(12) **Translation of European patent specification**

(11) **NO/EP 3820572 B1**

NORWAY

(19) NO

(51) Int Cl.

A61P 35/00 (2006.01)
A61K 31/4439 (2006.01)
A61K 31/444 (2006.01)
A61K 31/497 (2006.01)
C07D 213/74 (2006.01)
C07D 241/20 (2006.01)
C07D 401/06 (2006.01)
C07D 401/12 (2006.01)
C07D 401/14 (2006.01)
C07D 403/12 (2006.01)
C07D 403/14 (2006.01)
C07D 471/08 (2006.01)
C07D 487/10 (2006.01)

Norwegian Industrial Property Office

(45)	Translation Published	2023.12.11
(80)	Date of The European Patent Office Publication of the Granted Patent	2023.08.16
(86)	European Application Nr.	19746317.7
(86)	European Filing Date	2019.07.12
(87)	The European Application's Publication Date	2021.05.19
(30)	Priority	2018.07.13, US, 201862697932 P 2018.10.17, US, 201862747033 P 2019.02.21, US, 201962808763 P
(84)	Designated Contracting States:	AL ; AT ; BE ; BG ; CH ; CY ; CZ ; DE ; DK ; EE ; ES ; FI ; FR ; GB ; GR ; HR ; HU ; IE ; IS ; IT ; LI ; LT ; LU ; LV ; MC ; MK ; MT ; NL ; NO ; PL ; PT ; RO ; RS ; SE ; SI ; SK ; SM ; TR
(73)	Proprietor	GILEAD SCIENCES, INC., 333 Lakeside Drive, Foster City, California 94404, USA
(72)	Inventor	AKTOUDIANAKIS, Evangelos, c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA CHO, Aesop, c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA GRAUPE, Michael, c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA LAD, Lateshkumar Thakorlal, c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA MACHICAO TELLO, Paulo A., 570 21st Street Apt. 409, Oakland, CA 94612-1606, USA MEDLEY, Jonathan William, c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA METOBO, Samuel E., c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA NADUTHAMBI, Devan, c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA

PHILLIPS, Barton W., c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA
MONOVICH, Scott Preston, c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA
WANG, Peiyuan, c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA
WATKINS, William J., c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA
XU, Jie, c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA
YANG, Kin Shing, c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA
ZIEBENHAUS, Christopher Allen, c/o Gilead Sciences, Inc. 333 Lakeside Drive, Foster City, California 94404, USA

(74) Agent or Attorney AWA NORWAY AS, Postboks 1052 Hoff, 0218 OSLO, Norge

---

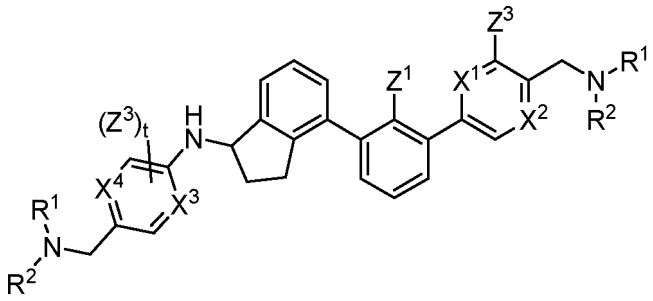
(54) Title **PD-1/PD-L1 INHIBITORS**

(56) References Cited:
WO-A1-2017/192961
WO-A1-2018/005374
US-A1- 2018 065 917
US-A1- 2017 174 679
WO-A1-2018/195321

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 (IIA):



(IIA)

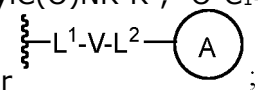
eller et farmasøytisk akseptabelt salt derav, hvor

hver av X^1, X^2, X^3 og X^4 er uavhengig N, CH eller CZ^3;

