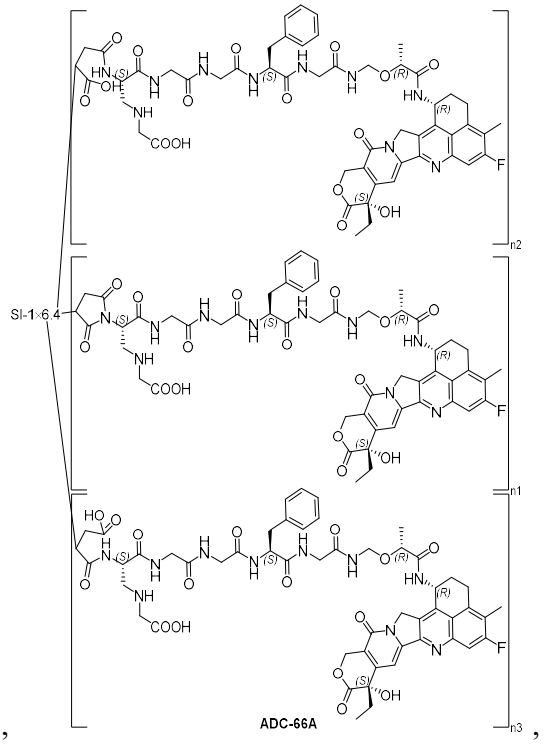
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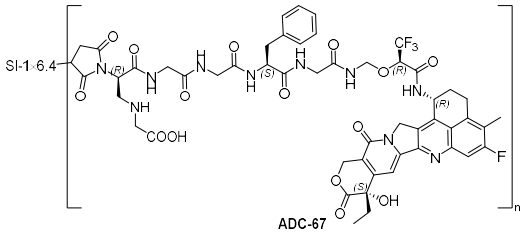
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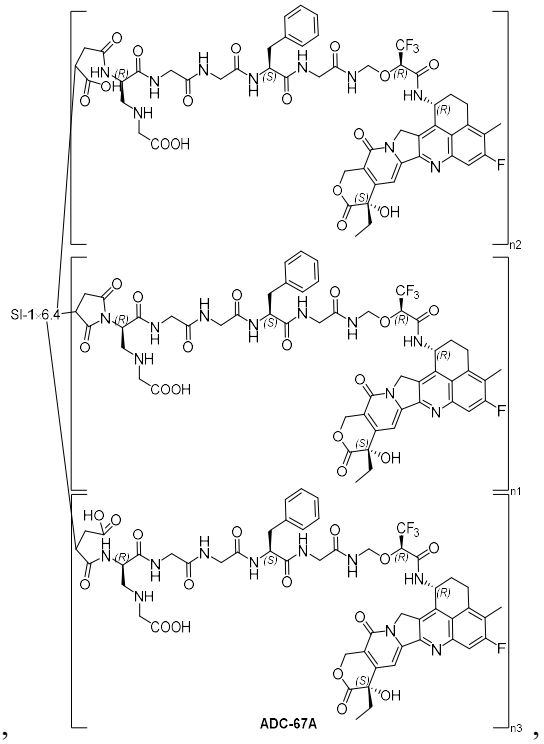
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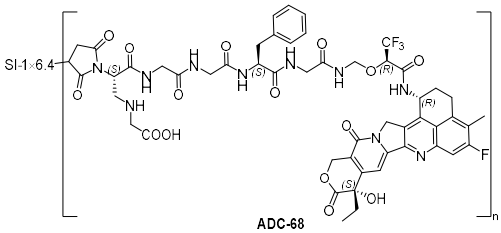
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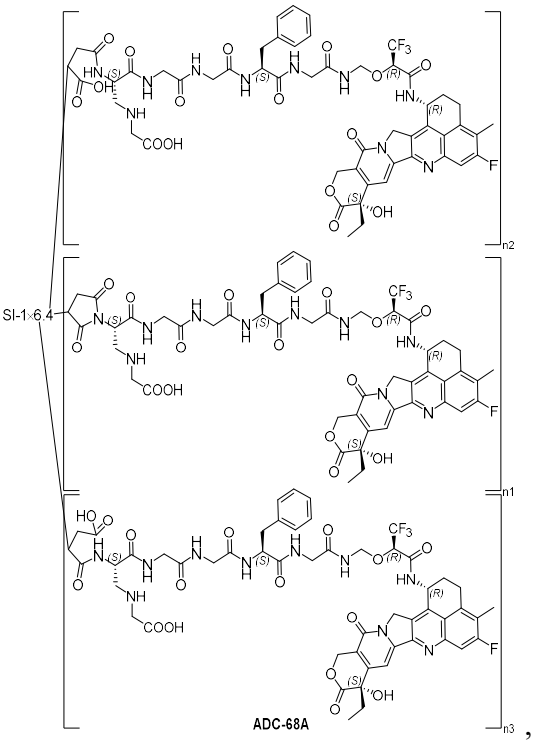
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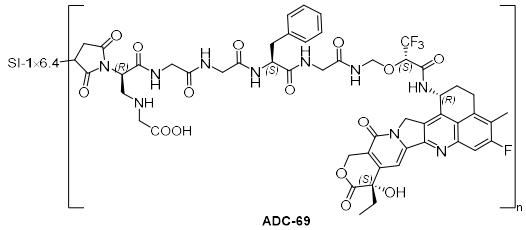
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ADC-68,

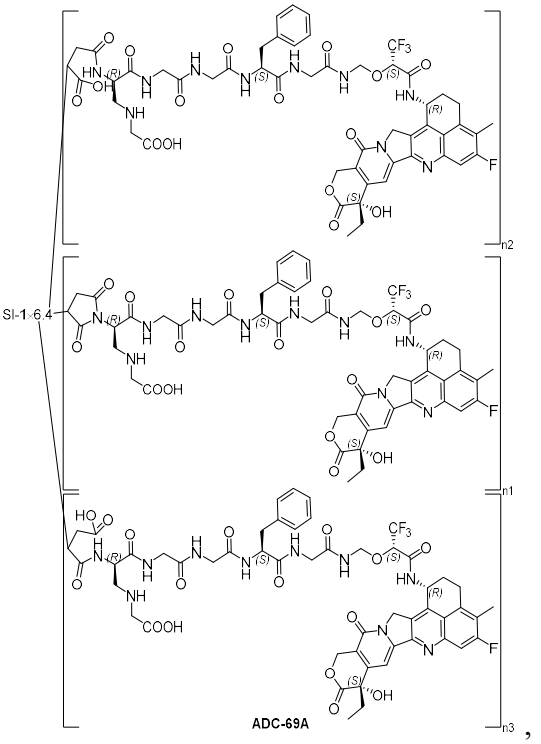


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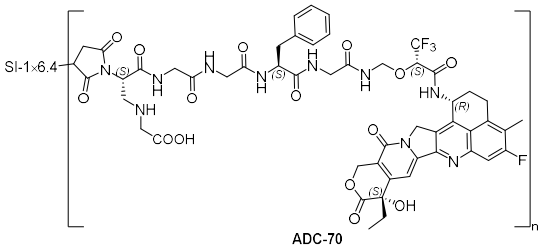
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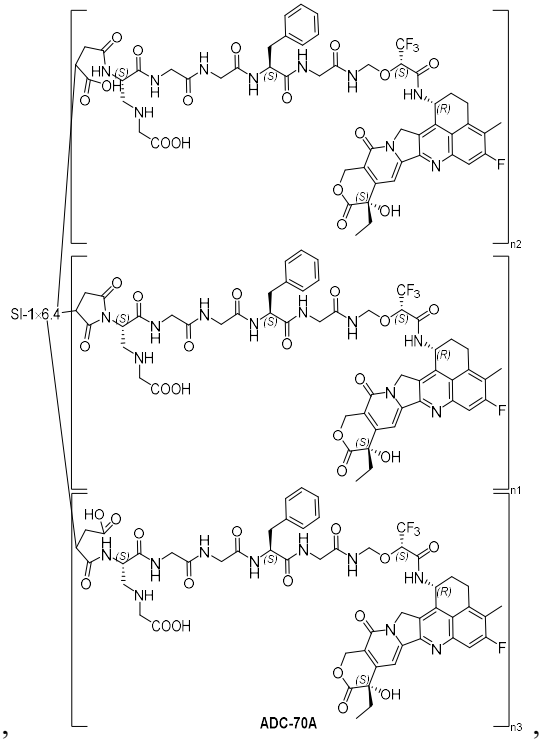
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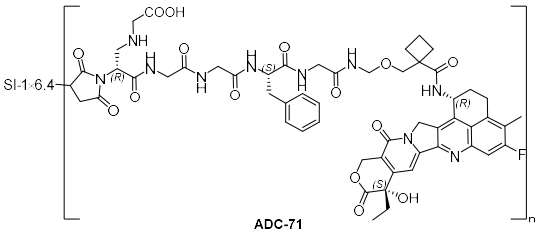
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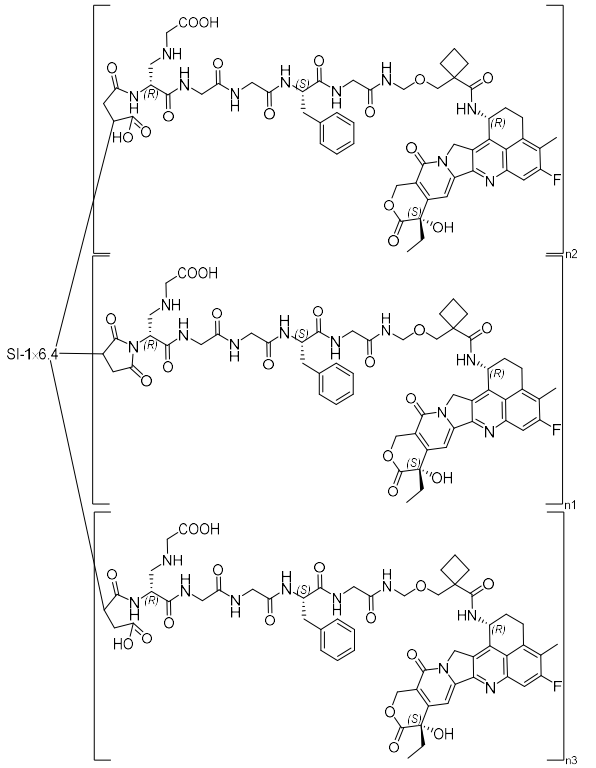


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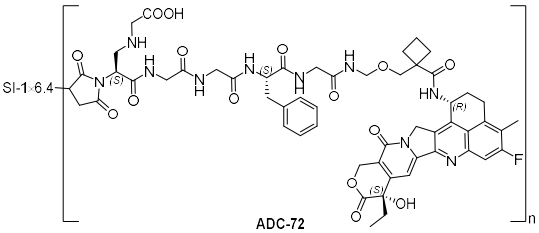
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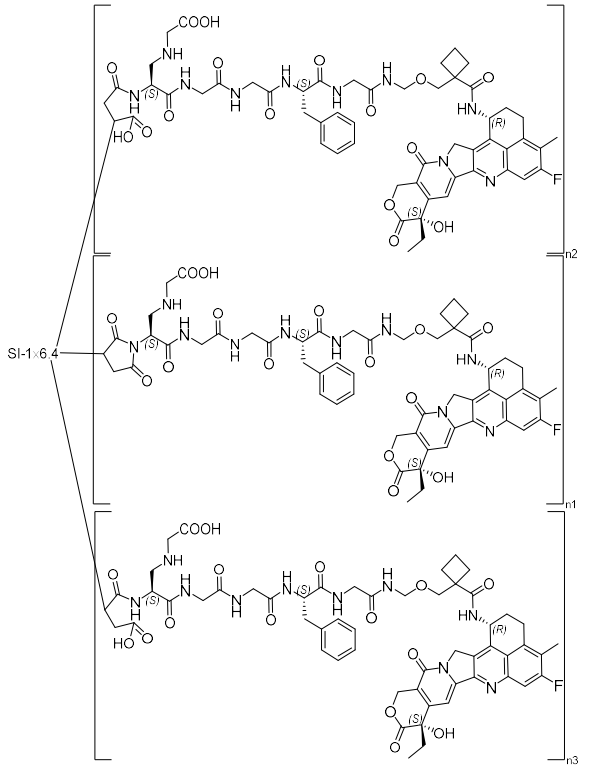
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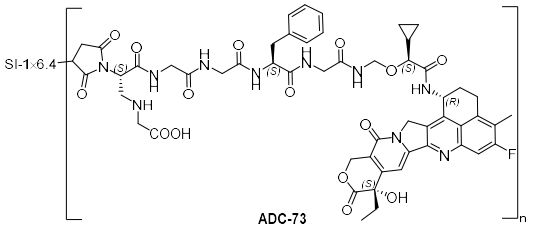
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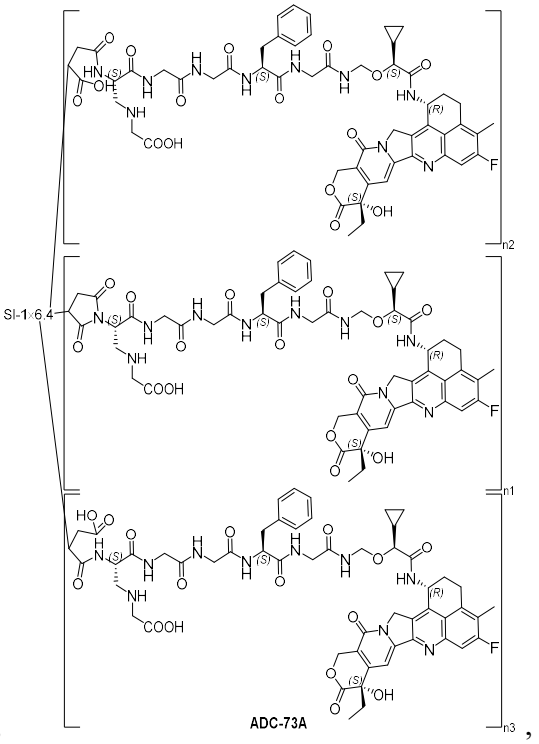
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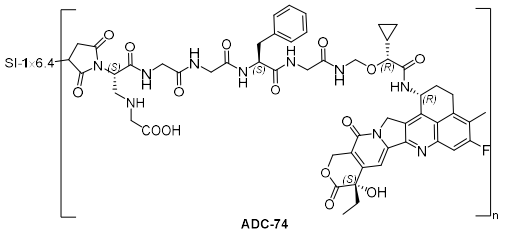
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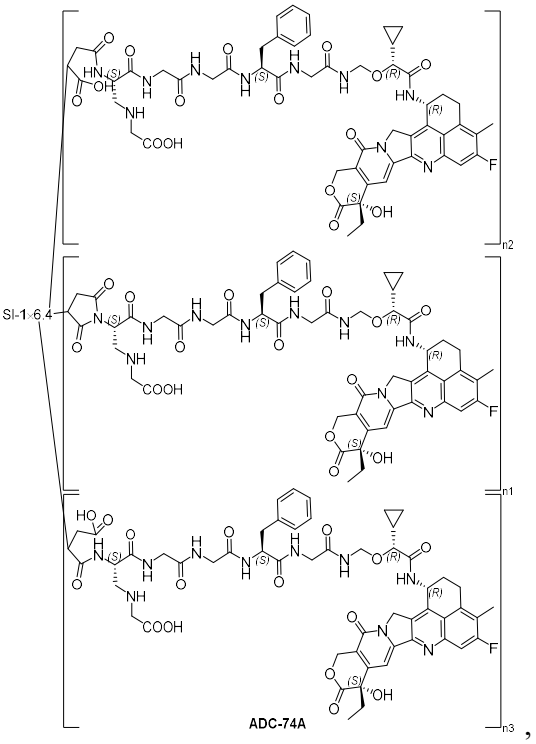
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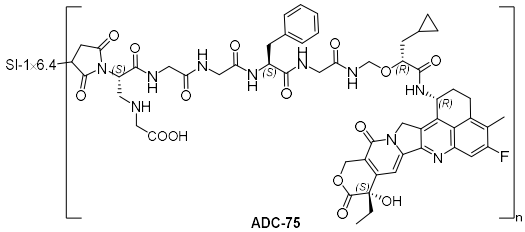
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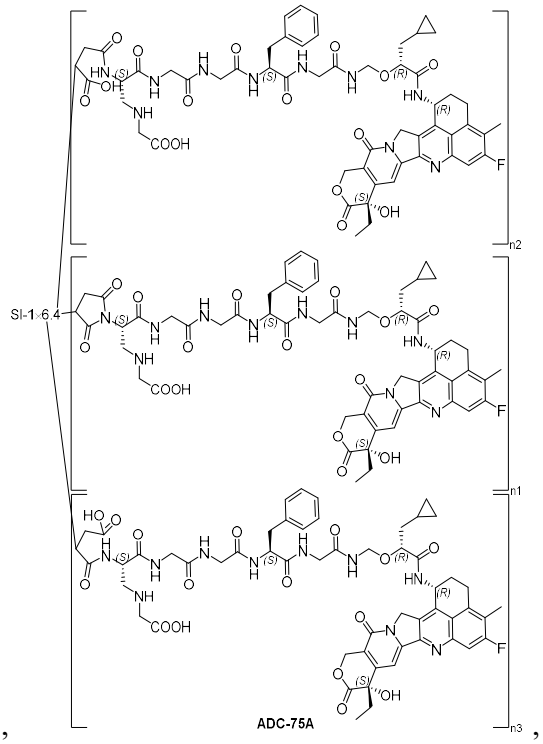
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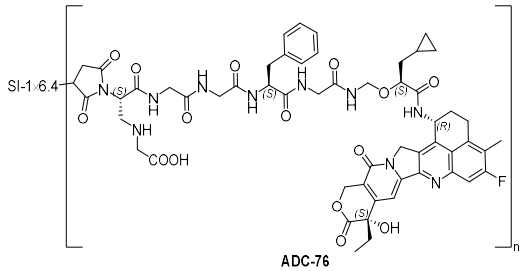
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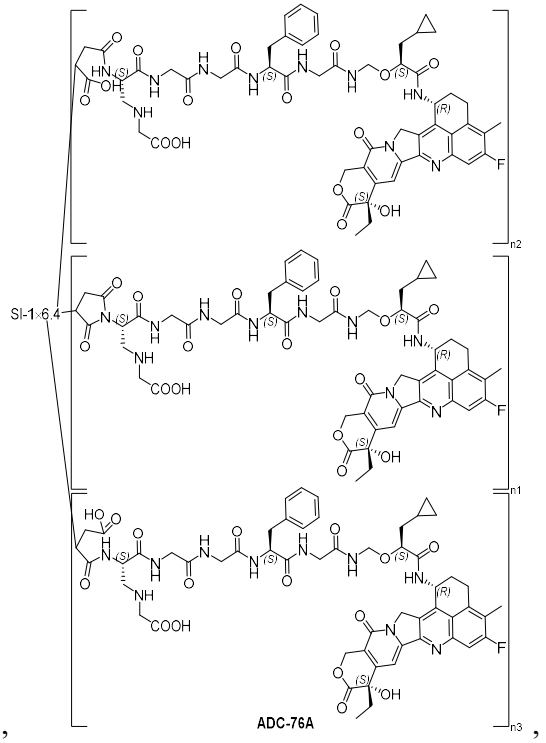
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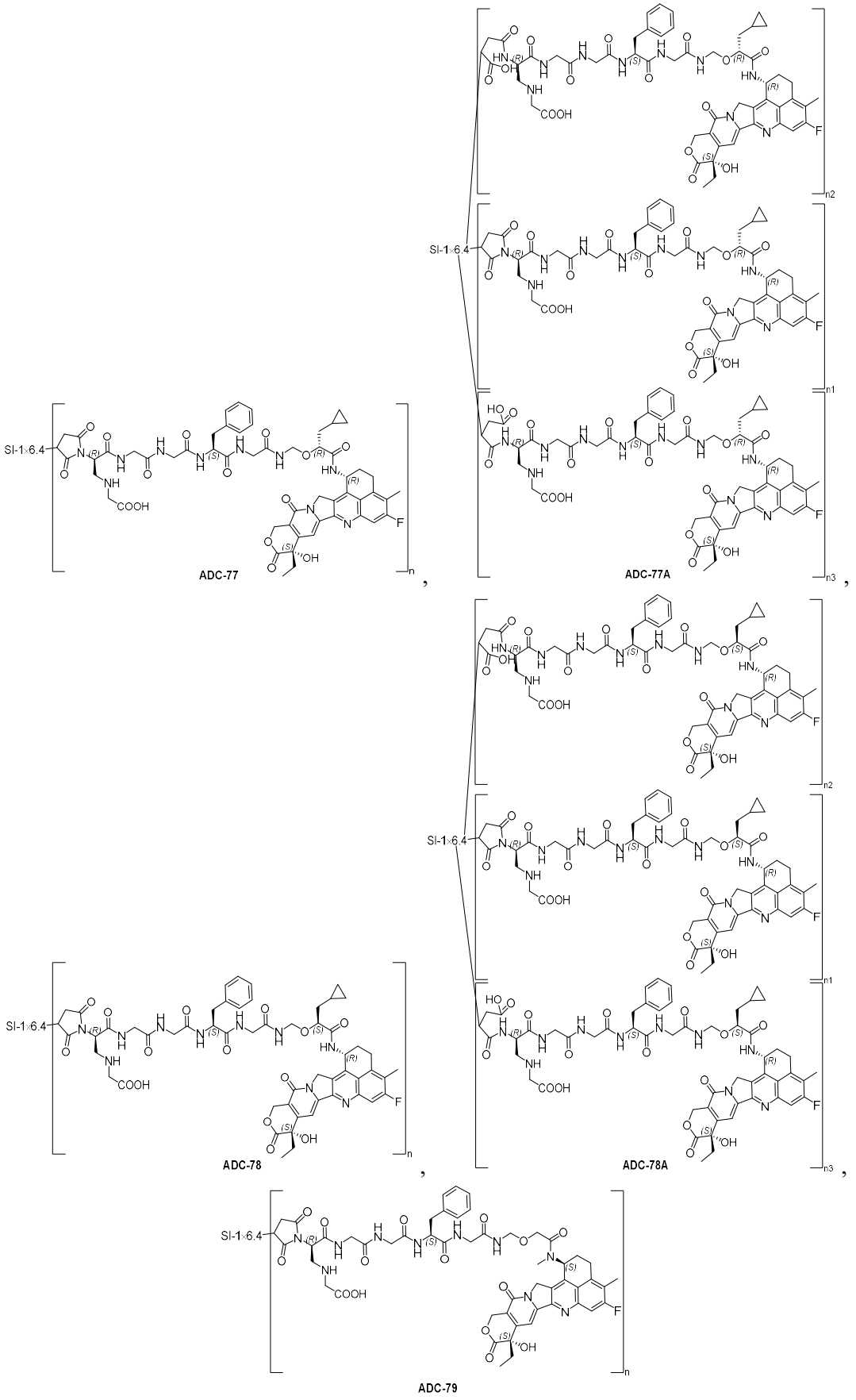
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ADC-76,



ADC-76A,



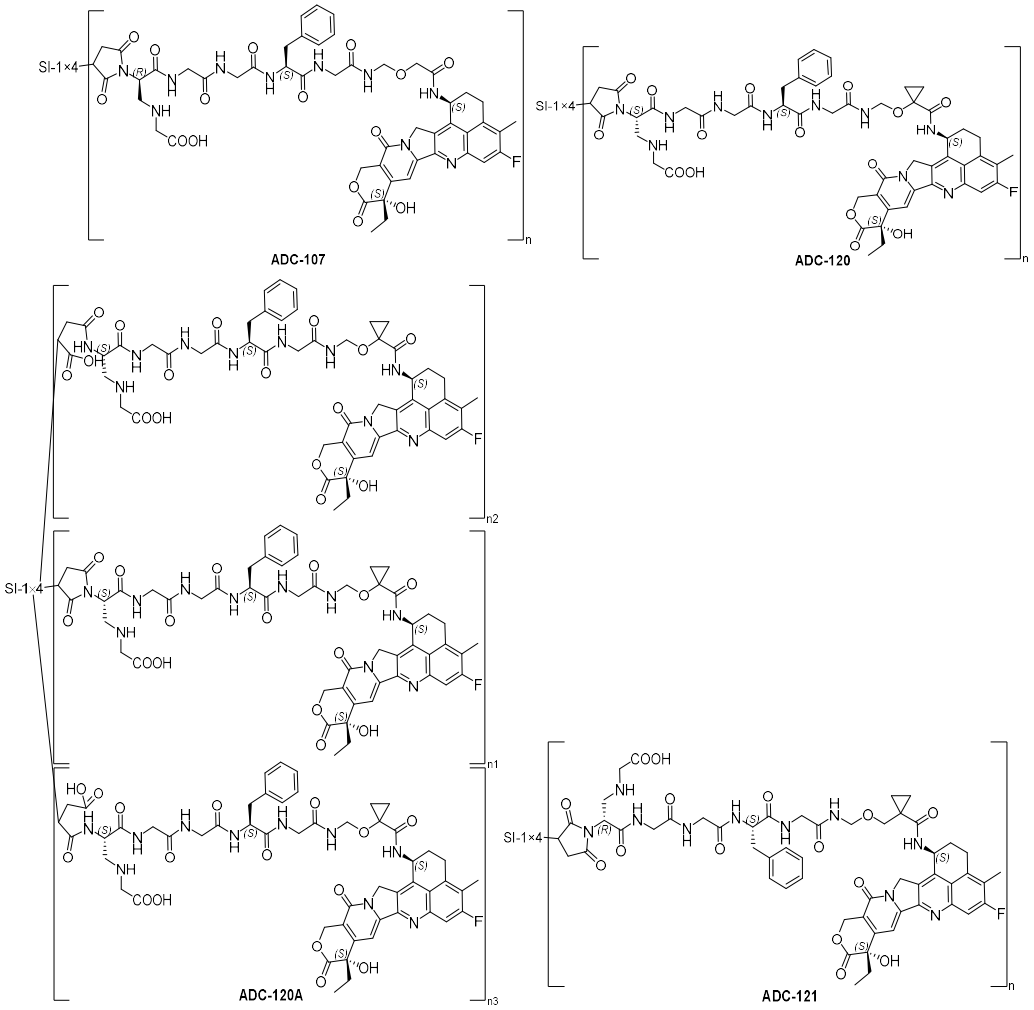
wherein:

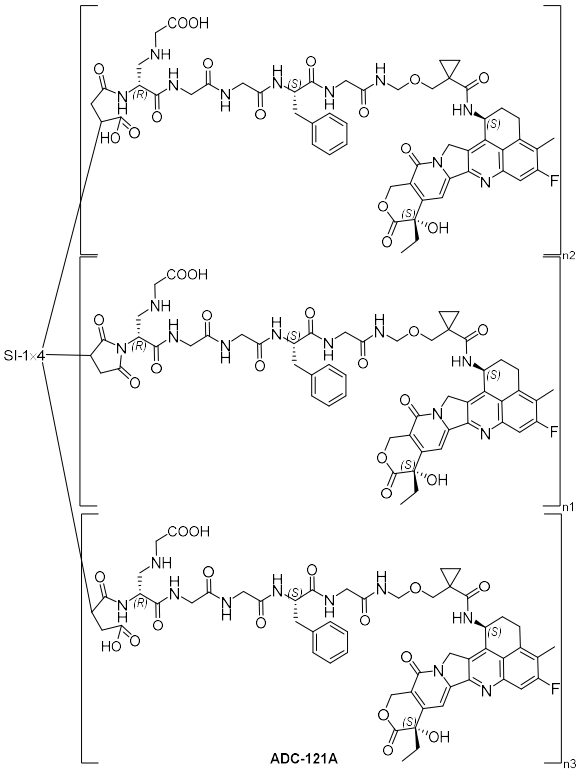
SI-1 x 6.4 is a bispecific antibody or antigen-binding fragment thereof having a binding affinity

to EGFR and HER3,

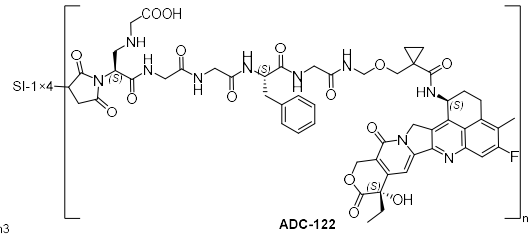
n is an integer of 1-10, n1, wherein n2, and n3 are each independently chosen from any integer or any decimal number from 0-10, n1, n2, and n3 are not simultaneously 0, and $1 \leq n1 + n2 + n3 \leq 10$.

51. The use as Claim 1-15, wherein the ligand-camptothecin derivative conjugate, or a pharmaceutically acceptable salt or solvate thereof, comprises the following structure, or a butanediimide ring-opening structure thereof, or an isomer thereof:

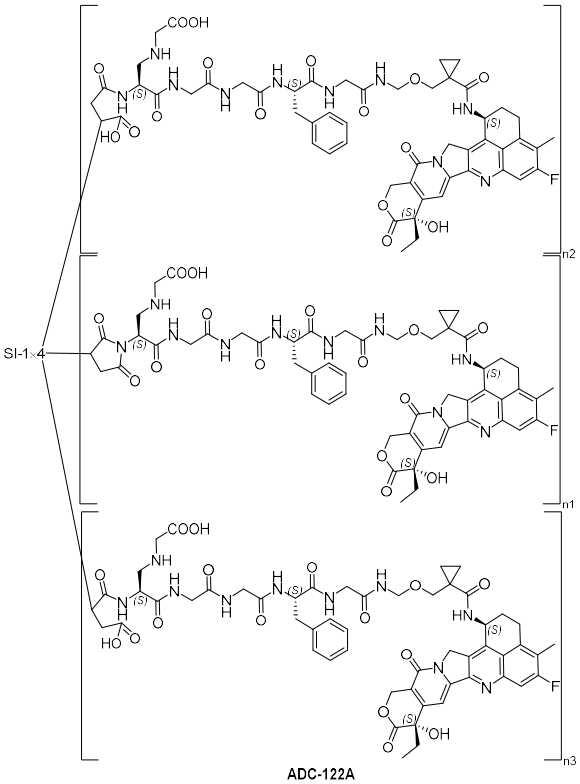




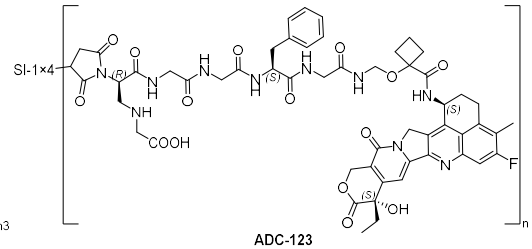
ADC-121A



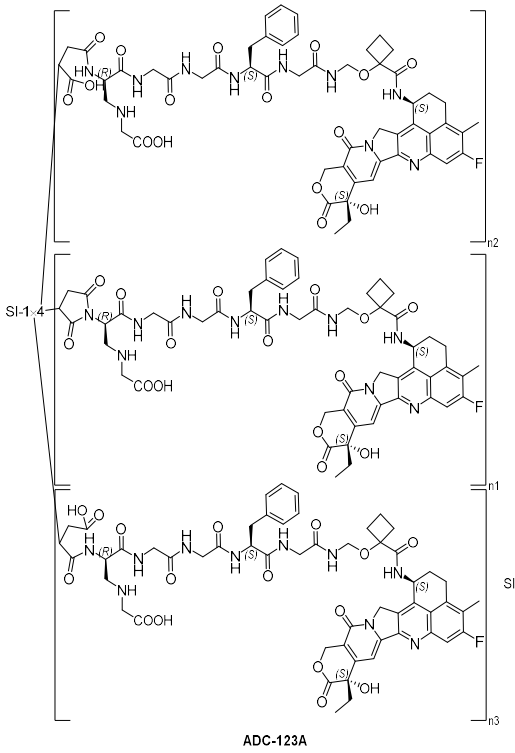
ADC-122



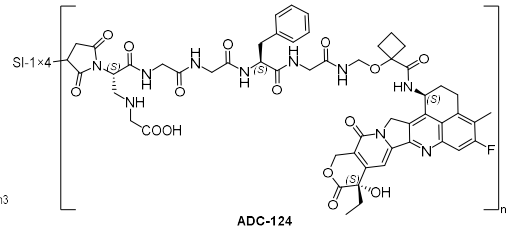
ADC-122A



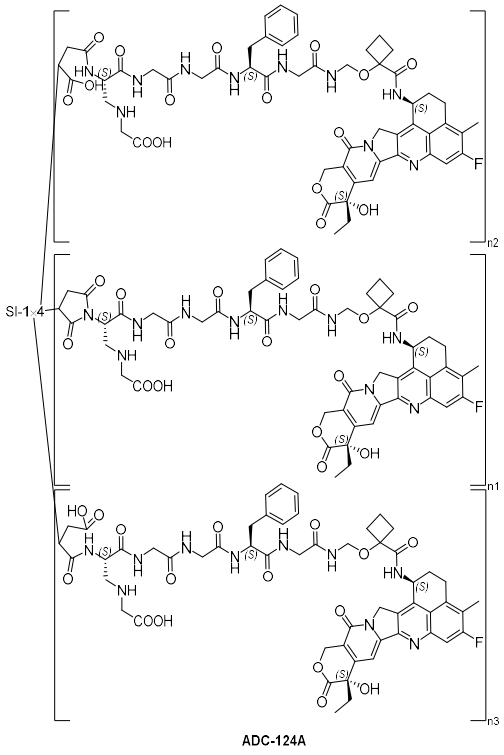
ADC-123



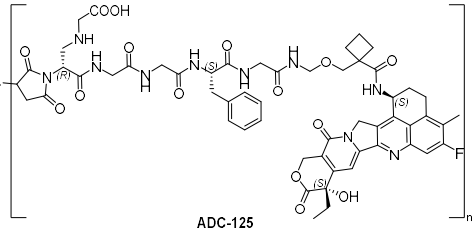
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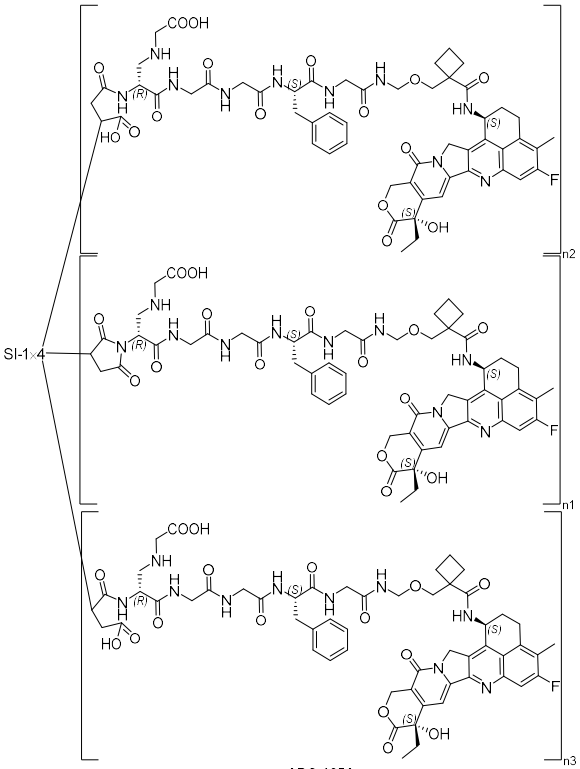
ADC-124



