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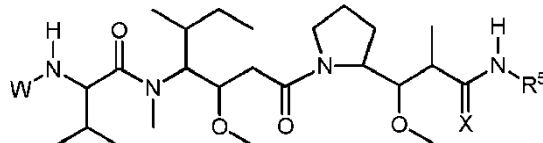
Norwegian Industrial Property Office

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(54) Title **CYTOTOXIC PEPTIDES AND ANTIBODY DRUG CONJUGATES THEREOF**

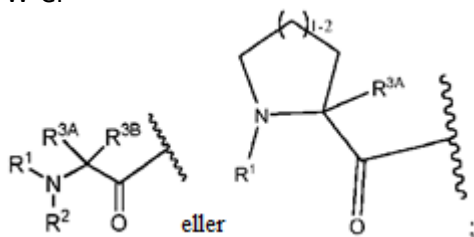
(56) References
Cited: WO-A2-2005/081711, WO-A2-2007/008848, SVETLANA O. DORONINA ET AL: "Enhanced Activity of Monomethylauristatin F through Monoclonal Antibody Delivery: Effects of Linker Technology on Efficacy and Toxicity", BIOCONJUGATE CHEMISTRY, vol. 17, no. 1, 1 January 2006 (2006-01-01), pages 114-124, XP055009264, ISSN: 1043-1802, DOI: 10.1021/bc0502917, DORONINA SVETLANA O ET AL: "Novel peptide linkers for highly potent antibody-auristatin conjugate", BIOCONJUGATE CHEMISTRY, ACS, WASHINGTON, DC, US, vol. 19, no. 10, 1 October 2008 (2008-10-01), pages 1960-1963, XP008098503, ISSN: 1043-1802, DOI: 10.1021/BC800289A [retrieved on 2008-09-20], WO-A2-2008/052187

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (<http://worldwide.espacenet.com>) or via the search engine on our website here: <https://search.patentstyret.no/>

Patentkrav**1. Forbindelse med formel I:****I**

5 eller et farmasøytisk akseptabelt salt eller solvat derav, hvori, uavhengig for hver forekomst,

W er



R^1 er hydrogen, C_1 - C_8 -alkyl eller C_1 - C_8 -haloalkyl;

10 R^2 er hydrogen, C_1 - C_8 -alkyl eller C_1 - C_8 -haloalkyl;

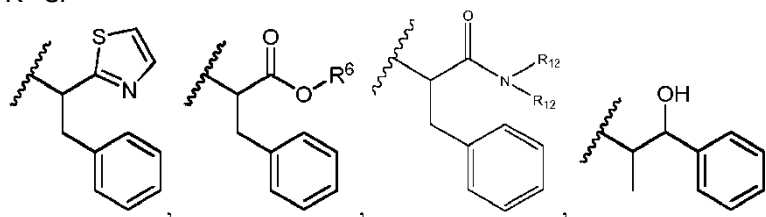
R^{3A} og R^{3B} er en av følgende:

(i) R^{3A} er C_1 - C_8 -alkyl, C_1 - C_8 -haloalkyl, C_3 - C_8 -karbocyklyl eller halogen; og

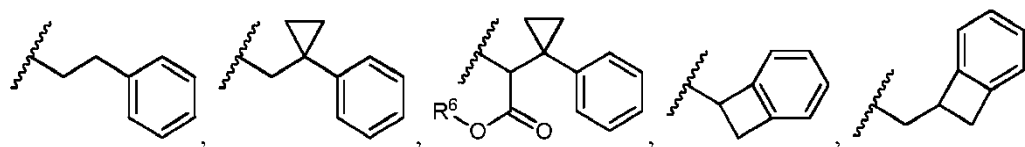
R^{3B} er C_1 - C_8 -alkyl, C_1 - C_8 -haloalkyl, C_3 - C_8 -karbocyklyl eller halogen; eller

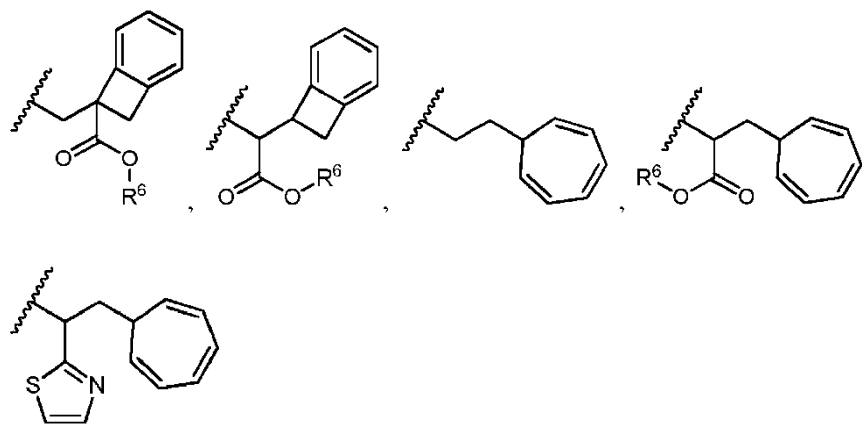
15 (ii) R^{3A} og R^{3B} sett under ett er enten C_2 - C_8 -alkylen, hvilket C_2 - C_8 -alkylen sett under ett med karbonet til hvilket det er bundet, danner en mettet karbocyklisk ring; eller C_1 - C_8 -heteroalkylen, hvilket C_1 - C_8 -heteroalkylen, sammen med karbonet til hvilket det er bundet, danner en mettet heterosyklisk ring;

R^5 er

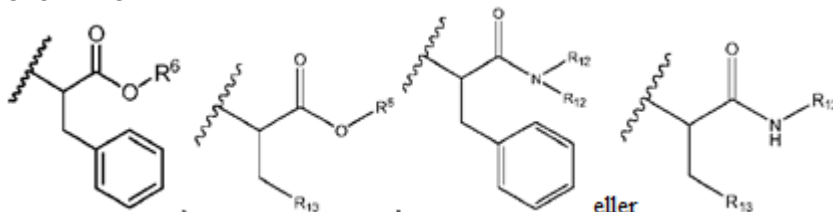


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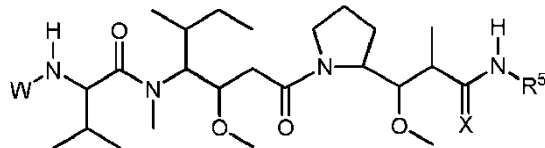




C_1 - C_{10} -heterosyklyl, C_3 - C_8 -karbosykly og C_6 - C_{14} -aryl, eventuelt substituert med
 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av $-C_1$ - C_8 -alkyl,
 $-C_1$ - C_8 -alkyl- $N(R')_2$, $-C_1$ - C_8 -alkyl- $C(O)R'$, $-C_1$ - C_8 -alkyl- $C(O)OR'$, $-O-(C_1$ - C_8 alkyl),
 $-C(O)R'$, $-OC(O)R'$, $-C(O)OR'$, $-C(O)N(R')_2$, $-NHC(O)R'$, $-S(O)_2R'$, $-S(O)R'$, $-OH$,
 halogen, $-N_3$, $-N(R')_2$, $-CN$, $-NHC(=NH)NH_2$, $-NHCONH_2$, $-S(=O)_2R'$ og $-SR'$, hvori
 hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C_1 - C_8 -alkyl og
 usubstituert aryl, eller to R' kan, sammen med nitrogenet til hvilket de er festet,
 danne et C_1 - C_{10} -heterosyklyl;
 eller R^5 er

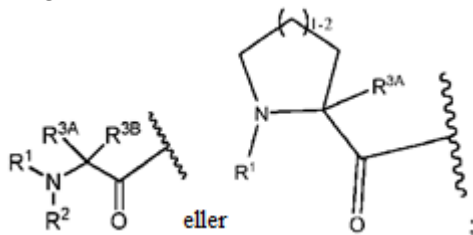


eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen
 bestående av C_1 - C_8 -alkyl, $-C_1$ - C_8 -alkyl- $N(R')_2$, $-C_1$ - C_8 -alkyl- $C(O)R'$, $-C_1$ - C_8 -alkyl-
 $C(O)OR'$, $-O-(C_1$ - C_8 -alkyl), $-C(O)R'$, $-OC(O)R'$, $-C(O)OR'$, $-C(O)N(R')_2$, $-NHC(O)R'$,
 $-S(O)_2R'$, $-S(O)R'$, $-OH$,
 halogen, $-N_3$, $-N(R')_2$, $-CN$, $-NHC(=NH)NH_2$, $-NHCONH_2$, $-S(=O)_2R'$, $-SR'$ og
 arylen- R' , hvori hver R' er uavhengig valgt fra gruppen bestående av hydrogen,
 C_1 - C_8 -alkyl, C_1 - C_8 -heterosyklyl, C_1 - C_{10} -alkylen- C_3 - C_8 -heterosyklyl og aryl, eller to R'
 kan, sammen med nitrogenet til hvilket de er festet, danne et C_1 - C_{10} -
 heterosyklyl;
 R^6 er hydrogen, $-C_1$ - C_8 -alkyl, $-C_2$ - C_8 -alkenyl, $-C_2$ - C_8 -alkynyl eller $-C_1$ - C_8 -
 haloalkyl;
 R^{12} er hydrogen, C_1 - C_4 -alkyl, C_1 - C_{10} -heterosyklyl eller C_6 - C_{14} -aryl;
 R^{13} er C_1 - C_{10} -heterosyklyl; og
 X er O.

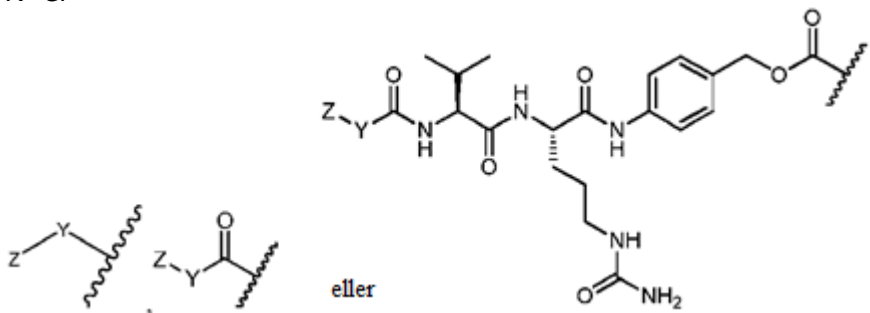
2. Forbindelse med formel IIa:**IIa**

eller et farmasøytisk akseptabelt salt eller solvat derav, hvori, uavhengig for hver forekomst,

5 W er



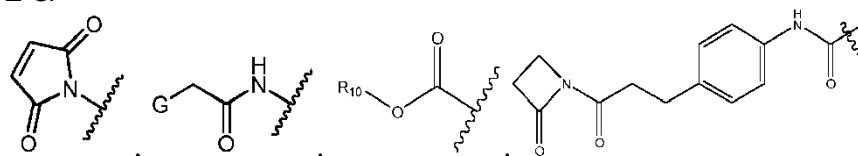
R¹ er



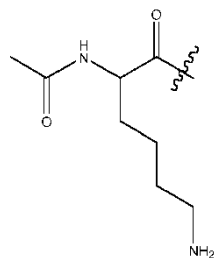
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Y er -C₂-C₂₀-alkylen-, -C₂-C₂₀-heteroalkylen-; -C₃-C₈-karbosyklo-, -arylen-, -C₃-C₈heterosyklo-, -C₁-C₁₀alkylen-arylen-, -arylen-C₁-C₁₀alkylen-, -C₁-C₁₀alkylen-(C₃-C₈karbosyklo)-, -(C₃-C₈karbosyklo)-C₁-C₁₀alkylen-, -C₁-C₁₀alkylen-(C₃-C₈heterosyklo)- eller-(C₃-C₈-heterosyklo)-C₁-C₁₀alkylen-;

Z er



15



eller -NH₂;

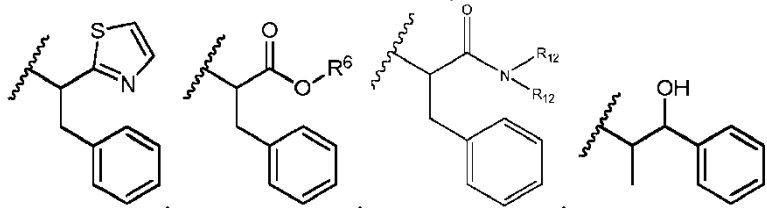
G er halogen, -OH, -SH eller -S-C₁-C₆-alkyl;

R^2 er hydrogen, C_1 - C_8 -alkyl eller C_1 - C_8 -haloalkyl;

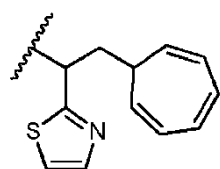
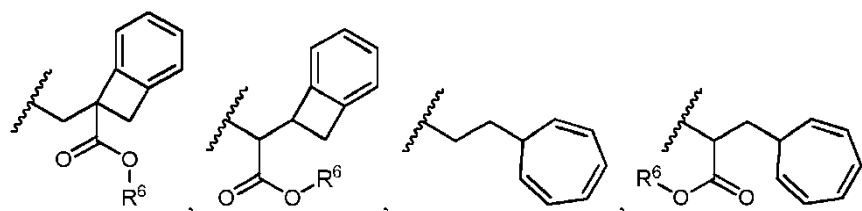
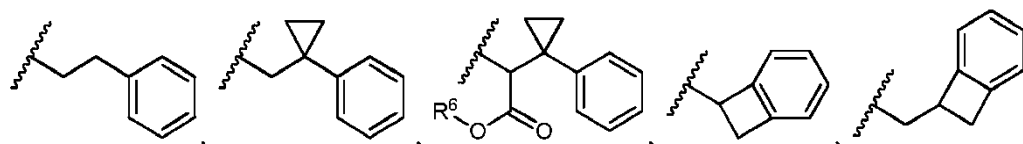
R^{3A} og R^{3B} er en av følgende:

(i) R^{3A} er C_1 - C_8 -alkyl, C_1 - C_8 -haloalkyl, C_3 - C_8 -karbocyklyl eller halogen; og R^{3B} er C_1 - C_8 -alkyl, C_1 - C_8 -haloalkyl, C_3 - C_8 -karbocyklyl eller halogen; eller

5 (ii) R^{3A} og R^{3B} sett under ett er enten C_2 - C_8 -alkylen, hvilket C_2 - C_8 -alkylen sett under ett med karbonet til hvilket det er bundet, danner en mettet karbocyklisk ring; eller C_1 - C_8 -heteroalkylen, hvilket C_1 - C_8 -heteroalkylen, sammen med karbonet til hvilket det er bundet, danner en mettet heterosyklisk ring; R^5 er



10

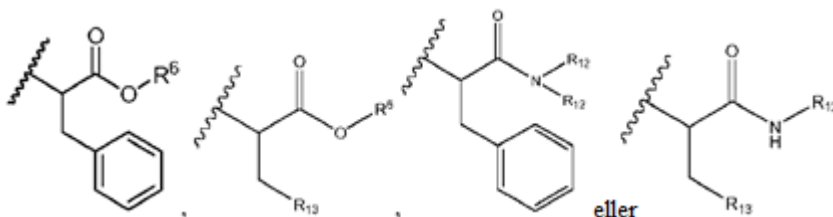


15

C_1 - C_{10} -heterosyklyl, C_3 - C_8 -karbocyklyl og C_6 - C_{14} -aryl, eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av $-C_1$ - C_8 -alkyl, $-C_1$ - C_8 -alkyl- $N(R')_2$, $-C_1$ - C_8 -alkyl- $C(O)R'$, $-C_1$ - C_8 -alkyl- $C(O)OR'$, $-O-(C_1$ - C_8 -alkyl)- $C(O)R'$, $-OC(O)R'$, $-C(O)OR'$, $-C(O)N(R')_2$, $-NHC(O)R'$, $-S(O)_2R'$, $-S(O)R'$, $-OH$, halogen, $-N_3$, $-N(R')_2$, $-CN$, $-NHC(=NH)NH_2$, $-NHCONH_2$, $-S(=O)_2R'$ og $-SR'$, hvori hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C_1 - C_8 -alkyl og usubstituert aryl, eller to R' kan, sammen med nitrogenet til hvilket de er festet, danne et C_1 - C_{10} -heterosyklyl; eller R^5 er

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5



eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av C₁-C₈-alkyl, -C₁-C₈-alkyl-N(R')₂, -C₁-C₈-alkyl-C(O)R', -C₁-C₈-alkyl-C(O)OR', -O-(C₁-C₈alkyl), -C(O)R', -OC(O)R', -C(O)OR', -C(O)N(R')₂, -NHC(O)R', -S(O)₂R', -S(O)R', -OH,

halogen, $-N_3$, $-N(R')_2$, $-CN$, $-NHC(=NH)NH_2$, $-NHCONH_2$, $-S(=O)_2R'$, $-SR'$ og arylen- R' , hvori hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C_1 - C_8 -alkyl, C_1 - C_8 heterosyklyl, C_1 - C_{10} alkylen- C_3 - C_8 heterosyklyl og aryl, eller to R' kan, sammen med nitrogenet til hvilket de er festet, danne et C_1 - C_{10} -heterosyklyl;

R⁶ er hydrogen, -C₁-C₈alkyl, -C₂-C₈alkenyl, -C₂-C₈alkynyl eller -C₁-C₈haloalkyl;

R¹² er hydrogen, C₁-C₄alkyl, C₁-C₁₀heterosyklyl eller C₆-C₁₄aryl;

R¹³ er C₁-C₁₀heterosyklyl; og

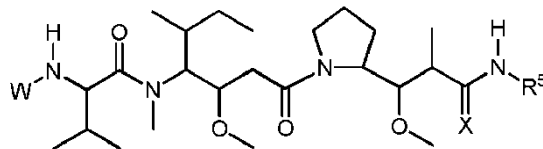
R⁷ er for hver forekomst uafhængig valgt fra gruppen bestående af F, Cl, I, Br, NO₂, CN og CF₃;

R¹⁰ er hydrogen, -C₁-C₁₀alkyl, -C₃-C₈karbosyklyl, -aryl, -C₁-C₁₀heteroalkyl, -C₃-C₈heterosyklo, -C₁-C₁₀alkylen-aryl, -arylen-C₁-C₁₀alkyl, -C₁-C₁₀alkylen-(C₃-C₈karbosyklo), -(C₃-C₈ karbosyklo)-C₁-C₁₀alkyl, -C₁-C₁₀alkylen-(C₃-C₈heterosyklo), og -(C₃-C₈-heterosyklo)-C₁-C₁₀alkyl, der aryl på R₁₀ omfattende aryl eventuelt er substitueret med [R₇]_h;

h er 1, 2, 3, 4 eller 5; og

$X \in \mathbb{R}^n$.