Z^1 er halo, $-OR^a$, cyano eller $-C_{1-6}$-alkyl;

hver Z^3 er uavhengig halo, $-OR^a$, $-N_3$, $-NO_2$, cyano, $-NR^1R^2$, $-SO_2R^a$. $-SO_2NR^aR^b$, $-NR^aSO_2R^a$, $-NR^aC(O)R^a$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-NR^aC(O)OR^a$, $-NR^aC(O)NR^1R^2$, $-OC(O)NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$, $-C_{1-6}$-alkyl, $-C_{2-6}$-alkenyl, $-C_{2-6}$-alkynyl, $-O-C_{1-6}$-alkyl, $-C_{1-6}$-cyanoalkyl, $-C_{1-6}$-haloalkyl, $-O-C_{1-6}$-cyanoalkyl, $-O-C_{1-6}$-haloalkyl, $-C_{3-8}$-cykloalkyl, $-C_{1-6}$-alkylC$_{3-8}$-cykloalkyl, aryl, heteroaryl, heterocyklyl og R^N; og

hvor alkyl-, alkenyl-, alkynyl-, C_{3-8}-cykloalkyl-, aryl-, heteroaryl- eller heterocyklylgruppen er valgfritt substituert med 1 til 4 grupper uavhengig valgt fra okso, $-NO_2$, $-N_3$, $-OR^a$, halo, cyano, $-NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-O-C_{1-6}$-cyanoalkyl, $-C(O)NR^aR^b$, $NR^aC(O)R^a$, $-NR^aC(O)OR^a$, $-S(O)_2R^a$, $-NR^aS(O)_2R^b$, $-S(O)_2NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$ og $-C_{3-8}$-cykloalkyl;

R^N er uavhengig $-C_{1-6}$-alkylNR^1R^2, $-OC_{1-6}$-alkylNR^1R^2, $-C_{1-6}$-alkylOC_{1-6}-alkylNR^1R^2, $-NR^a-C_{1-6}$-alkylNR^1R^2, $-C_{1-6}$-alkyl$C(O)NR^1R^2$, $-O-C_{1-6}$-alkyl$C(O)NR^1R^2$, $-O-C_{1-6}$-alkyl$C(O)OR^1$, $-S-C_{1-6}$-alkylNR^1R^2, $-C_{1-6}$-alkylOR^a eller  ;

hvor: L^1 er uavhengig en binding, -O-, -NR^a-, -S-, -S(O)- eller -$S(O)_2$-;

V er uavhengig valgt fra en binding, C_{1-6}-alkyl, C_{2-6}-alkenyl og C_{2-6}-alkynyl;

hvor hver alkyl, alkenyl eller alkynyl er valgfritt uavhengig substituert med -OR^a, halo, cyano, -NR^aR^b eller -C_{3-8}-cykloalkyl;

L^2 er uavhengig en binding, -O-, -NR^a-, -S-, -S(O)- eller -$S(O)_2$-;

ring A er uavhengig cykloalkyl, aryl, heteroaryl eller heterocyklyl;

hvor hver cykloalkyl, aryl, heteroaryl eller heterocyklyl er valgfritt substituert med 1 til 4 grupper uavhengig valgt fra okso, -NO_2, -N_3, -OR^a, halo, cyano, -C_{1-6}-alkyl, -C_{1-6}-haloalkyl, -C_{2-6}-alkenyl, -C_{2-6}-alkynyl, -O-C_{1-6}-haloalkyl, NR^aR^b, -C(O)R^a, -C(O)OR^a, -OC_{1-6}-alkylCN, -C(O)NR^aR^b, -$NR^aC(O)R^a$, -$NR^aC(O)OR^a$, -C(O)N(R^a)OR^b, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$NR^aS(O)_2R^b$, -$NR^aS(O)_2NR^aR^b$, -C(O)$NR^aS(O)_2NR^aR^b$, -C_{3-8}-cykloalkyl, heteroaryl og -C_{1-6}-alkylC_{3-8}-cykloalkyl; og

hvor alkyl-, alkenyl- eller alkynylgruppen er valgfritt uavhengig substituert med -OR^a, halo, cyano, -NR^aR^b eller -C_{3-8}-cykloalkyl;

t er 0, 1 eller 2;

hver R^1 er uavhengig valgt fra hydrogen, -C_{1-8}-alkyl, -C_{2-6}-alkenyl, -C_{2-6}-alkynyl, -C_{3-6}-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C_{1-6}-alkylaryl, -C_{1-6}-alkylheteroaryl, -C_{1-6}-alkylheterocyklyl, -C_{1-6}-alkylC(O)OR^a, -C_{2-6}-alkenylC(O)OR^a, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -C(O)$NR^aS(O)_2R^a$ og -C_{1-6}-alkylC_{3-8}-cykloalkyl;