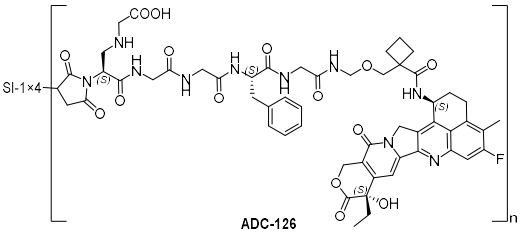
ADC-124A



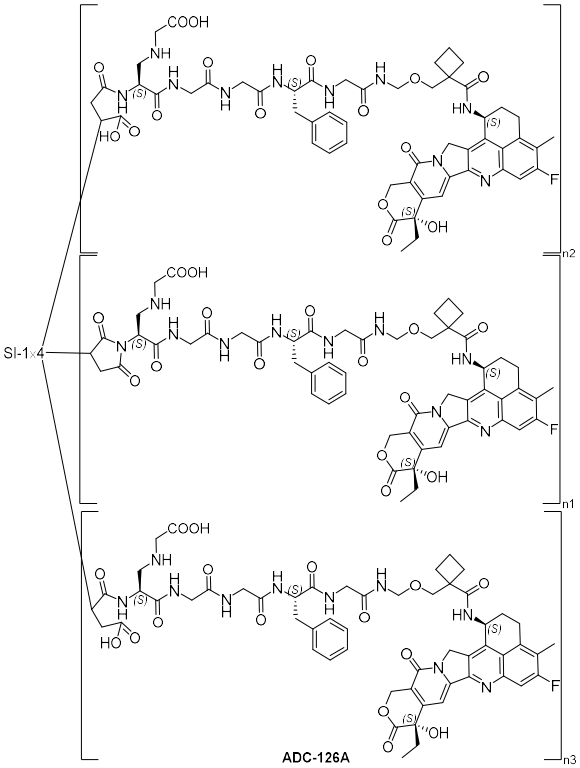
ADC-125



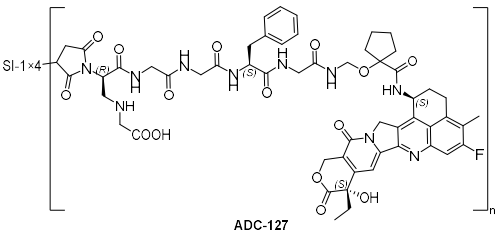
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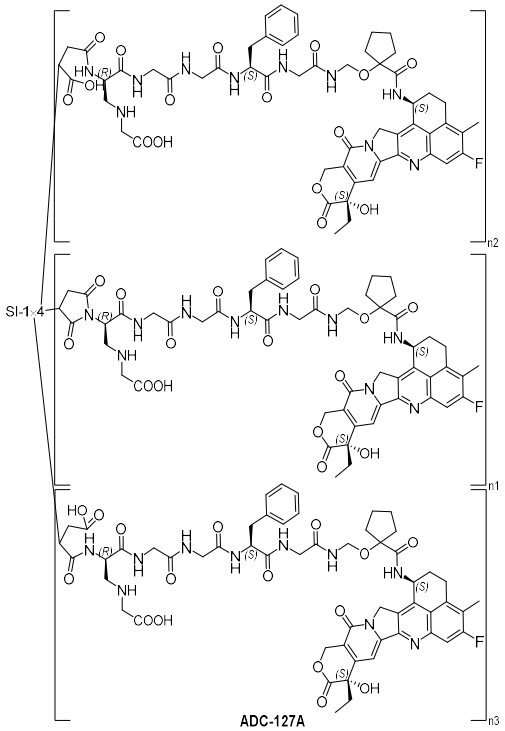
ADC-126



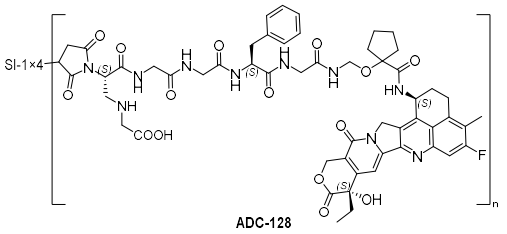
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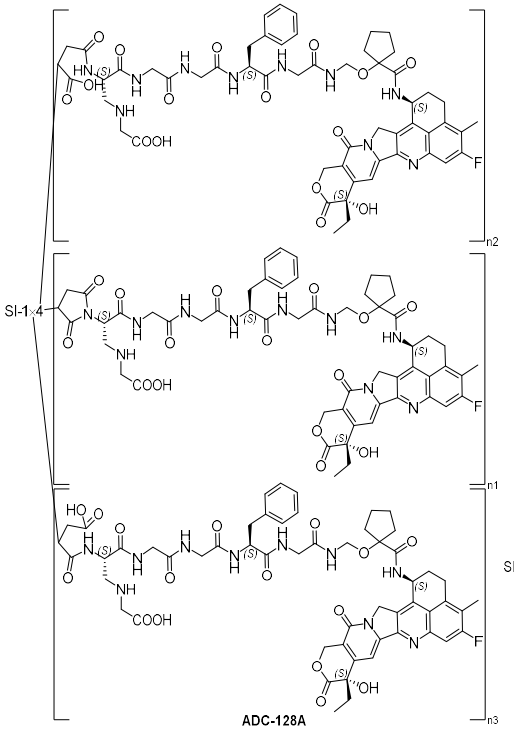
ADC-127



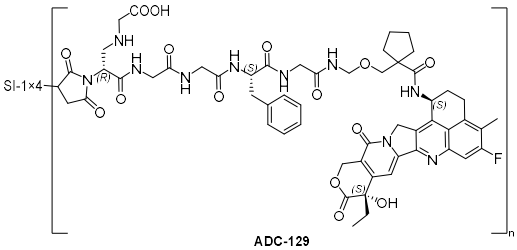
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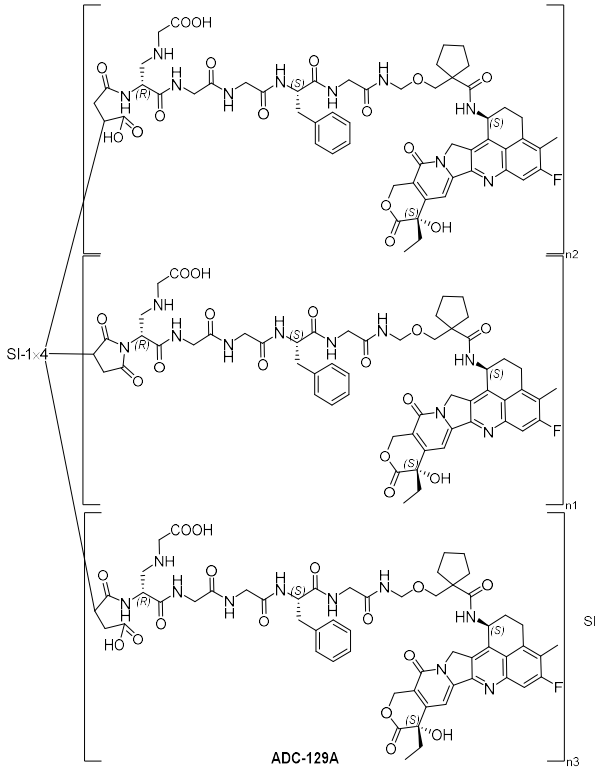
ADC-128



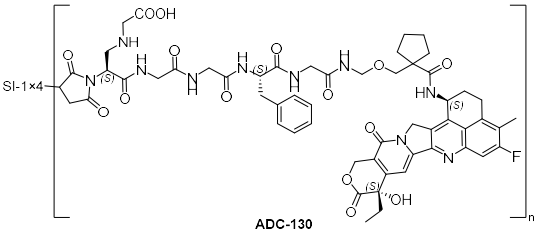
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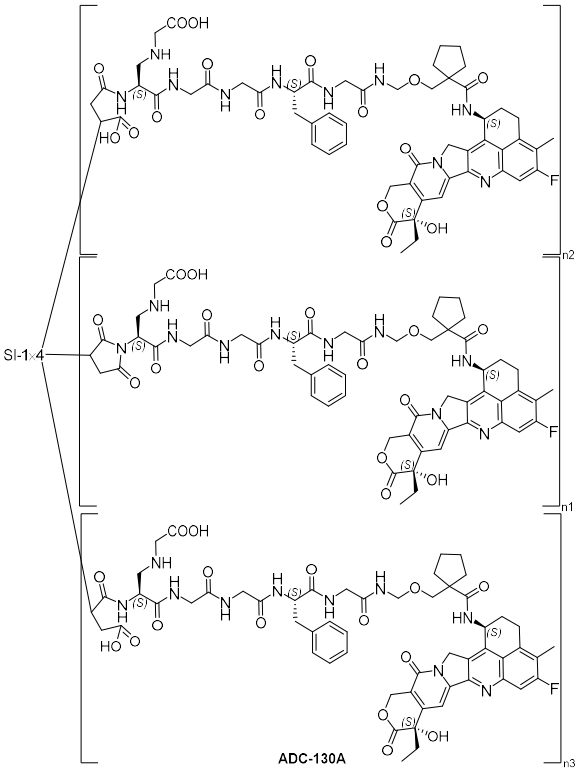
ADC-129



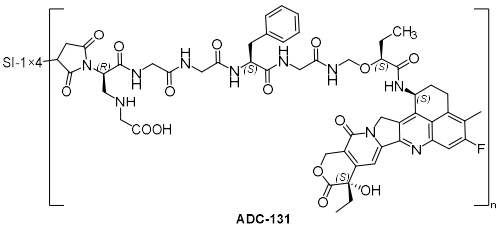
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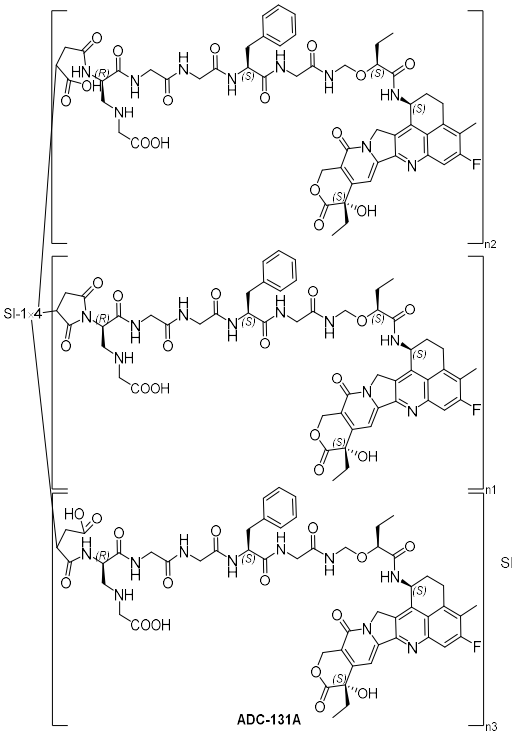
ADC-130



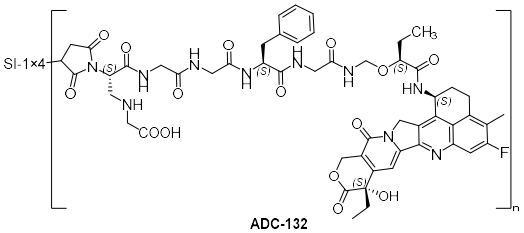
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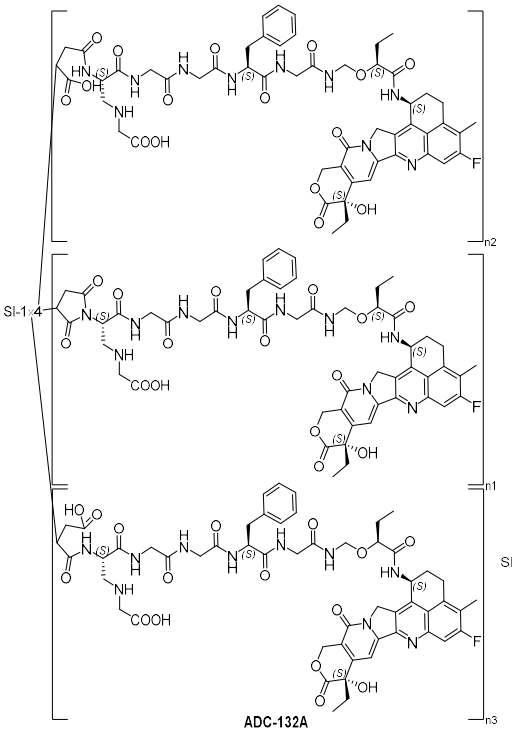
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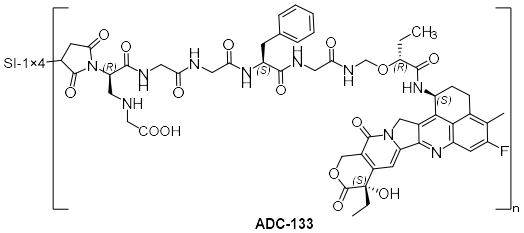
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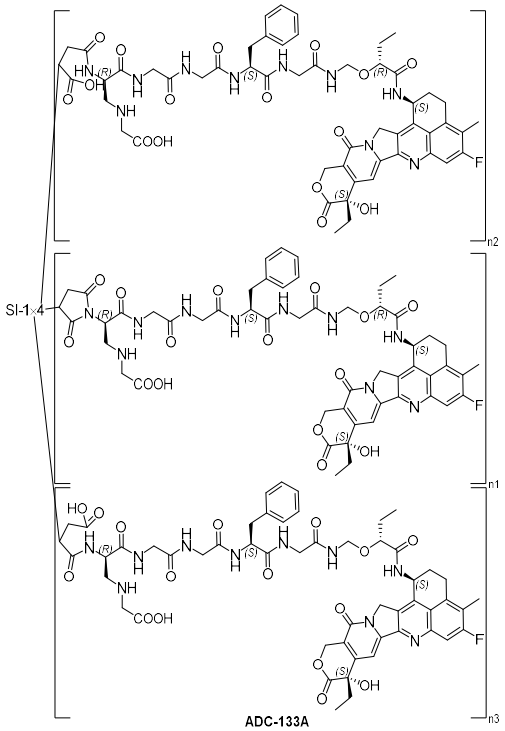
ADC-132



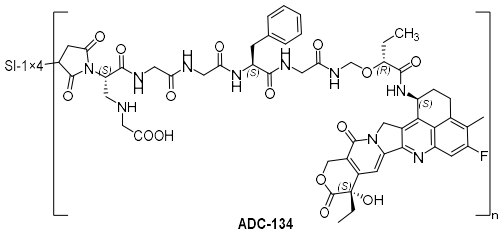
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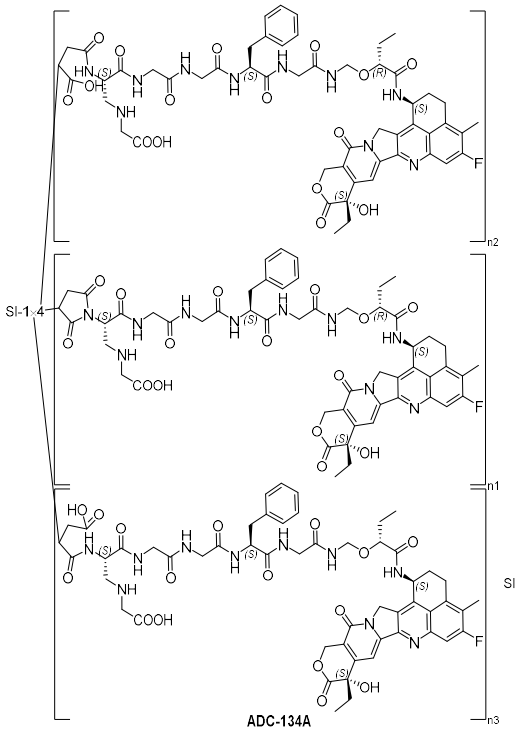
ADC-133



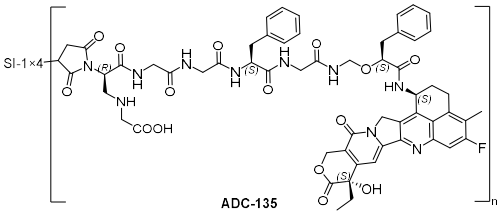
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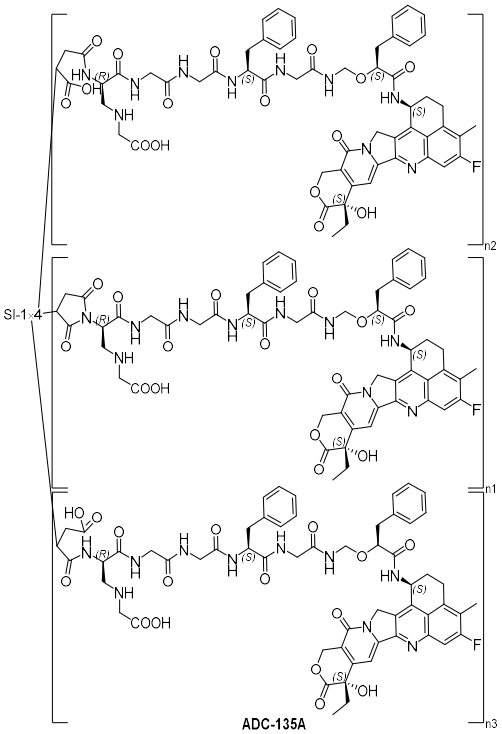
ADC-134



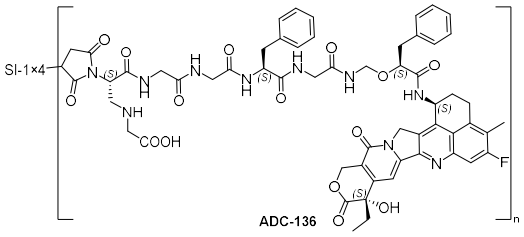
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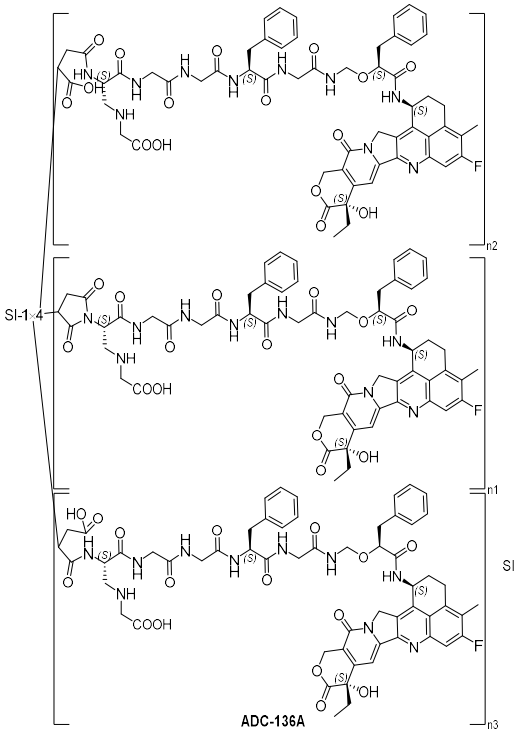
ADC-135



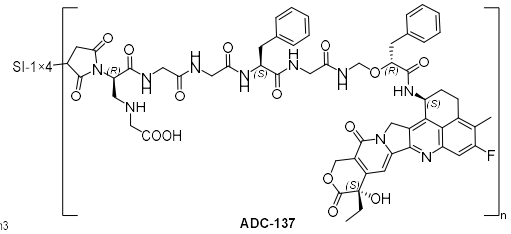
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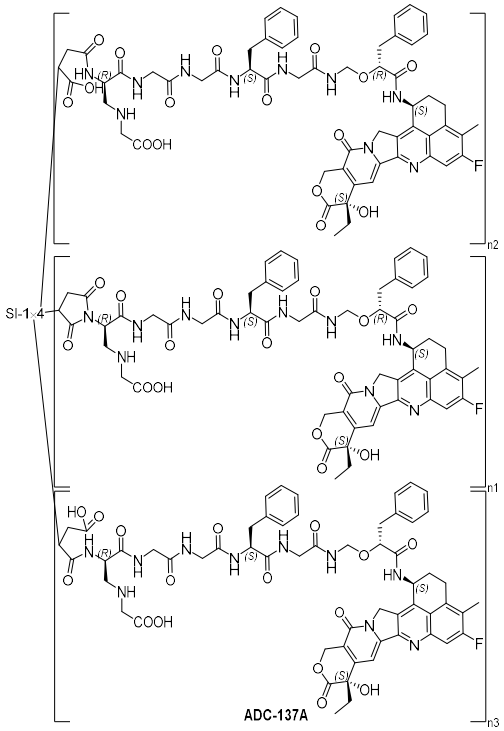
ADC-136



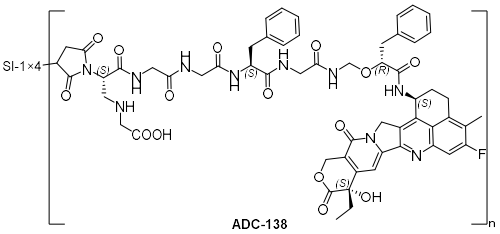
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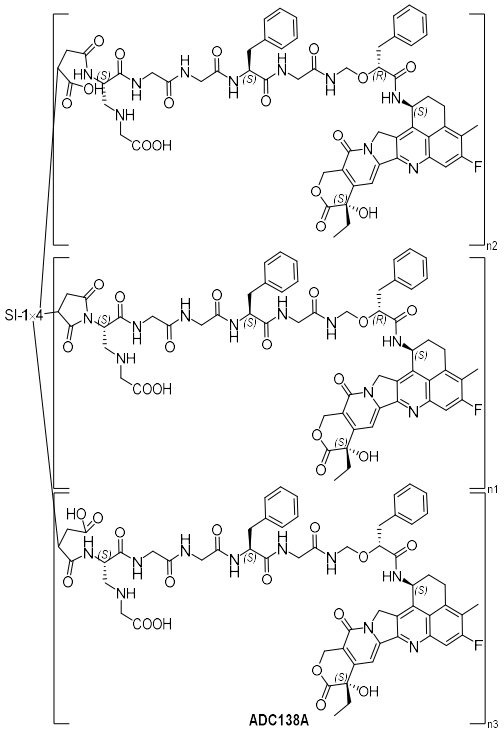
ADC-137



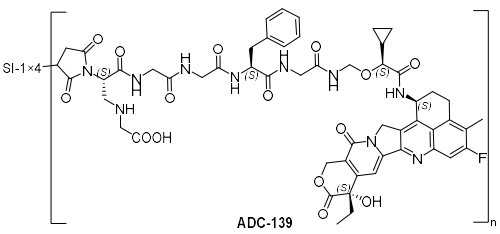
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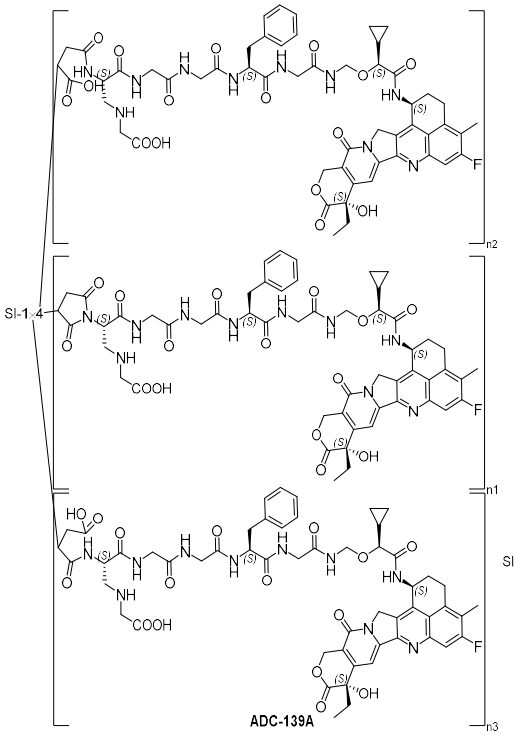
ADC-138



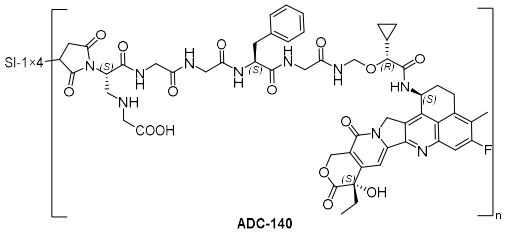
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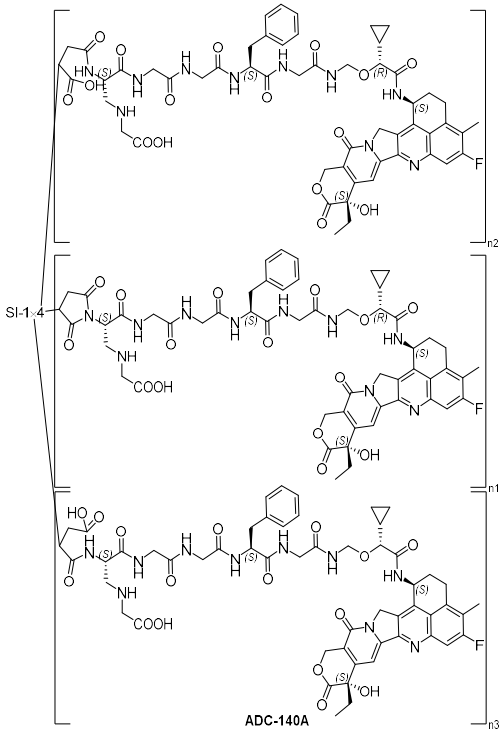
ADC-139



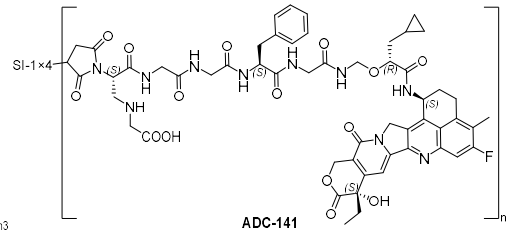
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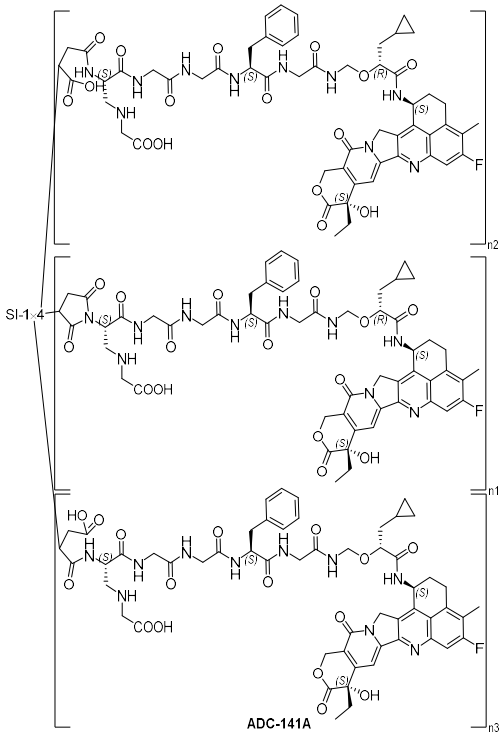
ADC-140



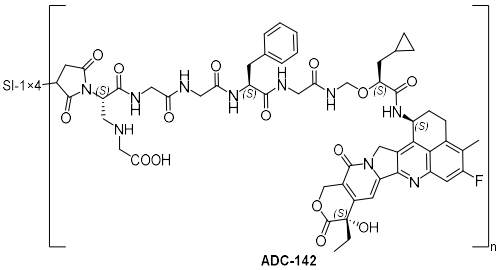
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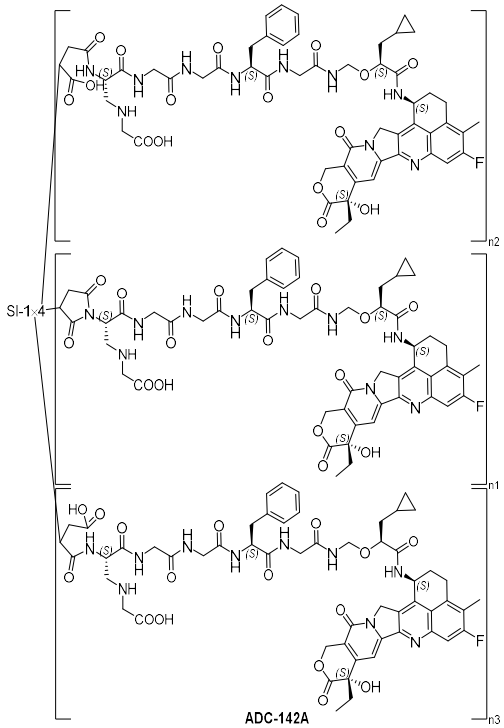
ADC-141



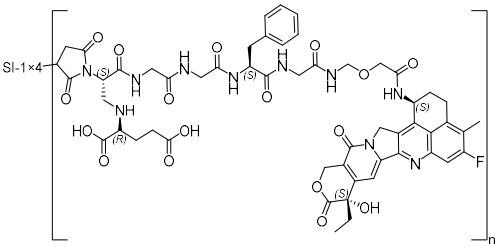
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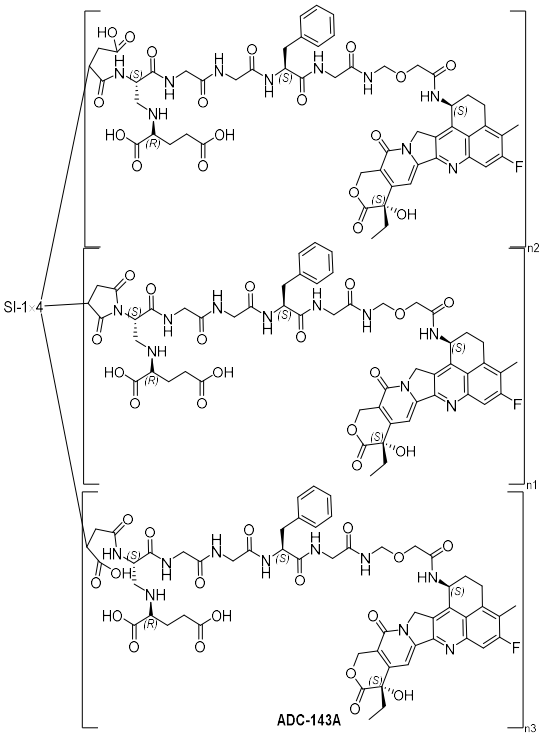
ADC-142