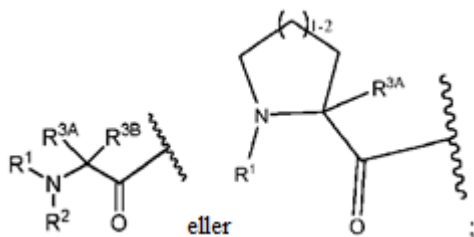
3. Forbindelse med formel **IIIa**:



IIIa

eller et farmasøytisk akseptabelt salt eller solvat derav, hvori, uavhengig for hver forekomst.

W er



R¹ er hydrogen, C₁-C₈-alkyl eller C₁-C₈-haloalkyl;

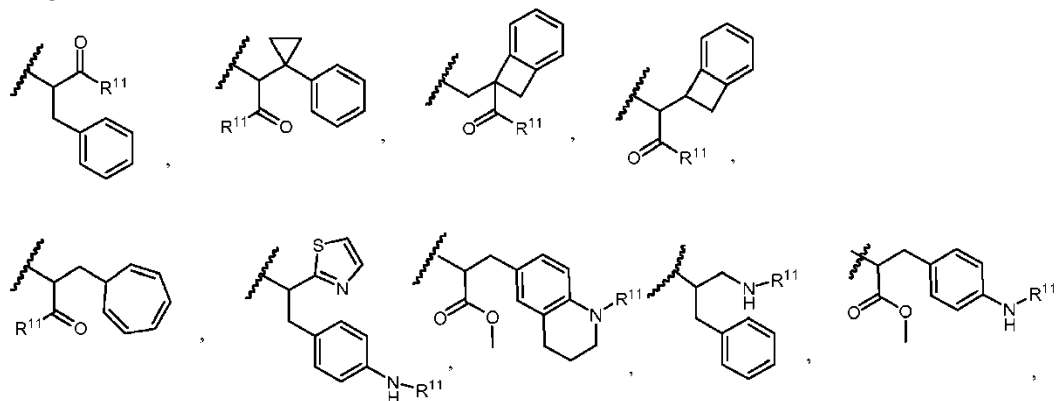
R² er hydrogen, C₁-C₈-alkyl eller C₁-C₈-haloalkyl;

R^{3A} og R^{3B} er en av følgende:

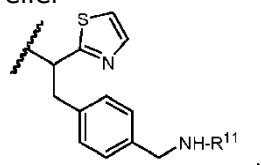
- 5 (i) R^{3A} er C₁-C₈-alkyl, C₁-C₈-haloalkyl, C₃-C₈-karbosyklyl eller halogen; og

R^{3B} er C₁-C₈-alkyl, C₁-C₈-haloalkyl, C₃-C₈-karbocyklyl eller halogen; eller

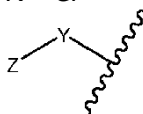
- (ii) R^{3A} og R^{3B} sett under ett er enten C₂-C₈-alkylen, hvilket C₂-C₈-alkylen sett under ett med karbonet til hvilket det er bundet, danner en mettet karbosyklisk ring; eller C₁-C₈-heteroalkylen, hvilket C₁-C₈-heteroalkylen, sammen med karbonet til hvilket det er bundet, danner en mettet heterosyklisk ring;

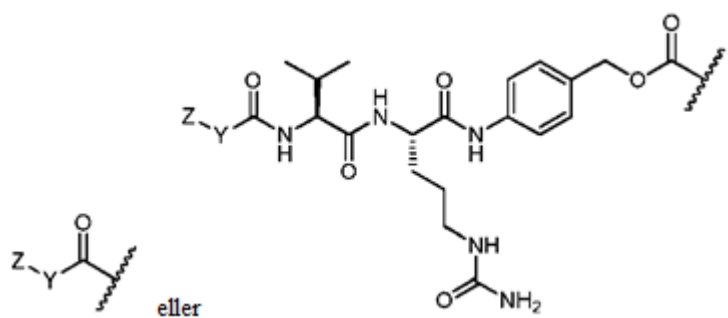
 R^5 er

eller



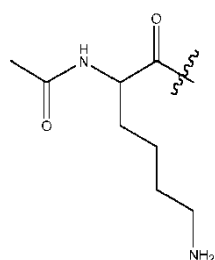
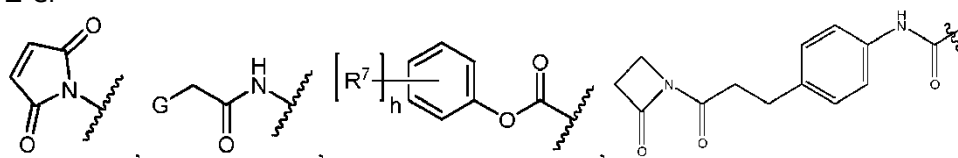
eventuelt substitueret med 1, 2, 3, 4 eller 5 grupper uafhængigt valgt fra gruppen bestående af C₁-C₈-alkyl, -O-(C₁-C₈alkyl), -C(O)R', -OC(O)R', -C(O)OR', -C(O)NH₂, -C(O)NHR', -C(O)N(R')₂, -NHC(O)R', -S(O)₂R', -S(O)R', -OH, halogen, -N₃, -NH₂, -NH(R'), -N(R')₂, -CN, -NHC(=NH)NH₂, -NHCONH₂, -S(=O)₂R' og -SR', hvori hver R' er uafhængigt valgt fra gruppen bestående af hydrogen, C₁-C₈-alkyl og usubstitueret aryl;

 R^{11} er



5 Y er -C₂-C₂₀-alkylen-, -C₂-C₂₀-heteroalkylen-, C₃-C₈-karbosyklo-, -arylen-, -C₃-C₈-heterosyklo-, -C₁-C₁₀-alkylen-arylen-, -arylen-C₁-C₁₀-alkylen-, -C₁-C₁₀-alkylen-(C₃-C₈-karbosyklo)-, -(C₃-C₈-karbosyklo)-C₁-C₁₀-alkylen-, -C₁-C₁₀-alkylen-(C₃-C₈-heterosyklo)- eller -(C₃-C₈-heterosyklo)-C₁-C₁₀-alkylen-;

Z er



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eller -NH₂;

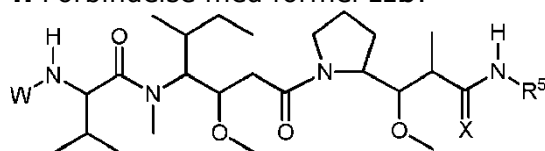
G er halogen, -OH, -SH eller -S-C₁-C₆alkyl;

R⁷ er for hver forekomst uavhengig valgt fra gruppen bestående av F, Cl, I, Br, NO₂, CN og CF₃;

15 h er 1, 2, 3, 4 eller 5; og

X er O.

4. Forbindelse med formel **IIb**:



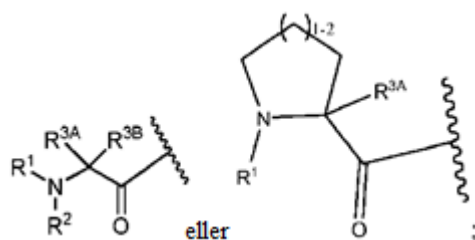
IIb

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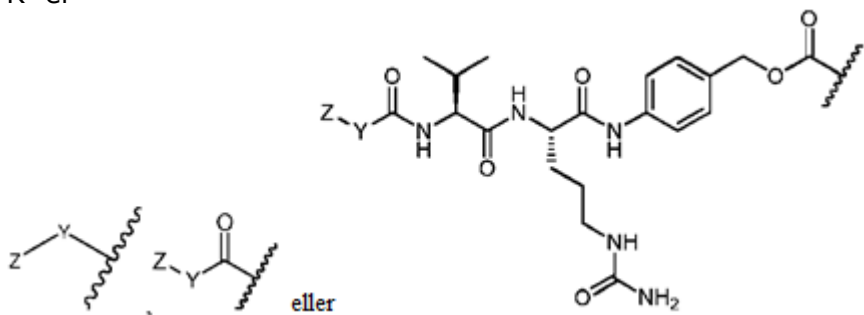
eller et farmasøytisk akseptabelt salt eller solvat derav, hvori, uavhengig for hver forekomst,

W er

8

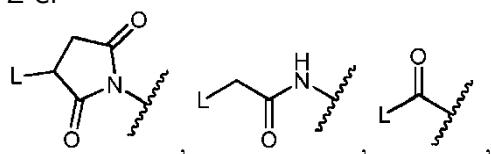


R^1 er

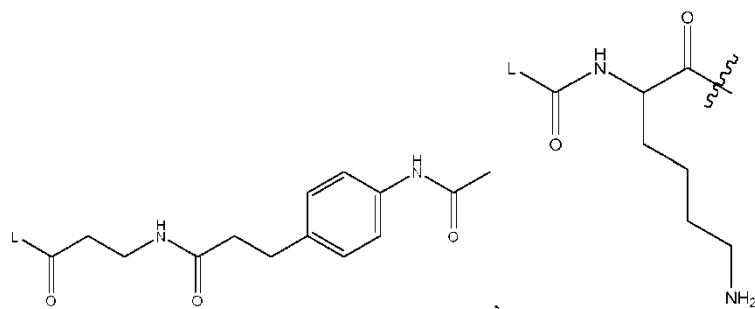


5 Y er $-C_2-C_{20}$ -alkylen-, $-C_2-C_{20}$ -heteroalkylen-, $-C_3-C_8$ -karbosyklo-, -arylen-, $-C_3-C_8$ heterosyklo-, $-C_1-C_{10}$ alkylen-arylen-, -arylen- $-C_1-C_{10}$ alkylen-, $-C_1-C_{10}$ alkylen- $(C_3-C_8$ karbosyklo)-, $-(C_3-C_8$ karbosyklo)- $-C_1-C_{10}$ alkylen-, $-C_1-C_{10}$ alkylen- $(C_3-C_8$ heterosyklo)-, eller- $(C_3-C_8$ -heterosyklo)- $-C_1-C_{10}$ alkylen-;

Z er



10



eller -NHL;

L er et antistoff;

R^2 er hydrogen, C_1-C_8 -alkyl eller C_1-C_8 -haloalkyl;

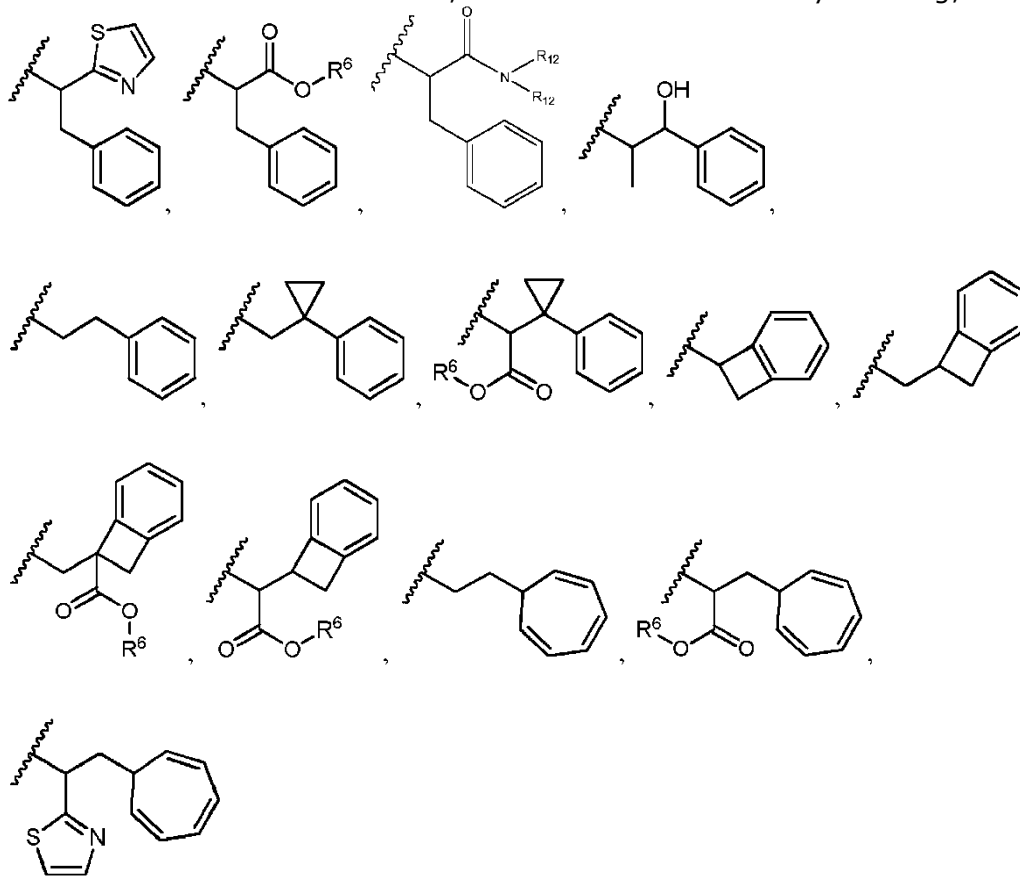
15 R^{3A} og R^{3B} er en av følgende:

(i) R^{3A} er C_1-C_8 -alkyl, C_1-C_8 -haloalkyl, C_3-C_8 -karbosyklil eller halogen; og

R^{3B} er C_1-C_8 -alkyl, C_1-C_8 -haloalkyl, C_3-C_8 -karbosyklil eller halogen; eller

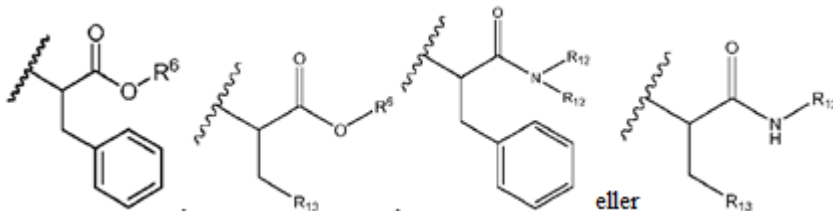
(ii) R^{3A} og R^{3B} sett under ett er enten C_2-C_8 -alkylen, hvilket C_2-C_8 -alkylen sett under ett med karbonet til hvilket det er bundet, danner en mettet karbosyklisk

ring; eller C₁-C₈-heteroalkylen, hvilket C₁-C₈-heteroalkylen, sammen med karbonet til hvilket det er bundet, danner en mettet heterosyklisk ring; R⁵ er



5

- 10 C₁-C₁₀-heterosyklyl, C₃-C₈-karbosykly og C₆-C₁₄-aryl eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av -C₁-C₈-alkyl, -C₁-C₈-alkyl-N(R')₂, -C₁-C₈-alkyl-C(O)R', -C₁-C₈-alkyl-C(O)OR' -O-(C₁-C₈alkyl), -C(O)R', -OC(O)R', -C(O)OR', -C(O)N(R')₂, -NHC(O)R', -S(O)₂R', -S(O)R', -OH, halogen, -N₃, -N(R')₂, -CN, -NHC(=NH)NH₂, -NHCONH₂, -S(=O)₂R' og -SR', hvori
- 15 hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C₁-C₈-alkyl og usubstituert aryl, eller to R' kan, sammen med nitrogenet til hvilket de er festet, danne et C₁-C₁₀-heterosyklyl;
- eller R⁵ er



eller

20

eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av C₁-C₈-alkyl, -C₁-C₈-alkyl-N(R')₂, -C₁-C₈-alkyl-C(O) R', -C₁-C₈-alkyl-

$C(O)OR'$, $-O-(C_1-C_8\text{alkyl})$, $-C(O)R'$, $-OC(O)R'$, $-C(O)OR'$, $-C(O)N(R')_2$, $-NHC(O)R'$, $-S(O)_2R'$, $-S(O)R'$, $-OH$,

halogen, $-N_3$, $-N(R')_2$, $-CN$, $-NHC(=NH)NH_2$, $-NHCONH_2$, $-S(=O)_2R'$, $-SR'$ og arylen- R' , hvori hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C_1-C_8 -alkyl, C_1-C_8 -heterosyklisk, C_1-C_{10} -alkylen- C_3-C_8 -heterosyklisk og aryl, eller to R' kan, sammen med nitrogenet til hvilket de er festet, danne et C_1-C_{10} -heterosyklisk;

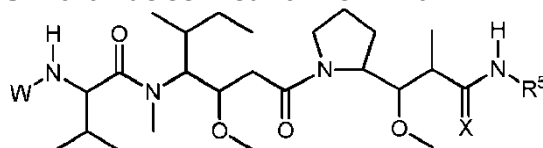
R^6 er hydrogen, $-C_1-C_8$ -alkyl, $-C_2-C_8$ -alkenyl, $-C_2-C_8$ -alkynyl eller $-C_1-C_8$ -haloalkyl;

R^{12} er hydrogen, C_1-C_4 -alkyl, C_1-C_{10} -heterosyklisk eller C_6-C_{14} -aryl;

R^{13} er C_1-C_{10} -heterosyklisk; og

X er O.