hvor hver alkyl, alkenyl, cykloalkyl, aryl, heteroaryl eller heterocyklyl er valgfritt substituert med 1 til 4 grupper uavhengig valgt fra -OR^a, cyano, halo, C_{1-6}-alkyl, -C_{1-6}-alkylOR^a, -C_{1-6}-cyanoalkyl, -C_{1-6}-haloalkyl, C_{3-8}-

cykloalkyl, -C_{1-3}-alkylC_{3-8}-cykloalkyl, -C(O)R^a, -C_{1-6}-alkylC(O)R^a, -C(O)OR^a, -C_{1-6}-alkylC(O)OR^a, -NR^aR^b, -OC(O)NR^aR^b, -$NR^aC(O)OR^b$, -C_{1-6}-alkylNR^aR^b, -C(O)NR^aR^b, -C_{1-6}-alkylC(O)NR^aR^b, -SO_2R^a, -C_{1-6}alkylSO_2R^a, -$SO_2NR^aR^b$, -C_{1-6}-alkyl$SO_2NR^aR^b$, -C(O)$NR^aSO_2R^b$, -C_{1-6}-alkylC(O)$NR^aSO_2R^b$, -$NR^aC(O)R^b$ og -C_{1-6}-alkyl$NR^aC(O)R^b$;

hver R^2 er uavhengig valgt fra hydrogen, -C_{1-6}-alkyl, -C_{2-6}-alkenyl, -C_{2-6}-alkynyl, -C_{3-6}-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C $_{1-6}$-alkylaryl, -C $_{1-6}$-alkylheteroaryl, -C_{1-6}-alkylheterocyklyl, -C_{2-6}-alkyl-OR^a, -C_{1-6}-alkylC(O)OR^a og -C_{2-6}-alkenylC(O)OR^a;

hvor hver alkyl, alkenyl, alkynyl, cykloalkyl, aryl, heteroaryl eller heterocyklyl er valgfritt substituert med 1 til 4 grupper uavhengig valgt fra -OR^a, cyano, halo, C_{1-6}-alkyl, -C_{1-6}-alkylOR^a, -C_{1-6}-cyanoalkyl, -C_{1-6}-haloalkyl, -C_{3-8}-cykloalkyl, -C_{1-3}-alkylC_{3-8}-cykloalkyl, -C(O)R^a, -C_{1-6}-alkylC(O)R^a, -C(O)OR^a, -C_{1-6}-alkylC(O)OR^a, -NR^aR^b, -C_{1-6}-alkylNR^aR^b, -C(O)NR^aR^b, C_{1-6}-alkylC(O)NR^aR^b, -$S(O)_2R^a$, -C_{1-6}-alkyl$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -C_{1-6}-alkyl$S(O)_2NR^aR^b$, -C(O)$NR^aS(O)_2R^b$ og -$NR^aC(O)R^b$;

eller R^1 og R^2 er slått sammen for å danne en heterocyklyl valgfritt substituert med 1 til 3 grupper uavhengig valgt fra okso, -C_{1-6}-alkyl, -C_{3-8}-cykloalkyl, -C_{2-6}-alkenyl, -C_{2-6}-alkynyl, -OR^a, -C(O)OR^a, -C_{1-6}-cyanoalkyl, -C_{1-6}-alkylOR^a, -C_{1-6}-haloalkyl, -C_{1-3}-alkylC_{3-8}-cykloalkyl, -C(O)R^a, -C_{1-6}-alkylC(O)R^a, -C_{1-6}-alkylC(O)OR^a, -NR^aR^b, -C_{1-6}-alkylNR^aR^b, -C(O)NR^aR^b, -C_{1-6}-alkylC(O)NR^aR^b, -$S(O)_2R^a$, -C_{1-6}-alkyl$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -C(O)N=S(O)$R^aNR^aR^b$, -C(O)N=S(O)$R^aNR^aC(O)R^b$ og -C_{1-6}-alkyl$S(O)_2NR^aR^b$;

hver R^a er uavhengig valgt fra hydrogen, -C_{1-6}-alkyl, -C_{1-6}-cyanoalkyl, -C_{1-6}-haloalkyl, -C_{3-8}-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C_{1-3}-alkylC_{3-8}-cykloalkyl, -C_{1-6}-alkylaryl, -C_{1-6}-alkylheteroaryl og -C_{1-6}-alkylheterocyklyl;

hver R^b er uavhengig valgt fra hydrogen, -C_{1-6}-alkyl, -C_{1-6}-cyanoalkyl, -C_{1-6}-haloalkyl, -C_{3-8}-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C_{1-3}-alkylC_{3-8}-cykloalkyl, -C_{1-6}-alkylaryl, -C_{1-6}-alkylheteroaryl og -C_{1-6}-alkylheterocyklyl;