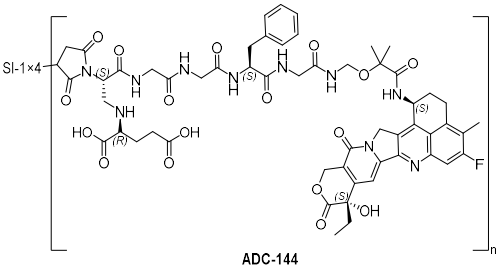
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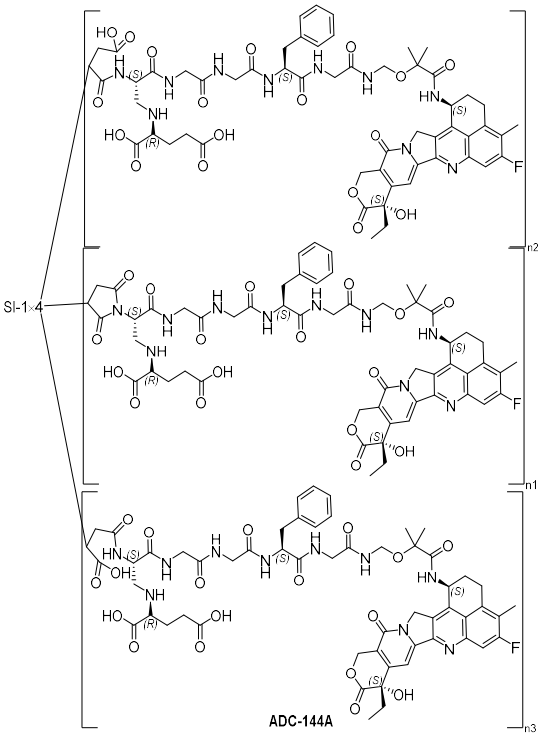
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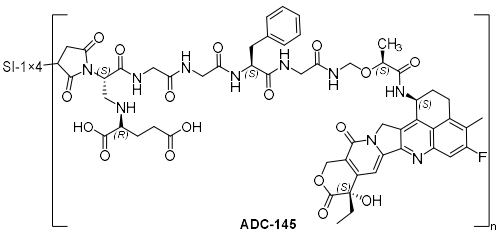
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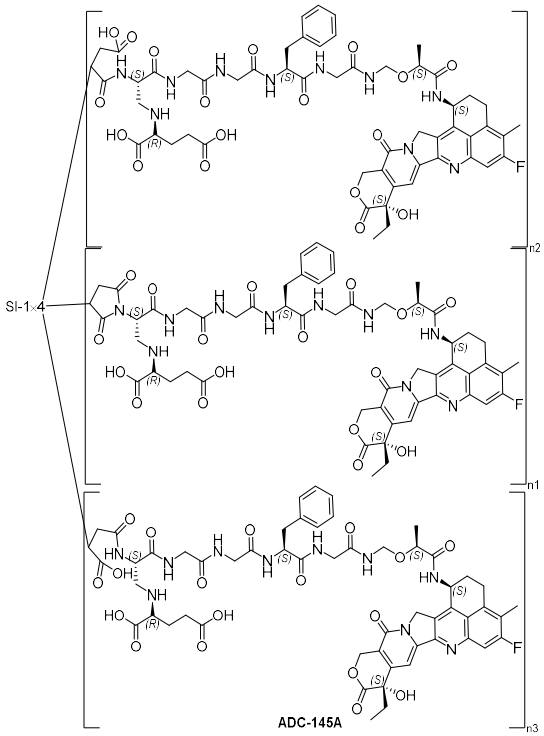
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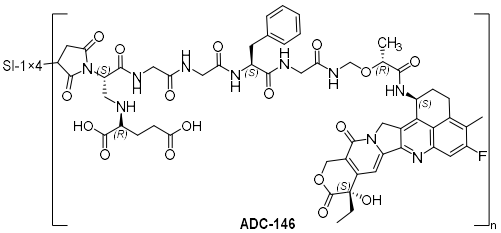
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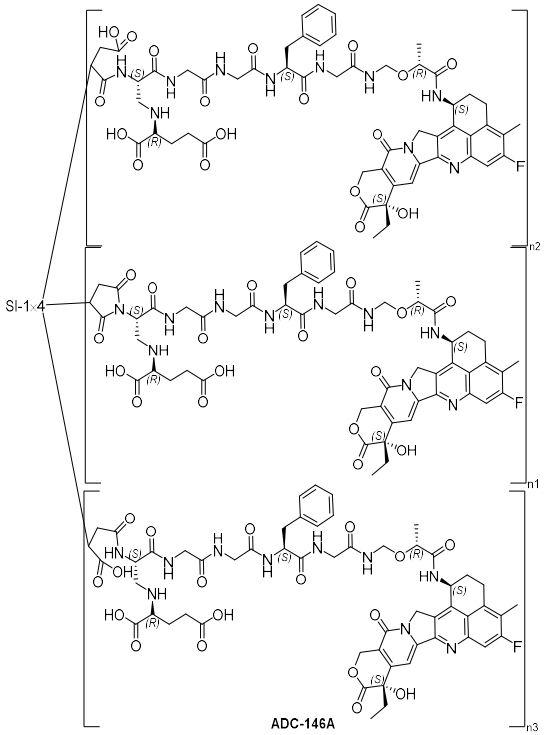
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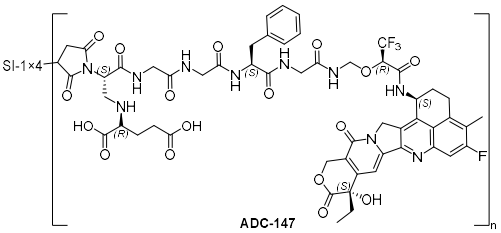
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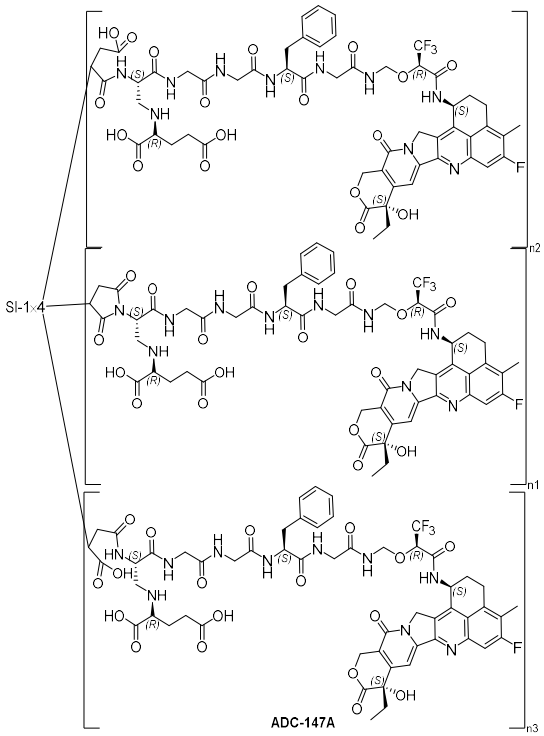
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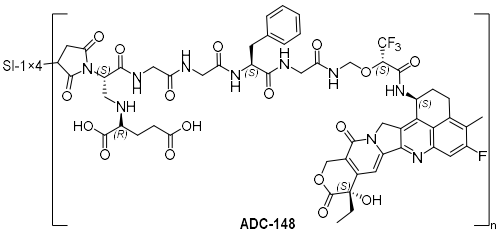
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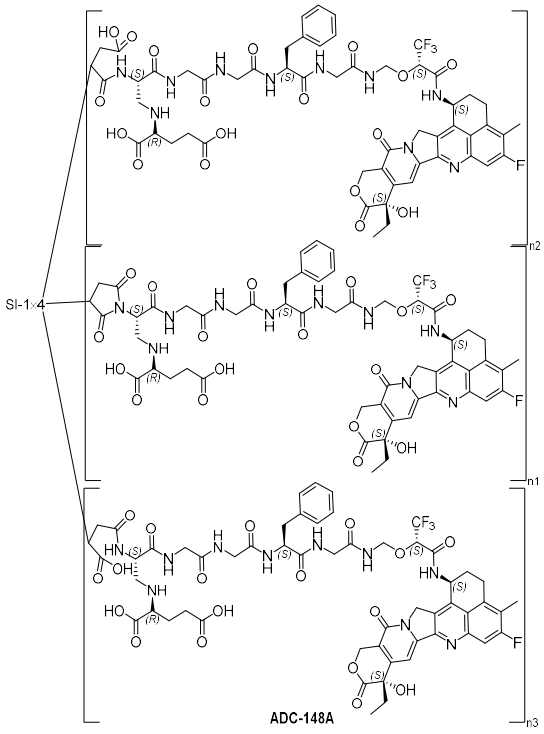
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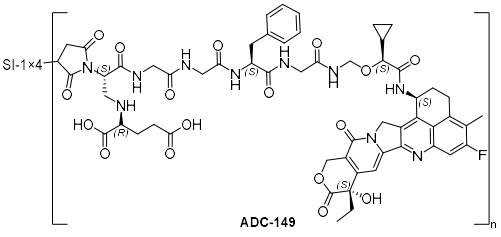
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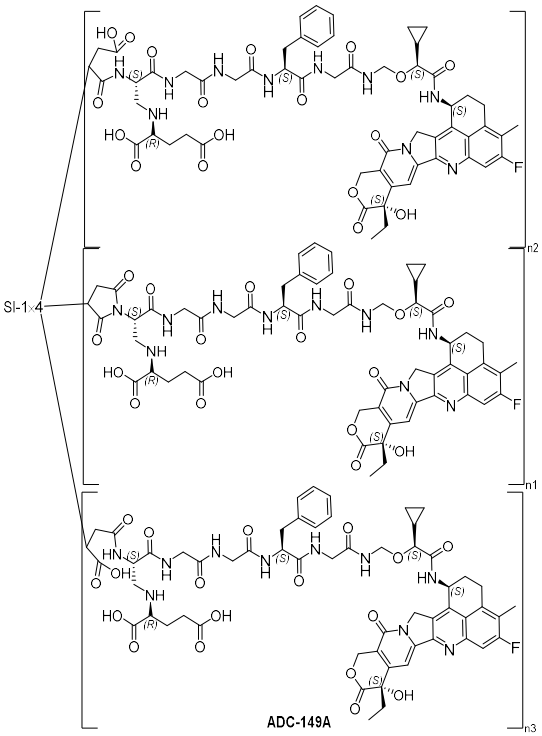
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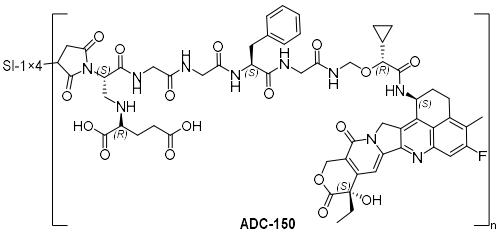
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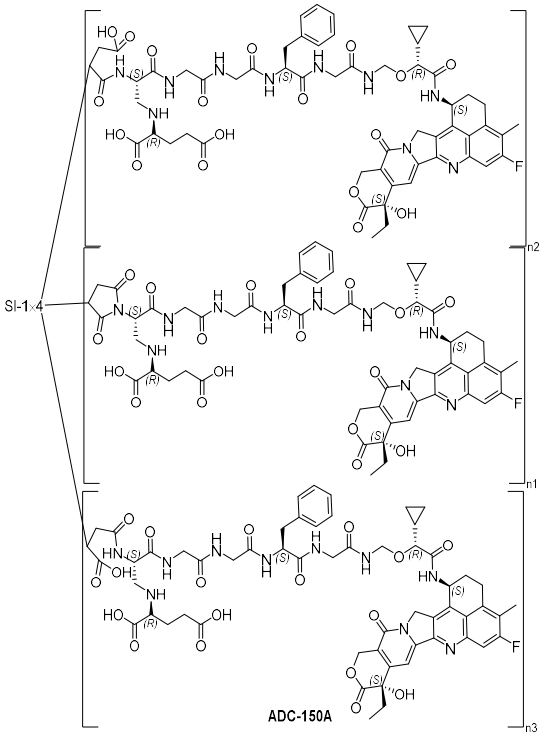
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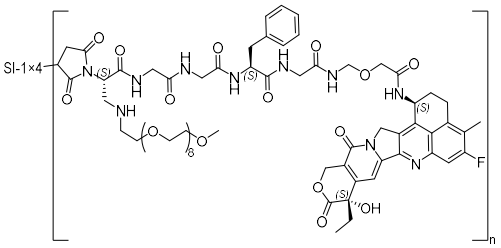
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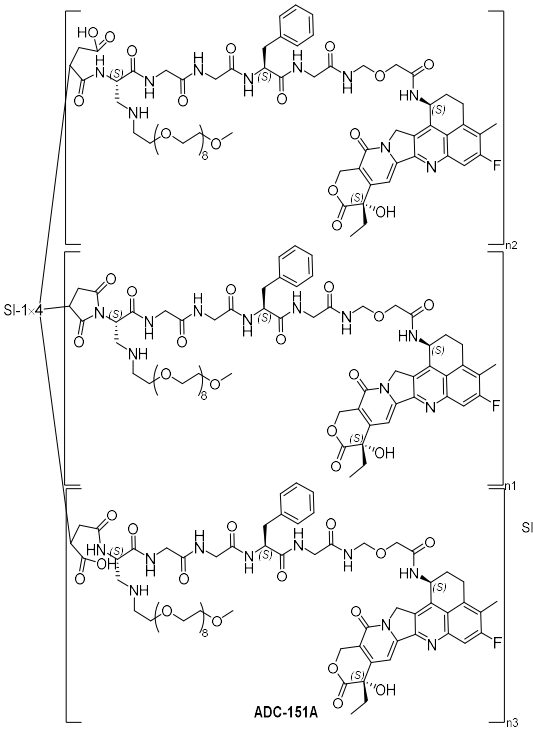
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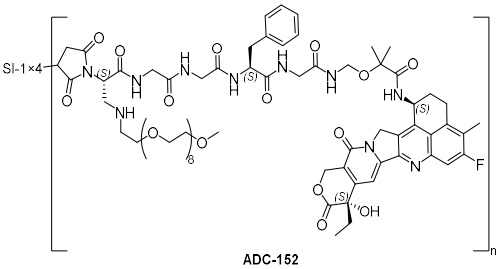
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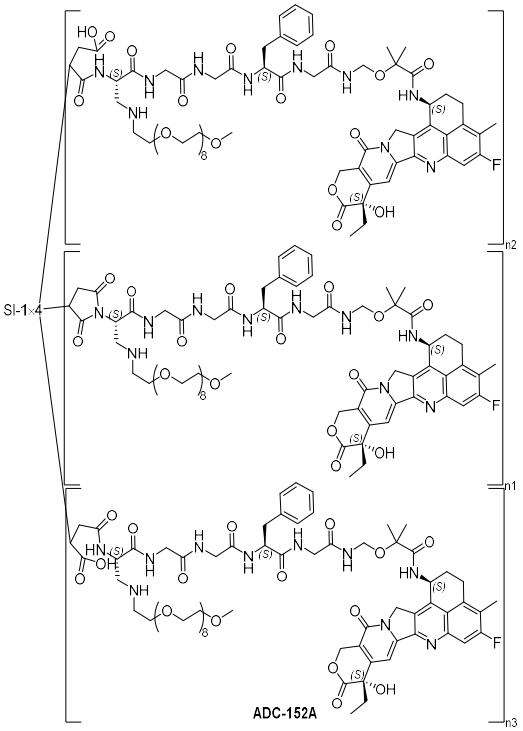
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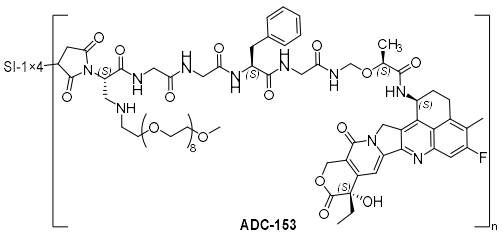
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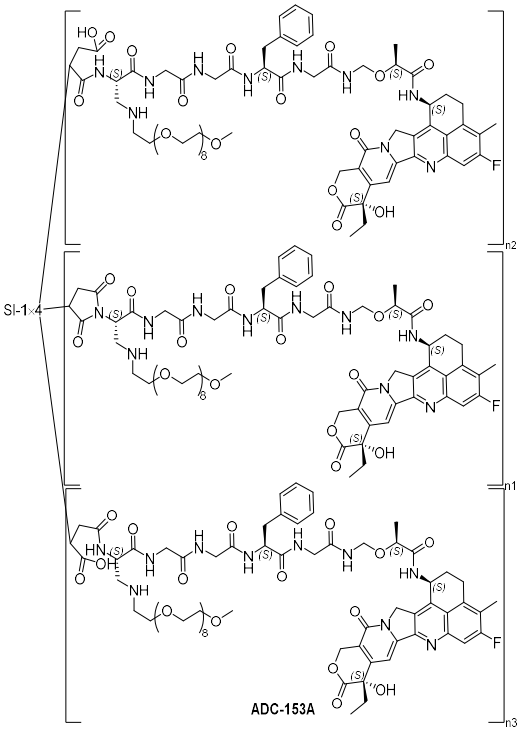
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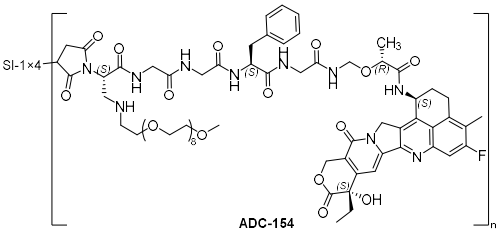
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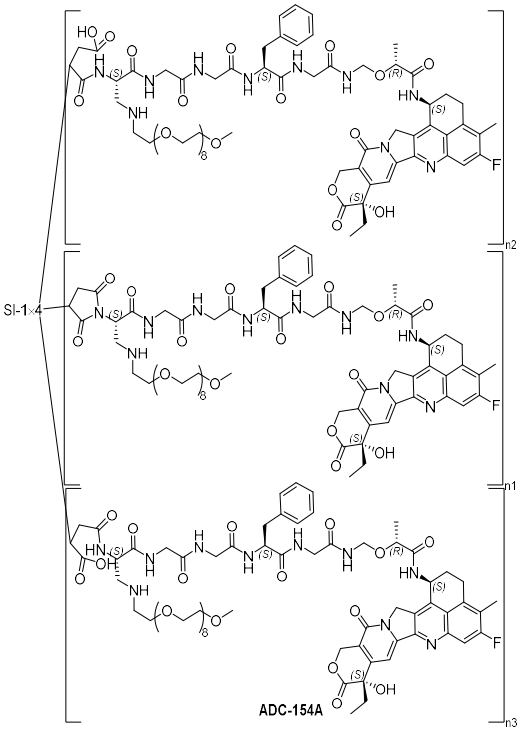
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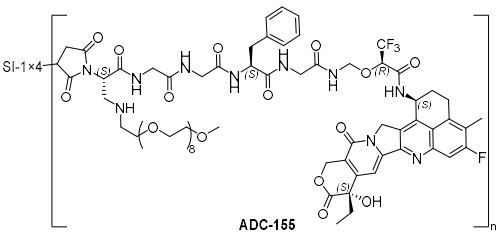
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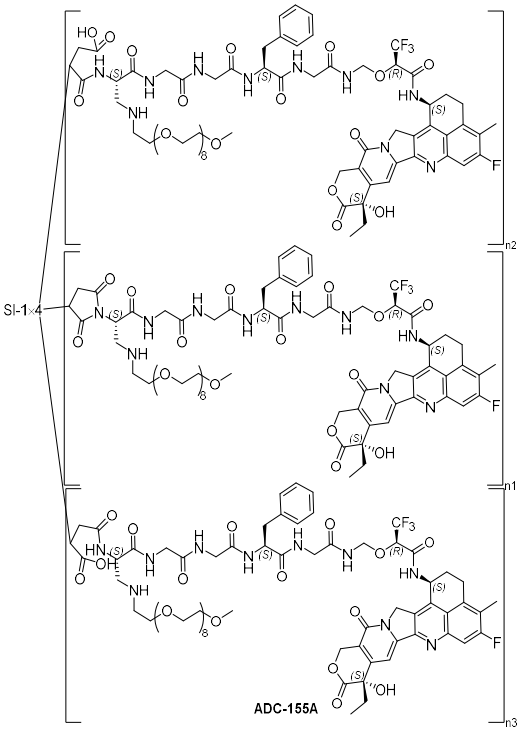
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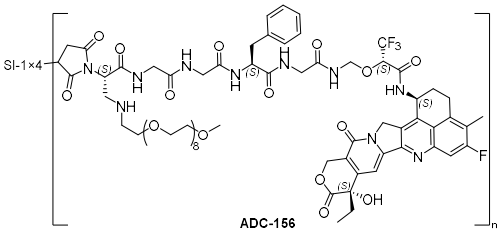
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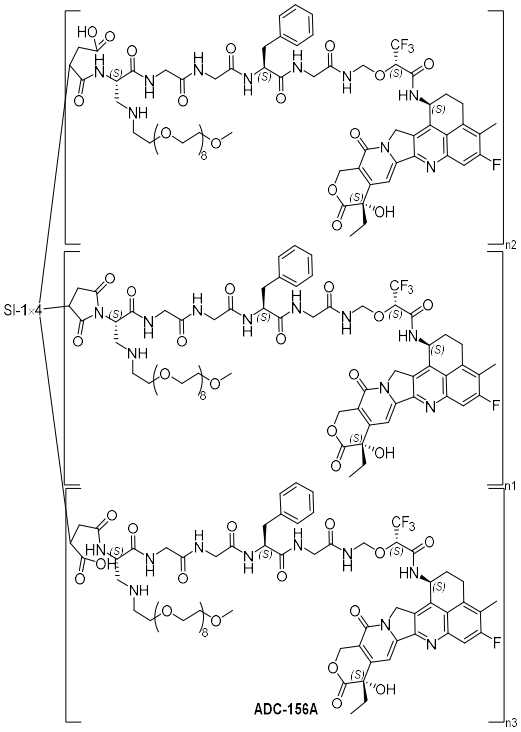
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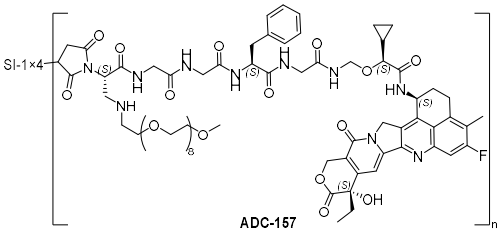
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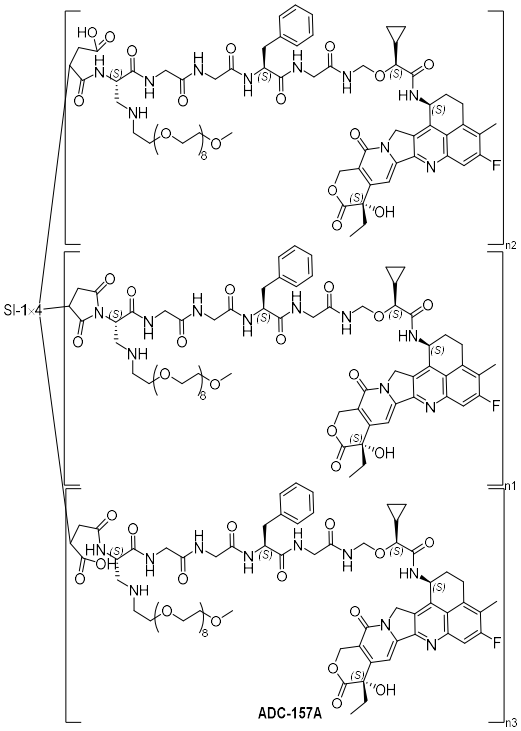
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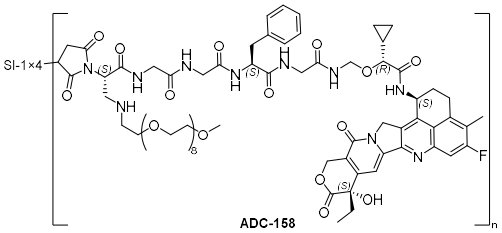
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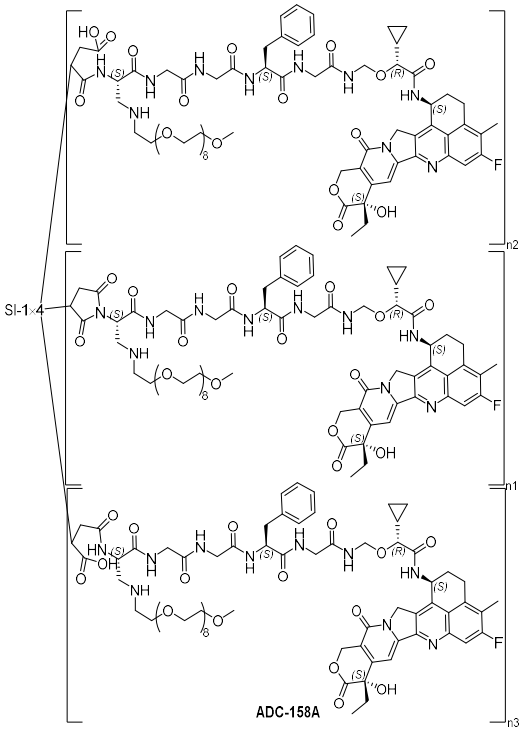
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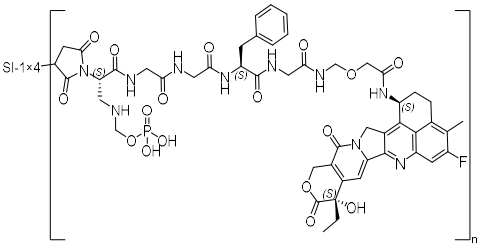
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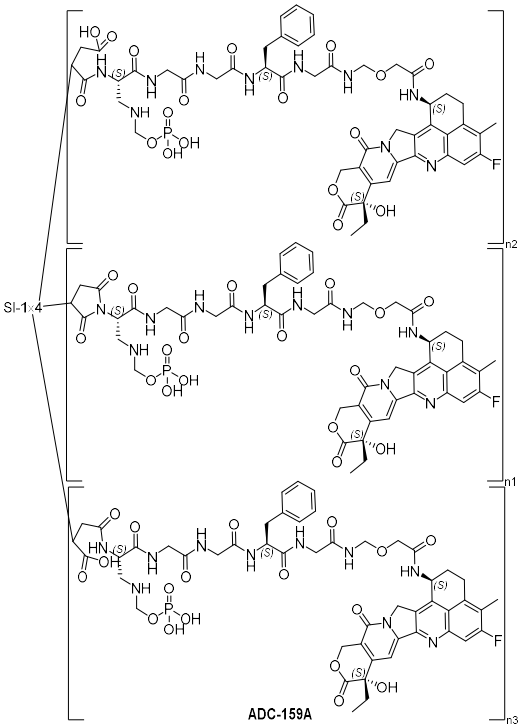
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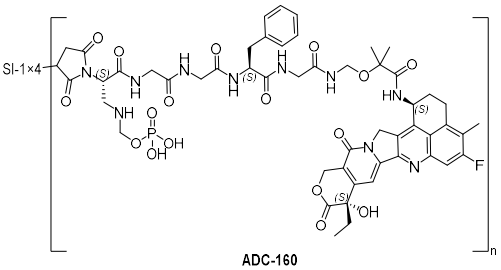
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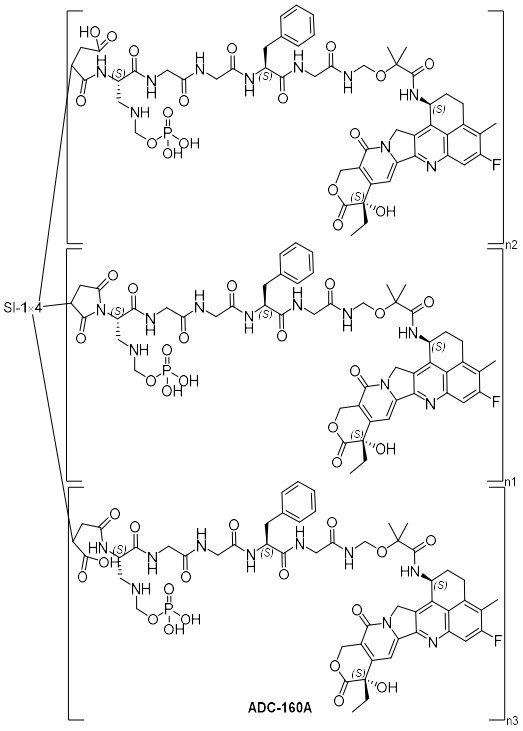
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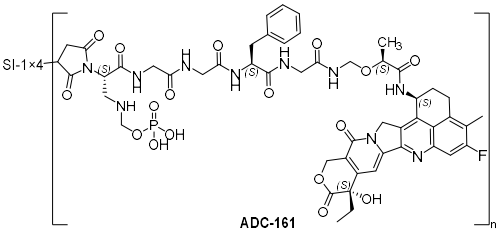
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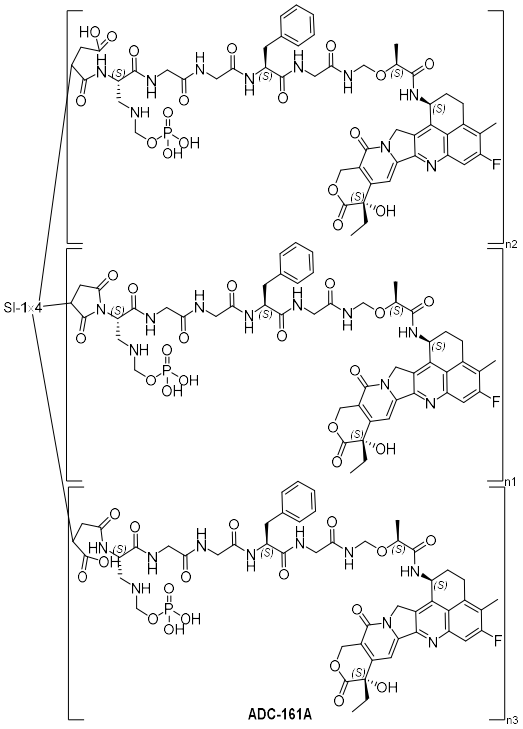
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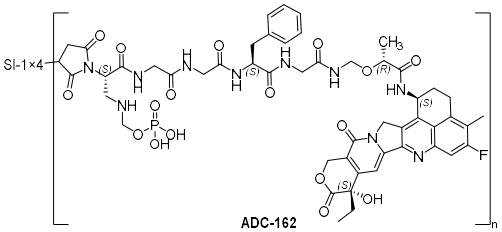
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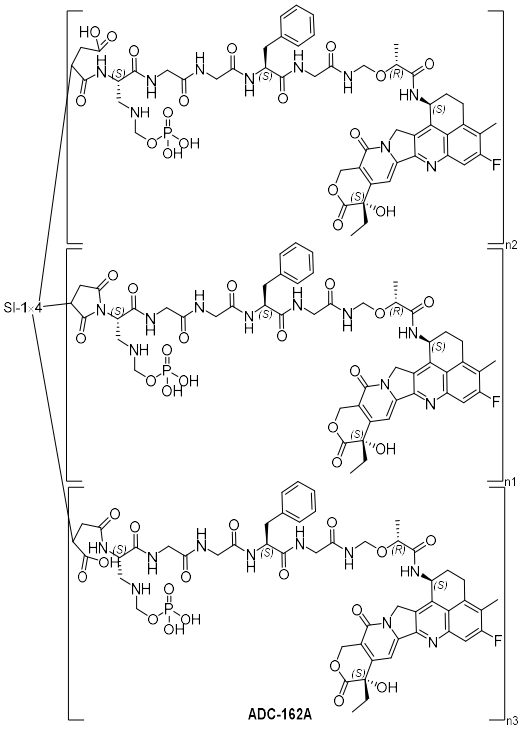
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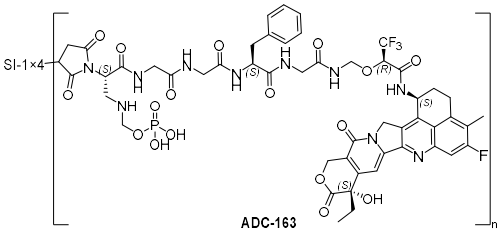
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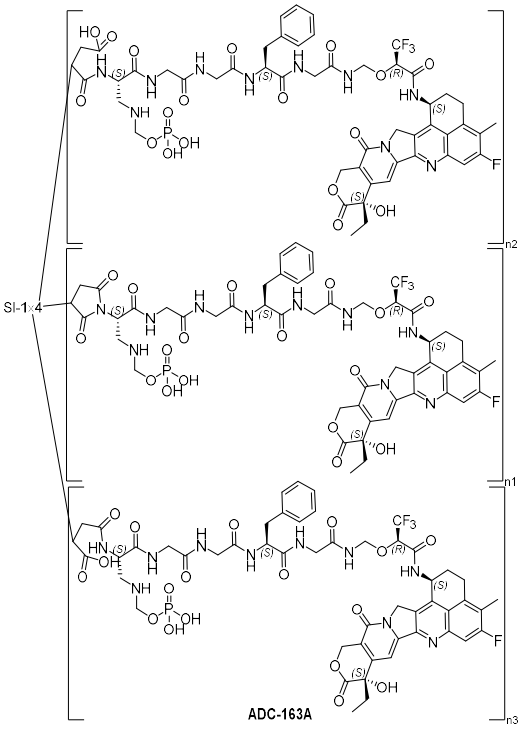
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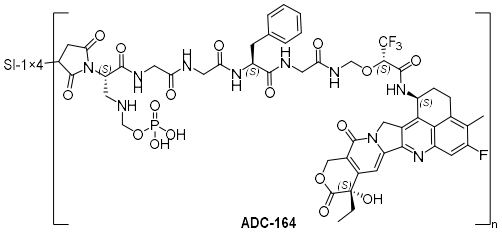
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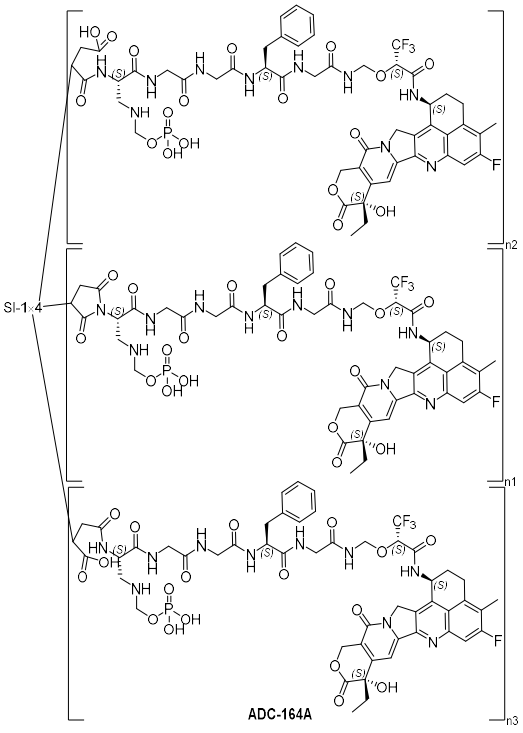
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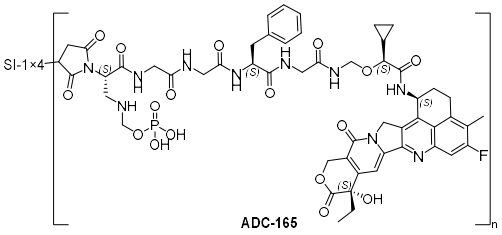
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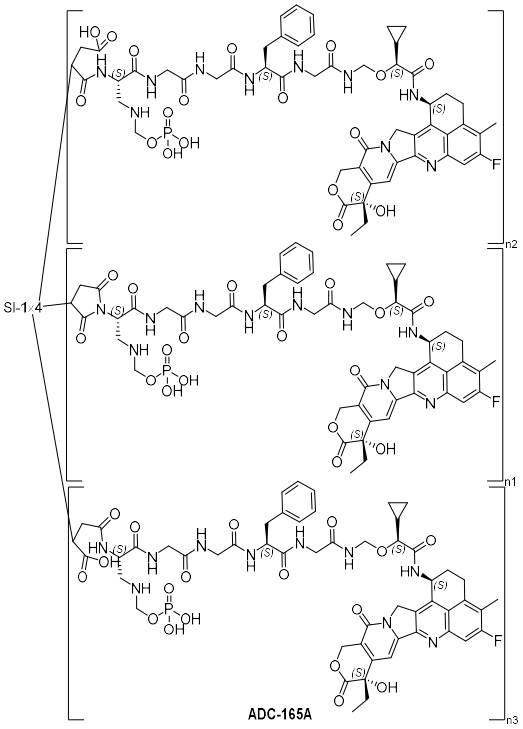
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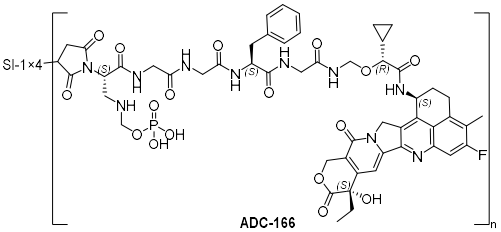
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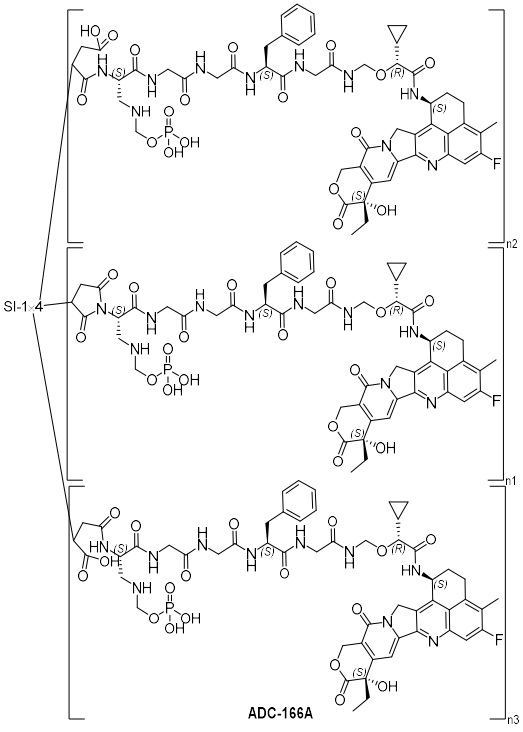
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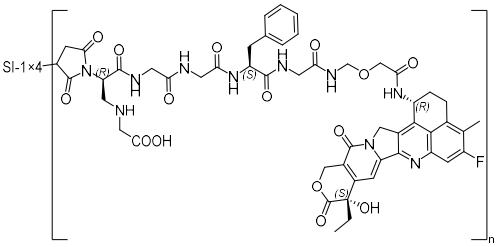
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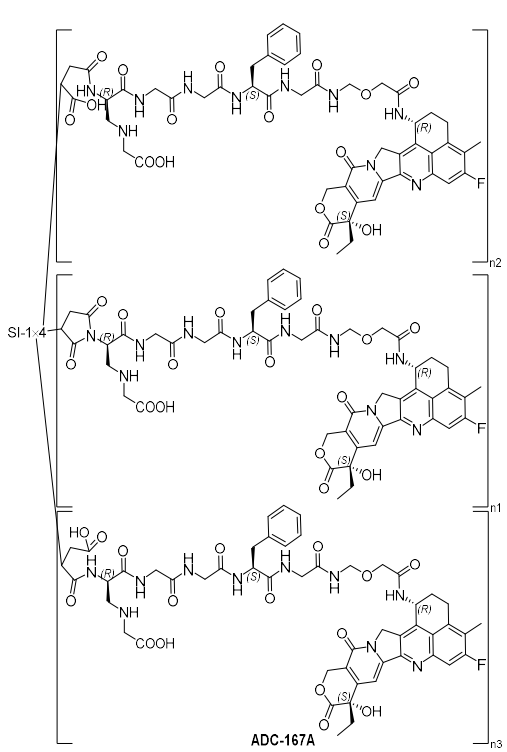
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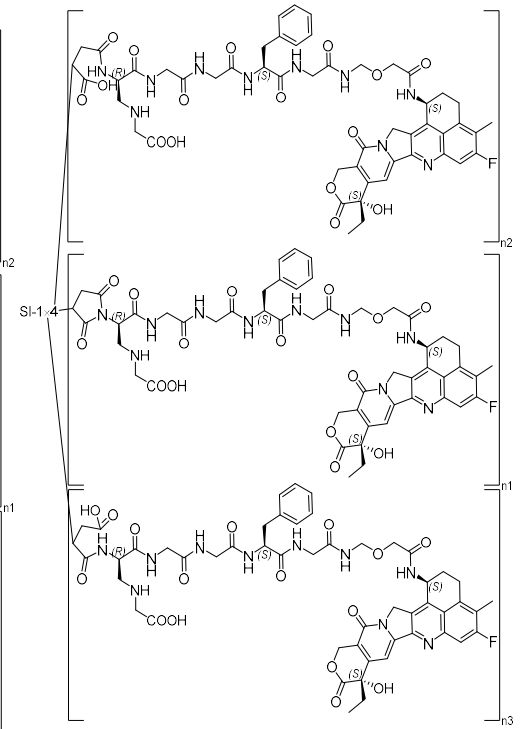
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ADC-167