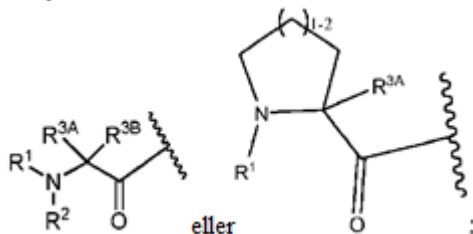
5. Forbindelse med formel **IIIb**:



IIIb

eller et farmasøytisk akseptabelt salt eller solvat derav, hvori, uavhengig for hver forekomst,

W er



R^1 er hydrogen, C_1-C_8 -alkyl eller C_1-C_8 -haloalkyl;

R^2 er hydrogen, C_1-C_8 -alkyl eller C_1-C_8 -haloalkyl;

R^{3A} og R^{3B} er en av følgende:

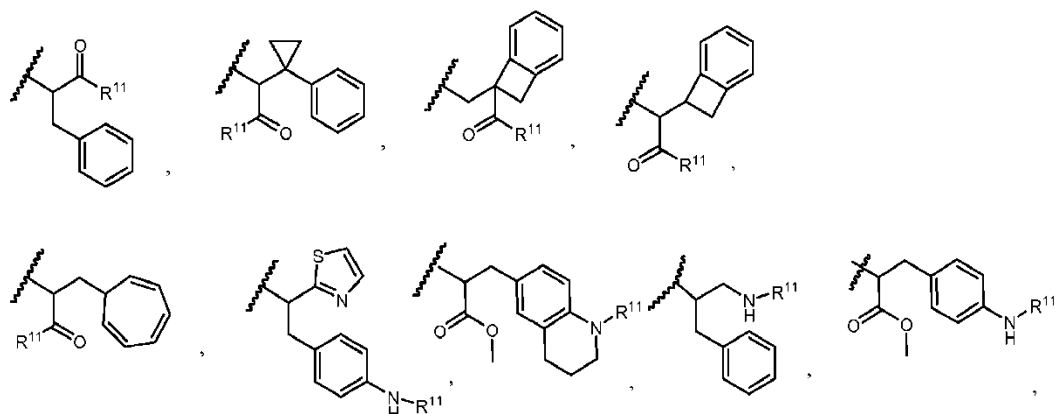
(i) R^{3A} er C_1-C_8 -alkyl, C_1-C_8 -haloalkyl, C_3-C_8 -karbosyklisk eller halogen; og

R^{3B} er C_1-C_8 -alkyl, C_1-C_8 -haloalkyl, C_3-C_8 -karbosyklisk eller halogen; eller

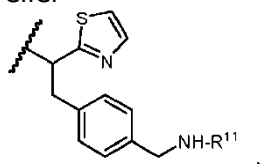
(ii) R^{3A} og R^{3B} sett under ett er enten C_2-C_8 -alkylen, hvilket C_2-C_8 -alkylen sett under ett med karbonet til hvilket det er bundet, danner en mettet karbosyklisk ring; eller C_1-C_8 -heteroalkylen, hvilket C_1-C_8 -heteroalkylen, sammen med karbonet til hvilket det er bundet, danner en mettet heterosyklisk ring;

R^5 er

11



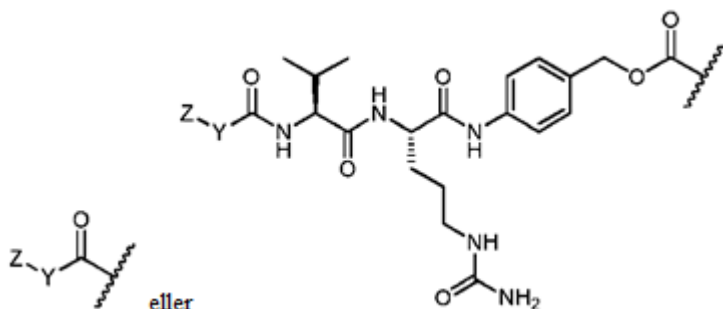
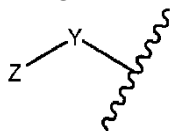
eller



5

eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av C₁-C₈-alkyl, -O-(C₁-C₈alkyl), -C(O)R', -OC(O)R', -C(O)OR', -C(O)NH₂, -C(O)NHR', -C(O)N(R')₂, -NHC(O)R', -S(O)₂R', -S(O)R', -OH, halogen, -N₃, -NH₂, -NH(R'), -N(R')₂, -CN, -NHC(=NH)NH₂, -NHCONH₂, -S(=O)₂R' og -SR', hvori hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C₁-C₈-alkyl og usubstituert aryl;

10

R¹¹ er

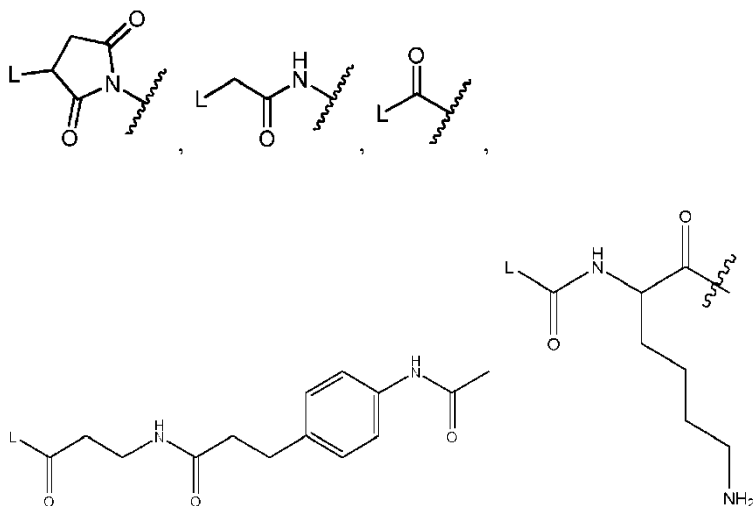
15

Y er -C₂-C₂₀-alkylen-, -C₂-C₂₀-heteroalkylen-, -C₃-C₈-karbocyklo-, -arylen-, -C₃-C₈heterocyklo-, -C₁-C₁₀alkylen-arylen-, -arylen-C₁-C₁₀alkylen-, -C₁-C₁₀alkylen-(C₃-C₈karbocyklo)-, -(C₃-C₈karbocyklo)-C₁-C₁₀alkylen-, -C₁-C₁₀alkylen-(C₃-C₈heterocyklo)- eller-(C₃-C₈ heterocyklo)-C₁-C₁₀alkylen-;

20

Z er

12

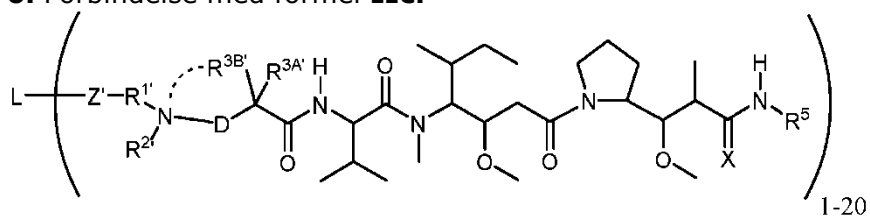


eller -NHL;

5 L er et antistoff;

X er O.

6. Forbindelse med formel **IIc**:

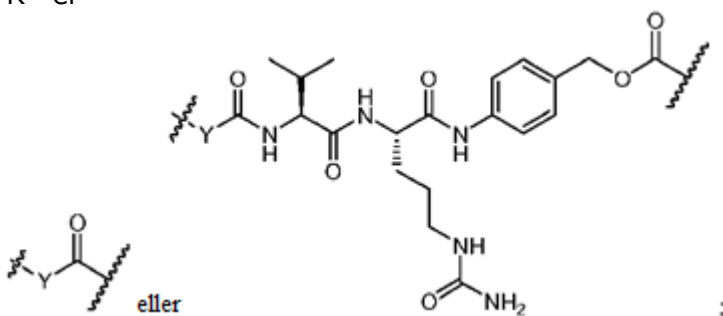


10

IIc

eller et farmasøytisk akseptabelt salt eller solvat derav, hvori, uafhængig for hver forekomst,

R^{1'} er

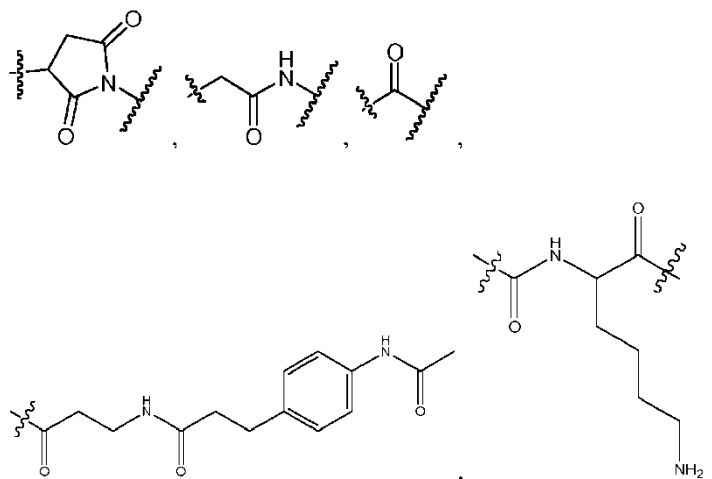


15

Y er -C₂-C₂₀-alkylen-, -C₂-C₂₀-heteroalkylen-, -C₃-C₈-karbosyklo-, -arylen-, -C₃-C₈heterosyklo-, -C₁-C₁₀alkylen-arylen-, -arylen-C₁-C₁₀alkylen-, -C₁-C₁₀alkylen-(C₃-C₈karbosyklo)-, -(C₃-C₈karbosyklo)-C₁-C₁₀alkylen-, -C₁-C₁₀alkylen-(C₃-C₈heterosyklo)- eller-(C₃-C₈ heterosyklo)-C₁-C₁₀alkylen-;

Z' er

13



eller -NH-;

5 L er et antistoff;

D er fraværende;

R^{2i} er hydrogen, C_1 - C_8 -alkyl, C_1 - C_8 -haloalkyl eller er fraværende hvis



er til stede;

10 R^{3A_i} og R^{3B_i} er en av følgende:

(i) R^{3A_i} er C_1 - C_8 -alkyl, C_1 - C_8 -haloalkyl, C_3 - C_8 -karbocyklyl eller halogen; og

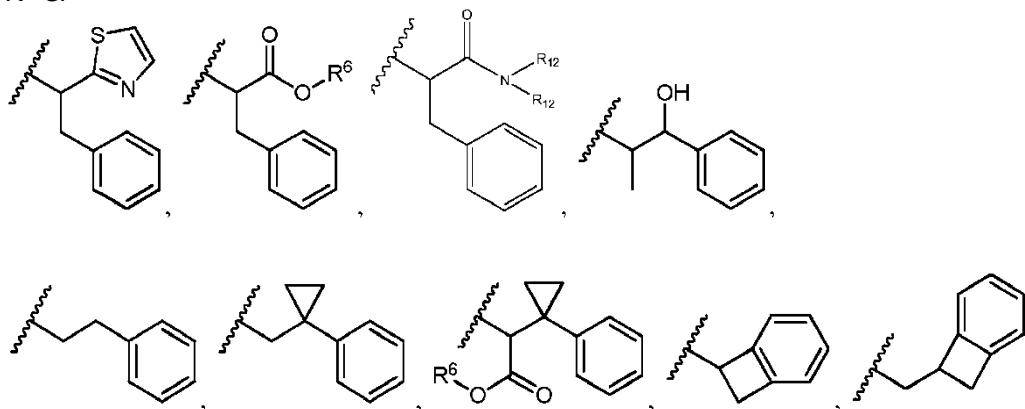
R^{3B_i} er C_1 - C_8 -alkyl, C_1 - C_8 -haloalkyl, C_3 - C_8 -karbocyklyl, eller halogen, eller R^{3B_i} er C_2 - C_4 -alkylen og danner en mettet 5- til 6-leddet ring som angitt ved

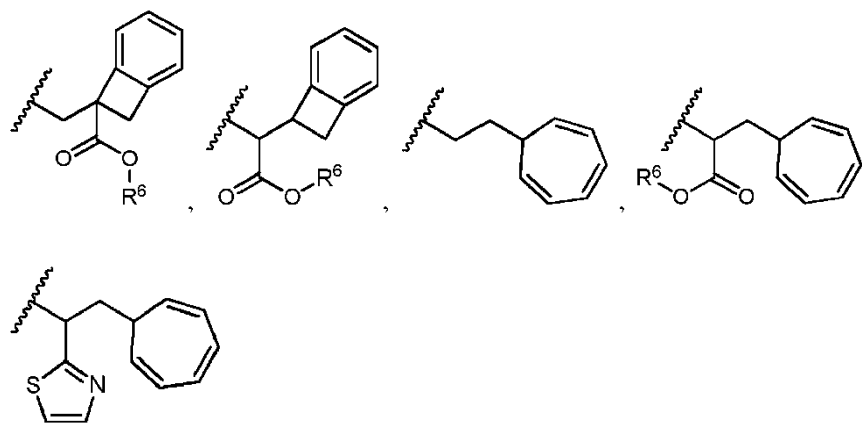


15 eller

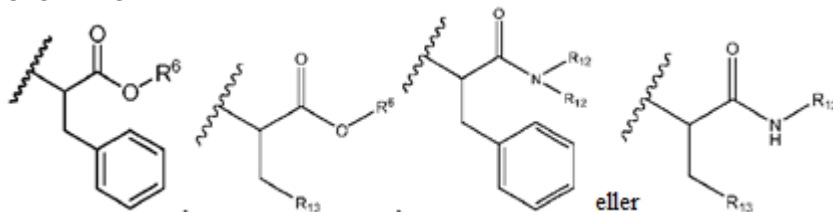
(ii) R^{3A_i} og R^{3B_i} sett under ett er begge C_2 - C_8 -alkylen, hvilket C_2 - C_8 -alkylen sett under ett med karbonet til hvilket det er bundet, danner en mettet karbocyklisk ring; eller C_1 - C_8 -heteroalkylen, hvilket C_1 - C_8 -heteroalkylen, sammen med karbonet til hvilket det er bundet, danner en mettet heterosyklisk ring;

20 R^5 er





C_1 - C_{10} -heterosyklyl, C_3 - C_8 -karbosykly og C_6 - C_{14} -aryl eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av - C_1 - C_8 -alkyl, - C_1 - C_8 -alkyl- $N(R')_2$, - C_1 - C_8 -alkyl- $C(O)R'$, - C_1 - C_8 -alkyl- $C(O)OR'$, - $O-(C_1-C_8alkyl)-C(O)R'$, - $OC(O)R'$, - $C(O)OR'$, - $C(O)N(R')_2$, - $NHC(O)R'$, - $S(O)_2R'$, - $S(O)R'$, -OH, halogen, - N_3 , - $N(R')_2$, -CN, - $NHC(=NH)NH_2$, - $NHCONH_2$, - $S(=O)_2R'$ og - SR' , hvori hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C_1 - C_8 -alkyl og usubstituert aryl, eller to R' kan, sammen med nitrogenet til hvilket de er festet, danne et C_1 - C_{10} -heterosyklyl; eller R^5 er



eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av C_1 - C_8 alkyl, - C_1 - C_8 alkyl- $N(R')_2$, - C_1 - C_8 alkyl- $C(O)R'$, - C_1 - C_8 alkyl- $C(O)OR'$, - $O-(C_1-C_8alkyl)-C(O)R'$, - $OC(O)R'$, - $C(O)OR'$, - $C(O)N(R')_2$, - $NHC(O)R'$, - $S(O)_2R'$, - $S(O)R'$, -OH, halogen, - N_3 , - $N(R')_2$, -CN, - $NHC(=NH)NH_2$, - $NHCONH_2$, - $S(=O)_2R'$, - SR' og arylen- R' , hvori hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C_1 - C_8 -alkyl, C_1 - C_8 heterosyklyl, C_1 - C_{10} alkylen- C_3 - C_8 heterosyklyl og aryl, eller to R' kan, sammen med nitrogenet til hvilket de er festet, danne et C_1 - C_{10} -heterosyklyl;

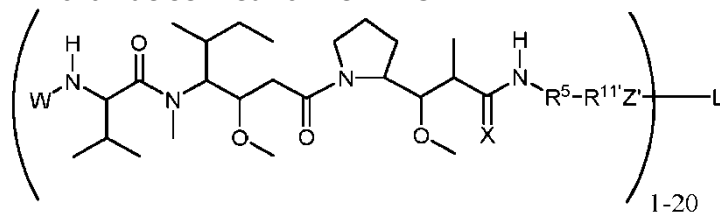
R^6 er hydrogen, - C_1 - C_8 -alkyl, - C_2 - C_8 -alkenyl, - C_2 - C_8 -alkynyl eller - C_1 - C_8 -haloalkyl;

R^{12} er hydrogen, C_1 - C_4 -alkyl, C_1 - C_{10} -heterosyklyl eller C_6 - C_{14} -aryl;

R^{13} er C_1 - C_{10} -heterosyklyl; og

X er O.

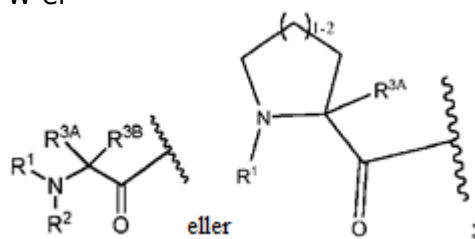
7. Forbindelse med formel **IIIc**:



IIIc

eller et farmasøytisk akseptabelt salt eller solvat derav, hvori, uavhengig for
hver forekomst,

W er



R^1 er hydrogen, C_1 - C_8 -alkyl eller C_1 - C_8 -haloalkyl;

R^2 er hydrogen, C_1 - C_8 -alkyl eller C_1 - C_8 -haloalkyl;

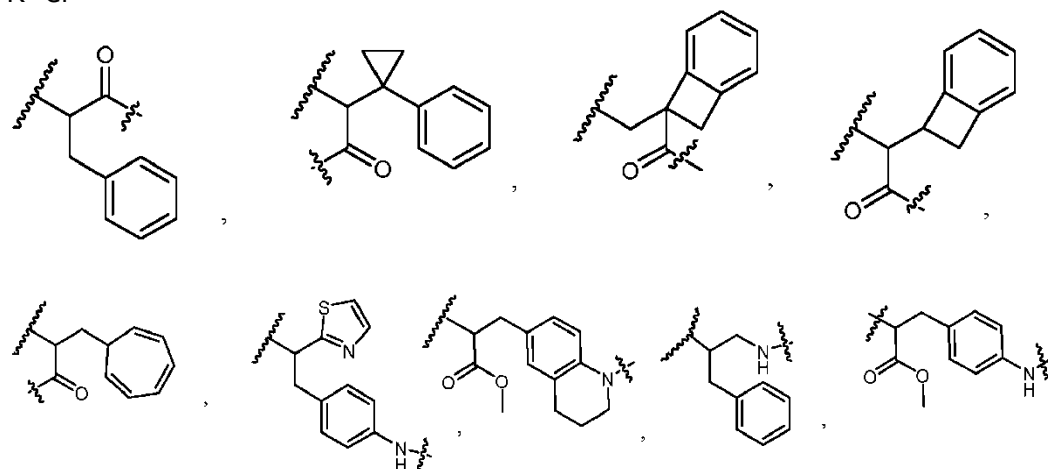
R^{3A} og R^{3B} er en av følgende:

(i) R^{3A} er C_1 - C_8 -alkyl, C_1 - C_8 -haloalkyl, C_3 - C_8 -karbocyklyl eller halogen; og

R^{3B} er C_1 - C_8 -alkyl, C_1 - C_8 -haloalkyl, C_3 - C_8 -karbocyklyl eller halogen; eller