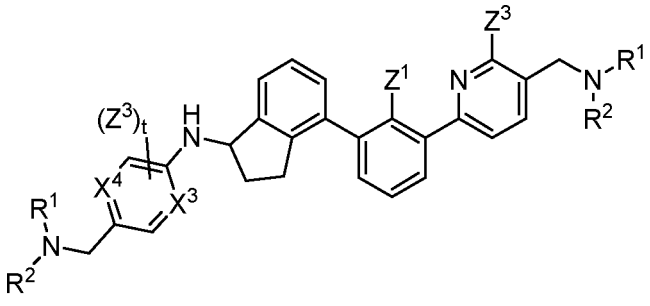
eller R^a og R^b kan være slått sammen for å danne en heterocyklyl valgfritt substituert med 1 til 4 grupper uavhengig valgt fra -OR^f, cyano, halo, -C_{1-6}-

alkylOR^f, -C$_1$-ecyanoalkyl, -C$_1$-ehaloalkyl, -C$_{3-8}$-cykloalkyl, -C$_{1-3}$-alkylC$_{3-8}$-cykloalkyl, -C(O)R^f, -C$_{1-6}$-alkylC(O)R^f, -C(O)OR^f, -C$_{1-6}$-alkylC(O)OR^f, -NR^{f}R^g, -C$_{1-6}$-alkylNR^{f}R^g, -C(O)NR^{f}R^g, -C$_{1-6}$-alkylC(O)NR^{f}R^g, -S(O)$_2$R^f, -C$_{1-6}$-alkylS(O)$_2$R^f, -S(O)$_2$NR^{f}R^g, -C$_{1-6}$-alkylS(O)$_2$NR^{f}R^g, -C(O)NR^{f}S(O)$_2$R^g og -NR^{f}C(O)R^g;

hver R^f er uavhengig valgt fra hydrogen, -C$_{1-6}$-alkyl, -C$_{3-8}$-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C$_{1-3}$-alkylC$_{3-8}$-cykloalkyl, -C$_{1-6}$-alkylaryl, -C$_{1-6}$-alkylheteroaryl og -C$_{1-6}$-alkylheterocyklyl; og

hver R^8 er uavhengig valgt fra hydrogen, -C$_{1-6}$-alkyl, -C$_{3-8}$-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C$_{1-3}$-alkylC$_{3-8}$-cykloalkyl, -C$_{1-6}$-alkylaryl, -C$_{1-6}$-alkylheteroaryl og -C$_{1-6}$-alkylheterocyklyl.

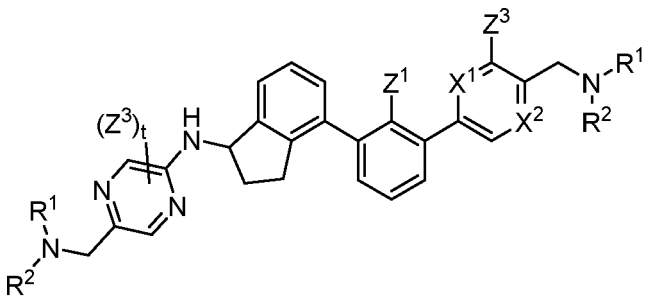
2. Forbindelse ifølge krav 1, hvor forbindelsen med formel (IIA) er en forbindelse med formel (IIC):



(IIC)

eller et farmasøytisk akseptabelt salt derav, hvor X^3, X^4, Z^1, Z^3, t, R^1 og R^2 har betydningene angitt i krav 1.

3. Forbindelse ifølge krav 1, hvor forbindelsen med formel (IIA) er en forbindelse med formel (VIA):



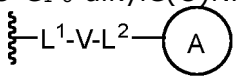
(VIA)

eller et farmasøytisk akseptabelt salt derav, hvor hver av X^1 og X^2 er uavhengig N, CH eller CZ^3;