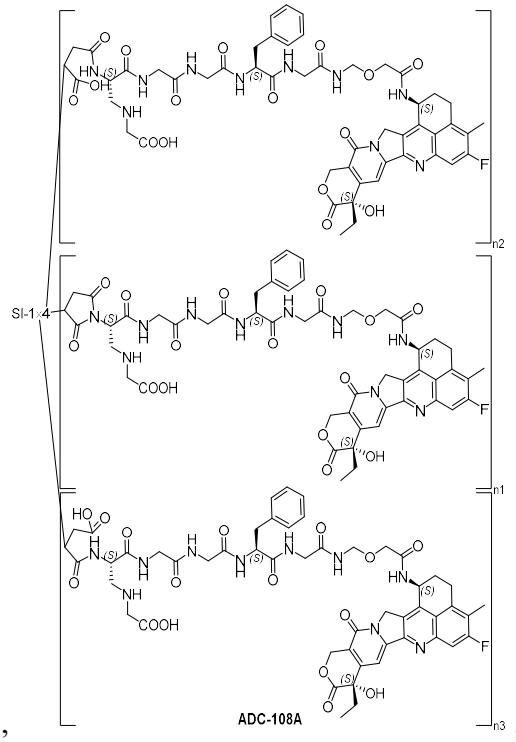


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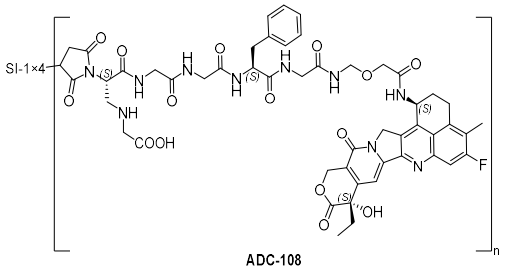
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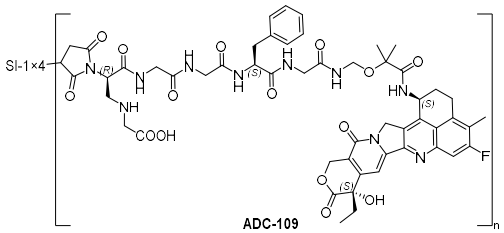
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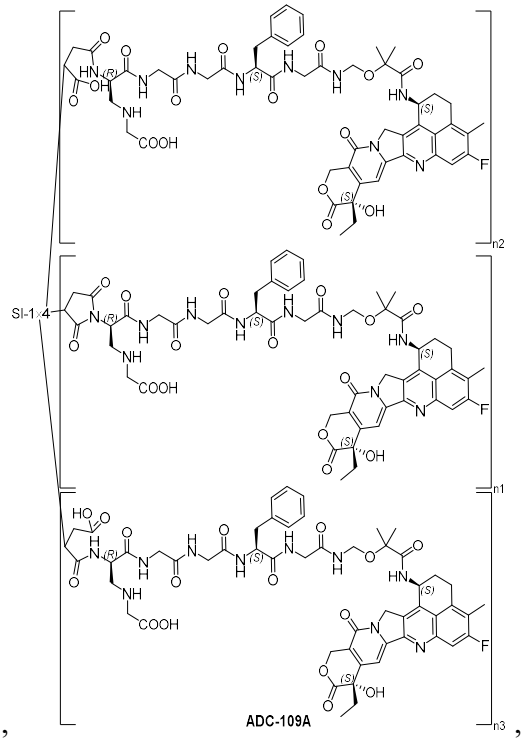
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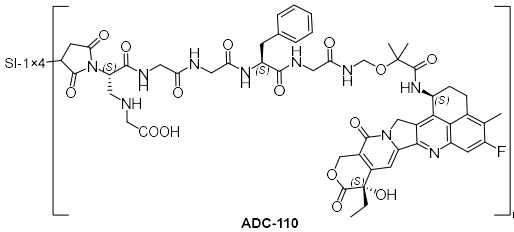
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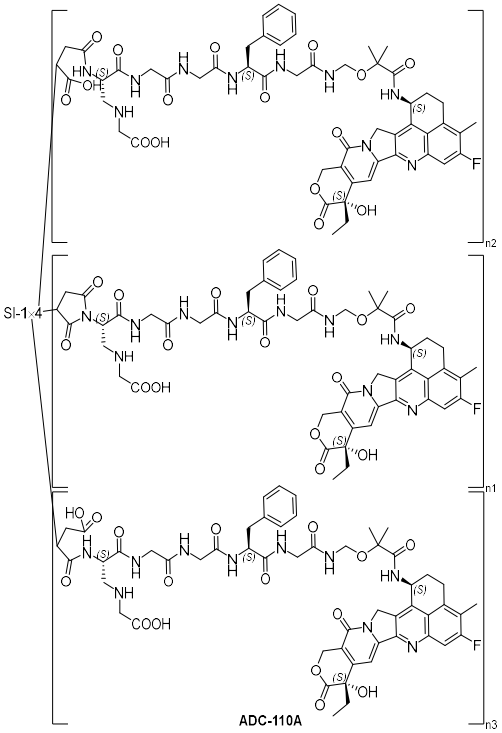
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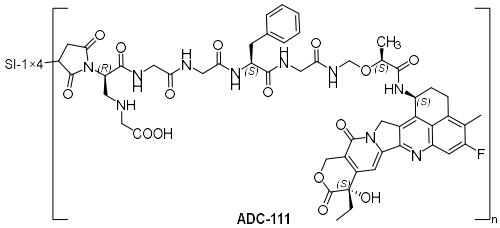
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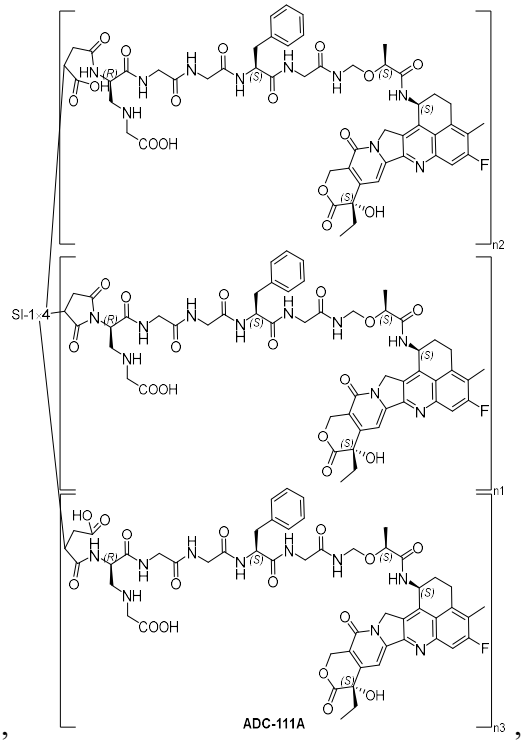


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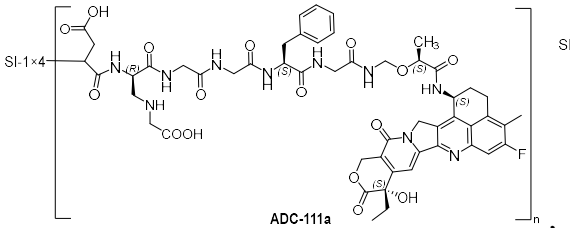
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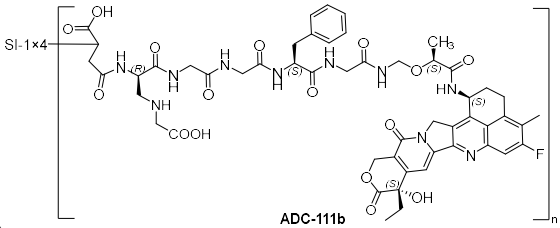
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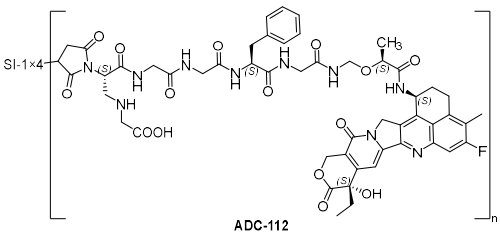
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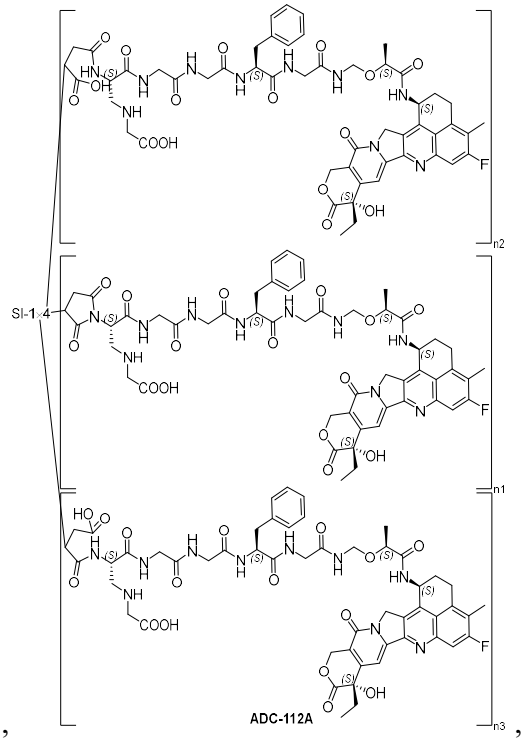
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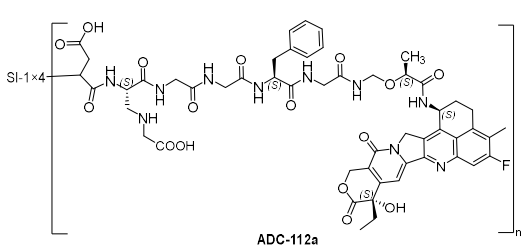
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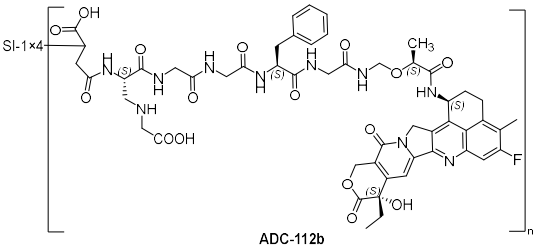
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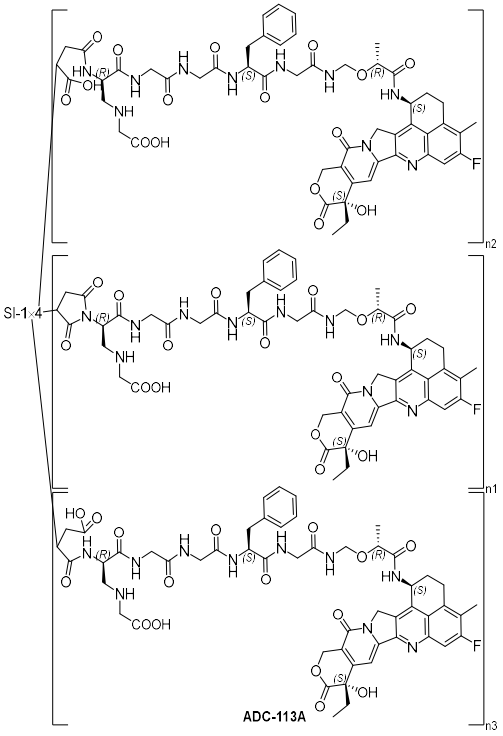
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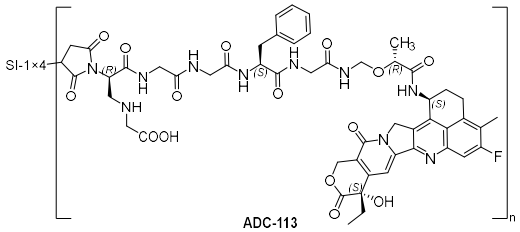
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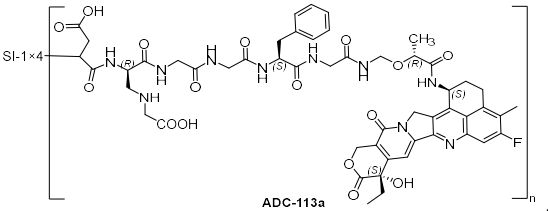
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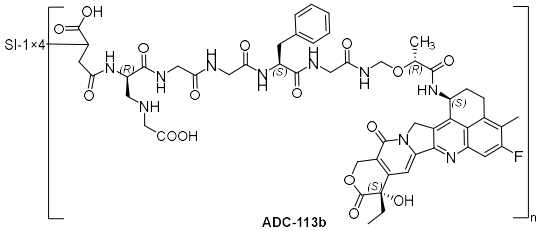
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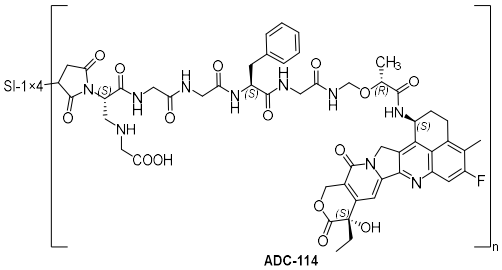
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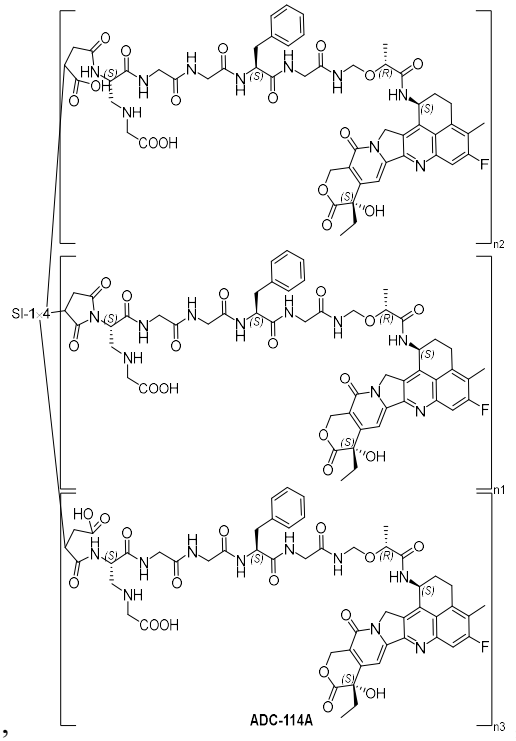
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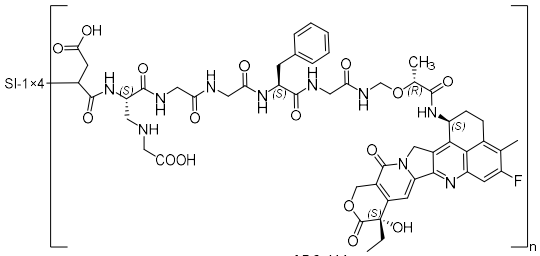
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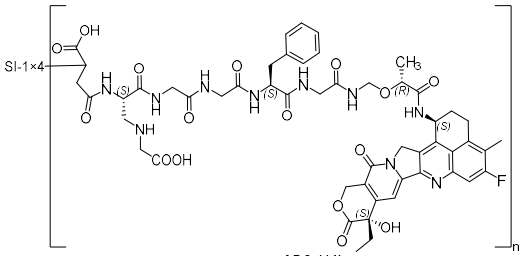
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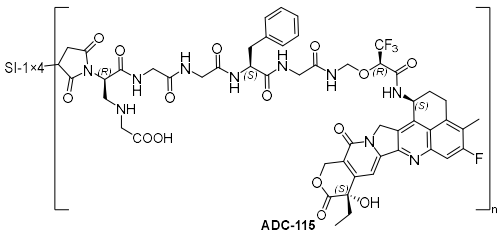
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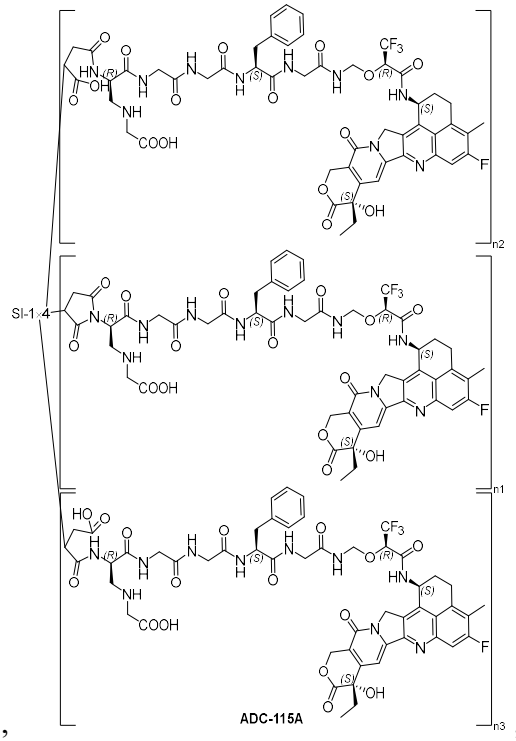
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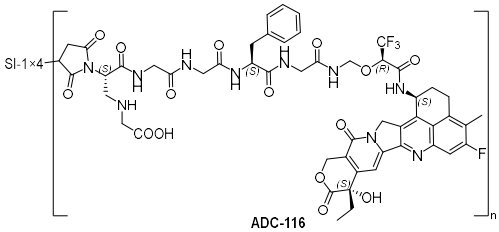
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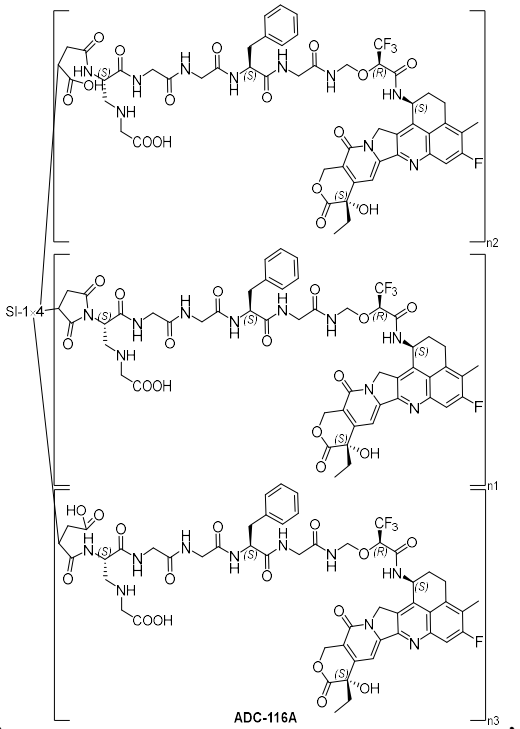
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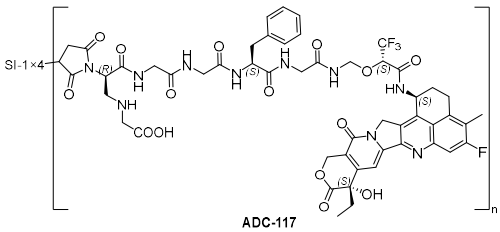
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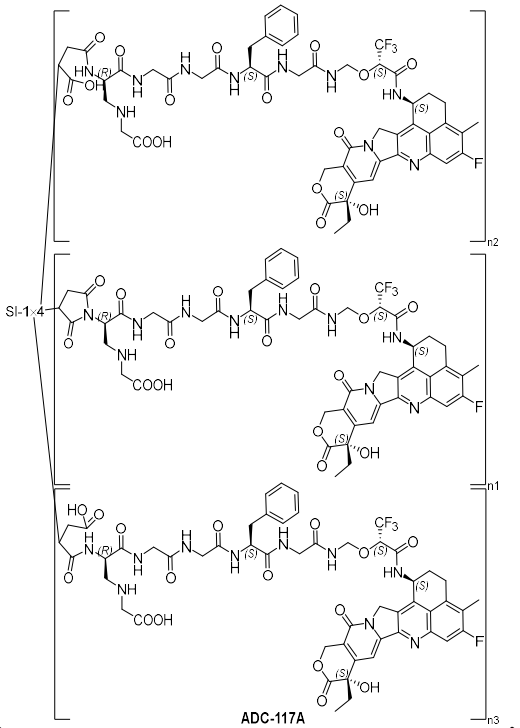
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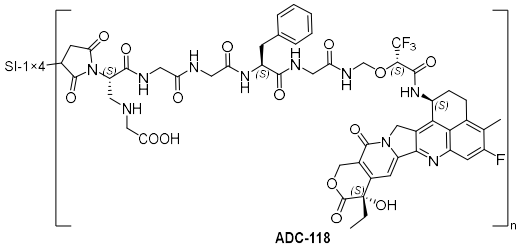
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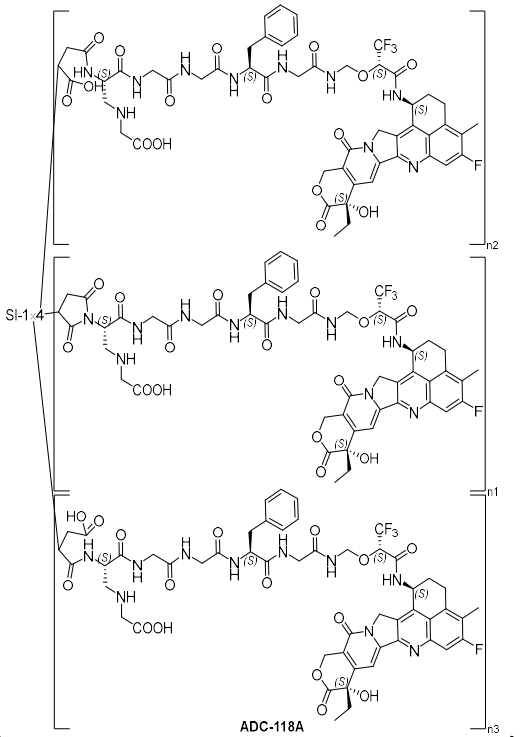


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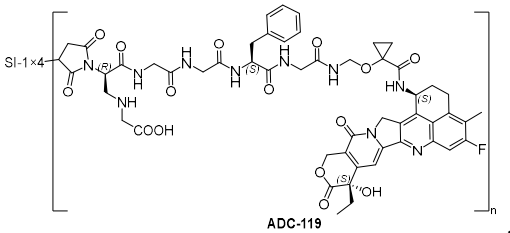
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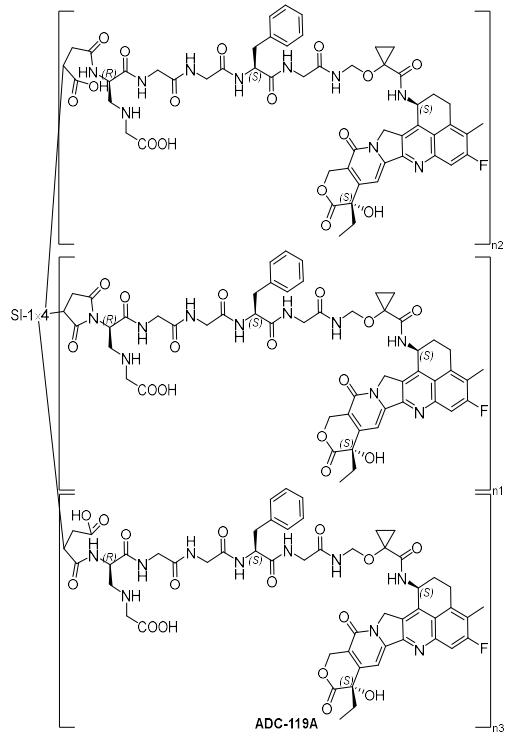
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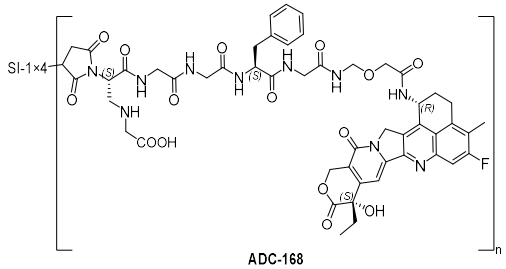