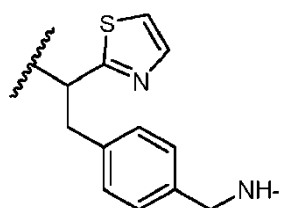
(ii) R^{3A} og R^{3B} sett under ett er enten C_2 - C_8 -alkylen, hvilket C_2 - C_8 -alkylen sett under ett med karbonet til hvilket det er bundet, danner en mettet karbocyklisk ring; eller C_1 - C_8 -heteroalkylen, hvilket C_1 - C_8 -heteroalkylen, sammen med karbonet til hvilket det er bundet, danner en mettet heterosyklisk ring;

R^5 er

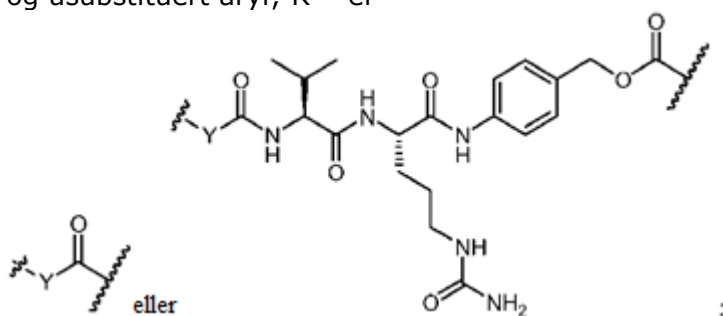


eller

16

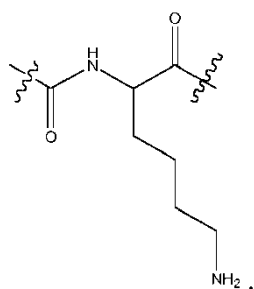
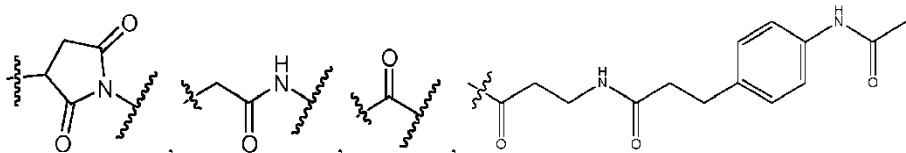


eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av C_1 - C_8 -alkyl, $-O-(C_1-C_8\text{alkyl})$, $-C(O)R'$, $-OC(O)R'$, $-C(O)OR'$, $-C(O)NH_2$, $-C(O)NHR'$, $-C(O)N(R')_2$, $-NHC(O)R'$, $-S(O)_2R'$, $-S(O)R'$, $-OH$, halogen, $-N_3$, $-NH_2$, $-NH(R')$, $-N(R')_2$, $-CN$, $-NHC(=NH)NH_2$, $-NHCONH_2$, $-S(=O)_2R'$ og $-SR'$, hvori hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C_1 - C_8 -alkyl og usubstituert aryl; R^{11} er



Y er $-C_2-C_{20}$ -alkylen-, $-C_2-C_{20}$ -heteroalkylen-, $-C_3-C_8$ -karbosyklo-, -arylen-, $-C_3-C_8$ heterosyklo-, $-C_1-C_{10}$ alkylen-arylen-, -arylen- $-C_1-C_{10}$ alkylen-, $-C_1-C_{10}$ alkylen- $(C_3-C_8\text{karbosyklo})$ -, $-(C_3-C_8\text{karbosyklo})-C_1-C_{10}$ alkylen-, $-C_1-C_{10}$ alkylen- $(C_3-C_8\text{heterosyklo})$ -, eller $-(C_3-C_8\text{heterosyklo})-C_1-C_{10}$ alkylen-;

Z' er



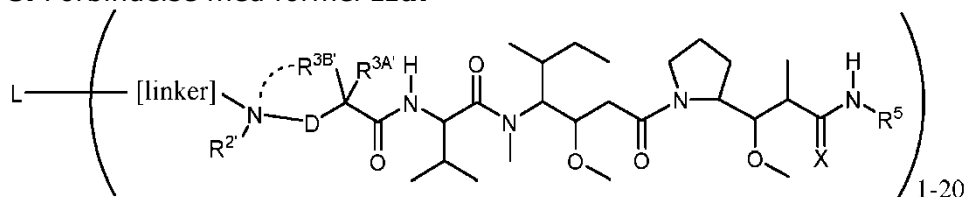
eller $-NH-$;

L er et antistoff;

X er O .

20

8. Forbindelse med formel **IId:**



Ild

eller et farmasøytisk akseptabelt salt eller solvat derav, hvori, uavhengig for hver forekomst.

5 L er et antistoff;

[linker] er en divalent linker;

D er fraværende;

R²¹ er hydrogen, C₁-C₈-alkyl, C₁-C₈-haloalkyl eller er fraværende hvis

10 er til stede;

$R^{3A'}$ og $R^{3B'}$ er en av følgende:

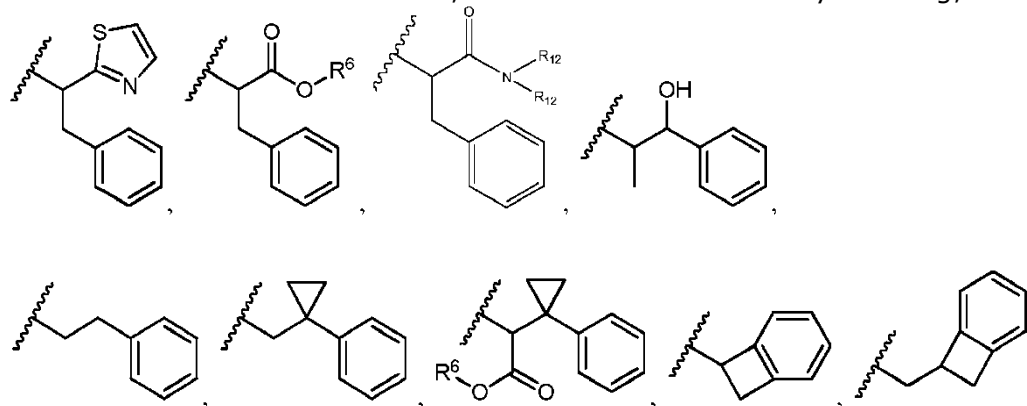
(i) R^{3A} er C₁-C₈-alkyl, C₁-C₈-haloalkyl, C₃-C₈-karbocyklyl eller halogen; og

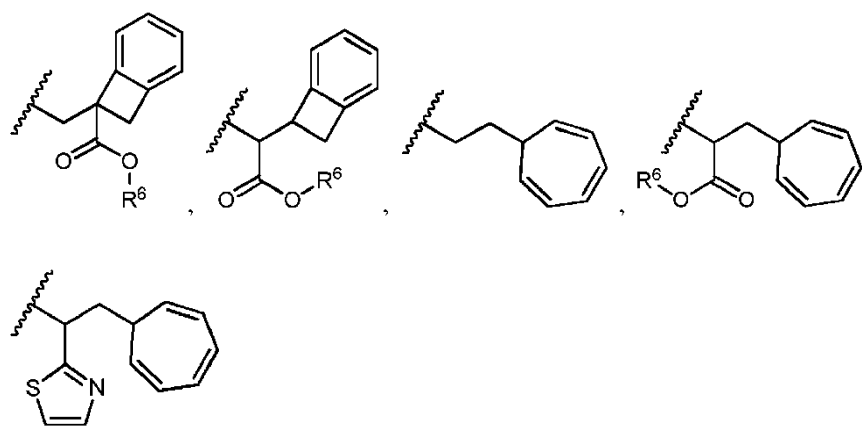
R^{3B1} er C₁-C₈-alkyl, C₁-C₈-haloalkyl, C₃-C₈-karbosyklyl, eller R^{3B1} er C₂-C₄-alkylen og danner en mettet 5- til 6-leddet ring som angitt ved ;

15

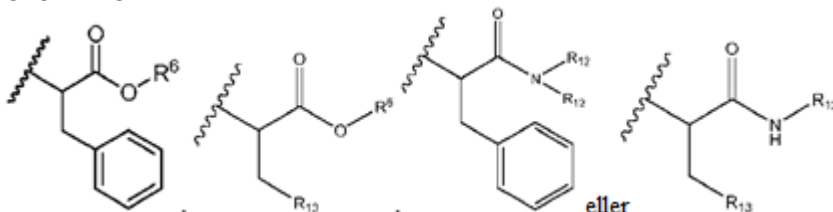
eller

(ii) R^{3A'} og R^{3B'} sett under ett er enten C₂-C₈-alkylen, hvilket C₂-C₈-alkylen sett under ett med karbonet til hvilket det er bundet, danner en mettet karbosyklisk ring; eller C₁-C₈-heteroalkylen, hvilket C₁-C₈-heteroalkylen, sammen med karbonet til hvilket det er bundet, danner en mettet heterosyklisk ring; R⁵ er





C_1 - C_{10} -heterosyklyl, C_3 - C_8 -karbosykly og C_6 - C_{14} -aryl eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av $-C_1$ - C_8 -alkyl, $-C_1$ - C_8 -alkyl- $N(R')_2$, $-C_1$ - C_8 -alkyl- $C(O)R'$, $-C_1$ - C_8 -alkyl- $C(O)OR'$, $-O-(C_1-C_8alkyl)-C(O)R'$, $-OC(O)R'$, $-C(O)OR'$, $-C(O)N(R')_2$, $-NHC(O)R'$, $-S(O)_2R'$, $-S(O)R'$, $-OH$, halogen, $-N_3$, $-N(R')_2$, $-CN$, $-NHC(=NH)NH_2$, $-NHCONH_2$, $-S(=O)_2R'$ og $-SR'$, hvori hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C_1 - C_8 -alkyl og usubstituert aryl, eller to R' kan, sammen med nitrogenet til hvilket de er festet, danne et C_1 - C_{10} -heterosyklyl; eller R^5 er



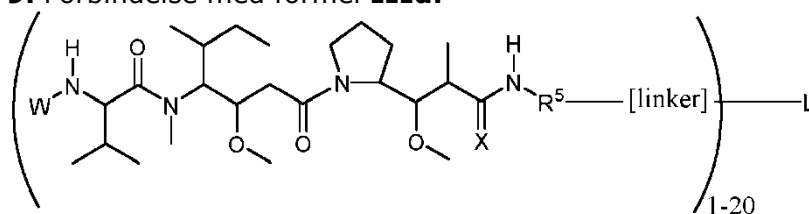
eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av C_1 - C_8 -alkyl, $-C_1$ - C_8 -alkyl- $N(R')_2$, $-C_1$ - C_8 -alkyl- $C(O)R'$, $-C_1$ - C_8 -alkyl- $C(O)OR'$, $-O-(C_1-C_8alkyl)-C(O)R'$, $-OC(O)R'$, $-C(O)OR'$, $-C(O)N(R')_2$, $-NHC(O)R'$, $-S(O)_2R'$, $-S(O)R'$, $-OH$, halogen, $-N_3$, $-N(R')_2$, $-CN$, $-NHC(=NH)NH_2$, $-NHCONH_2$, $-S(=O)_2R'$, $-SR'$ og arylen- R' , hvori hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C_1 - C_8 -alkyl, C_1 - C_8 -heterosyklyl, C_1 - C_{10} -alkylen- C_3 - C_8 -heterosyklyl og aryl, eller to R' kan, sammen med nitrogenet til hvilket de er festet, danne et C_1 - C_{10} -heterosyklyl;

R^6 er hydrogen, $-C_1$ - C_8 -alkyl, $-C_2$ - C_8 -alkenyl, $-C_2$ - C_8 -alkynyl eller $-C_1$ - C_8 -haloalkyl;

R^{12} er hydrogen, C_1 - C_4 -alkyl, C_1 - C_{10} -heterosyklyl eller C_6 - C_{14} -aryl;

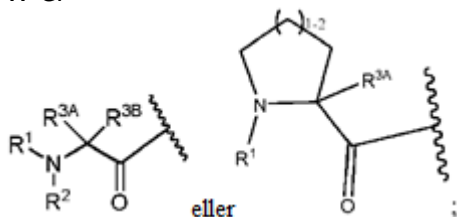
R^{13} er C_1 - C_{10} -heterosyklyl; og

X er O.

9. Forbindelse med formel IIIId:**IIIId**

eller et farmasøytisk akseptabelt salt eller solvat derav, hvori, uavhengig for hver forekomst,

5 W er



R^1 er hydrogen, C_1 - C_8 -alkyl eller C_1 - C_8 -haloalkyl;

R^2 er hydrogen, C_1 - C_8 -alkyl eller C_1 - C_8 -haloalkyl;

R^{3A} og R^{3B} er en av følgende:

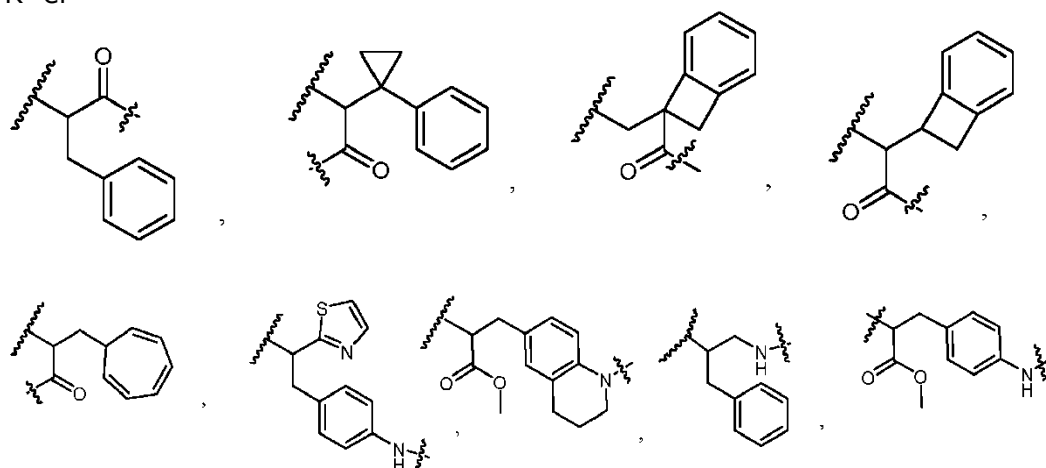
10 (i) R^{3A} er C_1 - C_8 -alkyl, C_1 - C_8 -haloalkyl, C_3 - C_8 -karbocyklil eller halogen; og

R^{3B} er C_1 - C_8 -alkyl, C_1 - C_8 -haloalkyl, C_3 - C_8 -karbocyklil eller halogen; eller

(ii) R^{3A} og R^{3B} sett under ett er enten C_2 - C_8 -alkylen, hvilket C_2 - C_8 -alkylen sett under ett med karbonet til hvilket det er bundet, danner en mettet karbocyklisk ring; eller C_1 - C_8 -heteroalkylen, hvilket C_1 - C_8 -heteroalkylen, sammen med

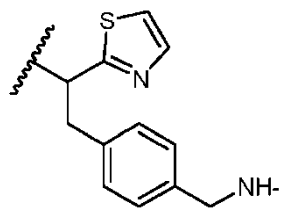
15 karbonet til hvilket det er bundet, danner en mettet heterosyklisk ring;

R^5 er



20 eller

20



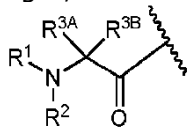
eventuelt substituert med 1, 2, 3, 4 eller 5 grupper uavhengig valgt fra gruppen bestående av C_1 - C_8 -alkyl, $-O-(C_1-C_8\text{alkyl})$, $-C(O)R'$, $-OC(O)R'$, $-C(O)OR'$, $-C(O)NH_2$, $-C(O)NHR'$, $-C(O)N(R')_2$, $-NHC(O)R'$, $-S(O)_2R'$, $-S(O)R'$, $-OH$, halogen, $-N_3$, $-NH_2$, $-NH(R')$, $-N(R')_2$, $-CN$, $-NHC(=NH)NH_2$, $-NHCONH_2$, $-S(=O)_2R'$ og $-SR'$, hvori hver R' er uavhengig valgt fra gruppen bestående av hydrogen, C_1 - C_8 -alkyl og usubstituert aryl;

[linker] er en divalent linker;

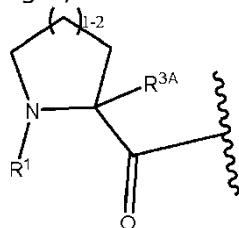
L er et antistoff;

X er O.

10. Forbindelsen, saltet eller solvatet ifølge hvilke som helst av kravene 1-5, 7 og 9, hvori W er



11. Forbindelsen, saltet eller solvatet ifølge hvilke som helst av kravene 1-5, 7 og 9, hvori W er



12. Forbindelsen, saltet eller solvatet ifølge hvilke som helst av kravene 1-5, 7 og 9, hvori R^2 er hydrogen eller C_1 - C_8 -alkyl.

13. Forbindelsen, saltet eller solvatet ifølge hvilke som helst av kravene 1-5, 7 og 9, hvori R^{3A} er C_1 - C_8 -alkyl, foretrukket metyl.

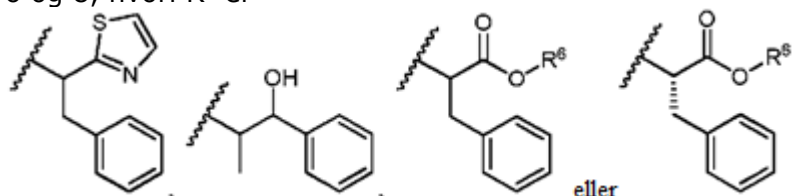
14. Forbindelsen, saltet eller solvatet ifølge hvilke som helst av kravene 1-5, 7 og 9, hvori R^{3A} og R^{3B} sett under ett er enten C_2 - C_8 -alkylen, hvilket C_2 - C_8 -alkylen sett under ett med karbonet til hvilket det er bundet, danner en mettet karbosyklisk ring; eller C_1 - C_8 -heteroalkylen, hvilket C_1 - C_8 -heteroalkylen, sammen med karbonet til hvilket det er bundet, danner en mettet heterosyklisk ring.

15. Forbindelsen, saltet eller solvatet ifølge krav 14, hvori R^{3A} og R^{3B} sett under ett er $-CH_2CH_2-$, hvilket $-CH_2CH_2-$ sett under ett med karbonet til hvilket det er bundet danner syklopropyl.

16. Forbindelsen, saltet eller solvatet ifølge krav 14, hvori R^{3A} og R^{3B} sett under ett er $-CH_2CH_2CH_2CH_2-$, hvilket $-CH_2CH_2CH_2CH_2-$ sett under ett med karbonet til hvilket det er bundet danner syklopentyl.