Z^1 er halo, -OR^a, cyano eller -C_{1-6}-alkyl;

hver Z^3 er uavhengig halo, -OR^a, -N_3, -NO_2, cyano, -NR^1R^2, -SO_2R^a. -$SO_2NR^aR^b$, -$NR^aSO_2R^a$, -$NR^aC(O)R^a$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^aR^b$, -$NR^aC(O)OR^a$, -$NR^aC(O)NR^1R^2$, -$OC(O)NR^aR^b$, -$NR^aS(O)_2NR^aR^b$, -$C(O)NR^aS(O)_2NR^aR^b$, -C_{1-6}-alkyl, -C_{2-6}-alkenyl, -C_{2-6}-alkynyl, -O-C_{1-6}-alkyl, -C_{1-6}-cyanoalkyl, -C_{1-6}-haloalkyl, -O-C_{1-6}-cyanoalkyl, -O-C_{1-6}-haloalkyl, -C_{3-8}-cykloalkyl, -C_{1-6}-alkylC_{3-8}-cykloalkyl, aryl, heteroaryl, heterocyklyl og R^N; og

hvor alkyl-, alkenyl-, alkynyl-, C_{3-8}-cykloalkyl-, aryl-, heteroaryl- eller heterocyklylgruppen er valgfritt substituert med 1 til 4 grupper uavhengig valgt fra okso, -NO_2, -N_3, -OR^a, halo, cyano, -NR^aR^b, -$C(O)R^a$, -$C(O)OR^a$, -O-C_{1-6}-cyanoalkyl, -$C(O)NR^aR^b$, $NR^aC(O)R^a$, -$NR^aC(O)OR^a$, -$S(O)_2R^a$, -$NR^aS(O)_2R^b$, -$S(O)_2NR^aR^b$, -$NR^aS(O)_2NR^aR^b$, -$C(O)NR^aS(O)_2NR^aR^b$ og -C_{3-8}-cykloalkyl;

R^N er uavhengig -C_{1-6}-alkylNR^1R^2, -OC_{1-6}-alkylNR^1R^2, -C_{1-6}-alkylOC_{1-6}-alkylNR^1R^2, -NR^a-C_{1-6}-alkylNR^1R^2, -C_{1-6}-alkyl$C(O)NR^1R^2$, -O-C_{1-6}-alkyl$C(O)NR^1R^2$, -O-C_{1-6}-alkyl$C(O)OR^1$, -S-C_{1-6}-alkylNR^1R^2, -C_{1-6}-alkylOR^a eller 

;

hvor: L^1 er uavhengig en binding, -O-, -NR^a-, -S-, -S(O)- eller -$S(O)_2$-;

V er uavhengig valgt fra en binding, C_{1-6}-alkyl, C_{2-6}-alkenyl og C_{2-6}-alkynyl;

hvor hver alkyl, alkenyl eller alkynyl er valgfritt uavhengig substituert med -OR^a, halo, cyano, -NR^aR^b eller -C_{3-8}-cykloalkyl;

L^2 er uavhengig en binding, -O-, -NR^a-, -S-, -S(O)- eller -$S(O)_2$-;

ring A er uavhengig cykloalkyl, aryl, heteroaryl eller heterocyklyl;

hvor hver cykloalkyl, aryl, heteroaryl eller heterocyklyl er valgfritt substituert med 1 til 4 grupper uavhengig valgt fra okso, -NO_2, -N_3, -OR^a, halo, cyano, -C_{1-6}-alkyl, -C_{1-6}-haloalkyl, -C_{2-6}-alkenyl, -C_{2-6}-alkynyl, -O-C_{1-6}-haloalkyl, NR^aR^b, -$C(O)R^a$, -$C(O)OR^a$, -OC_{1-6}-alkylCN, -$C(O)NR^aR^b$, -$NR^aC(O)R^a$, -$NR^aC(O)OR^a$, -$C(O)N(R^a)OR^b$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$NR^aS(O)_2R^b$, -$NR^aS(O)_2NR^aR^b$, -$C(O)NR^aS(O)_2NR^aR^b$, -C_{3-8}-cykloalkyl, heteroaryl og -C_{1-6}-alkylC_{3-8}-cykloalkyl; og

hvor alkyl-, alkenyl- eller alkynylgruppen er valgfritt uavhengig substituert med -OR^a, halo, cyano, -NR^aR^b eller -C_{3-8}-cykloalkyl;

t er 0, 1 eller 2;