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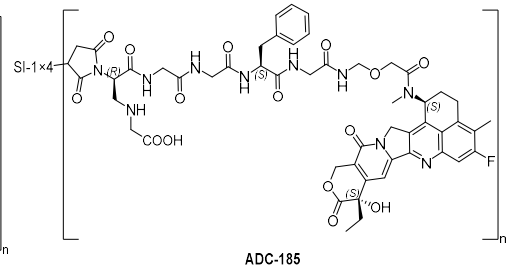
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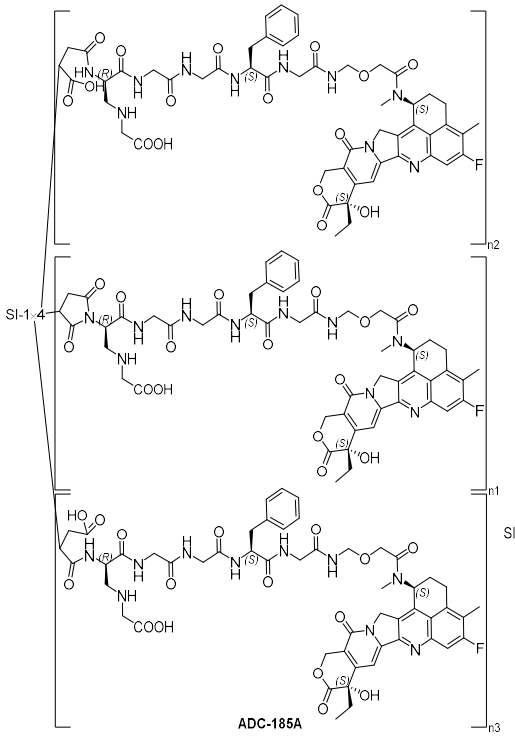
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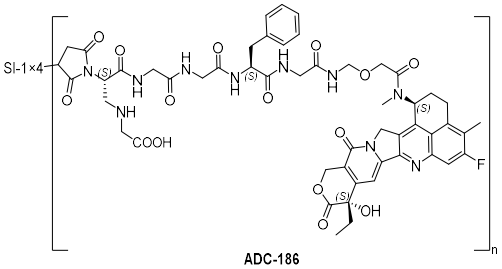
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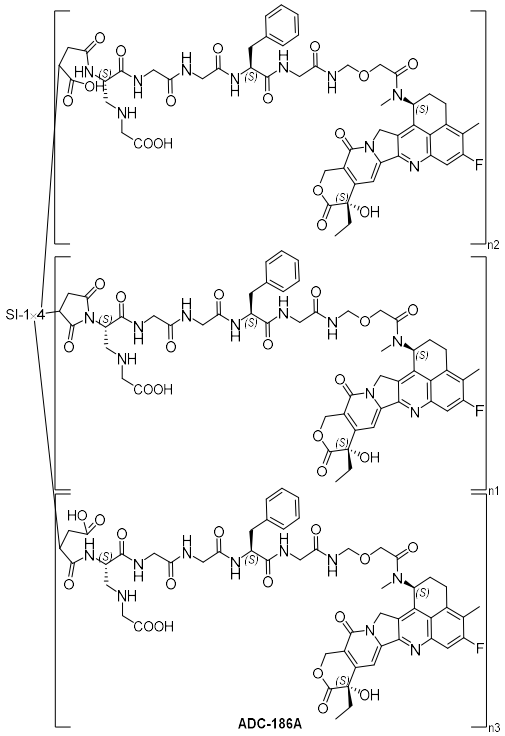
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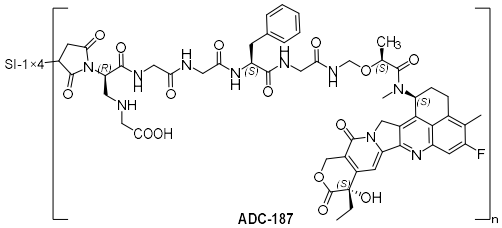
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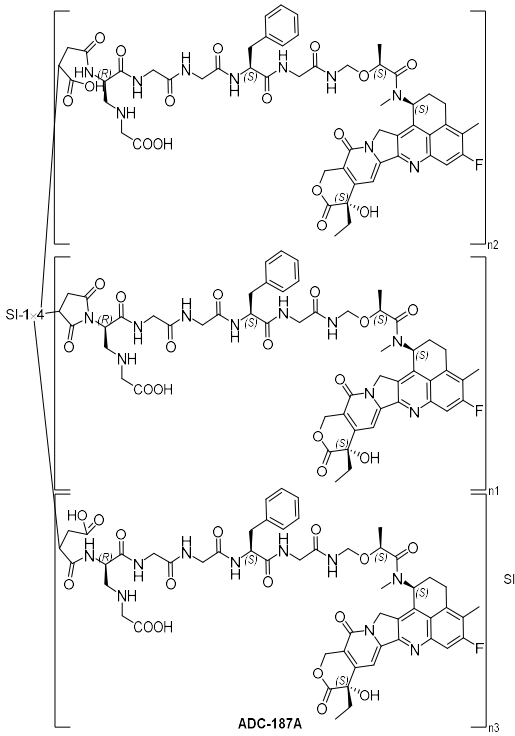
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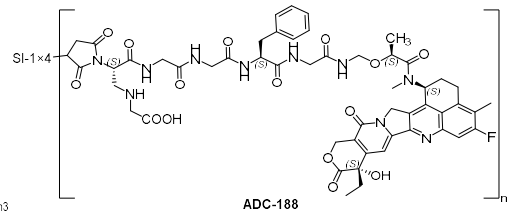
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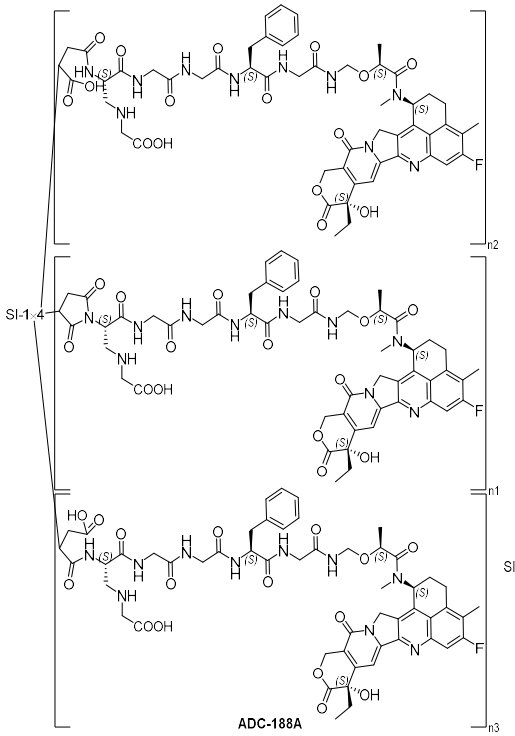
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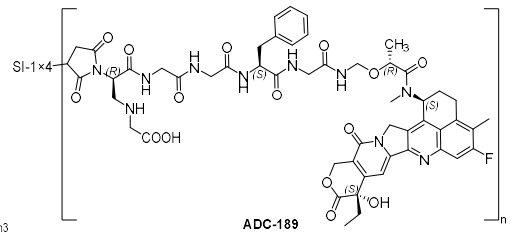
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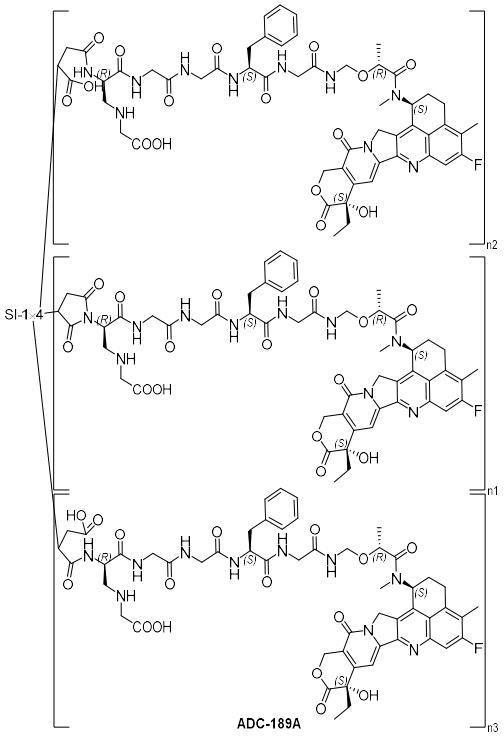
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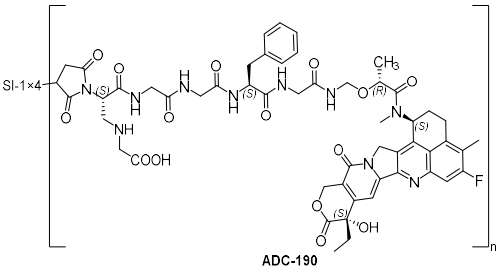
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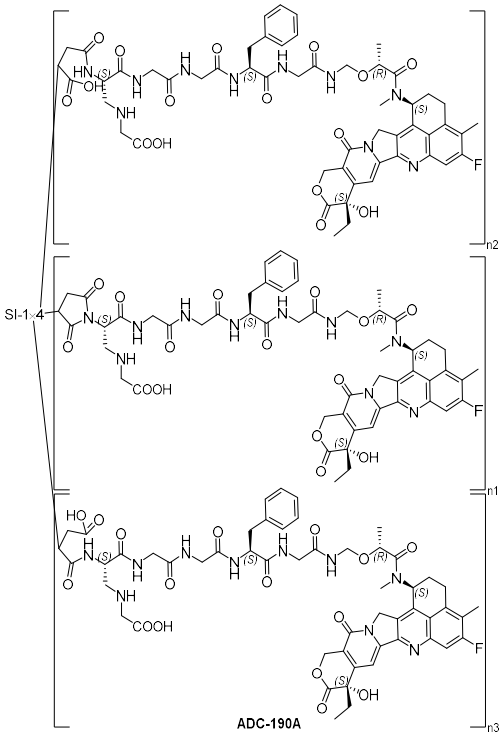
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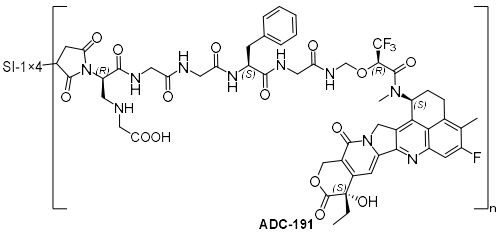
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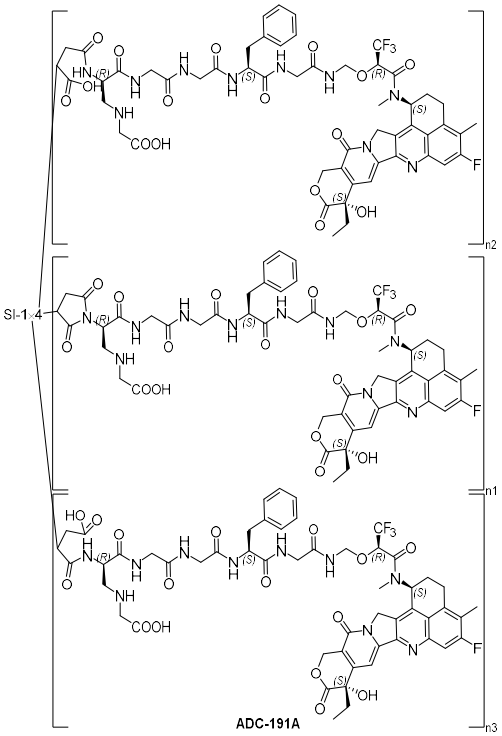
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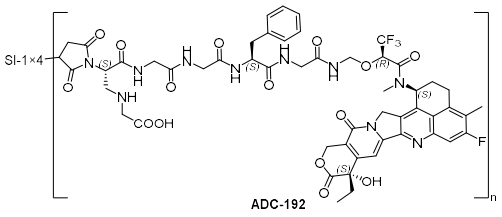
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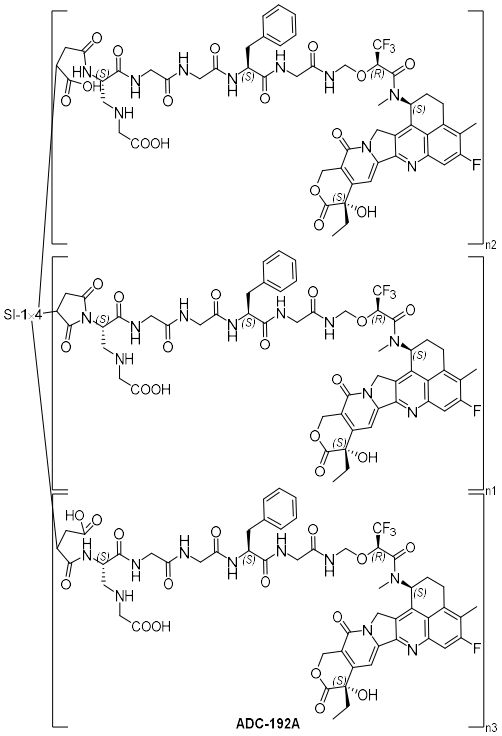
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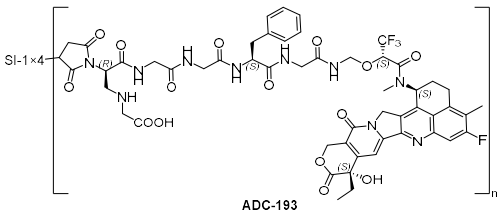
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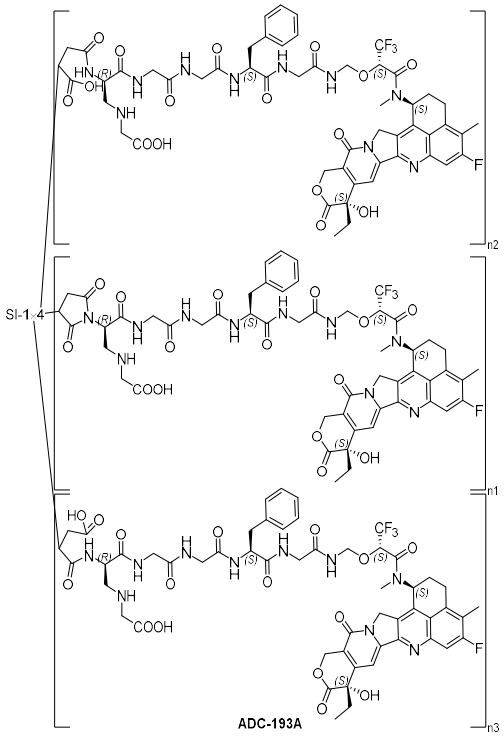
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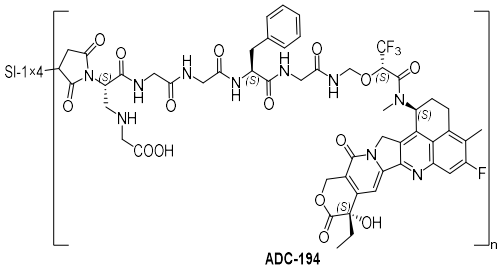
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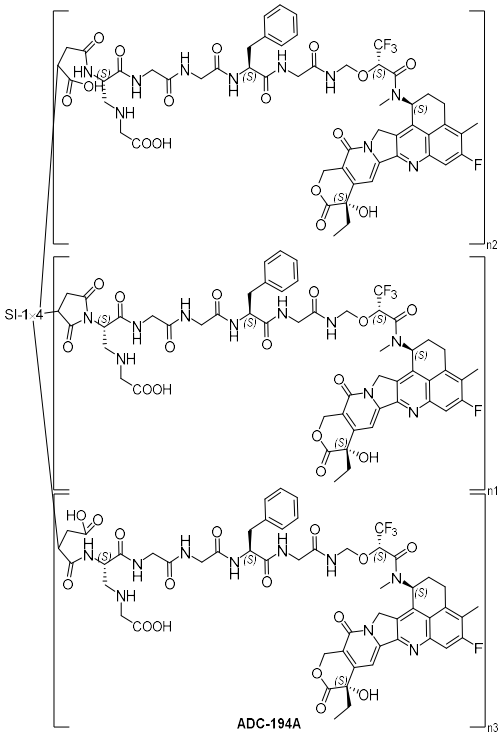
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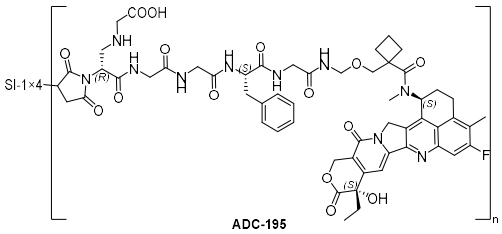
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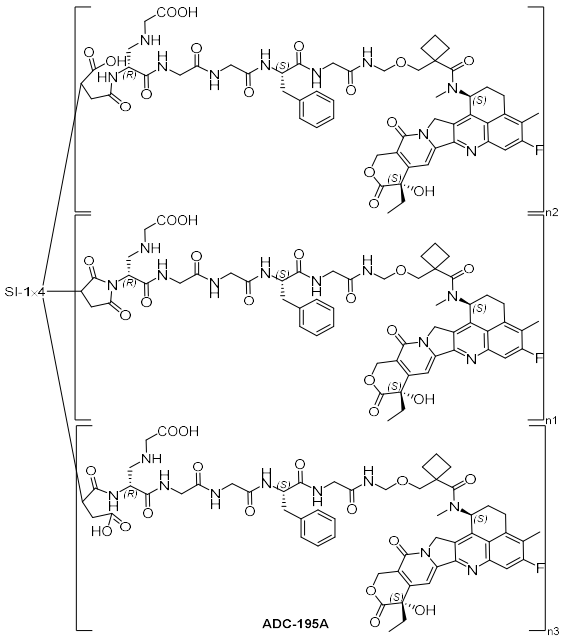
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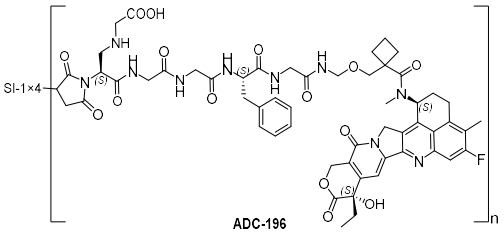
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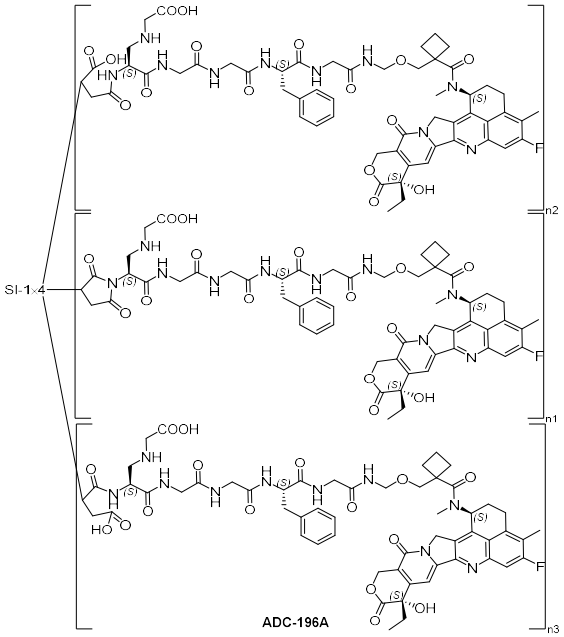
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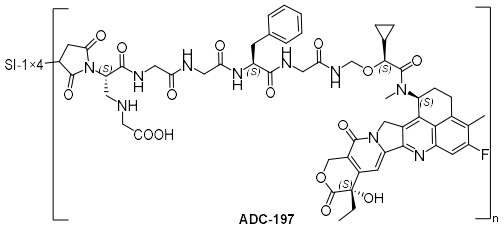
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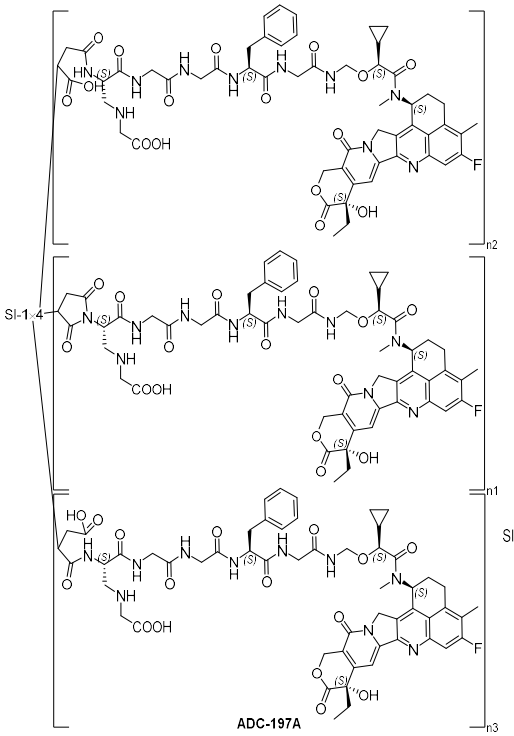
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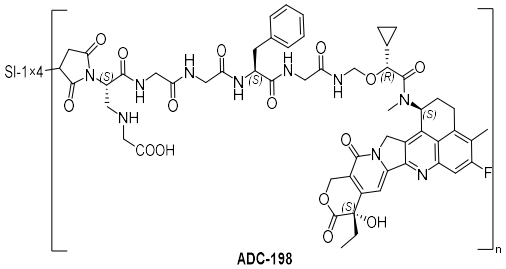
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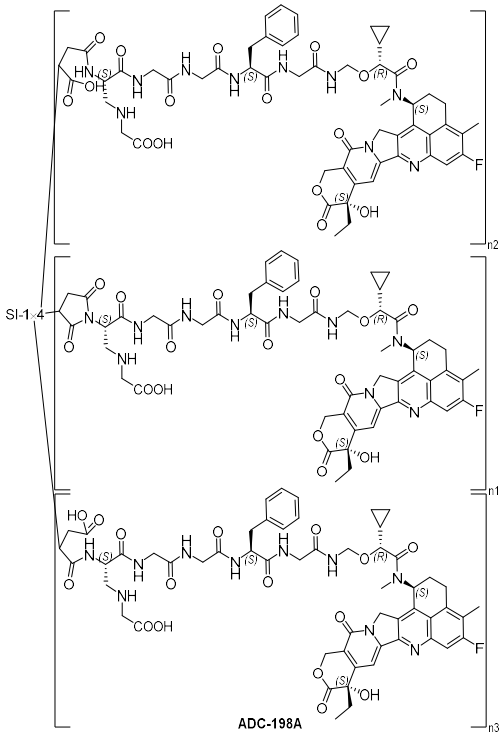
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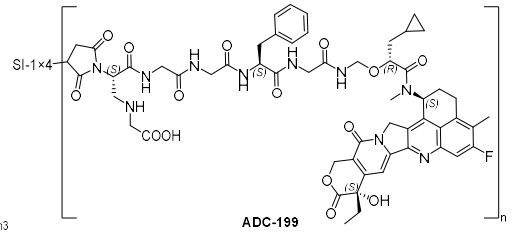
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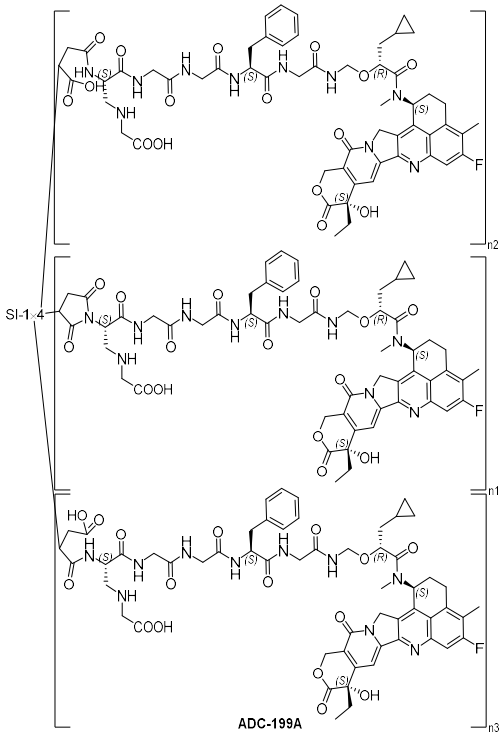
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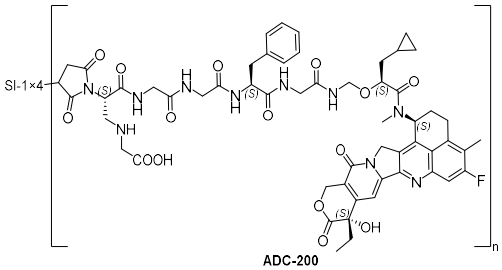
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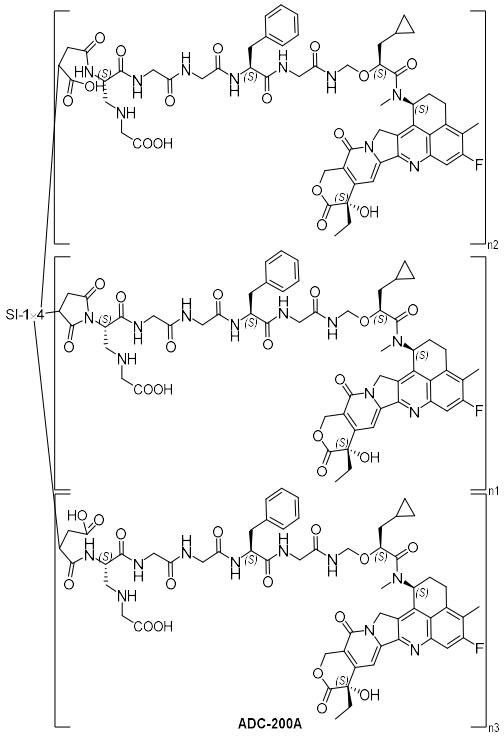
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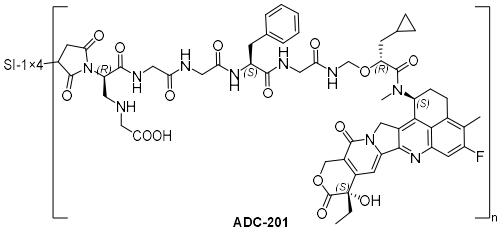
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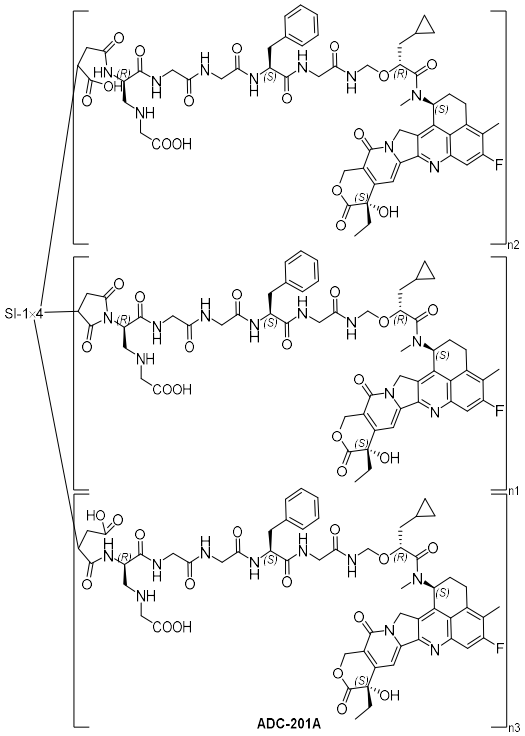
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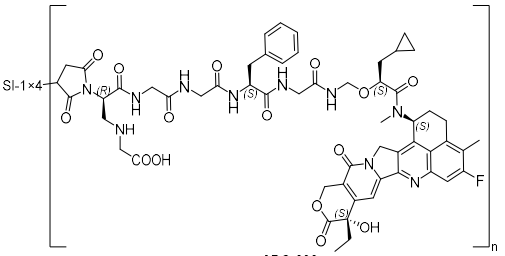
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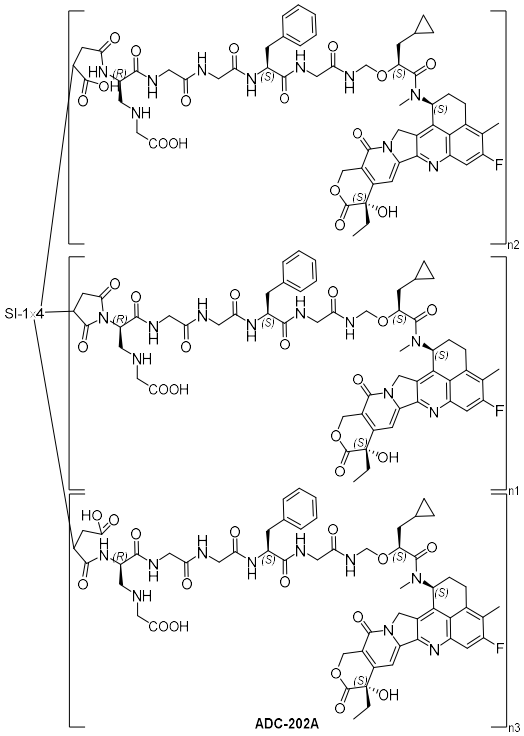
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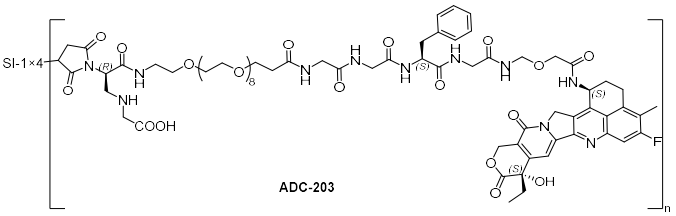
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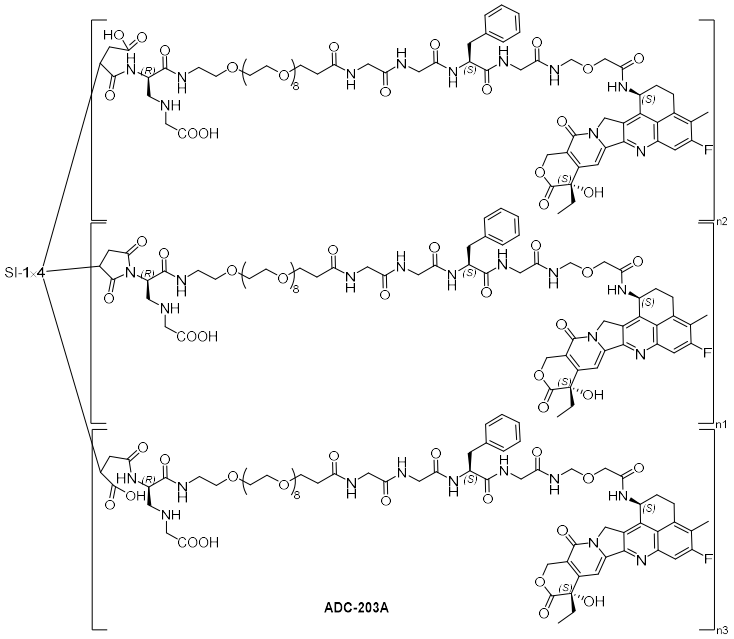
ADC-202



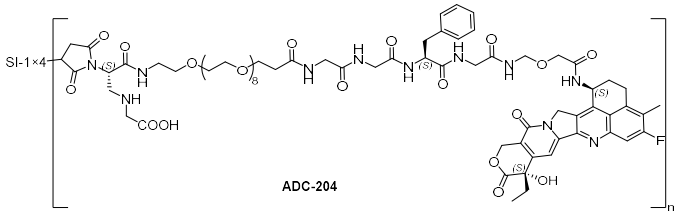
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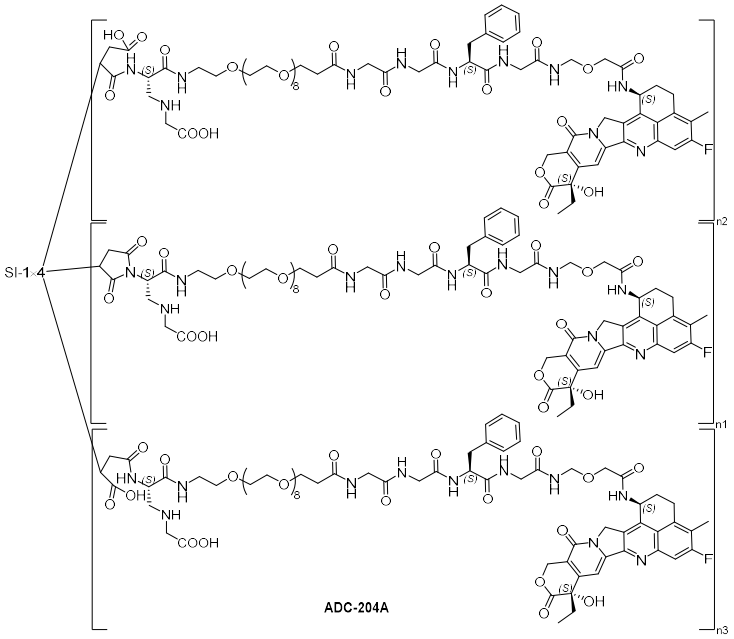
ADC-203



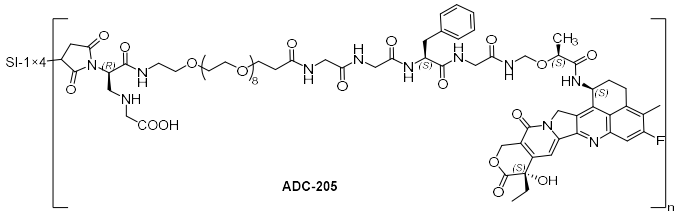
ADC-203A



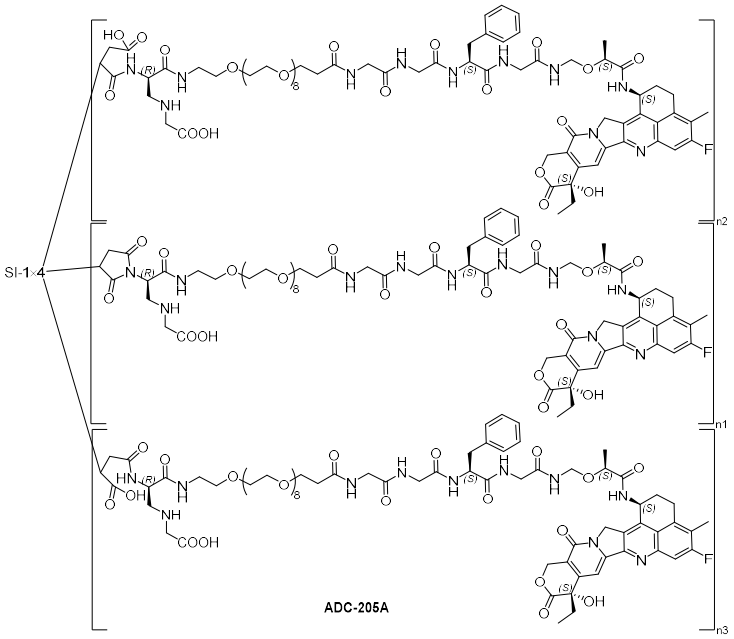
ADC-204



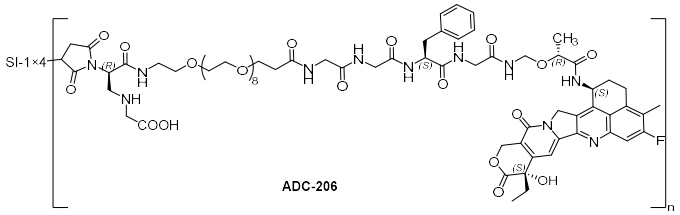
ADC-204A



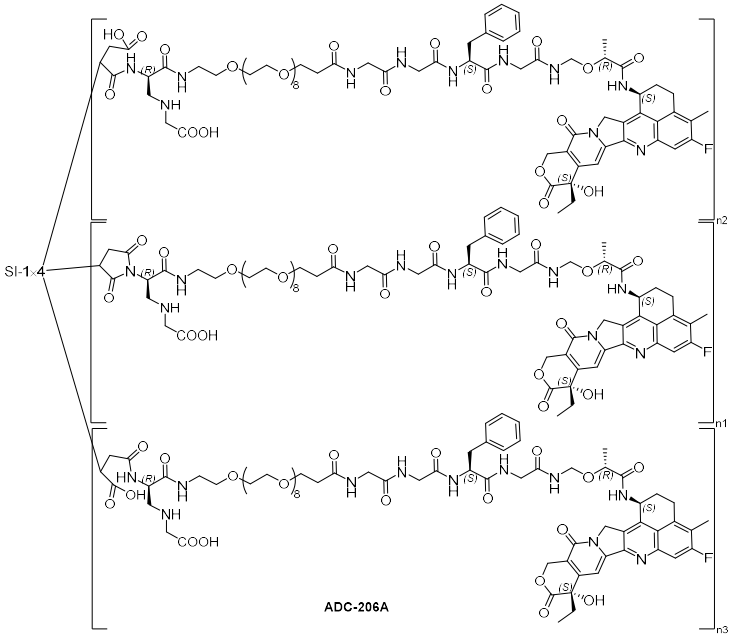
ADC-205



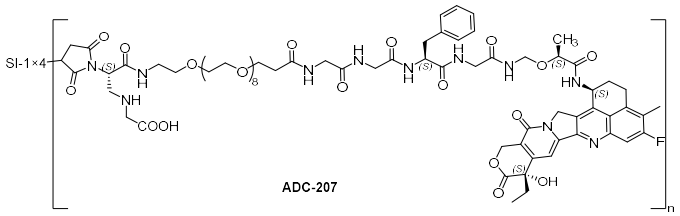
ADC-205A



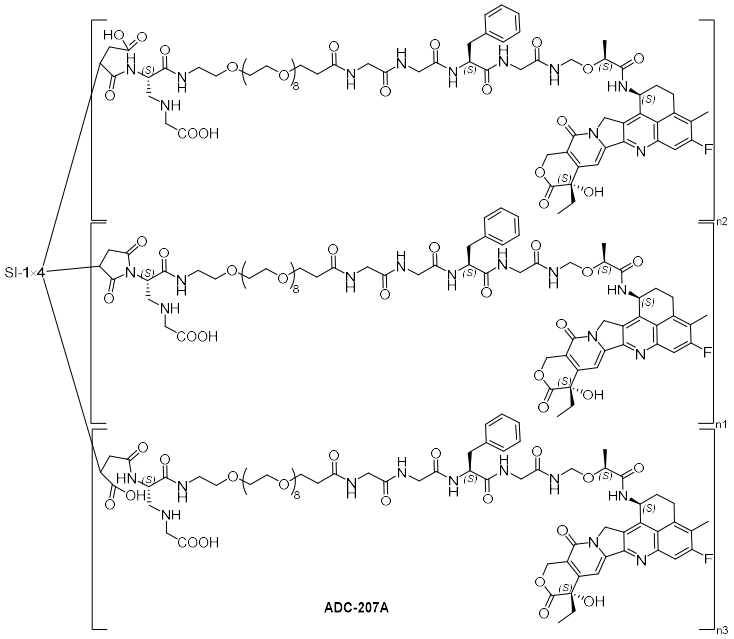
ADC-206



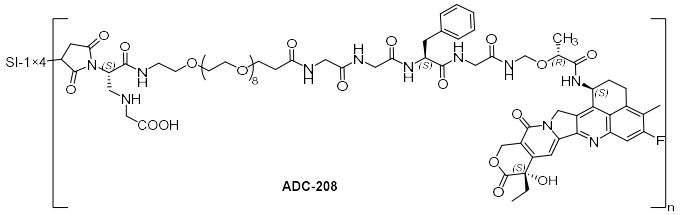
ADC-206A



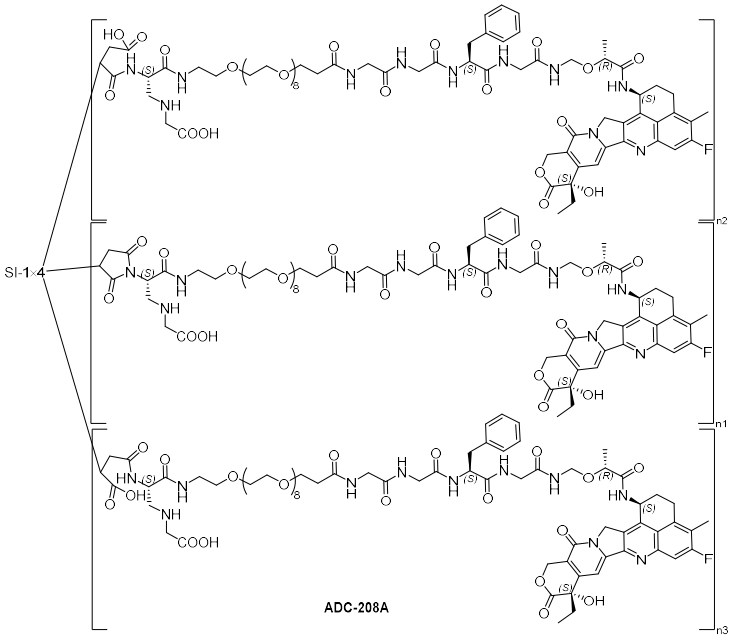
ADC-207



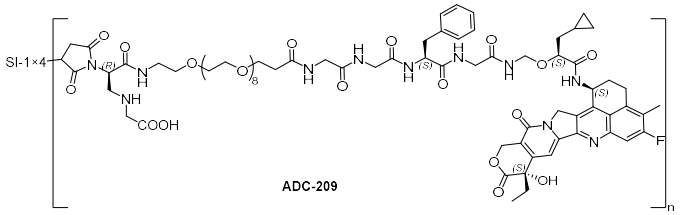
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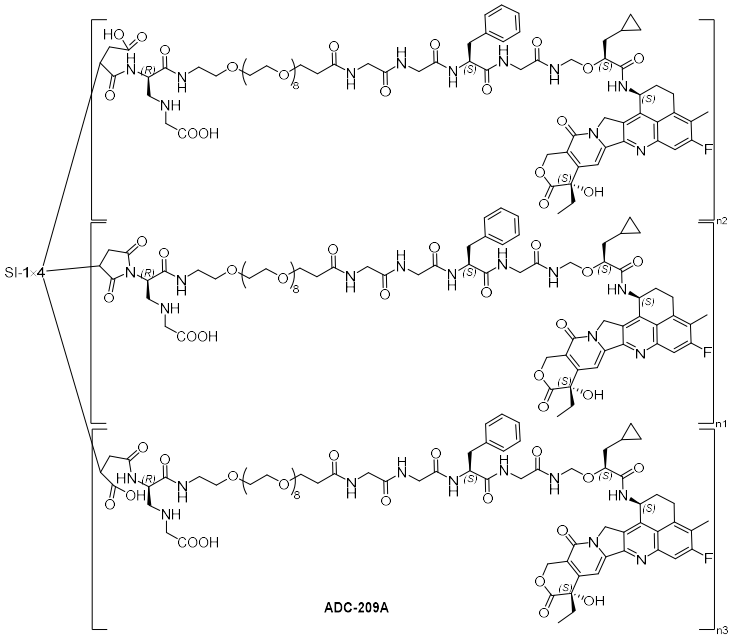
ADC-208