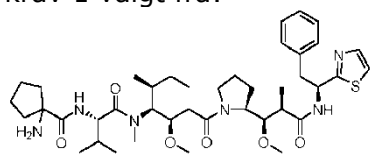
17. Forbindelsen, saltet eller solvatet ifølge krav 14, hvori R^{3A} og R^{3B} sett under ett er $-CH_2OCH_2-$, hvilket $-CH_2OCH_2-$ sett under ett med karbonet til hvilket det er bundet danner oksetanyl.

18. Forbindelsen, saltet eller solvatet ifølge hvilke som helst av kravene 1-2, 4, 6 og 8, hvori R^5 er

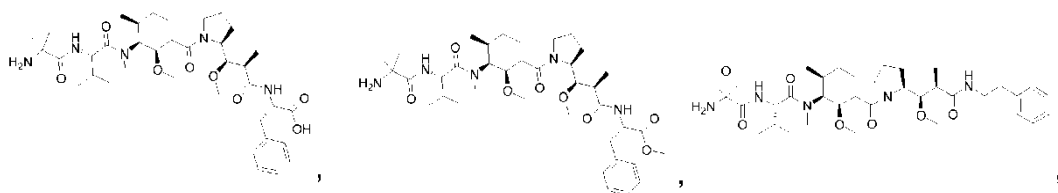
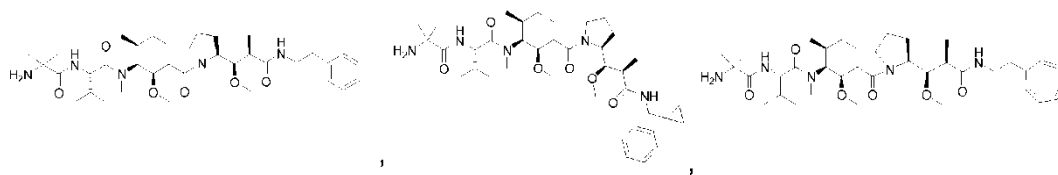
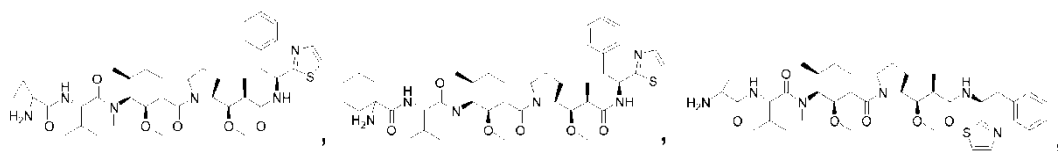


19. Forbindelsen, saltet eller solvatet ifølge hvilke som helst av kravene 4-9, hvori antistoffet er valgt fra trastuzumab, oregovomab, edrecolomab, cetuximab, et humanisert monoklonalt antistoff til vitronektinreseptoren ($\alpha_v\beta_3$); alemtuzumab; et humanisert anti-HLA-DR-antistoff for behandling av non-Hodgkins lymfom; 1311 Lym-1; et murint anti-HLA-Dr10-antistoff for behandling av non-Hodgkins lymfom; et humanisert anti-CD2 mAb for behandling av Hodgkins sykdom eller non-Hodgkins lymfom; labetuzumab; bevacizumab; ibritumomab tiuxetan; ofatumumab; panitumumab; rituximab; tositumomab; ipilimumab; gemtuzumab; et anti-IL13-antistoff; og et anti-Notch-antistoff.

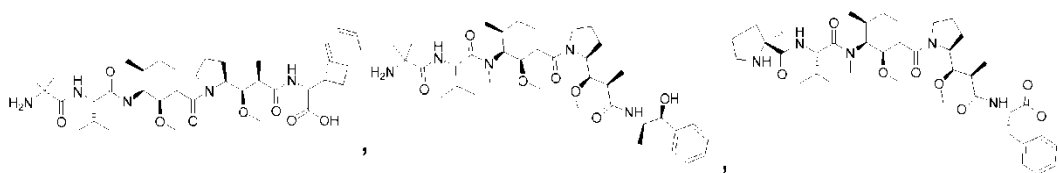
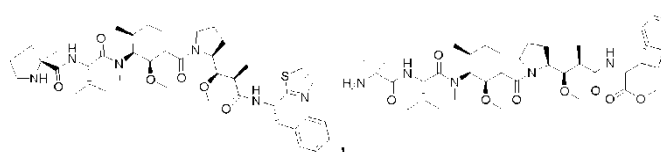
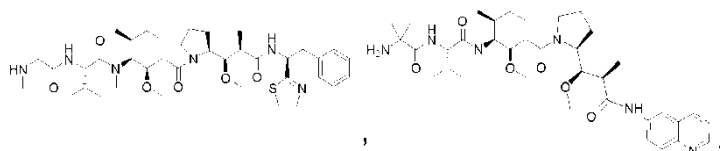
20. Forbindelse eller et farmasøytisk akseptabelt salt eller solvat derav ifølge krav 1 valgt fra:



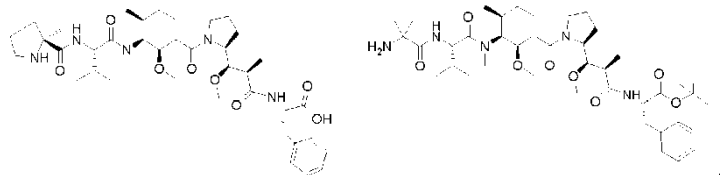
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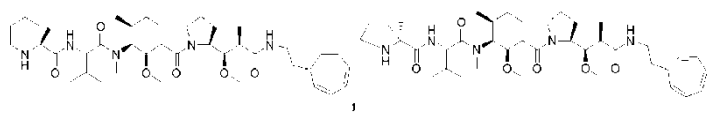
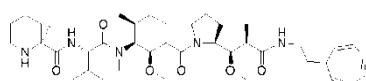
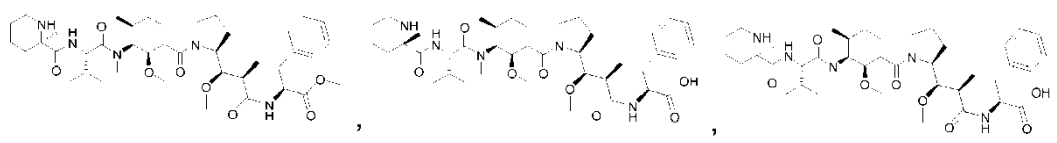
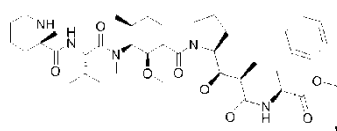
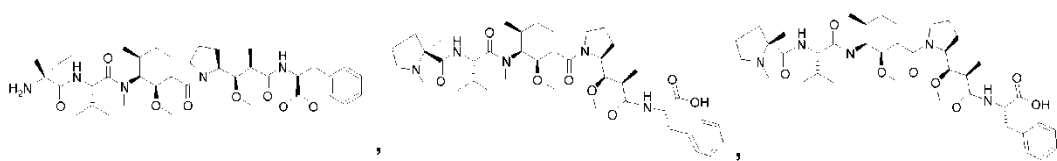
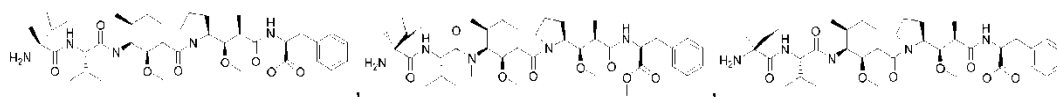
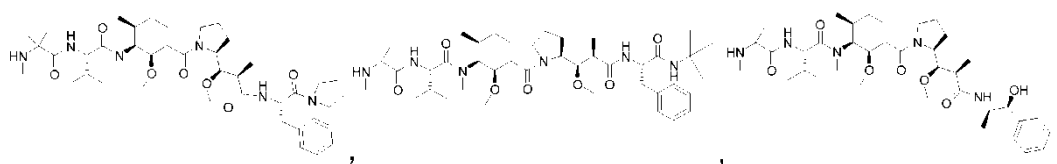
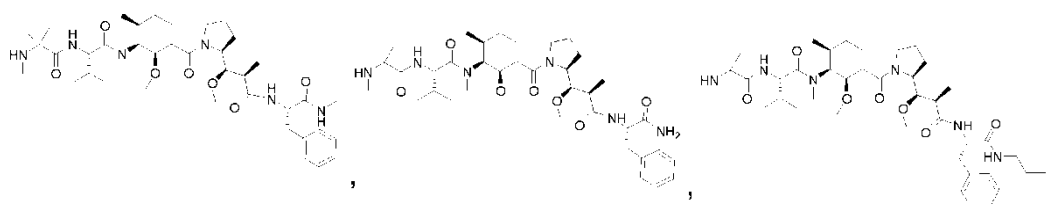
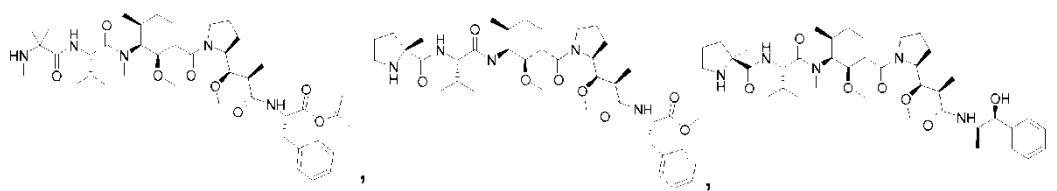
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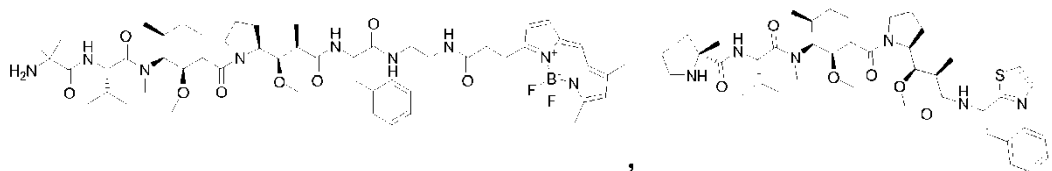
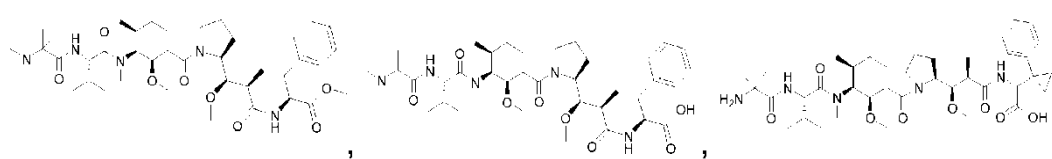
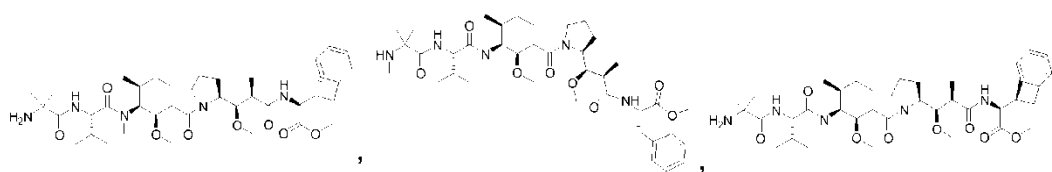
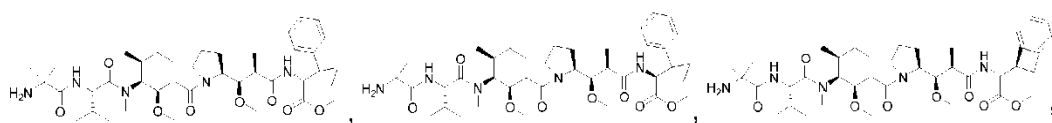
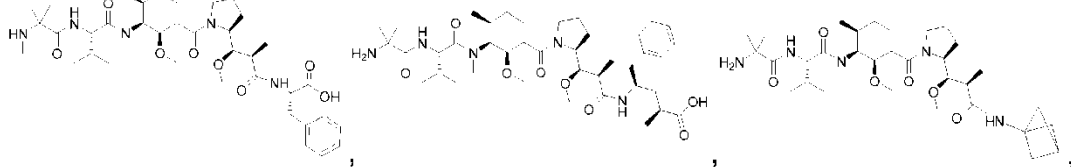
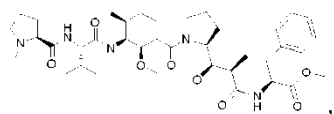
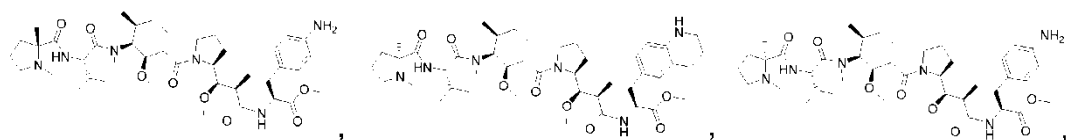
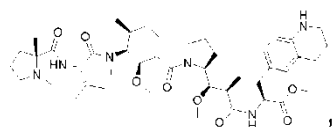
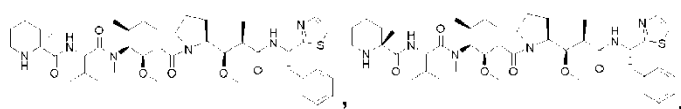
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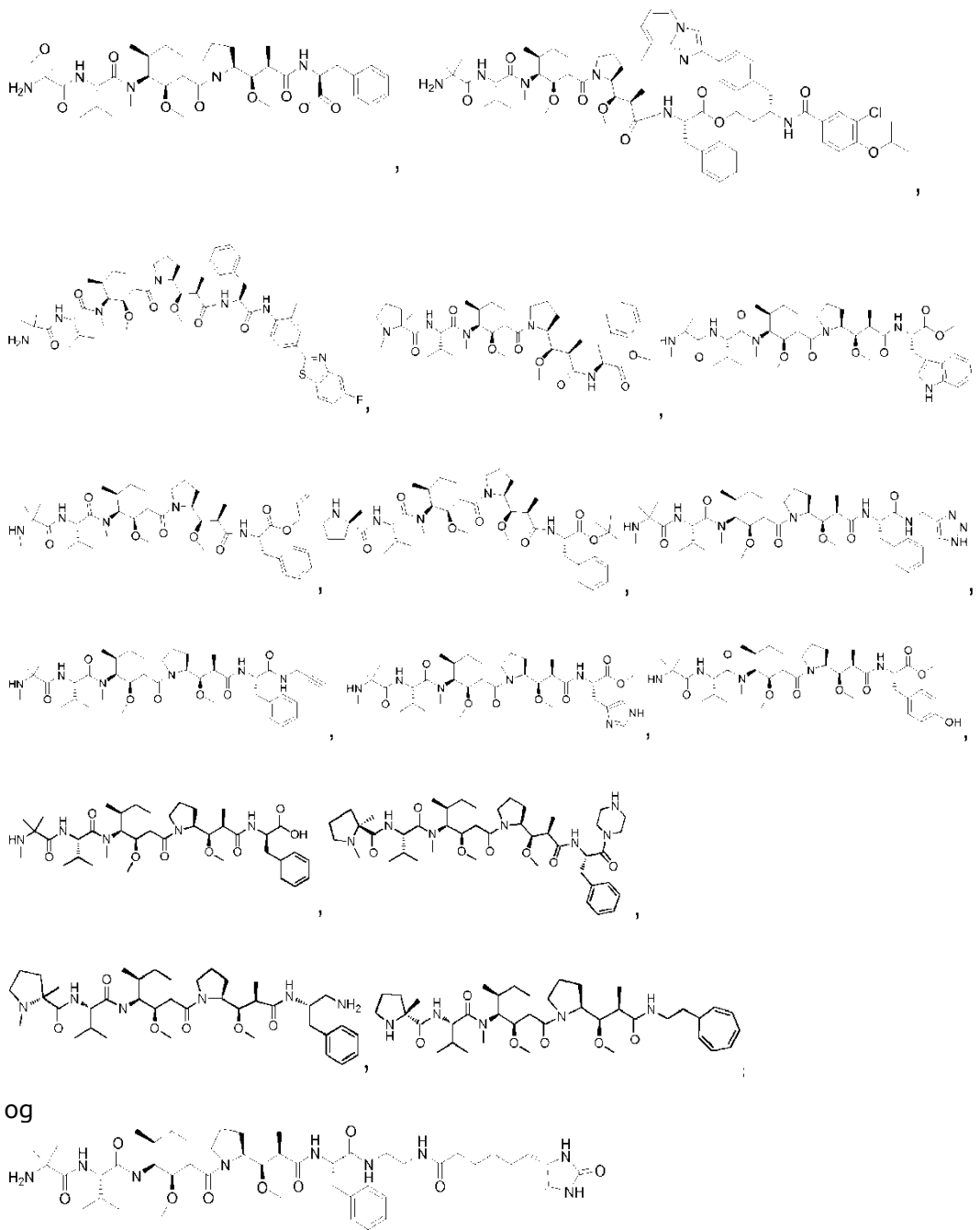


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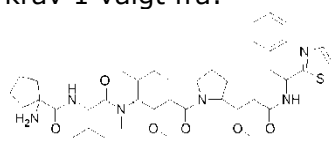
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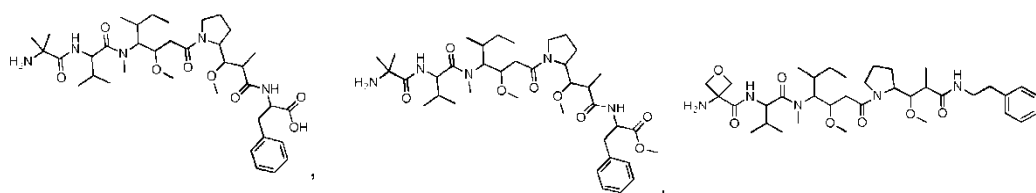
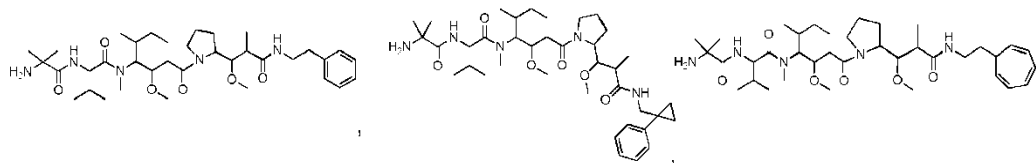
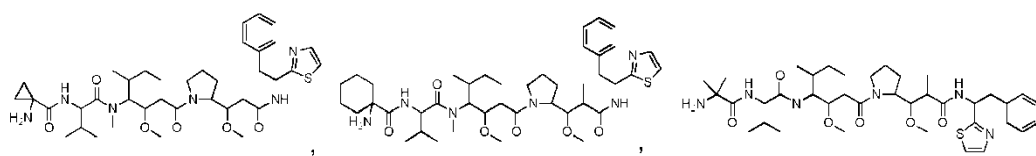
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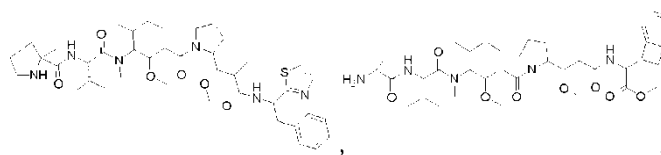
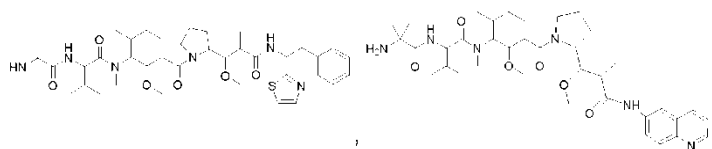
21. Forbindelse eller et farmasøytisk akseptabelt salt eller solvat derav ifølge krav 1 valgt fra:



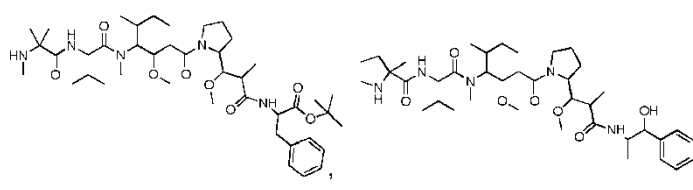
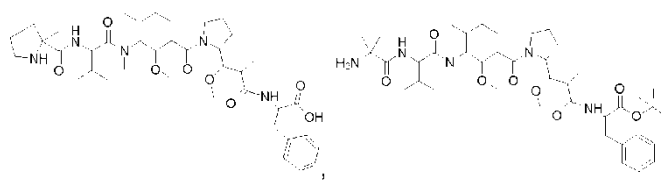
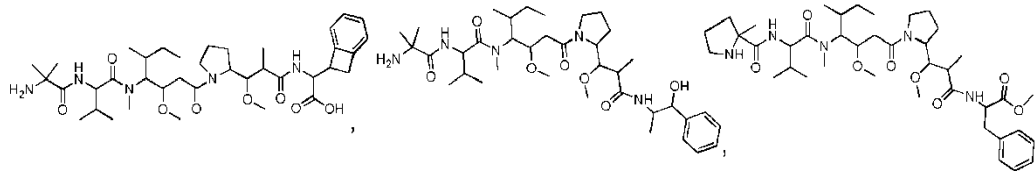
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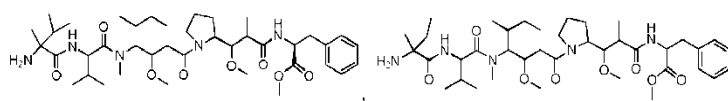
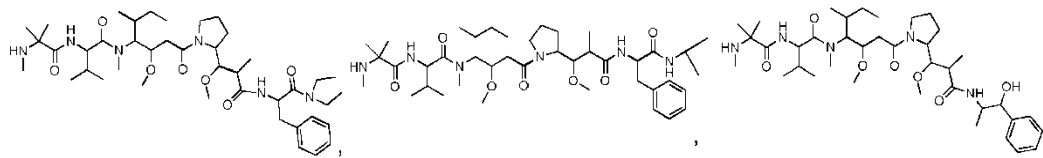
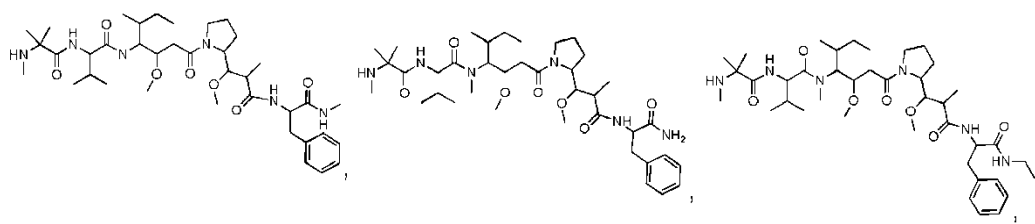


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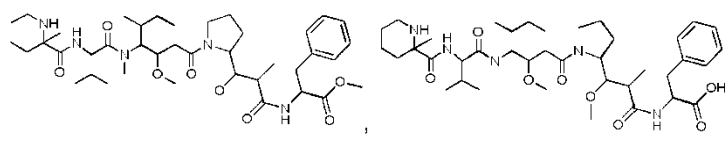
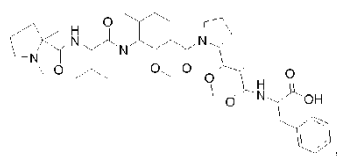


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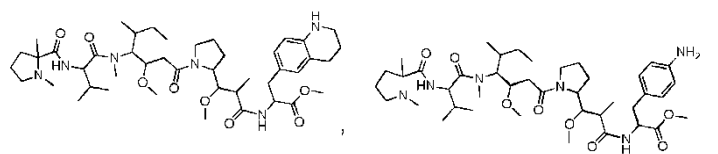
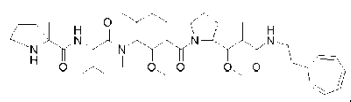
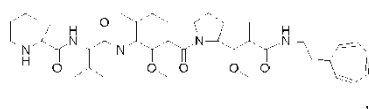
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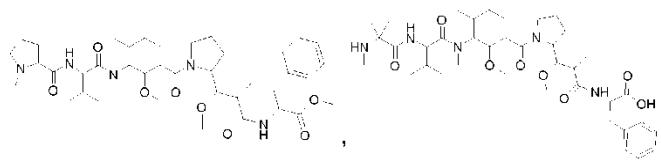
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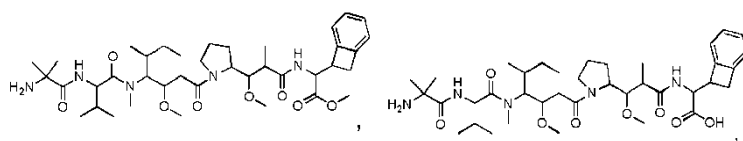
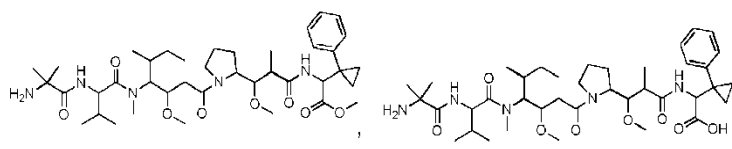
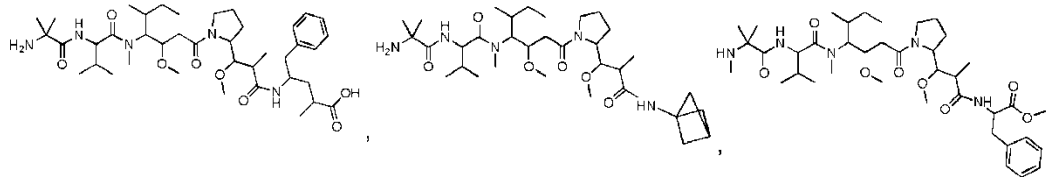
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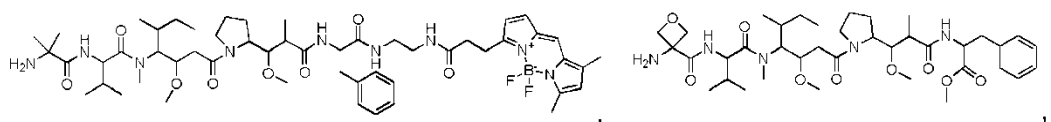
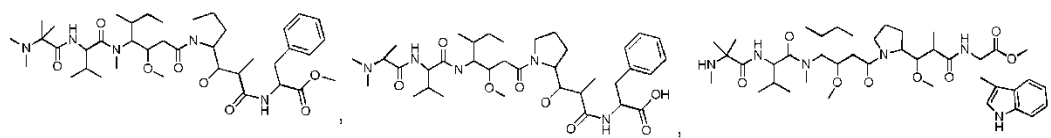
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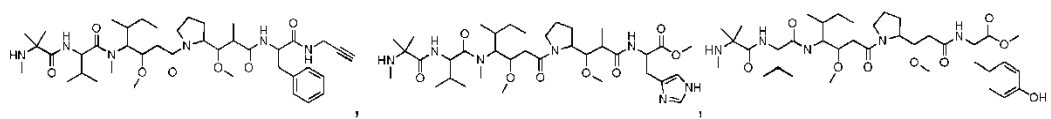
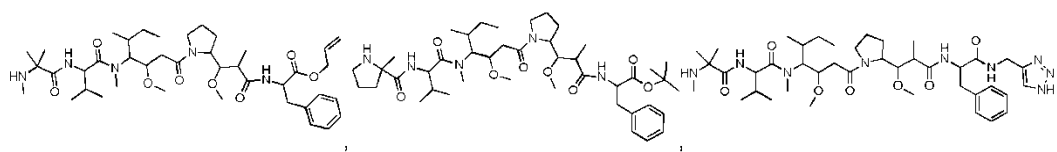
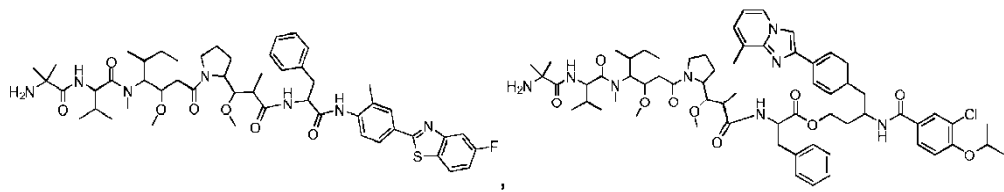
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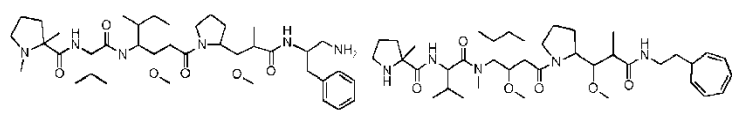
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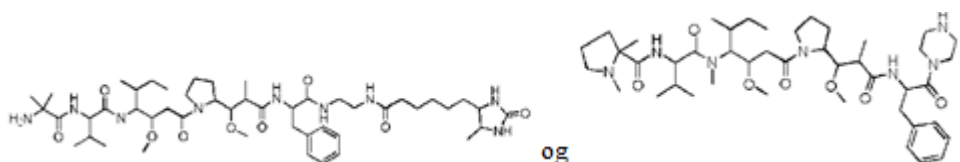
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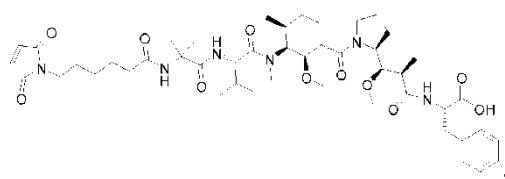
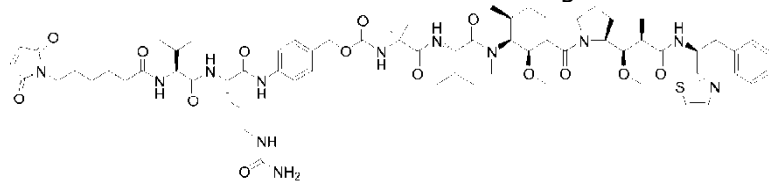
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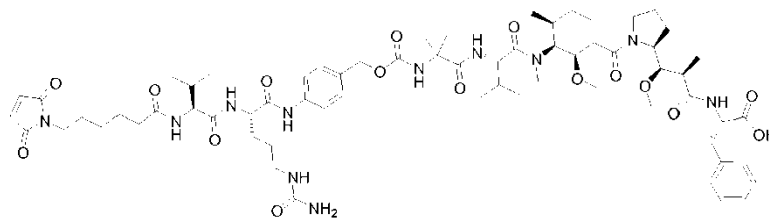
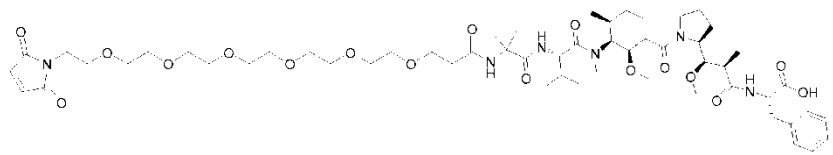
5 **22.** Nyttelast-linker eller et antistofflegemiddelkonjugat eller et farmasøytisk akseptabelt salt eller solvat derav ifølge et hvilket som helst av kravene 2 til 9, omfattende et radikal av en forbindelse ifølge krav 20 eller 21.

10 **23.** Antistofflegemiddelkonjugat eller et farmasøytisk akseptabelt salt eller solvat derav, omfattende et radikal av en forbindelse ifølge krav 1-3.

24. Forbindelse eller et farmasøytisk akseptabelt salt eller solvat derav ifølge hvilket som helst av kravene 2 eller 3 valgt fra:

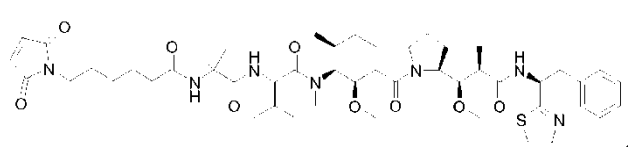
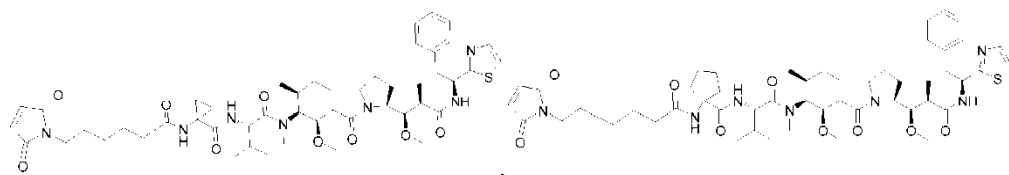
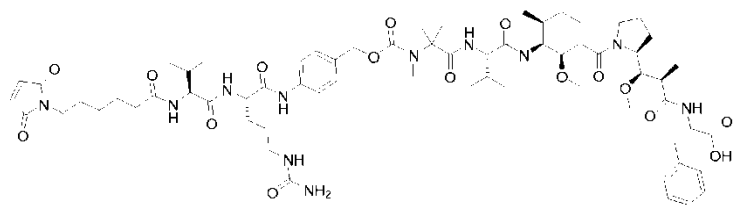
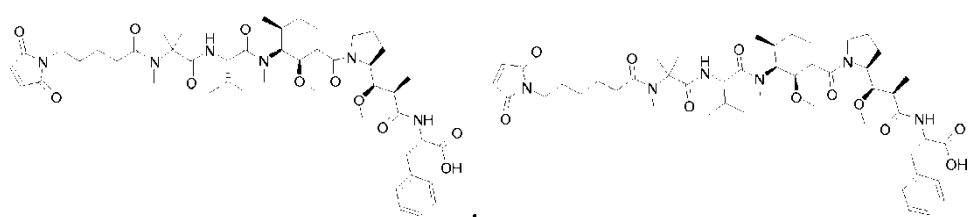
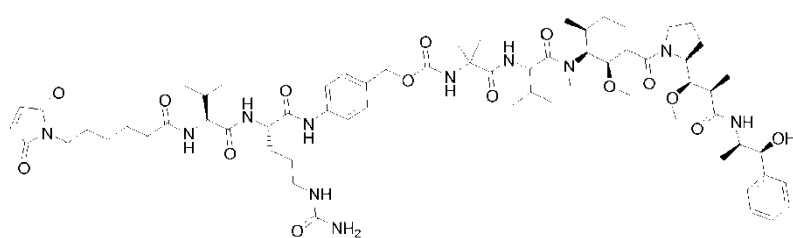
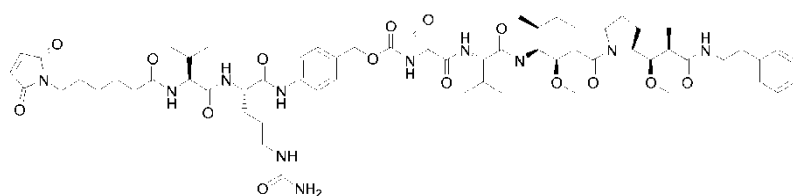
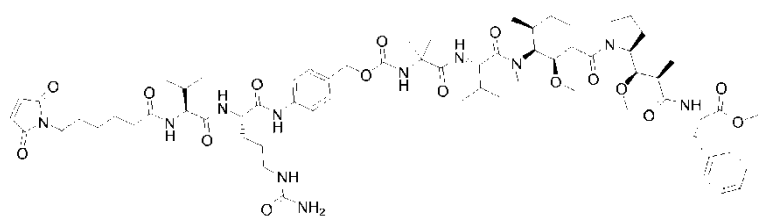


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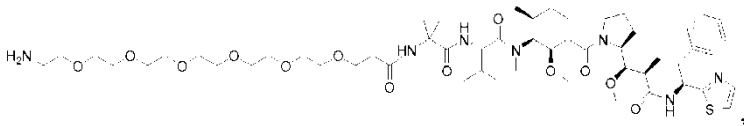
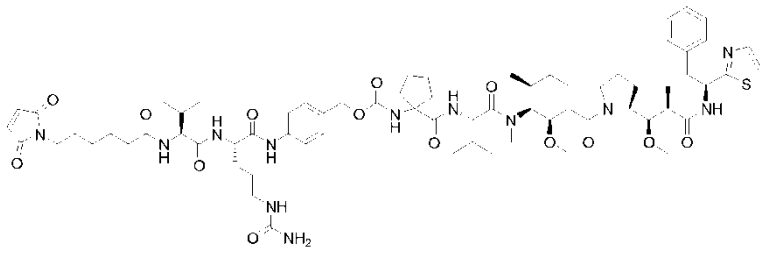