hver R^1 er uavhengig valgt fra hydrogen, -C_{1-8}-alkyl, -C_{2-6}-alkenyl, -C_{2-6}-alkynyl, -C_{3-6}-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C_{1-6}-alkylaryl, -C_{1-6}-alkylheteroaryl, -C_{1-6}-alkylheterocyklyl, -C_{1-6}-alkylC(O)OR^a, -C_{2-6}-alkenylC(O)OR^a, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)NR^aS(O)_2R^a$ og -C_{1-6}-alkylC$_{3-8}$-cykloalkyl;

hvor hver alkyl, alkenyl, cykloalkyl, aryl, heteroaryl eller heterocyklyl er valgfritt substituert med 1 til 4 grupper uavhengig valgt fra -OR^a, cyano, halo, C_{1-6}-alkyl, -C_{1-6}-alkylOR^a, -C_{1-6}-cyanoalkyl, -C_{1-6}-haloalkyl, C_{3-8}-cykloalkyl, -C_{1-3}-alkylC$_{3-8}$-cykloalkyl, -C(O)R^a, -C_{1-6}-alkylC(O)R^a, -C(O)OR^a, -C_{1-6}-alkylC(O)OR^a, -NR^aR^b, -OC(O)NR^aR^b, -$NR^aC(O)OR^b$, -C_{1-6}-alkylNR^aR^b, -C(O)NR^aR^b, -C_{1-6}-alkylC(O)NR^aR^b, -SO_2R^a, -C_{1-6}-alkylSO_2R^a, -$SO_2NR^aR^b$, -C_{1-6}-alkyl$SO_2NR^aR^b$, -C(O)$NR^aSO_2R^b$, -C_{1-6}-alkylC(O)$NR^aSO_2R^b$, -$NR^aC(O)R^b$ og -C_{1-6}-alkyl$NR^aC(O)R^b$;

hver R^2 er uavhengig valgt fra hydrogen, -C_{1-6}-alkyl, -C_{2-6}-alkenyl, -C_{2-6}-alkynyl, -C_{3-6}-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C_{1-6}-alkylaryl, -C_{1-6}-alkylheteroaryl, -C_{1-6}-alkylheterocyklyl, -C_{2-6}-alkyl-OR^a, -C_{1-6}-alkylC(O)OR^a og -C_{2-6}-alkenylC(O)OR^a;

hvor hver alkyl, alkenyl, alkynyl, cykloalkyl, aryl, heteroaryl eller heterocyklyl er valgfritt substituert med 1 til 4 grupper uavhengig valgt fra -OR^a, cyano, halo, C_{1-6}-alkyl, -C_{1-6}-alkylOR^a, -C_{1-6}-cyanoalkyl, -C_{1-6}-haloalkyl, -C_{3-8}-cykloalkyl, -C_{1-3}-alkylC$_{3-8}$-cykloalkyl, -C(O)R^a, -C_{1-6}-alkylC(O)R^a, -C(O)OR^a, -C_{1-6}-alkylC(O)OR^a, -NR^aR^b, -C_{1-6}-alkylNR^aR^b, -C(O)NR^aR^b, C_{1-6}-alkylC(O)NR^aR^b, -$S(O)_2R^a$, -C_{1-6}-alkyl$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -C_{1-6}-alkyl$S(O)_2NR^aR^b$, -C(O)$NR^aS(O)_2R^b$ og -$NR^aC(O)R^b$;

eller R^1 og R^2 er slått sammen for å danne en heterocyklyl valgfritt substituert med 1 til 3 grupper uavhengig valgt fra okso, -C_{1-6}-alkyl, -C_{3-8}-cykloalkyl, -C_{2-6}-alkenyl, -C_{2-6}-alkynyl, -OR^a, -C(O)OR^a, -C_{1-6}-cyanoalkyl, -C_{1-6}-alkylOR^a, -C_{1-6}-haloalkyl, -C_{1-3}-alkylC$_{3-8}$-cykloalkyl, -C(O)R^a, -C_{1-6}-alkylC(O)R^a, -C_{1-6}-alkylC(O)OR^a, -NR^aR^b, -C_{1-6}-alkylNR^aR^b, -C(O)NR^aR^b, -C_{1-6}-alkylC(O)NR^aR^b, -$S(O)_2R^a$, -C_{1-6}-

alkylS(O)$_2$R^a, -S(O)$_2$NR^{a}R^b, -C(O)N=S(O)R^{a}NR^{a}R^b, -C(O)N=S(O)R^{a}NR^{a}C(O)R^b og -C$_{1-6}$-alkylS(O)$_2$NR^{a}R^b;

hver R^a er uavhengig valgt fra hydrogen, -C$_{1-6}$-alkyl, -C$_{1-6}$-cyanoalkyl, -C$_{1-6}$-haloalkyl, -C$_{3-8}$-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C$_{1-3}$-alkylC$_{3-8}$-cykloalkyl, -C$_{1-6}$-alkylaryl, -C$_{1-6}$-alkylheteroaryl og -C$_{1-6}$-alkylheterocyklyl;