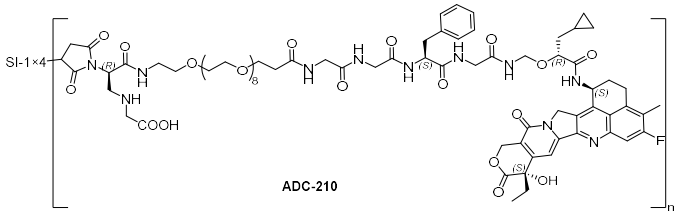
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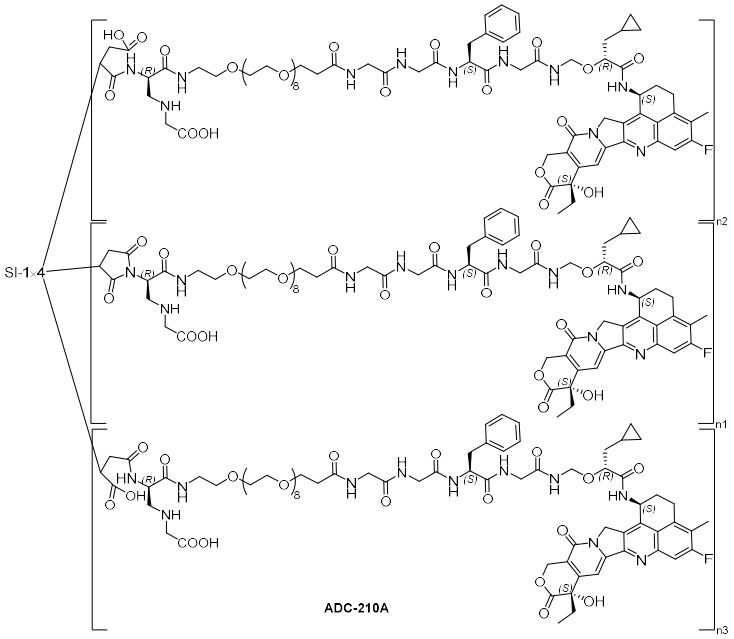
ADC-209



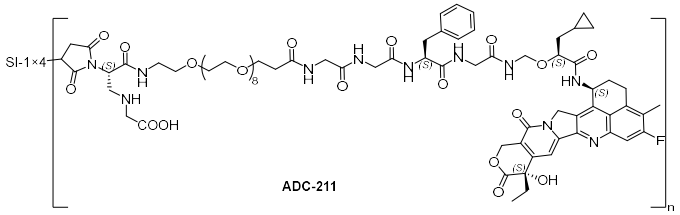
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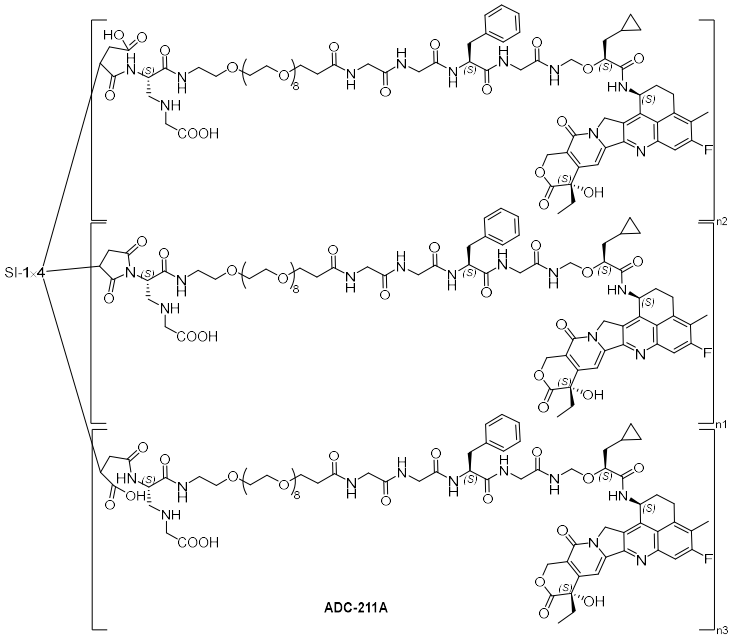
ADC-210



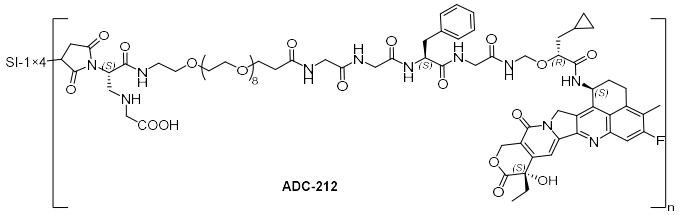
ADC-210A



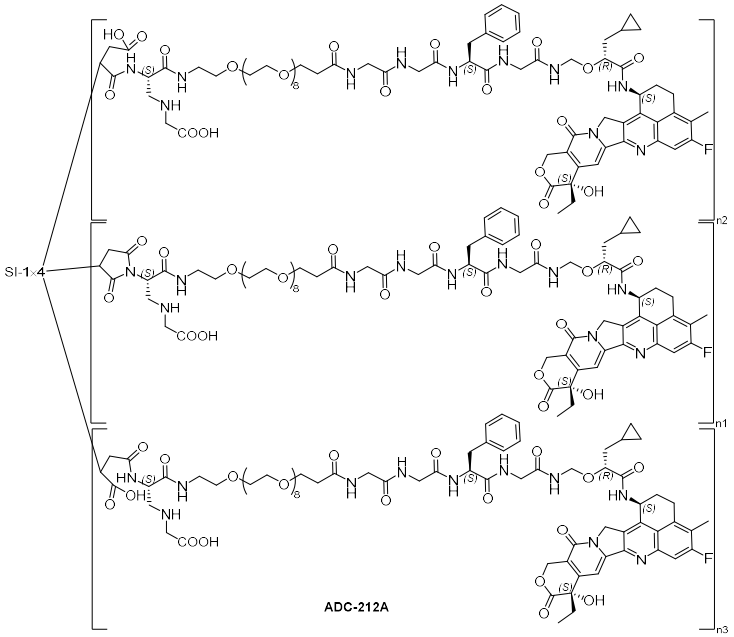
ADC-211



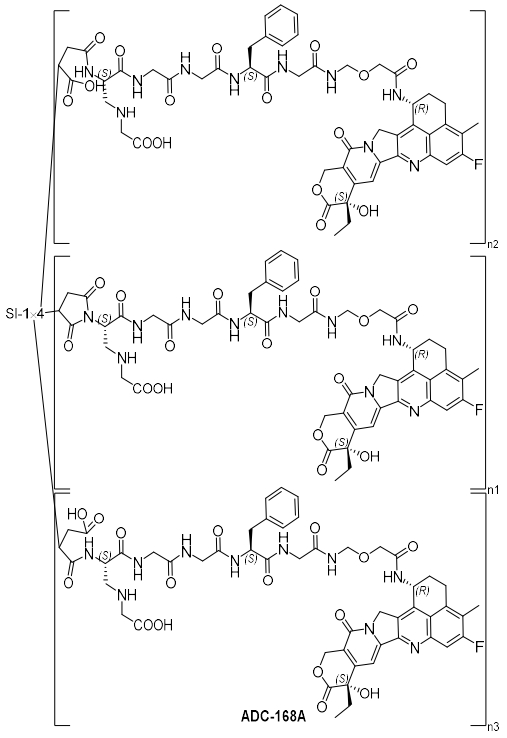
ADC-211A



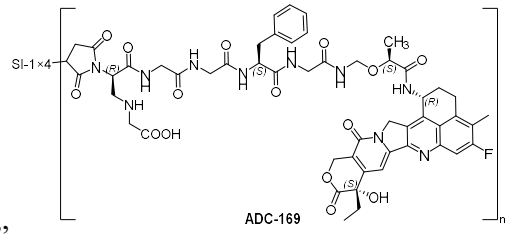
ADC-212



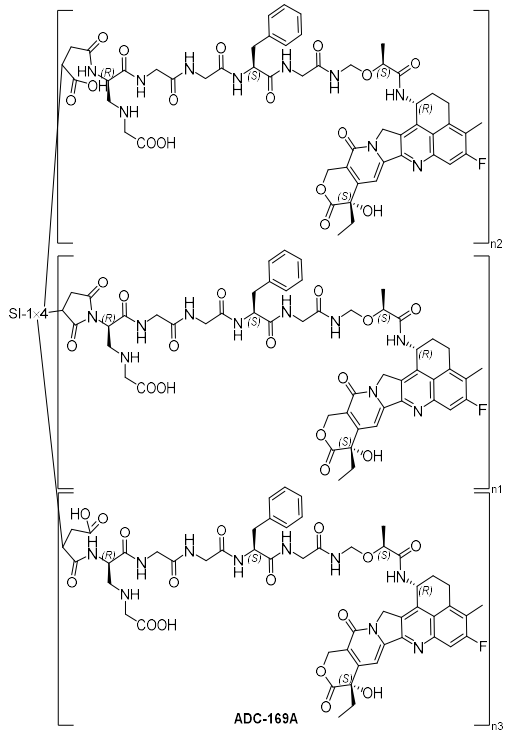
ADC-212A



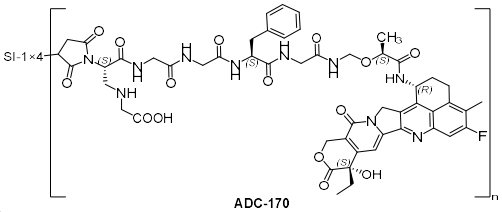
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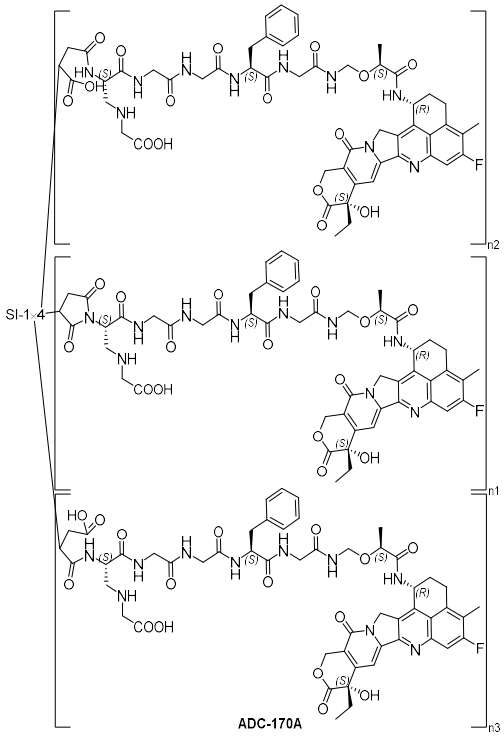
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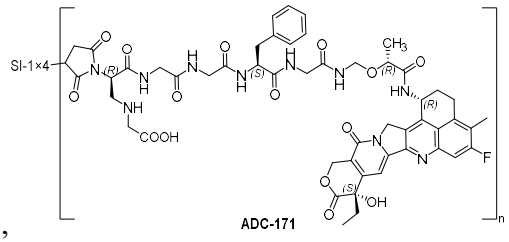
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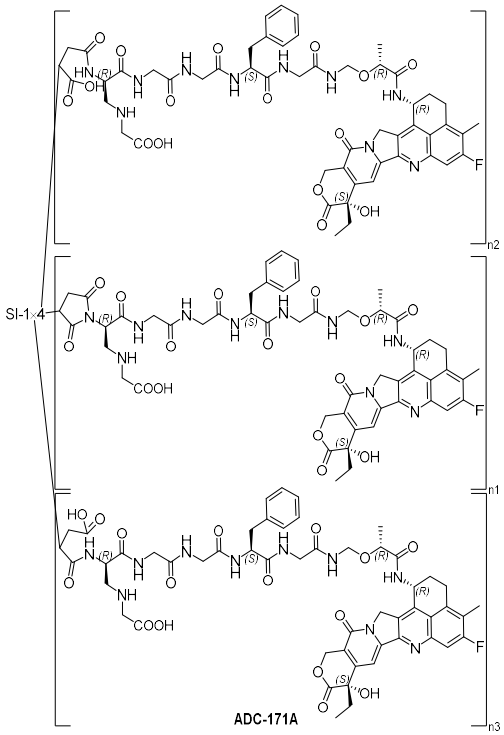
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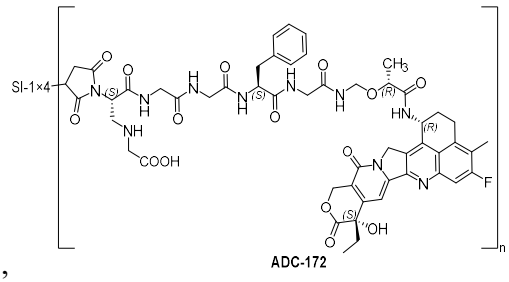
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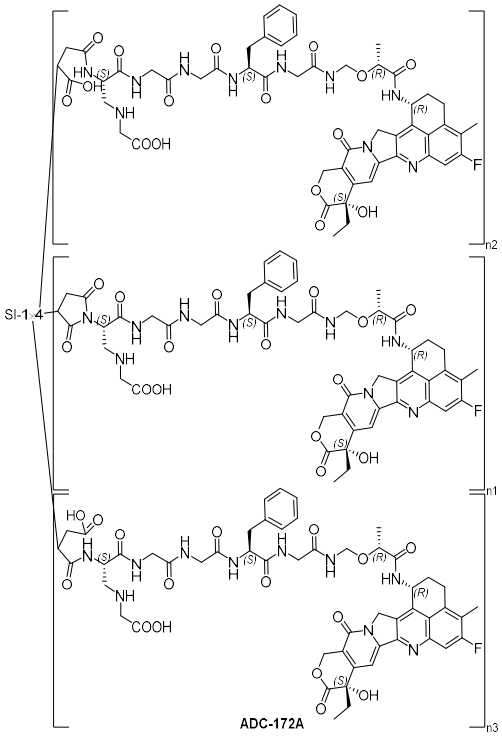
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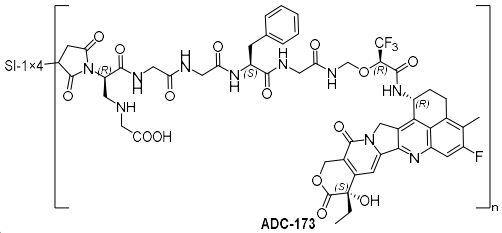
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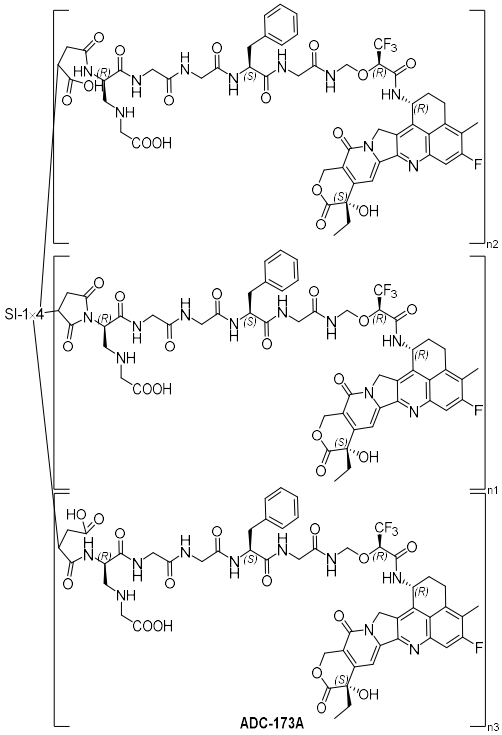
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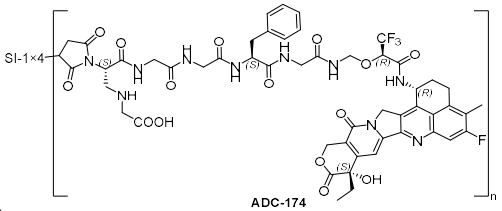
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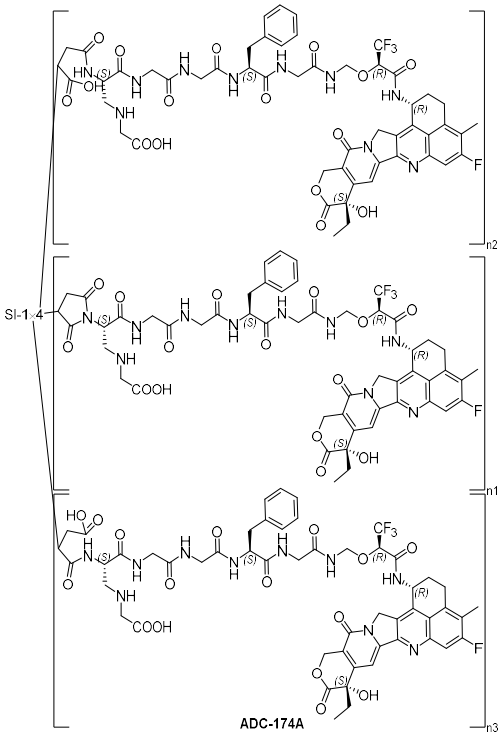
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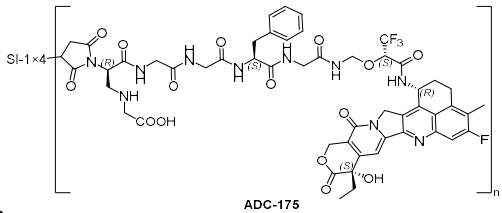
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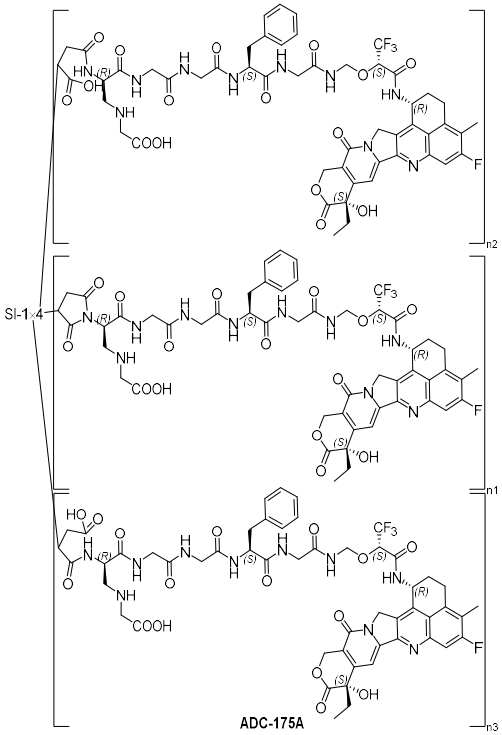
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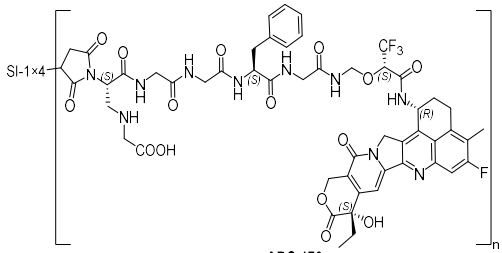
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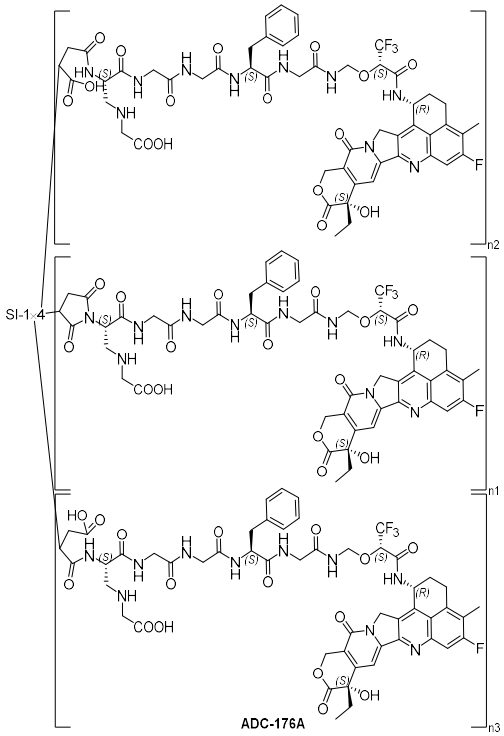
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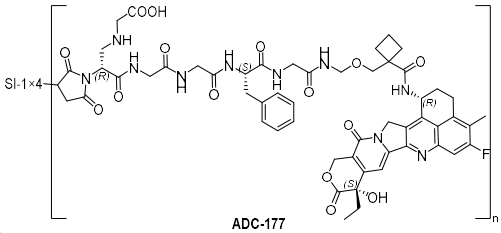
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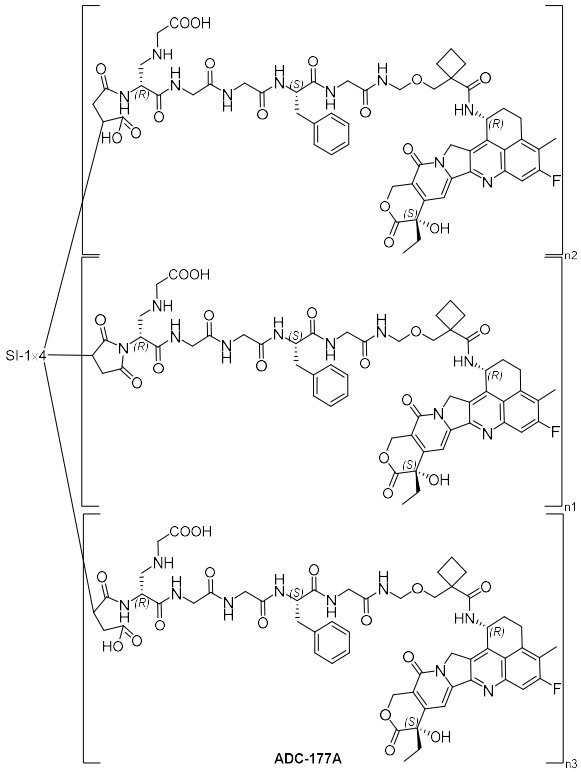
ADC-176 ,



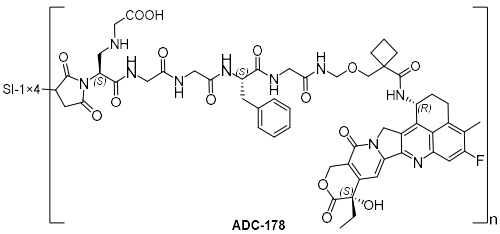
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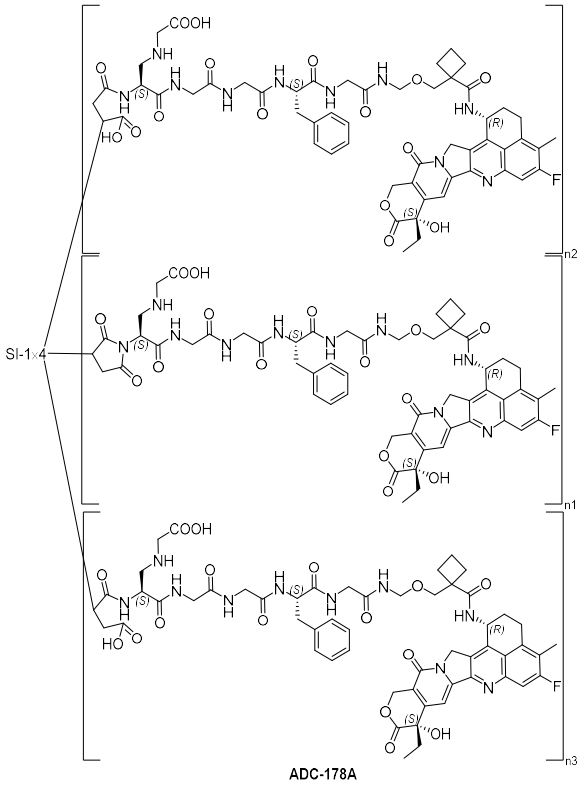
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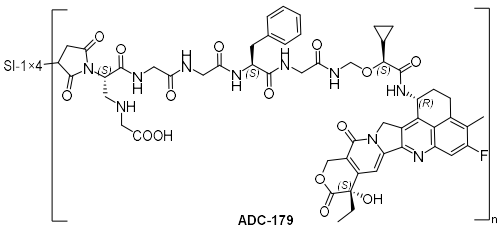
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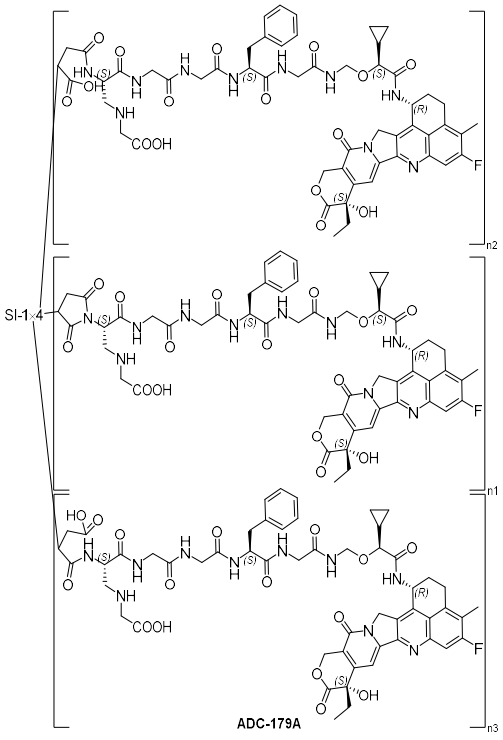
ADC-178 ,



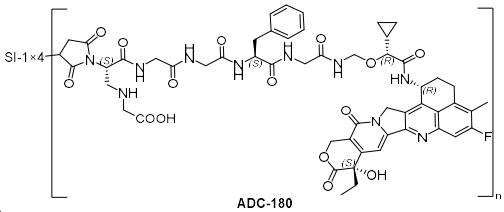
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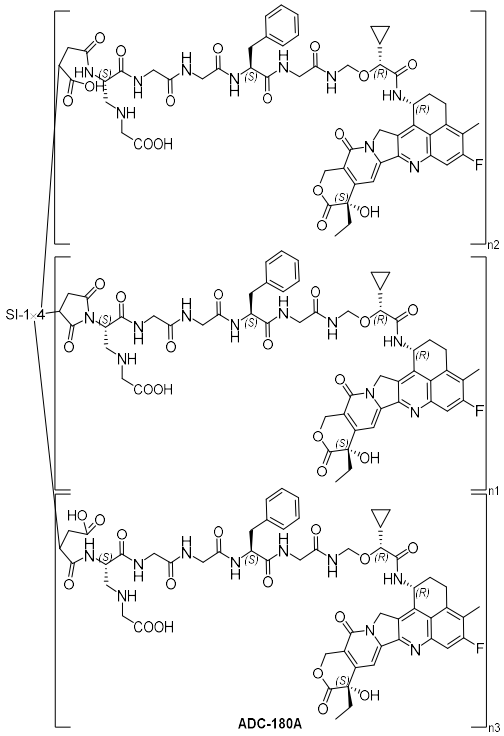
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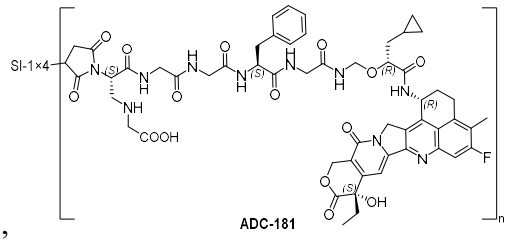
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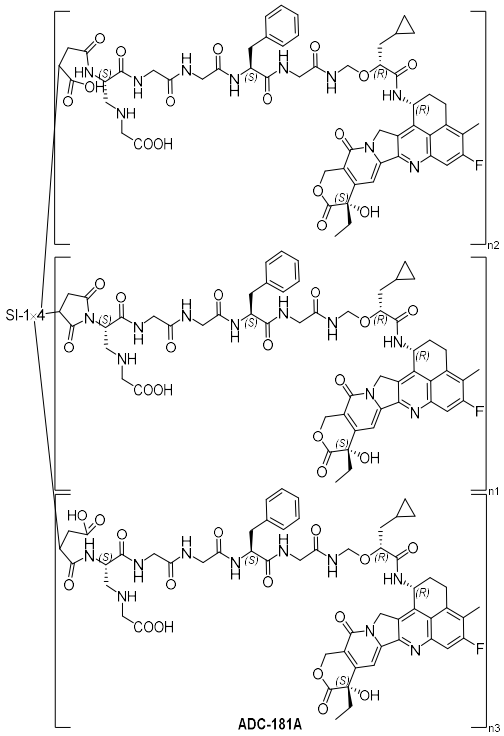
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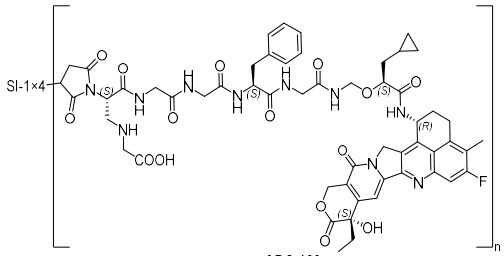
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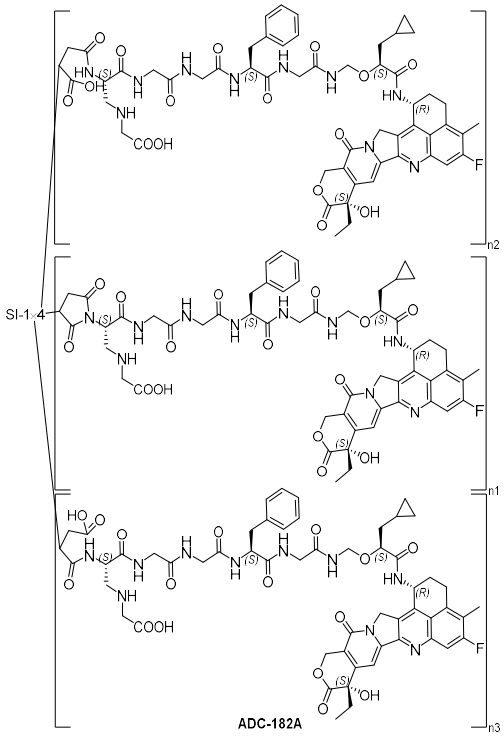
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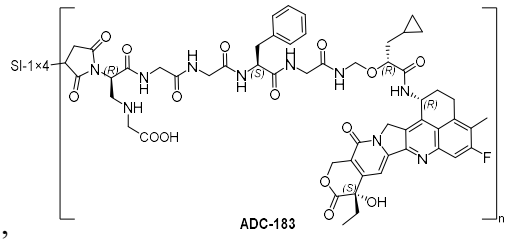
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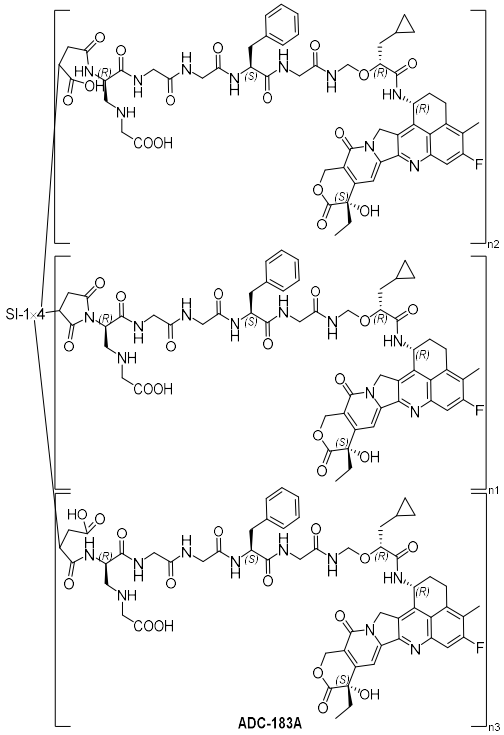
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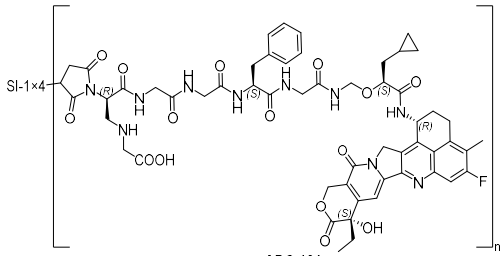
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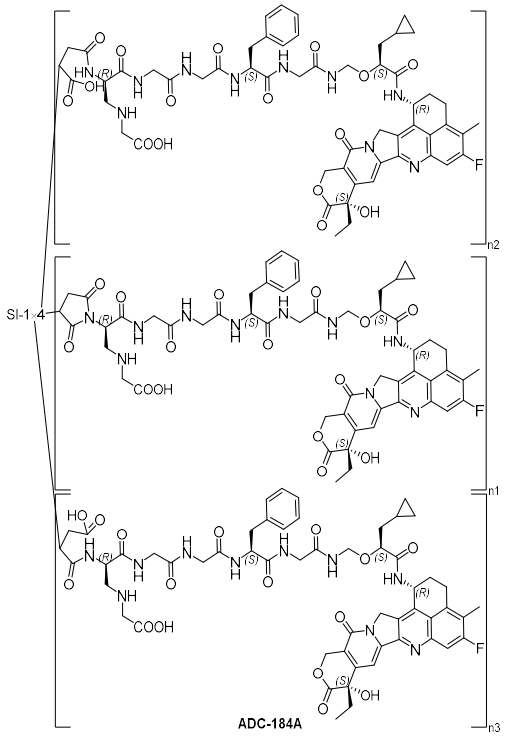
ADC-183,



ADC-183A,



ADC-184,



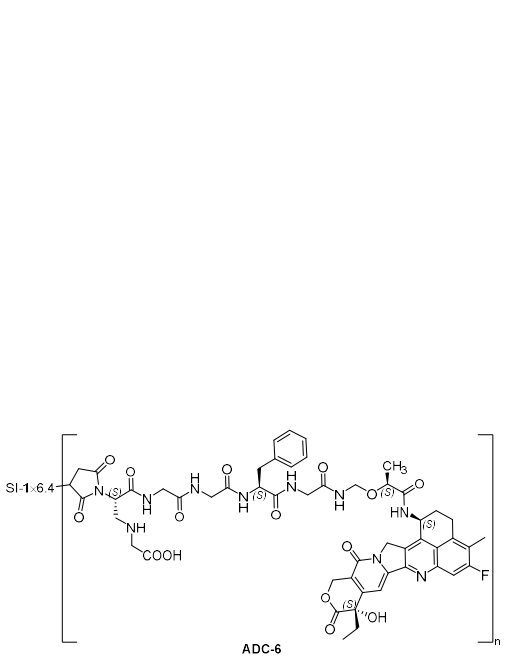
ADC-184A

wherein:

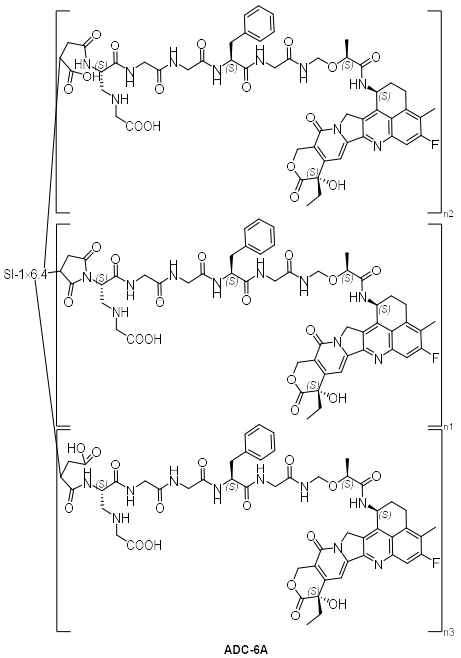
SI-1 x 4 is a bispecific antibody or antigen-binding fragment thereof having a binding specificity to both EGFR and HER3,

n is an integer of1-10, wherein n1, n2, and n3 are each independently chosen from any integer or any decimal number from 0-10, n1, n2, and n3 are not simultaneously 0, and $1 \leq n1 + n2 + n3 \leq 10$.