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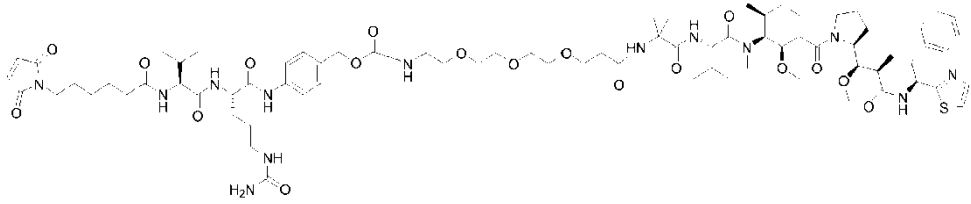
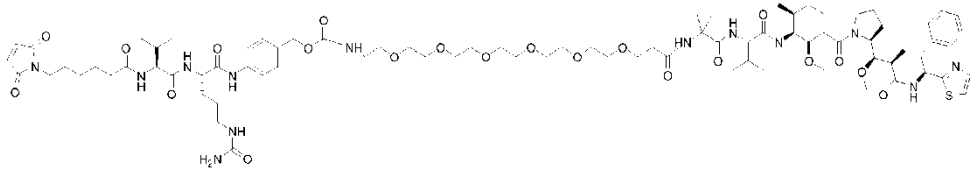
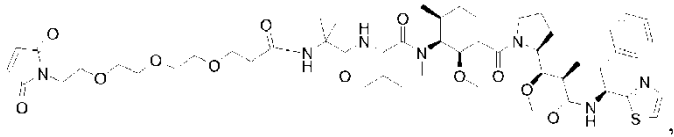
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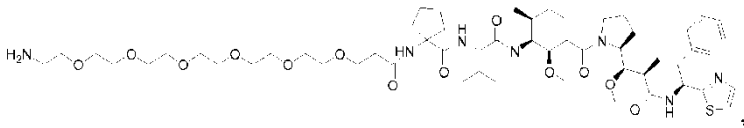
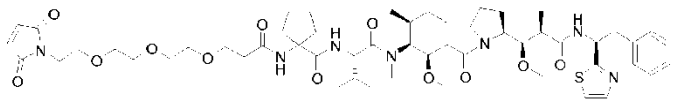
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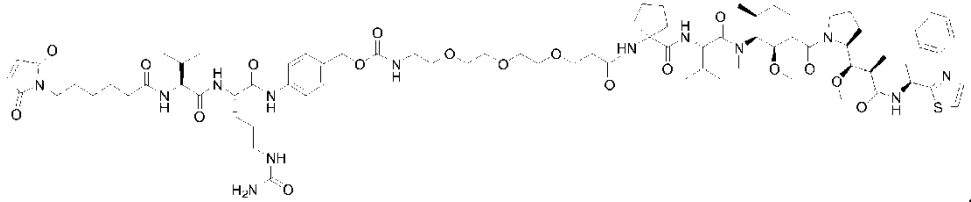
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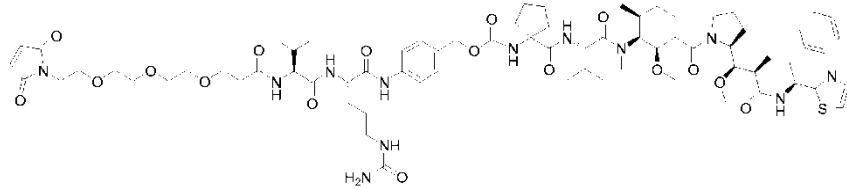
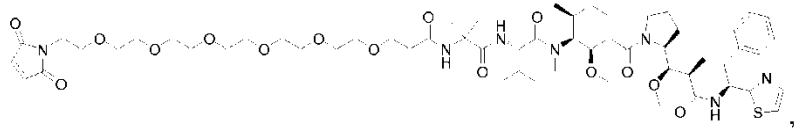
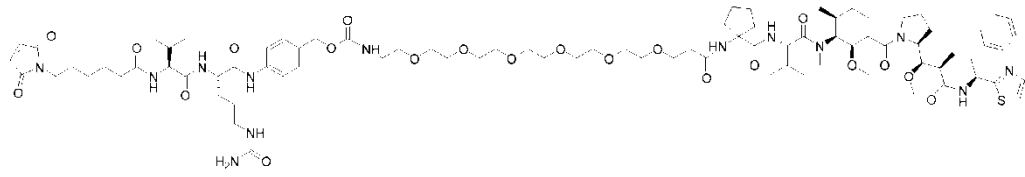
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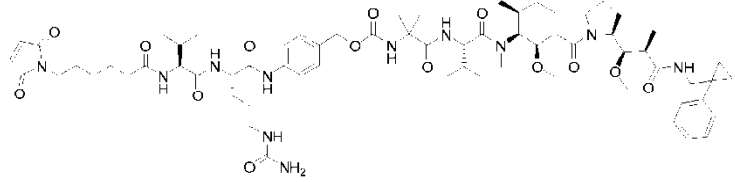
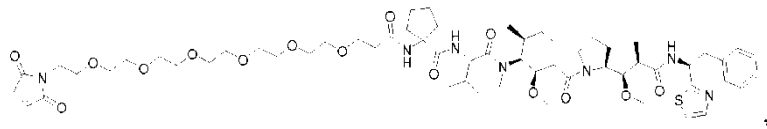
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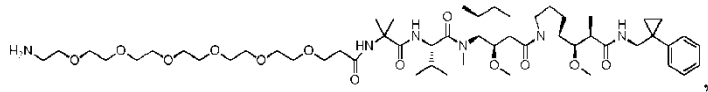
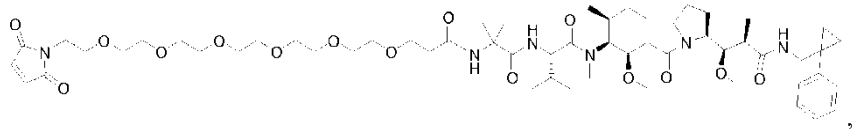
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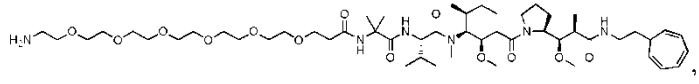
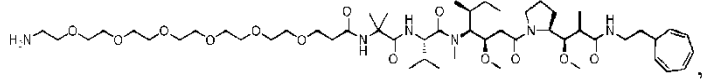
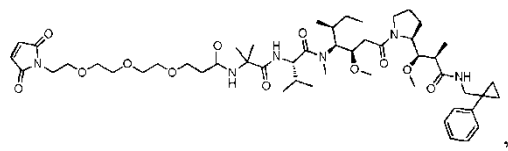
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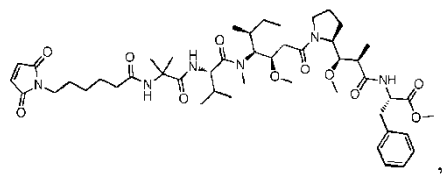
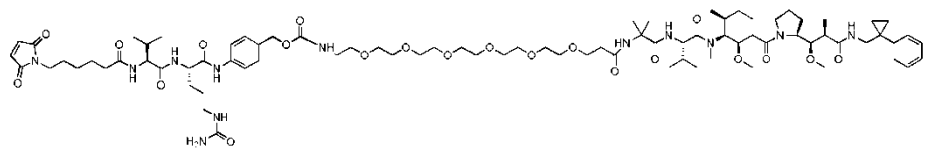


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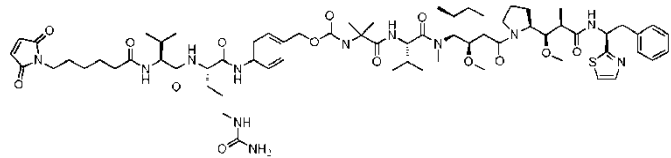
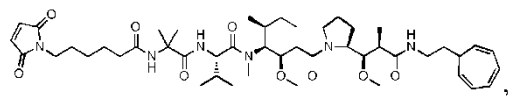
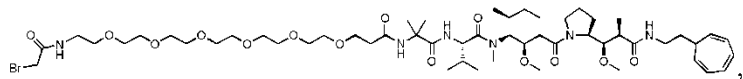


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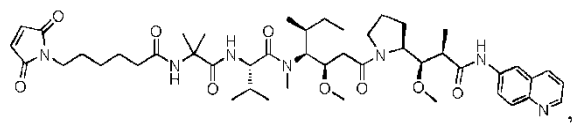
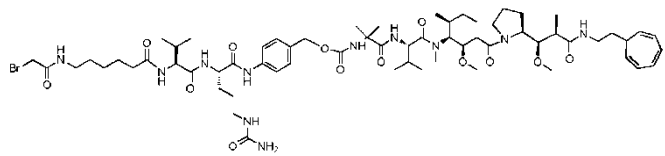




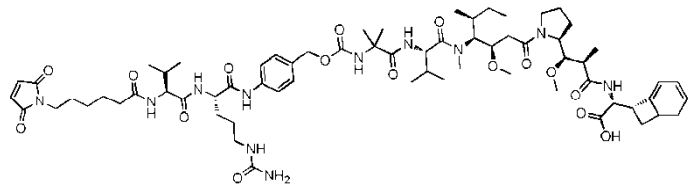
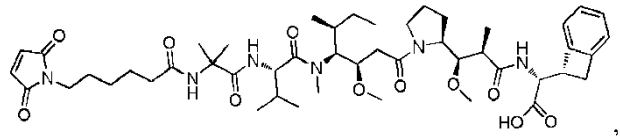
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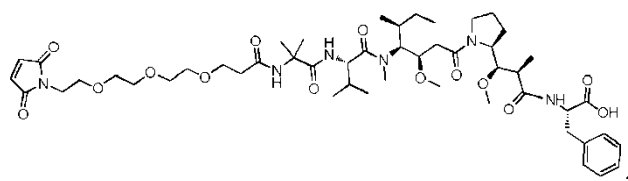
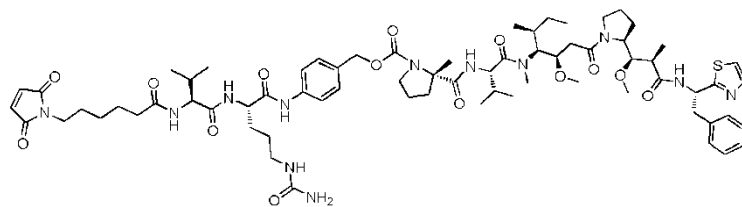
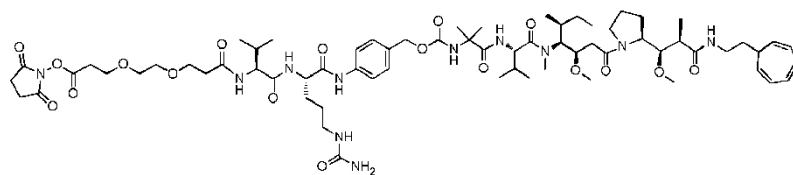
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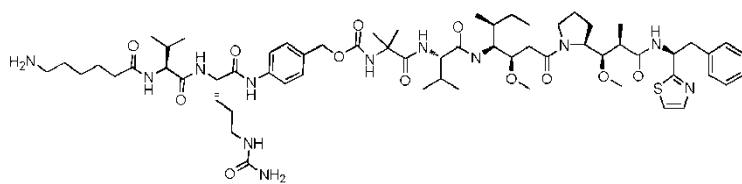
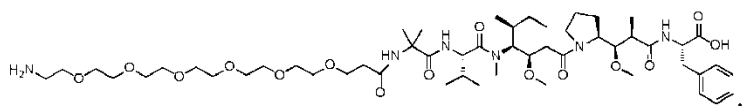
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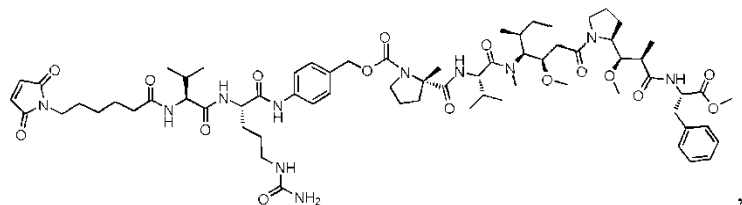
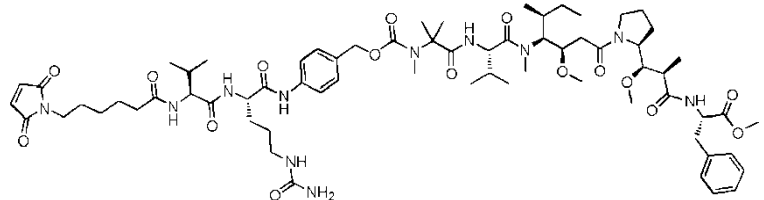
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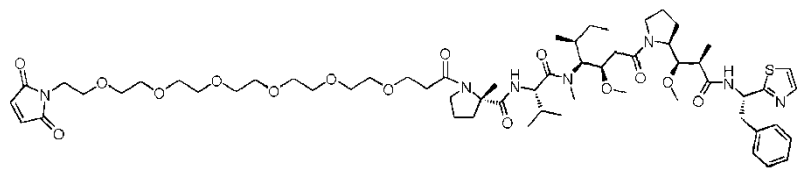
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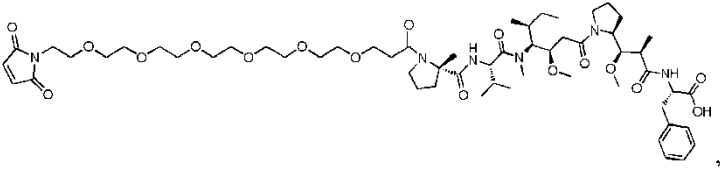
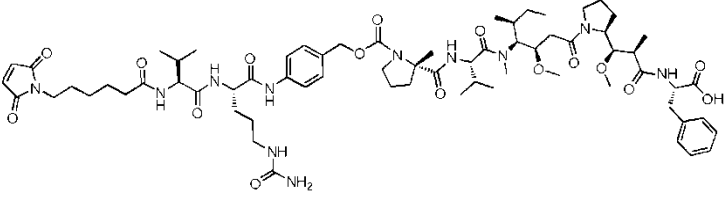
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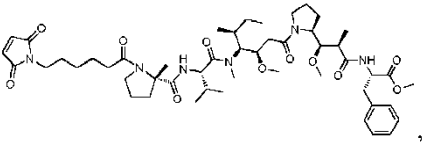
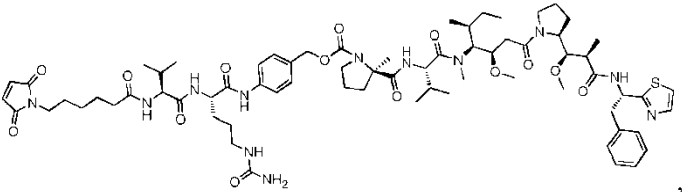
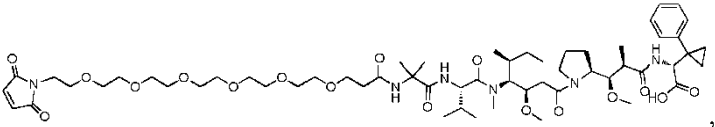
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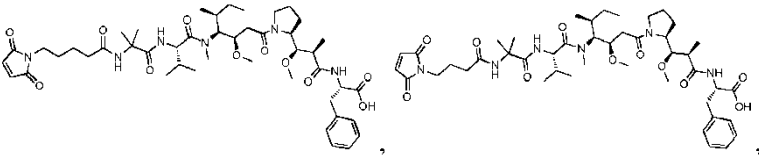
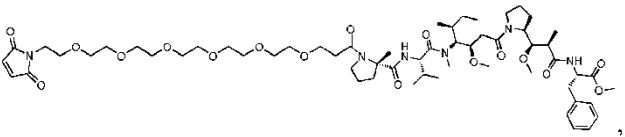
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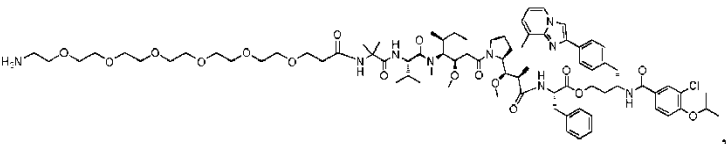
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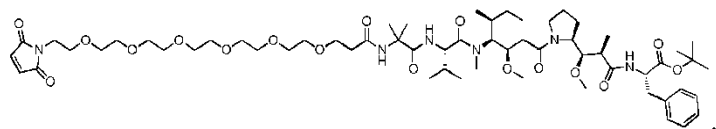


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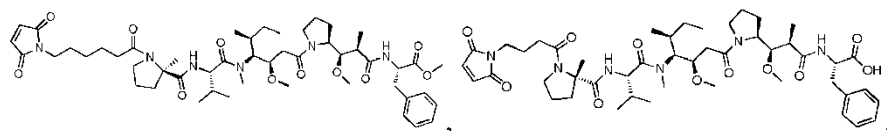
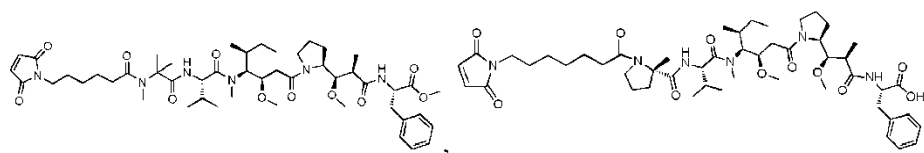


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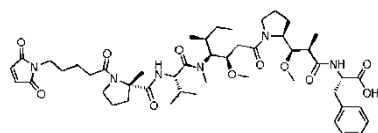
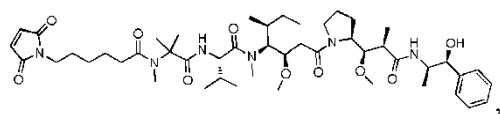
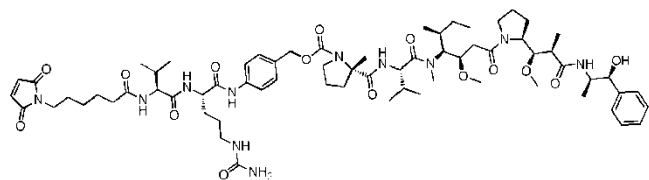