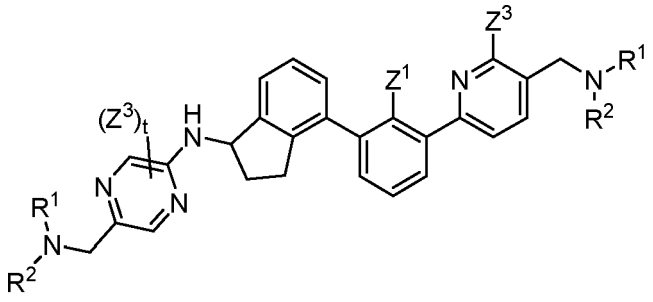
hver R^b er uavhengig valgt fra hydrogen, -C$_{1-6}$-alkyl, -C$_{1-6}$-cyanoalkyl, -C$_{1-6}$-haloalkyl, -C$_{3-8}$-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C$_{1-3}$-alkylC$_{3-8}$-cykloalkyl, -C$_{1-6}$-alkylaryl, -C$_{1-6}$-alkylheteroaryl og -C$_{1-6}$-alkylheterocyklyl;

eller R^a og R^b kan være slått sammen for å danne en heterocyklyl valgfritt substituert med 1 til 4 grupper uavhengig valgt fra -OR^f, cyano, halo, -C$_{1-6}$-alkylOR^f, -C$_{1-6}$-cyanoalkyl, -C$_{1-6}$-haloalkyl, -C$_{3-8}$-cykloalkyl, -C$_{1-3}$-alkylC$_{3-8}$-cykloalkyl, -C(O)R^f, -C$_{1-6}$-alkylC(O)R^f, -C(O)OR^f, -C$_{1-6}$-alkylC(O)OR^f, -NR^{f}R^g, -C$_{1-6}$-alkylNR^{f}R^g, -C(O)NR^{f}R^g, -C$_{1-6}$-alkylC(O)NR^{f}R^g, -S(O)$_2$R^f, -C$_{1-6}$-alkylS(O)$_2$R^f, -S(O)$_2$NR^{f}R^g, -C$_{1-6}$-alkylS(O)$_2$NR^{f}R^g, -C(O)NR^{f}S(O)$_2$R^g og -NR^{f}C(O)R^g;

hver R^f er uavhengig valgt fra hydrogen, -C$_{1-6}$-alkyl, -C$_{3-8}$-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C$_{1-3}$-alkylC$_{3-8}$-cykloalkyl, -C$_{1-6}$-alkylaryl, -C$_{1-6}$-alkylheteroaryl og -C$_{1-6}$-alkylheterocyklyl; og

hver R^g er uavhengig valgt fra hydrogen, -C$_{1-6}$-alkyl, -C$_{3-8}$-cykloalkyl, aryl, heteroaryl, heterocyklyl, -C$_{1-3}$-alkylC$_{3-8}$-cykloalkyl, -C$_{1-6}$-alkylaryl, -C$_{1-6}$-alkylheteroaryl og -C$_{1-6}$-alkylheterocyklyl.

4. Forbindelse ifølge krav 3, hvor forbindelsen med formel (VIA) er en forbindelse med formel (VIC):



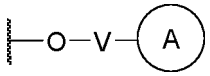
(VIC)

eller et farmasøytisk akseptabelt salt derav, hvor Z^1, Z^3, t, R^1 og R^2 har betydningene angitt i krav 3.

5. Forbindelse ifølge et hvilket som helst av de forutgående krav, hvor Z^1 er halo.

6. Forbindelse ifølge et hvilket som helst av de forutgående krav, hvor i det minste én Z^3 er halo, -C_{1-6}-alkyl, C_{1-6}-haloalkyl, -O-cyanoalkyl, -O-C_{1-6}-haloalkyl eller C_{1-6}-alkoksy.