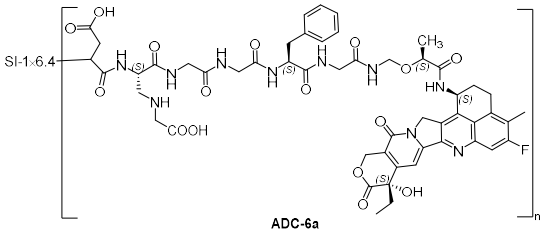
52. The use of Claim 1-15, wherein the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent compound thereof, comprises the following structure or a butanediimide ring-opening structure thereof or an isomer thereof:

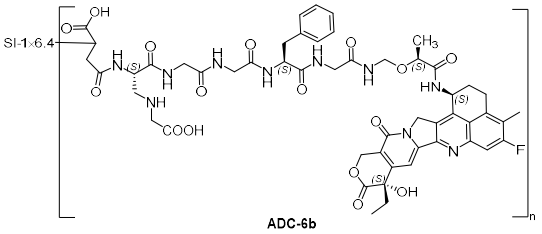


ADC-6



ADC-6A



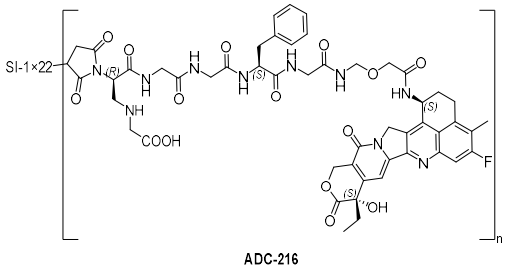


wherein:

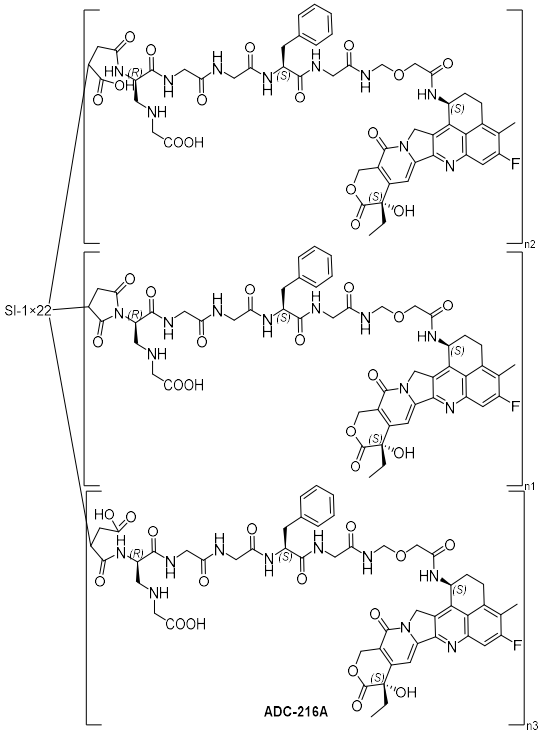
SI-1 x 24 is a bispecific antibody or antigen-binding fragment thereof having a binding specificity to both EGFR and HER3;

n is an integer of 1-10, wherein n1, n2, and n3 are each independently chosen from any integer or any decimal number from 0-10, n1, n2, and n3 are not simultaneously 0, and $1 \leq n1 + n2 + n3 \leq 10$.

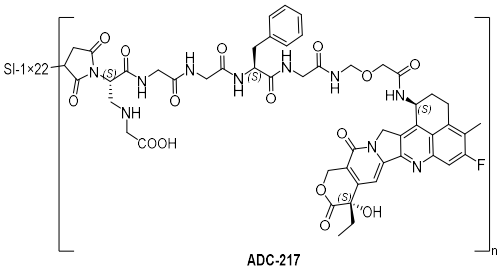
53. The use of Claim 1-15, wherein the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent compound thereof, comprises the following structure, or a butanediimide ring-opening structure thereof, or an isomer thereof:



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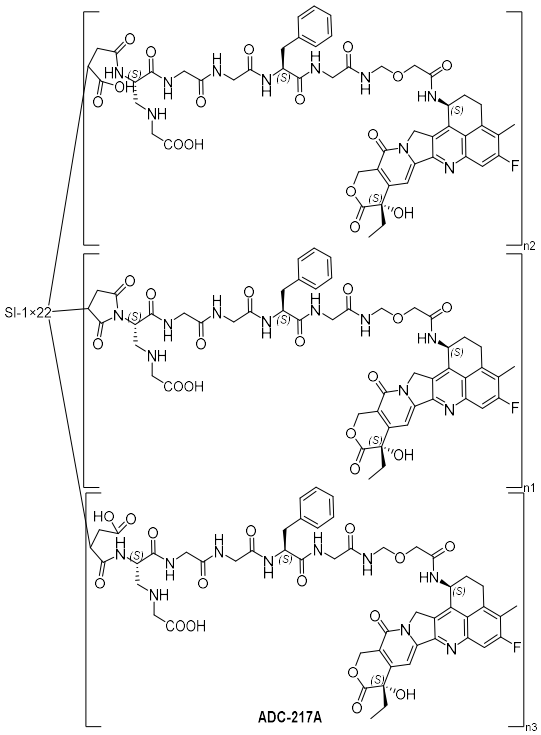


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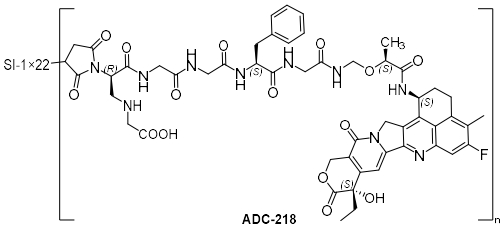
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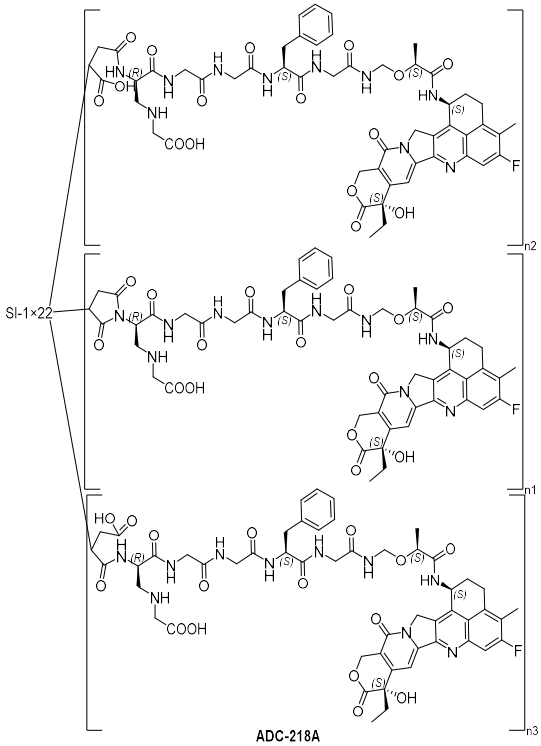
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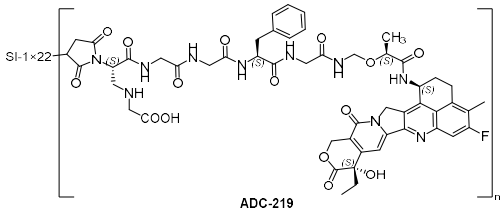
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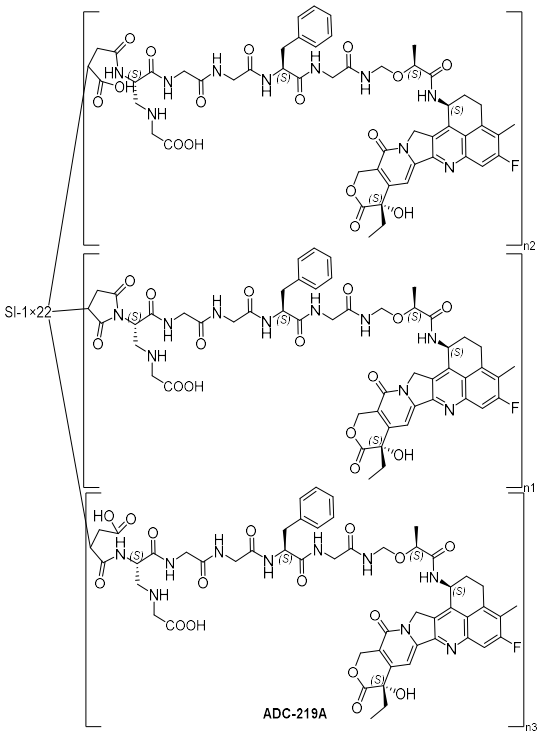
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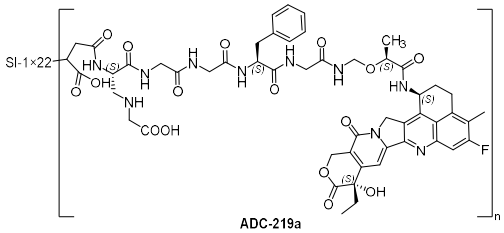
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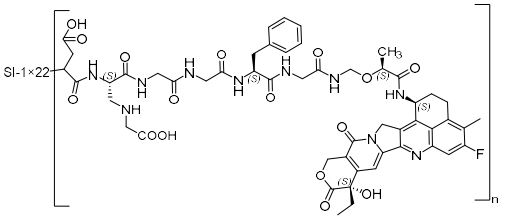
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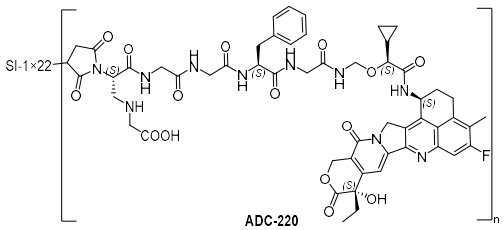
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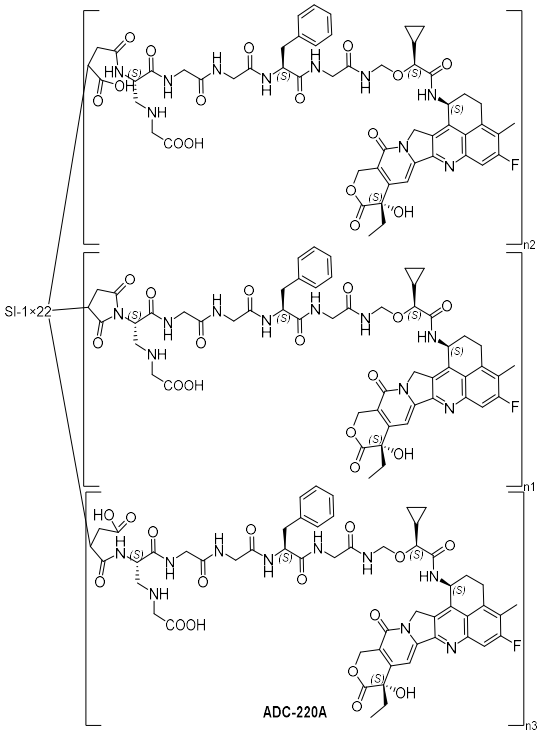
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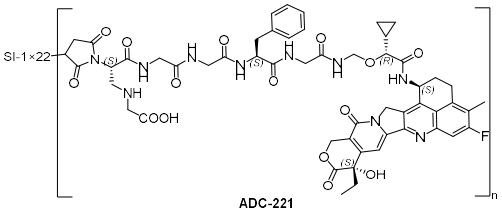
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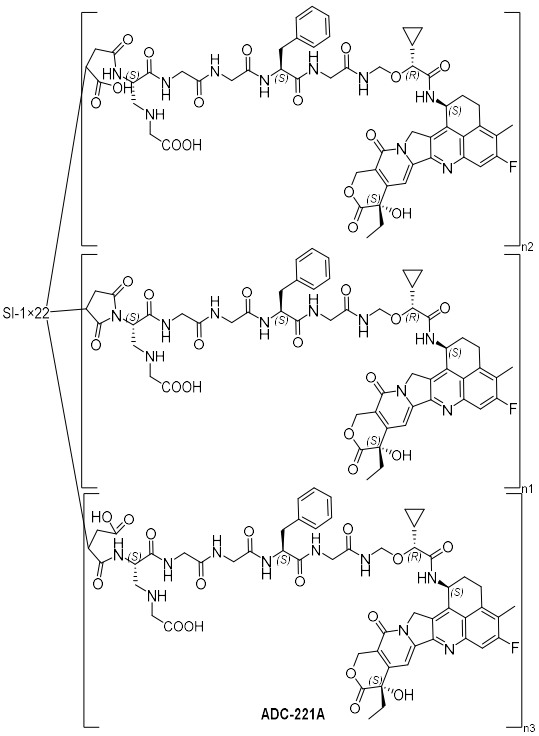
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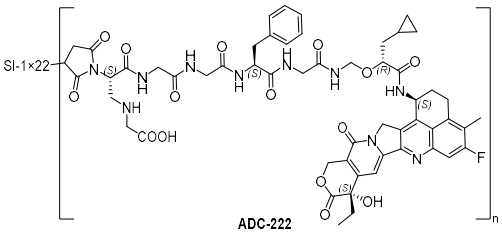
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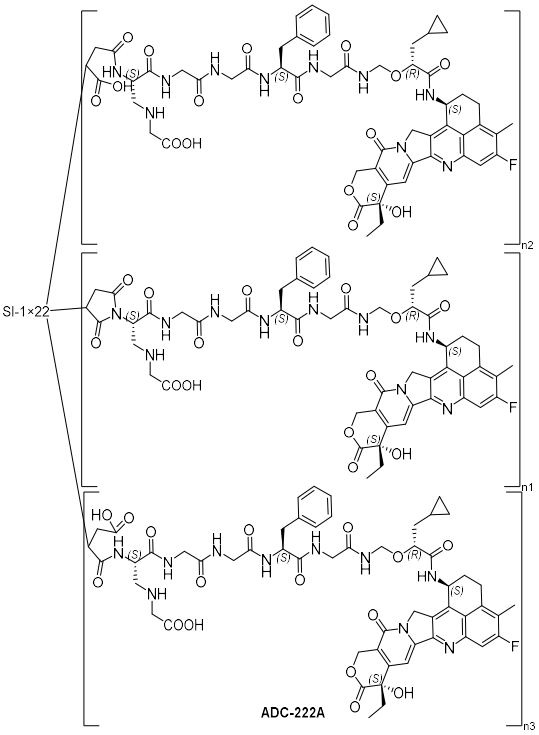
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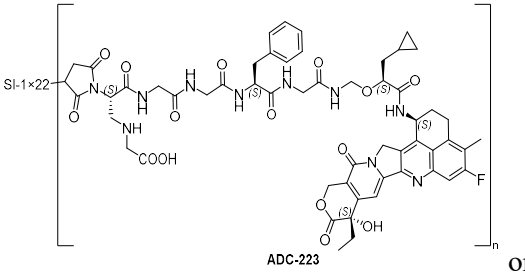
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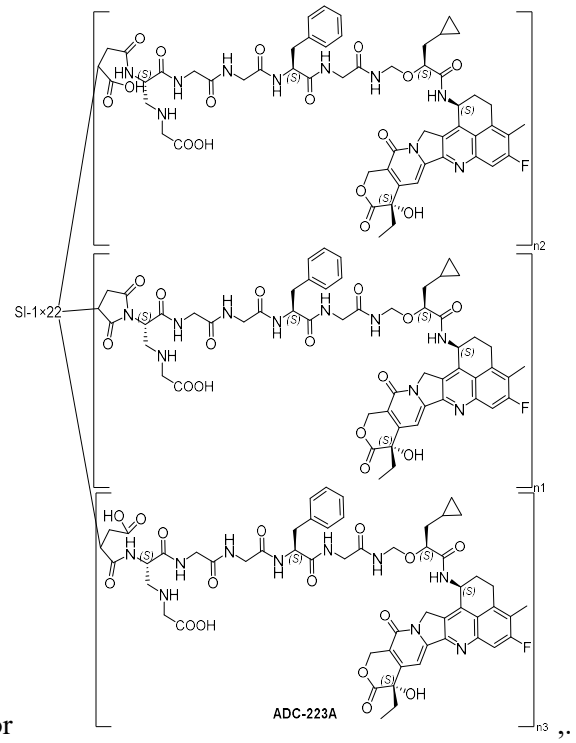
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ADC-223

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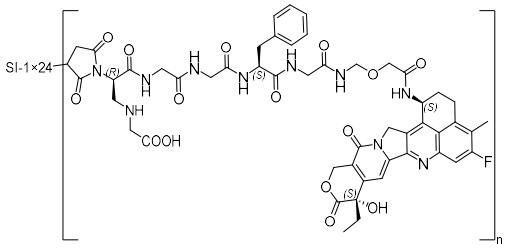
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wherein:

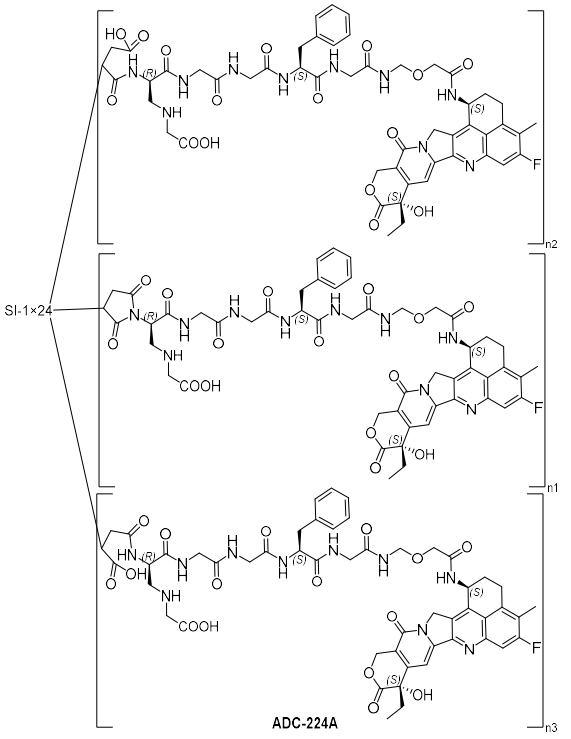
SI-1 x 22 is a bispecific antibody or antigen-binding fragment thereof having a binding specificity to both EGFR and HER3;

n is an integer of 1-10, wherein n1, n2, and n3 are each independently chosen from any integer or any decimal number from 0-10, n1, n2, and n3 are not simultaneously 0, and $1 \leq n1 + n2 + n3 \leq 10$.

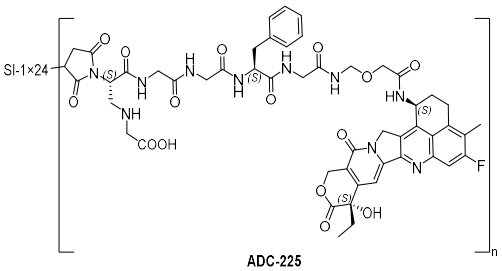
54. The use of Claim 1-15, wherein the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent compound thereof, comprises the following structure, or a butanediimide ring-opening structure thereof, or an isomer thereof:



ADC-224 ,

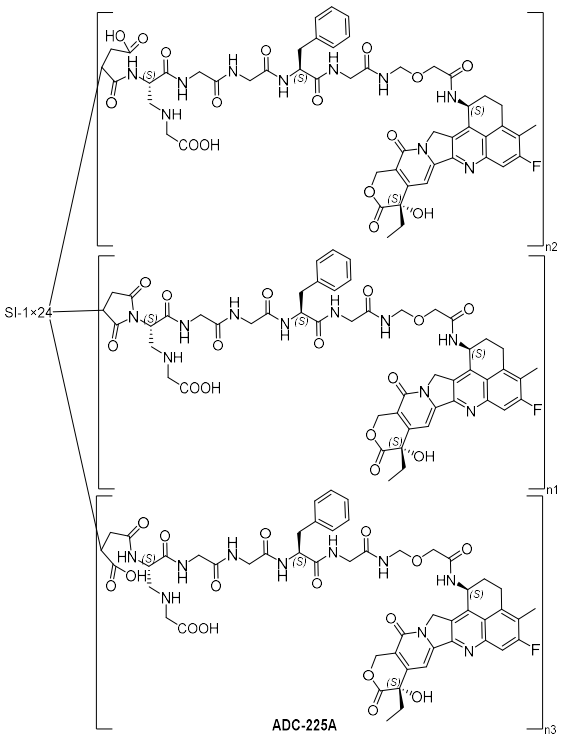


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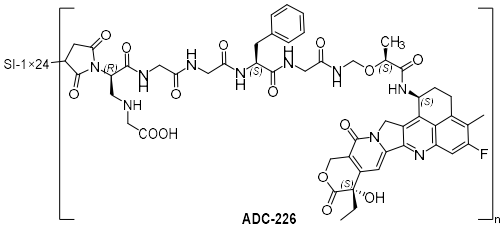
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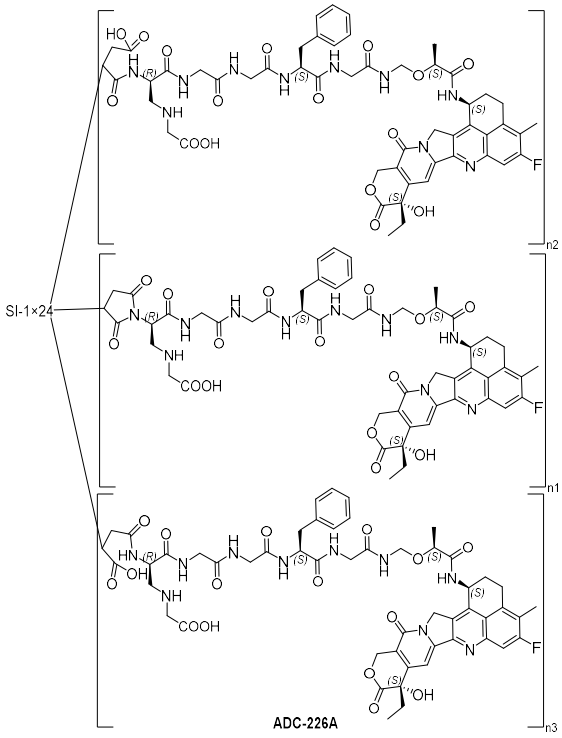
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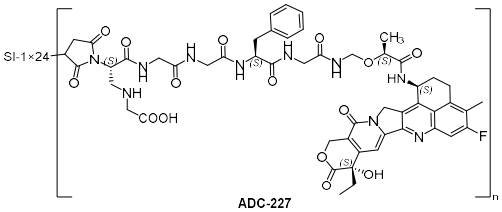
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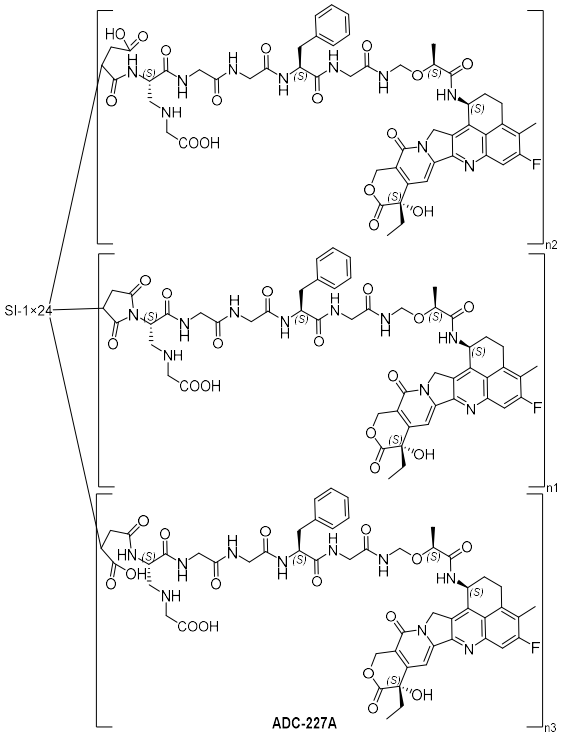
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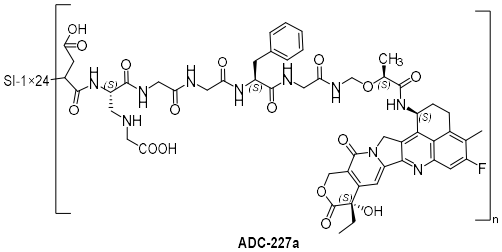
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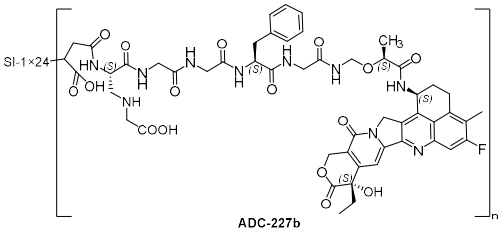
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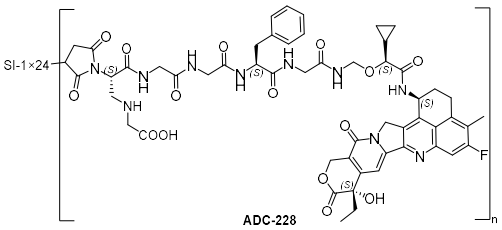
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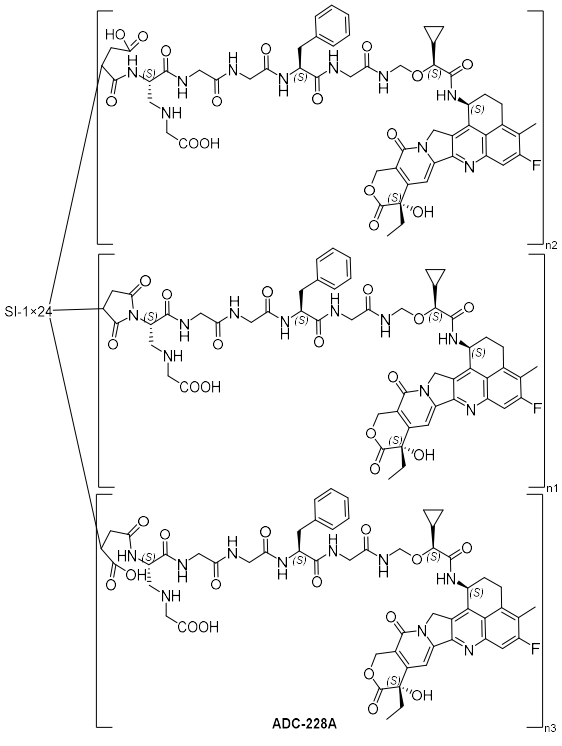
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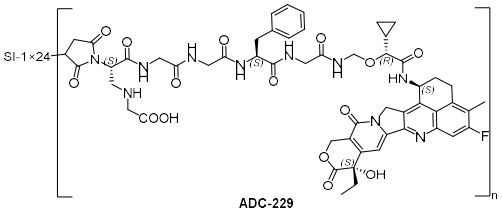
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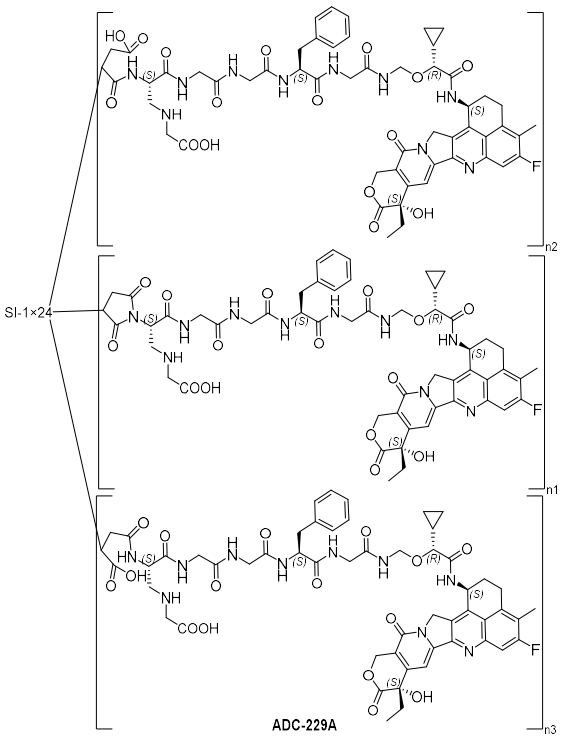
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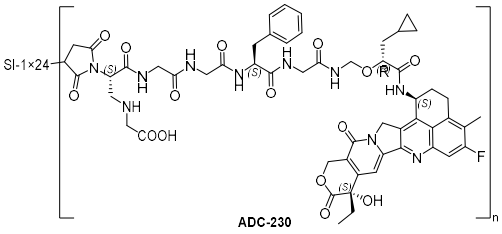
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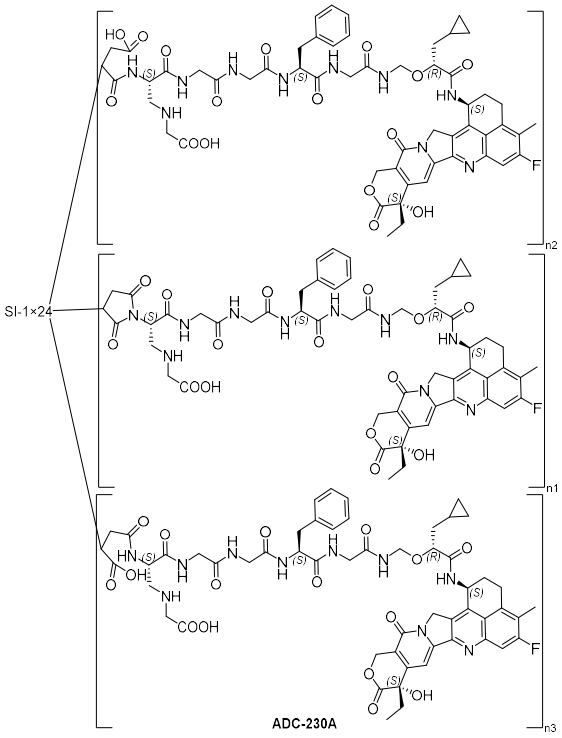
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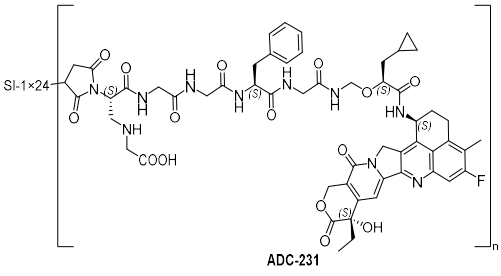
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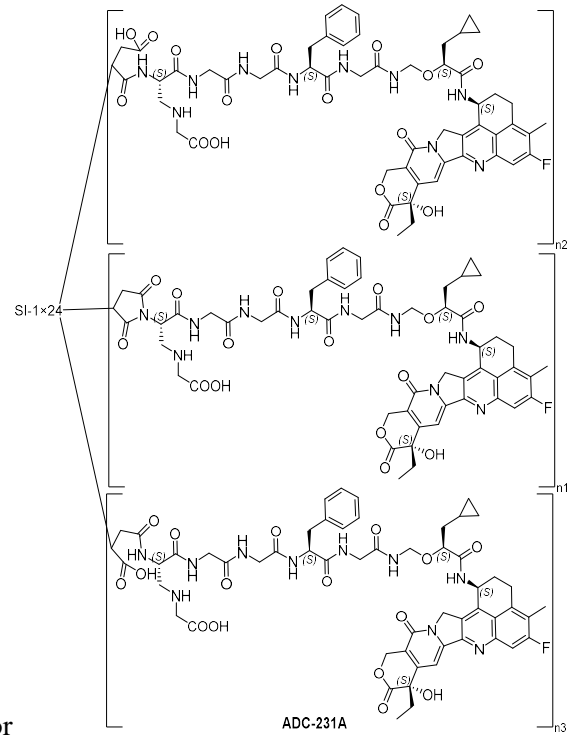
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ADC-231

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ADC-231A

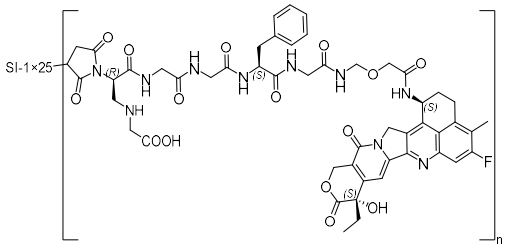
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wherein:

SI-1 x 24 is a bispecific antibody or antigen-binding fragment thereof having a binding specificity to both EGFR and HER3;

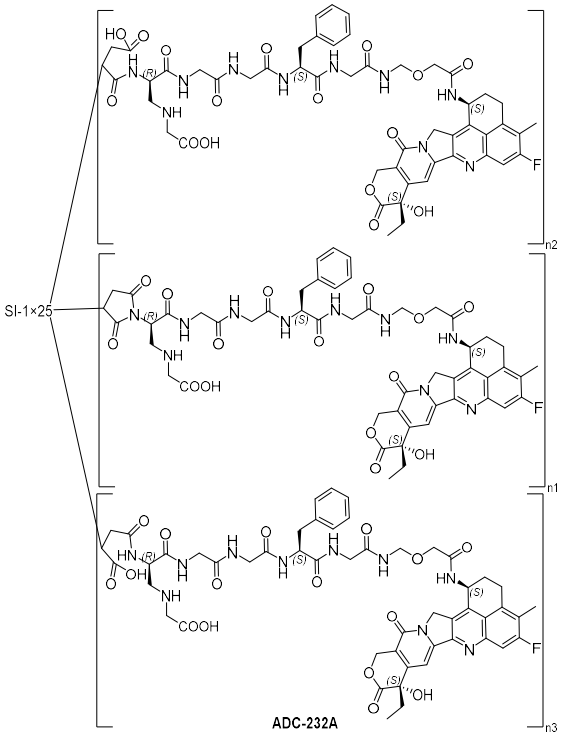
n is an integer of 1-10, wherein n1, n2, and n3 are each independently chosen from any integer or any decimal number from 0-10, n1, n2, and n3 are not simultaneously 0, and $1 \leq n1 + n2 + n3 \leq 10$.