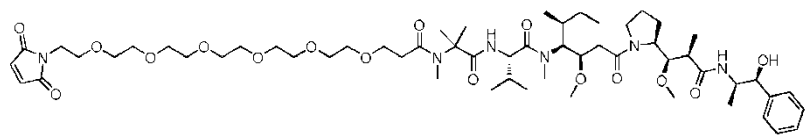
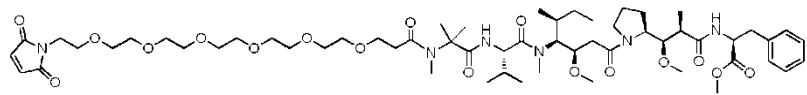
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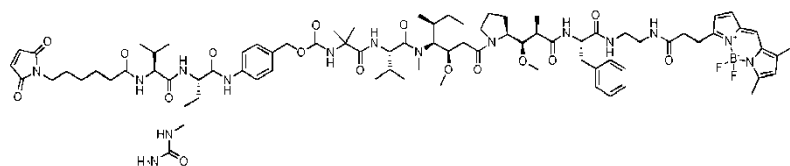
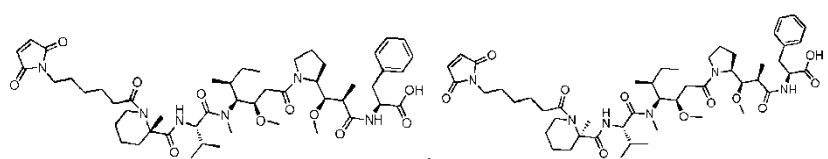


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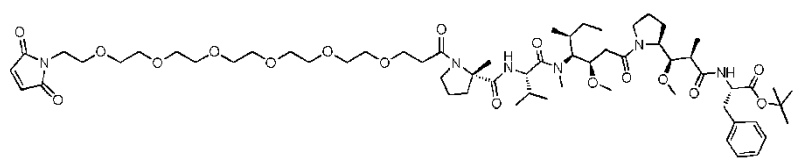
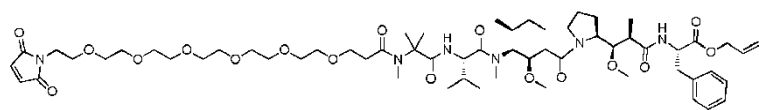


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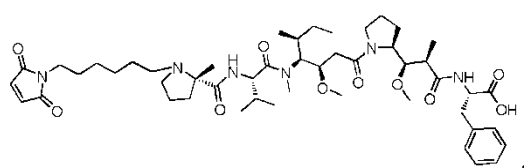
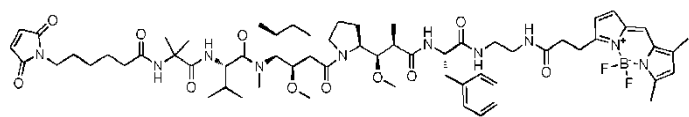
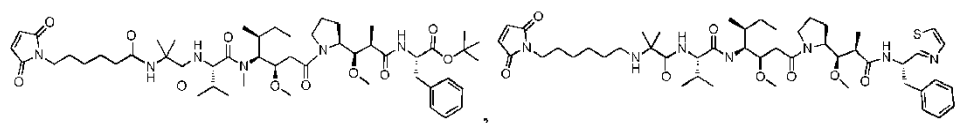




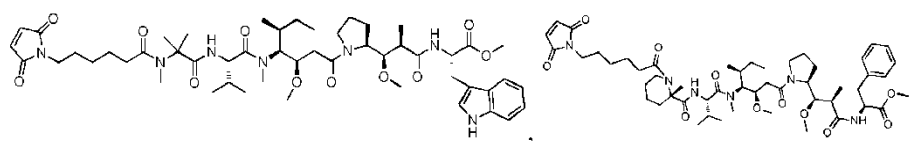
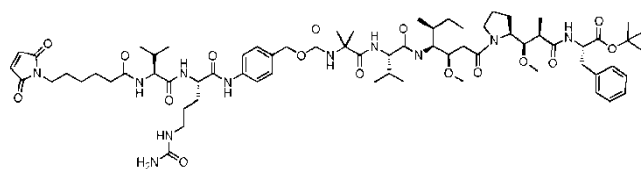
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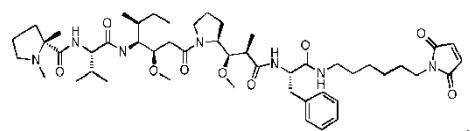
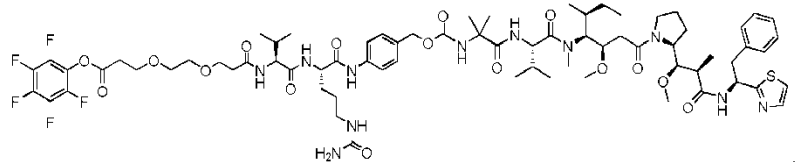
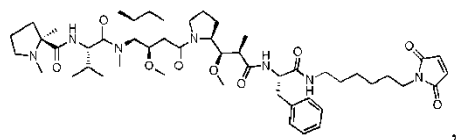
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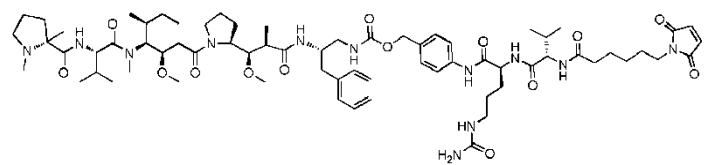
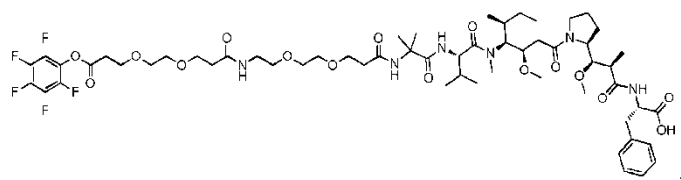
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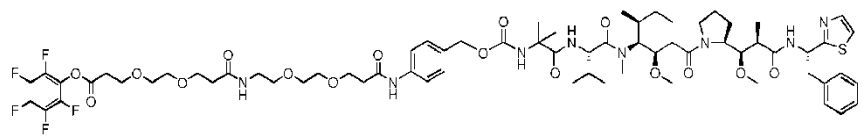
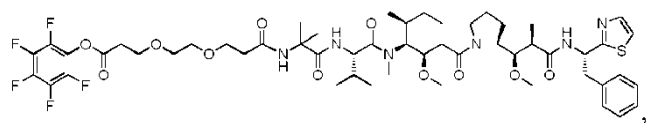
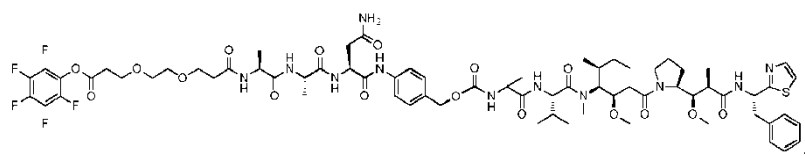
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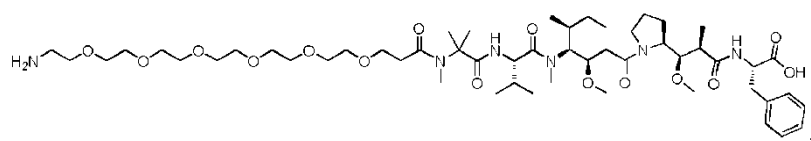
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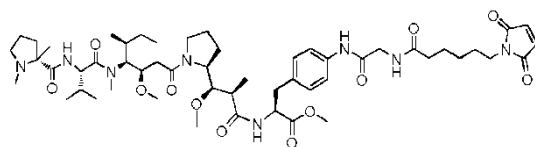
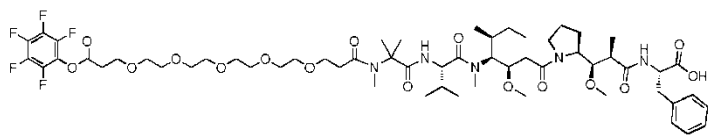
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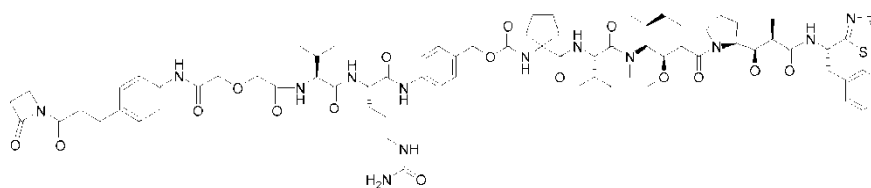
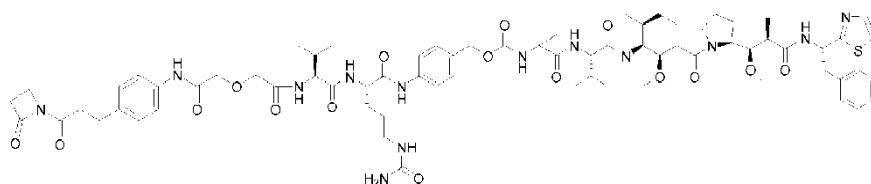
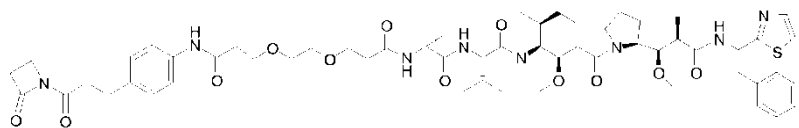
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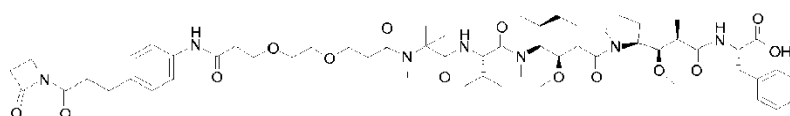
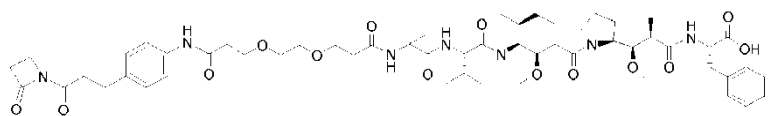
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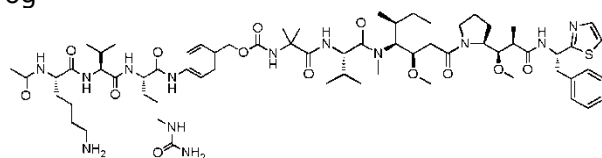
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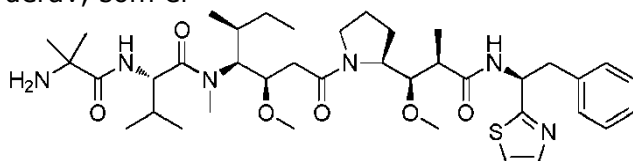


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25. Antistofflegemiddelkonjugat eller et farmasøytisk akseptabelt salt eller solvat derav ifølge et hvilket som helst av kravene 4, 5, 7 eller 9 omfattende et radikal av en forbindelse ifølge krav 24.

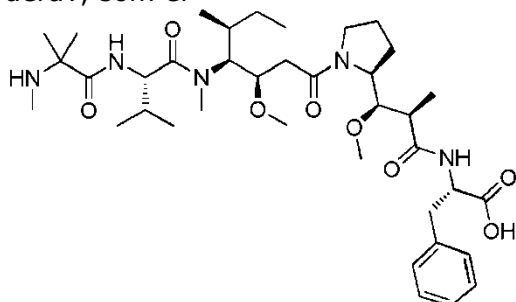
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26. Forbindelse ifølge krav 1 eller et farmasøytisk akseptabelt salt eller solvat derav, som er



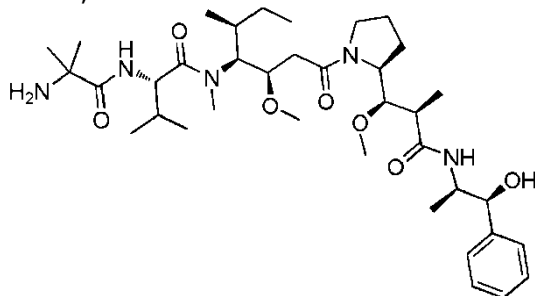
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27. Forbindelse ifølge krav 1 eller et farmasøytisk akseptabelt salt eller solvat derav, som er



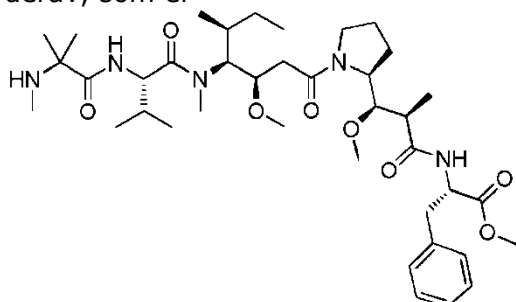
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28. Forbindelse ifølge krav 1 eller et farmasøytisk akseptabelt salt eller solvat derav, som er

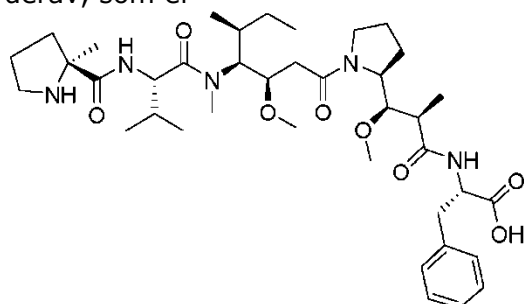


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29. Forbindelse ifølge krav 1 eller et farmasøytisk akseptabelt salt eller solvat derav, som er

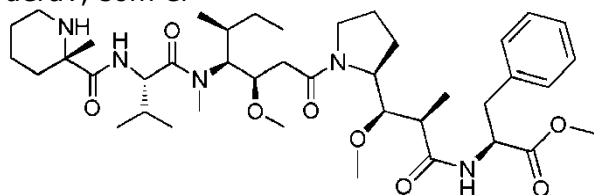


30. Forbindelse ifølge krav 1 eller et farmasøytisk akseptabelt salt eller solvat derav, som er



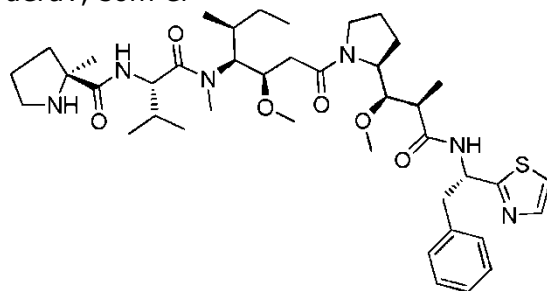
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31. Forbindelse ifølge krav 1 eller et farmasøytisk akseptabelt salt eller solvat derav, som er



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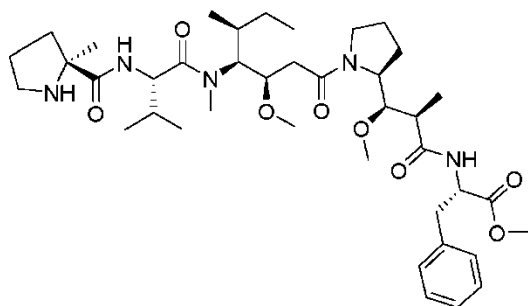
32. Forbindelse ifølge krav 1 eller et farmasøytisk akseptabelt salt eller solvat derav, som er



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33. Forbindelse ifølge krav 1 eller et farmasøytisk akseptabelt salt eller solvat derav, som er

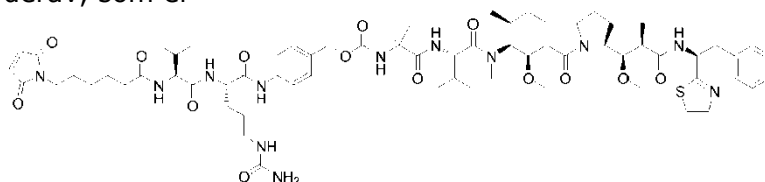
42



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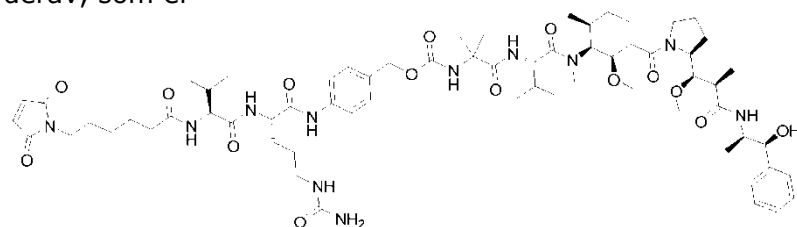
34. Nyttelast-linker eller et antistofflegemiddelkonjugat eller et farmasøytisk akseptabelt salt eller solvat derav ifølge et hvilket som helst av kravene 2 til 9, omfattende et radikal av en forbindelse ifølge krav 26-33.

35. Forbindelse ifølge krav 24 eller et farmasøytisk akseptabelt salt eller solvat derav, som er



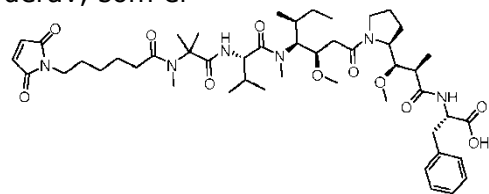
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36. Forbindelse ifølge krav 24 eller et farmasøytisk akseptabelt salt eller solvat derav, som er



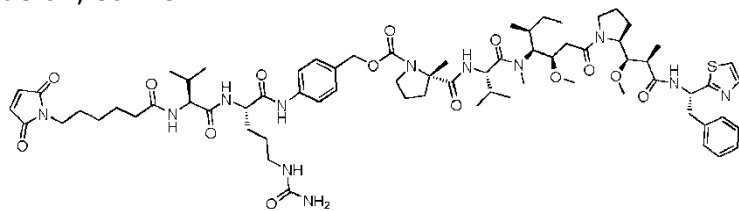
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37. Forbindelse ifølge krav 24 eller et farmasøytisk akseptabelt salt eller solvat derav, som er



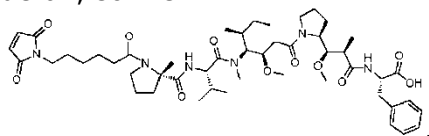
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38. Forbindelse ifølge krav 24 eller et farmasøytisk akseptabelt salt eller solvat derav, som er



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39. Forbindelse ifølge krav 24 eller et farmasøytisk akseptabelt salt eller solvat derav, som er



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40. Antistofflegemiddelkonjugat eller et farmasøytisk akseptabelt salt eller solvat derav ifølge et hvilket som helst av kravene 4, 5, 7 eller 9, omfattende et radikal av en forbindelse ifølge krav 35-39.

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41. Farmasøytisk sammensetning omfattende en forbindelse ifølge et hvilket som helst av kravene 1-40 eller et farmasøytisk akseptabelt salt eller solvat derav og farmasøytisk akseptabel eksipient.

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42. Forbindelse ifølge et hvilket som helst av kravene 1-40 eller et farmasøytisk akseptabelt salt eller solvat derav eller en farmasøytisk sammensetning ifølge krav 41, for anvendelse i behandling av kreft.