55. The use of Claim 1-15, wherein the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent compound thereof, comprises the following structure, or a butanediimide ring-opening structure thereof, or an isomer thereof.



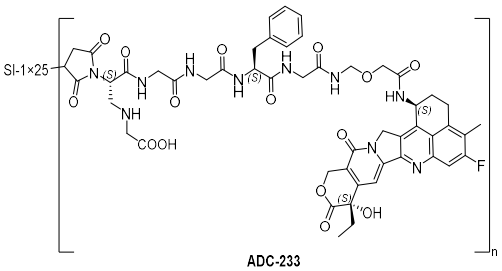
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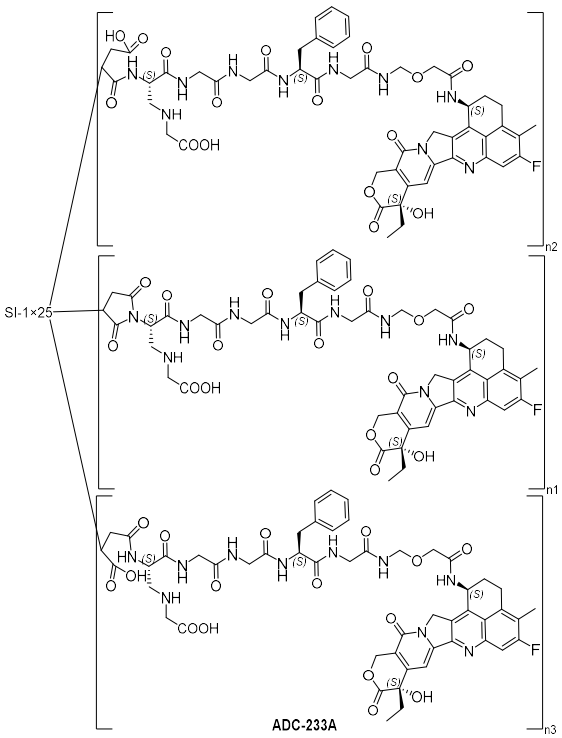
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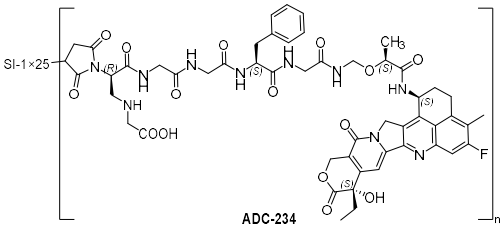
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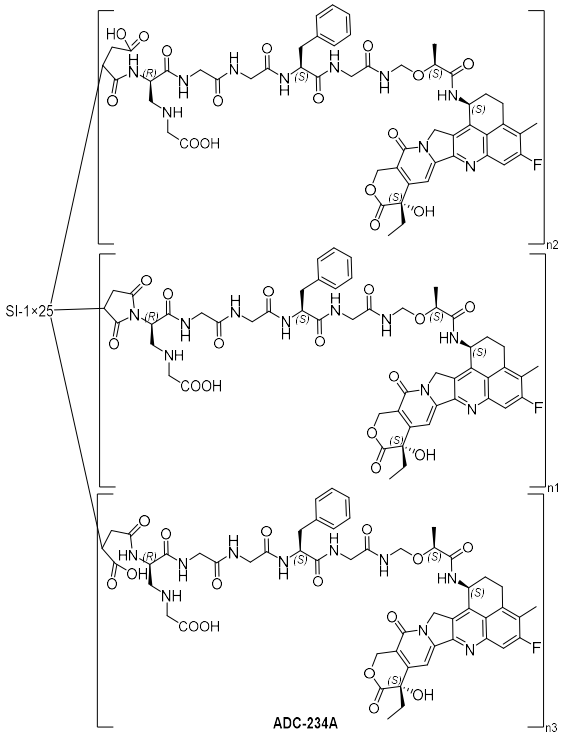
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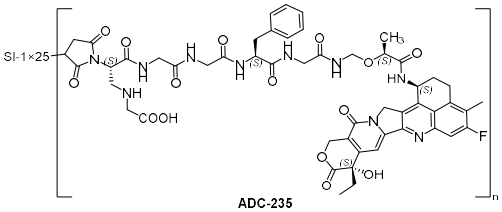
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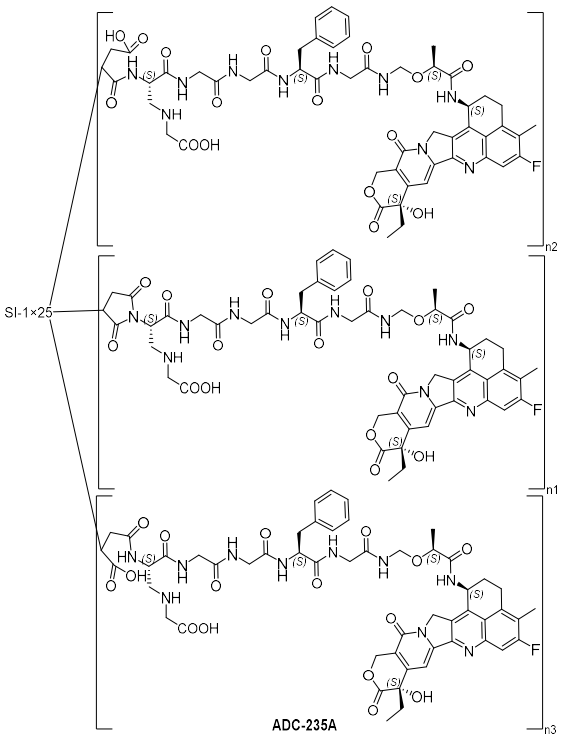
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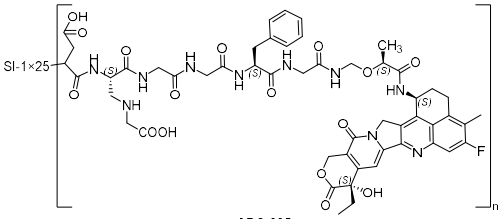
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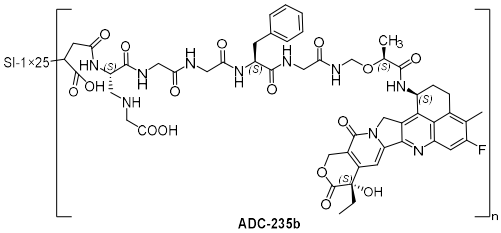
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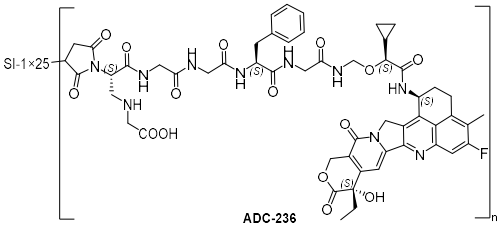
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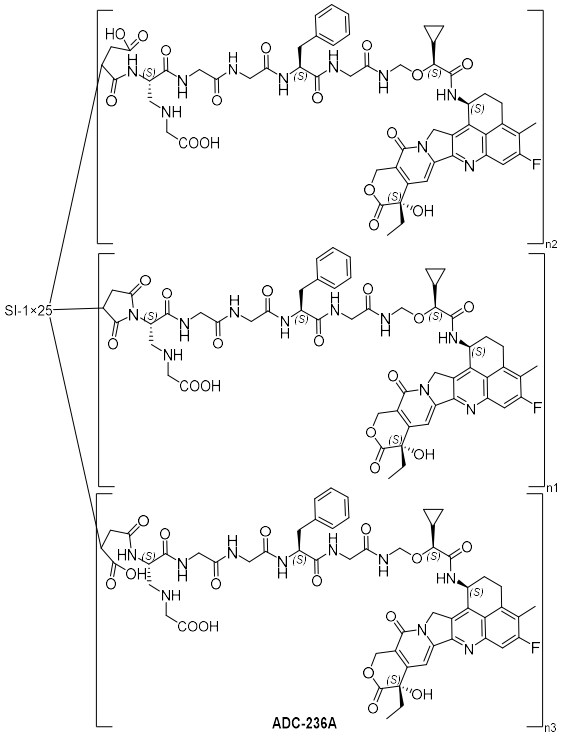
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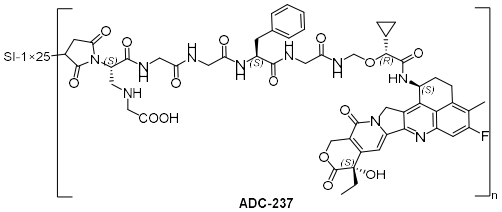
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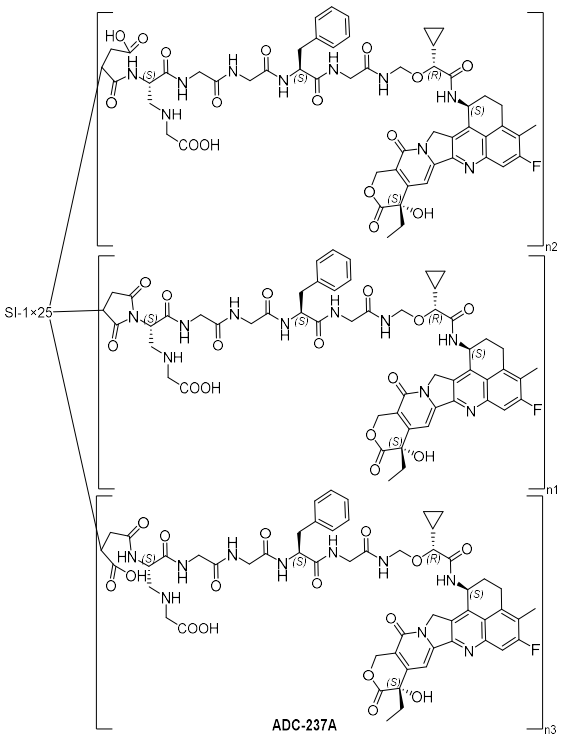
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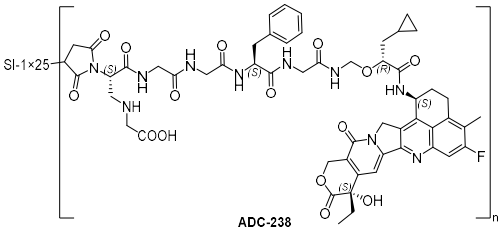
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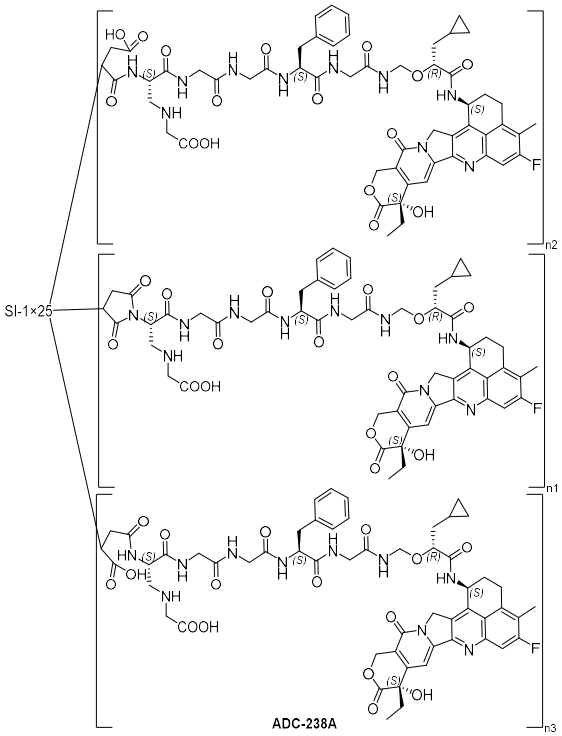
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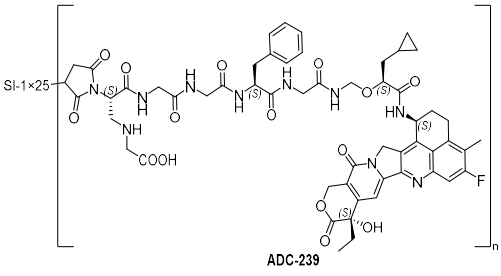
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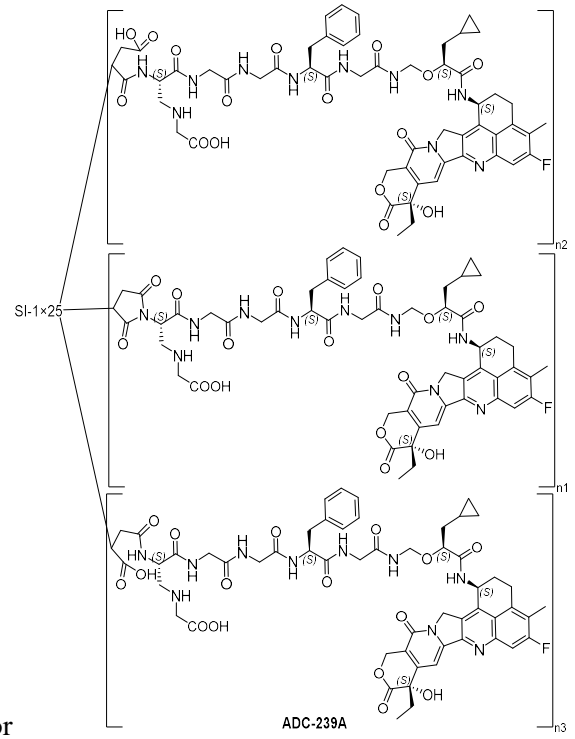
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ADC-239

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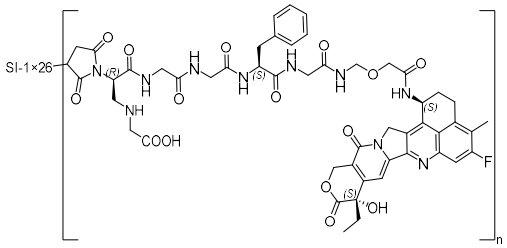
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wherein:

SI-1 x 25 is a bispecific antibody or antigen-binding fragment thereof having a binding specificity to both EGFR and HER3,

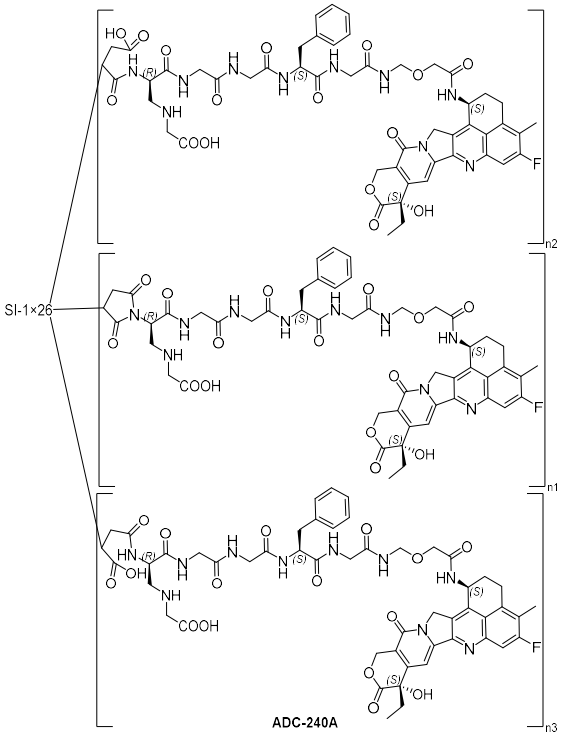
n is an integer of 1-10, wherein n1, n2, and n3 are each independently chosen from any integer or any decimal number from 0-10, n1, n2, and n3 are not simultaneously 0, and $1 \leq n1 + n2 + n3 \leq 10$.

56. The use of Claim 1-15, wherein the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent compound thereof, comprises the following structure, or a butanediimide ring-opening structure thereof, or an isomer thereof:



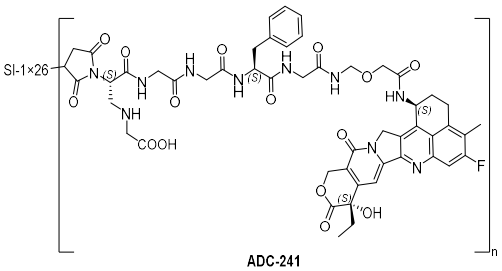
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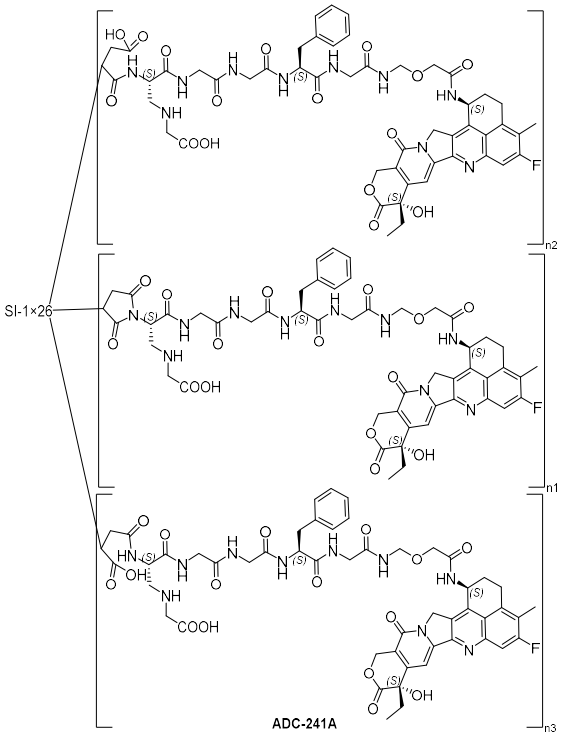
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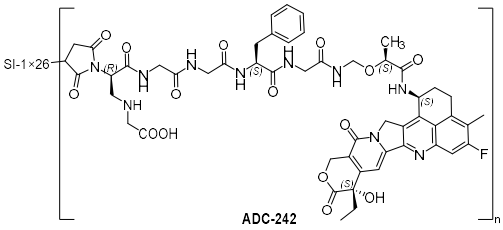
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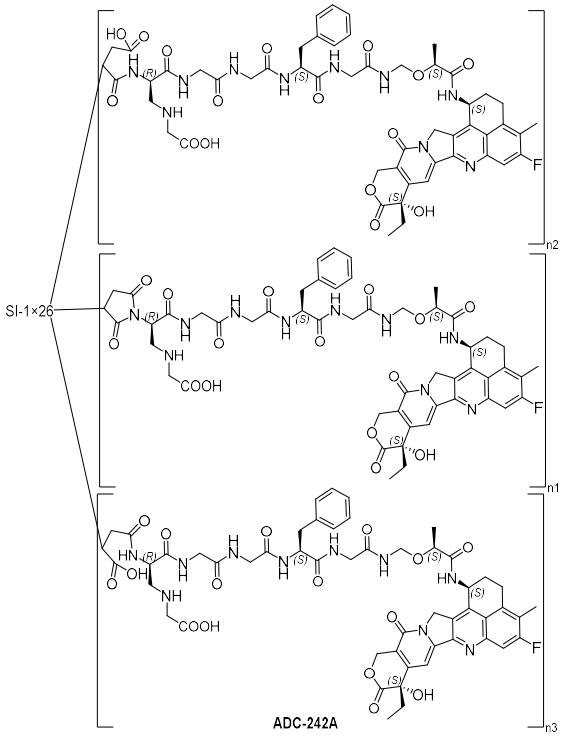
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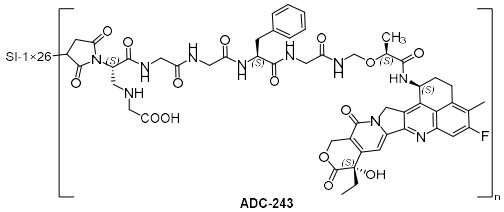
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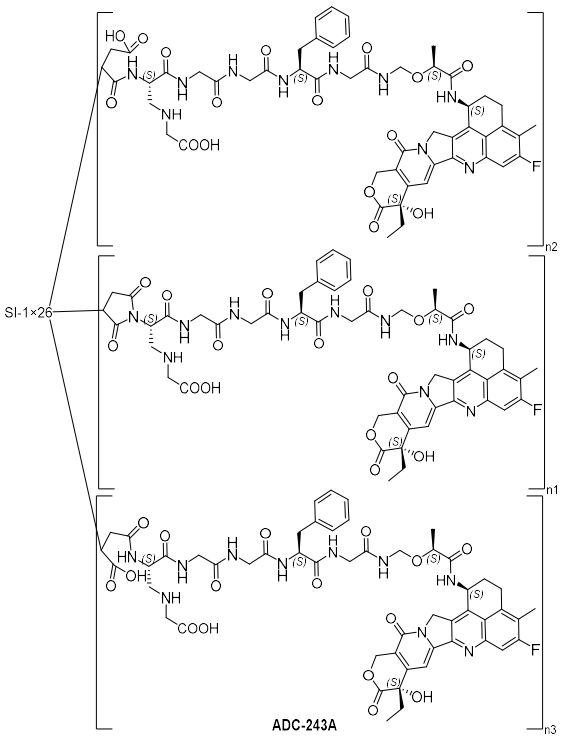
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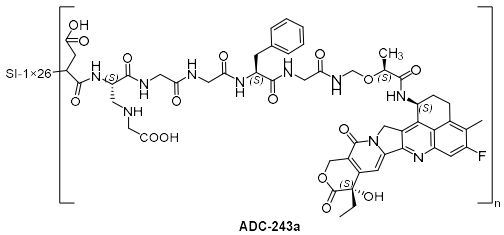
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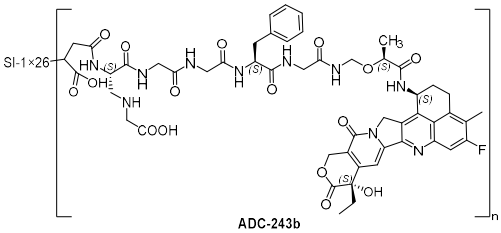
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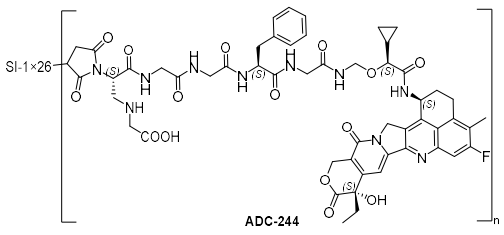
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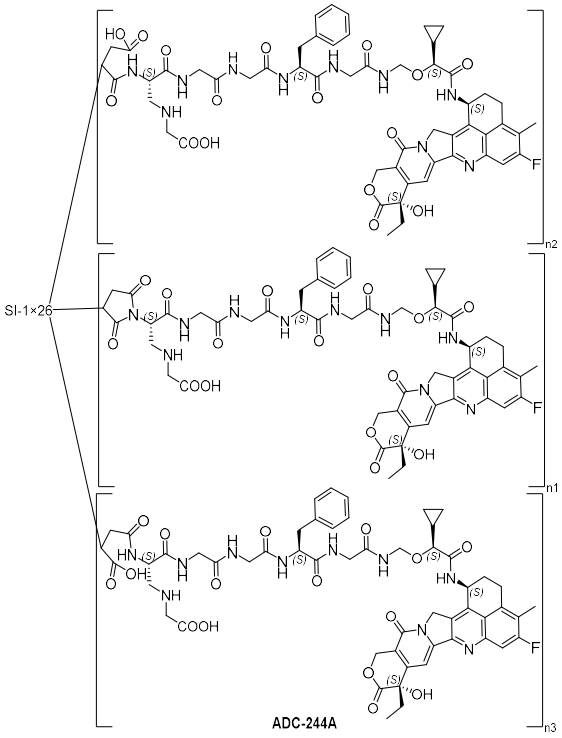
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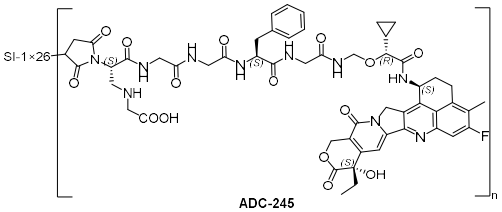
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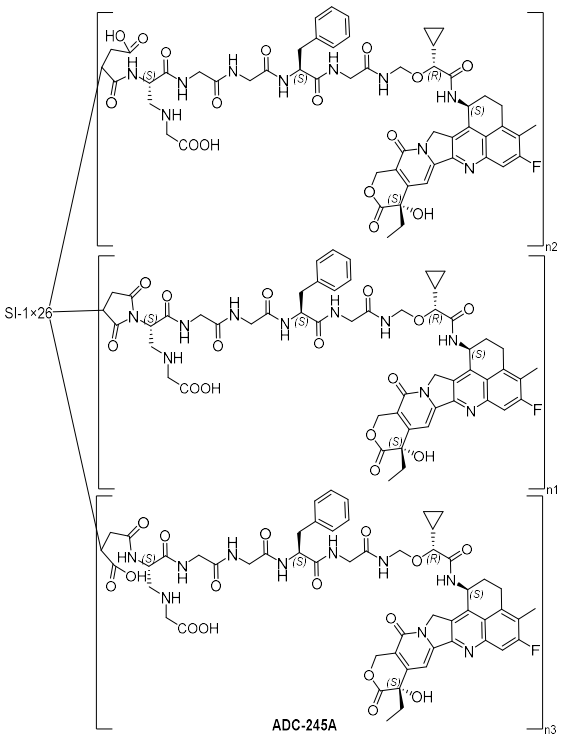
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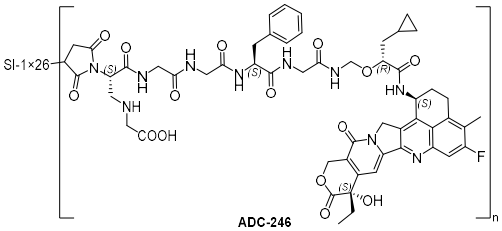
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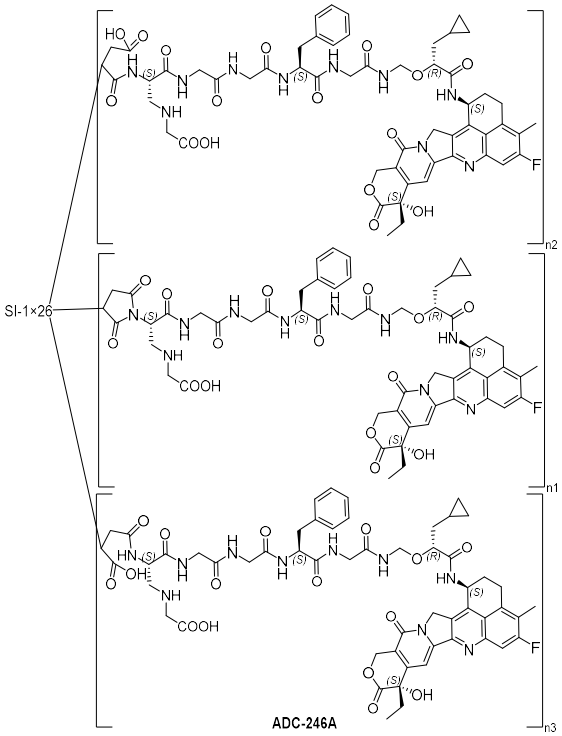
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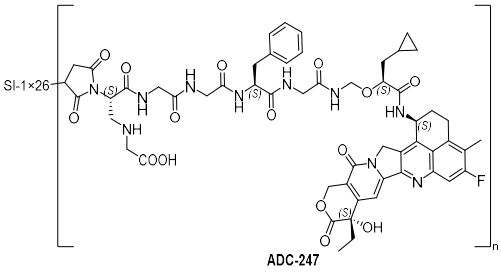
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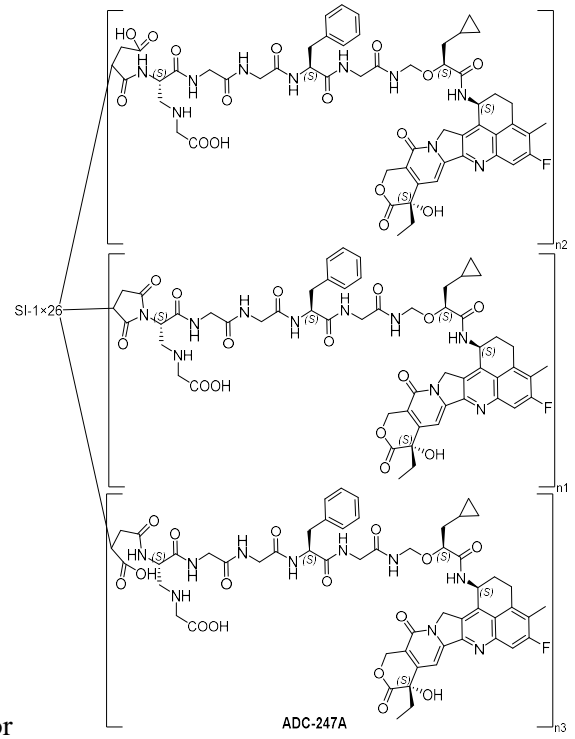
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or



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wherein:

SI-1 x 26 is a bispecific antibody or antigen-binding fragment thereof targeting having a binding specificity to both EGFR and HER3,

n is an integer of 1-10, wherein n1, n2, and n3 are each independently chosen from any integer or any decimal number from 0-10, n1, n2, and n3 are not simultaneously 0, and $1 \leq n1 + n2 + n3 \leq 10$.

57. The use of Claim 1, wherein the pharmaceutically acceptable salt comprises a sodium, potassium, calcium, or magnesium salt formed with an acidic functional group in the structural formula, and acetate, trifluoroacetate, citrate, oxalate, oxalate, tartrate, malate, nitrate, chloride, bromide, iodide, sulphate, bisulfate, phosphate, lactate, oleate, ascorbate, salicylic acid , tartrate, malate, nitrate, chloride, bromide, iodide, sulfate, bisulfate, phosphate, lactate, oleate, ascorbate, salicylate, formate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate, or a combination thereof.

58. A pharmaceutical composition, comprising a lyophilized powder injection formula, wherein the lyophilized powder injection formula comprises the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvate thereof, of Claim 1 and a pharmaceutical carrier composition.

59. The pharmaceutical composition of Claim 58, wherein the lyophilized powder injection formula comprises the ligand-camptothecin conjugate of Formula I, or a pharmaceutically acceptable salt or solvate thereof, in an amount from about 10% to about 20% w/w, from about 12% to about 16% w/w, or from about 14% to about 15% w/w.

60. The pharmaceutical composition of Claim 58, wherein the pharmaceutical carrier composition comprises a buffer composition, an excipient, a preservative, an emulsifier, or a combination thereof.

61. A method for making the pharmaceutical composition of Claim 58, comprising

combining the ligand-camptothecin derivative conjugate of Formula I, or a pharmaceutically acceptable salt or solvent thereof, of Claim 1 and a pharmaceutical carrier composition to provide a pharmaceutical mixture, and

lyophilizing the pharmaceutical mixture to provide the lyophilized powder injection formula.

62. The method of Claim 61, further comprising combining the lyophilized powder injection formula with water to provide an injection solution.

63. A treatment kit, comprising a first container and a package insert, wherein the first container comprises at least one dose of the pharmaceutical composition of Claim 58, and wherein the package insert comprises instructions for treating the subject using the pharmaceutical composition.

64. The treatment kit of Claim 63, further comprising a second container, wherein the second container comprises at least one dose of a second treatment composition, wherein the second treatment composition comprises a platinum-containing or platinum-free chemotherapeutic agent, an immune checkpoint inhibitor, an EGFR-TKI, or a combination thereof.

65. The treatment kit of Claim 63, wherein the instructions state that the treatment kit is intended for use in treating the subject having cancer or tumor that tests positive for EGFR, HER3 or both.

66. The treatment kit of Claim 63, wherein the instructions state that the treatment kit is intended for use in treating the subject having non-small cell lung cancer, small cell lung cancer, head and neck squamous carcinoma, nasopharyngeal cancer, breast cancer, bladder cancer, esophageal squamous cell carcinoma, or biliary tract carcinoma.