7. Forbindelse ifølge et hvilket som helst av de forutgående krav, hvor i det minste én Z^3 har formel:



V er uavhengig valgt fra en binding, C_{1-6}-alkyl, C_{2-6}-alkenyl og C_{2-6}-alkynyl;

hvor hver alkyl, alkenyl eller alkynyl er valgfritt uavhengig substituert med -OR^a, halo, cyano, -NR^aR^b eller -C_{3-8}-cykloalkyl;

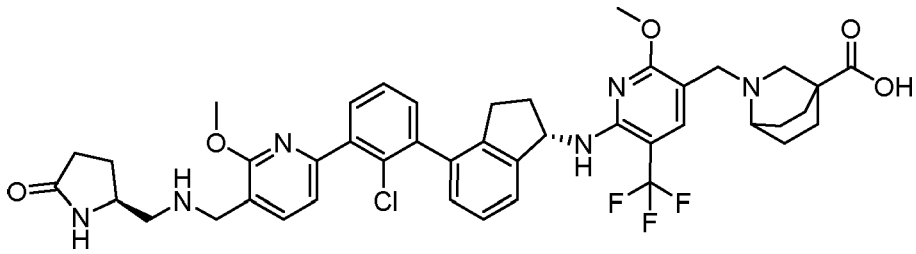
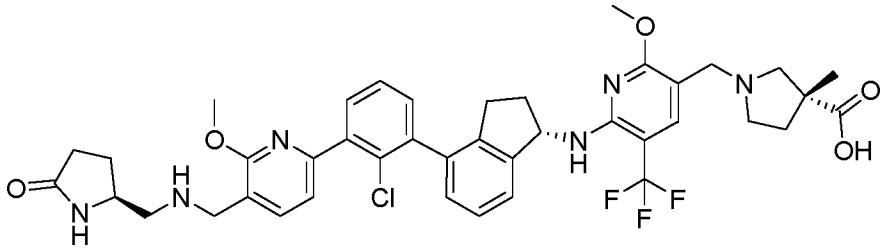
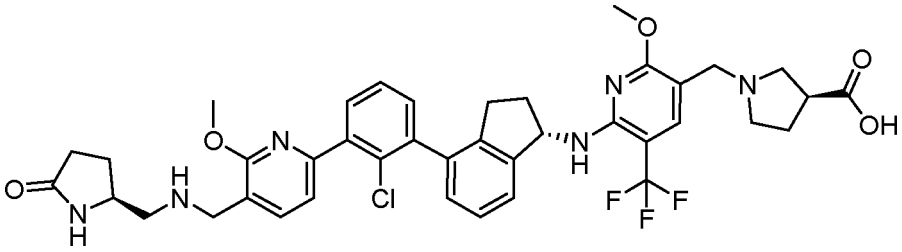
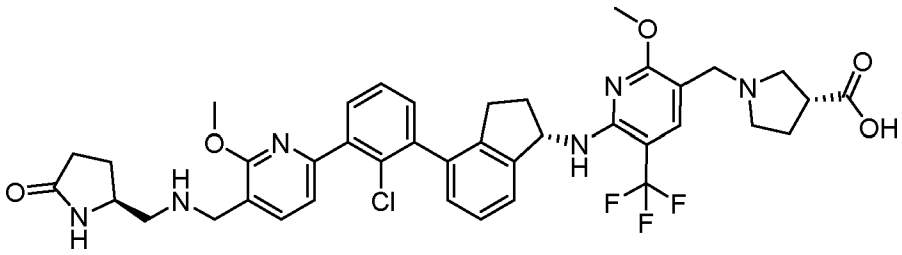
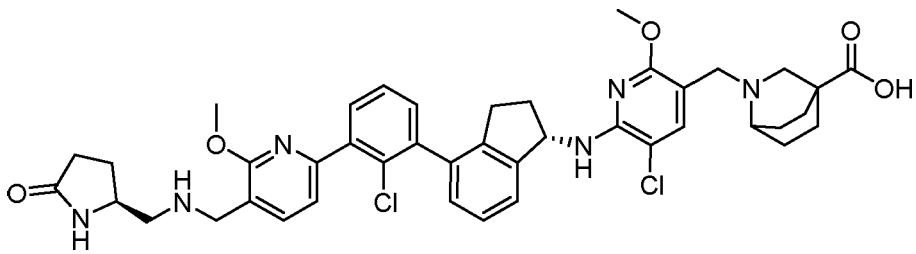
ring A er uavhengig cykloalkyl, aryl, heteroaryl eller heterocyklyl;

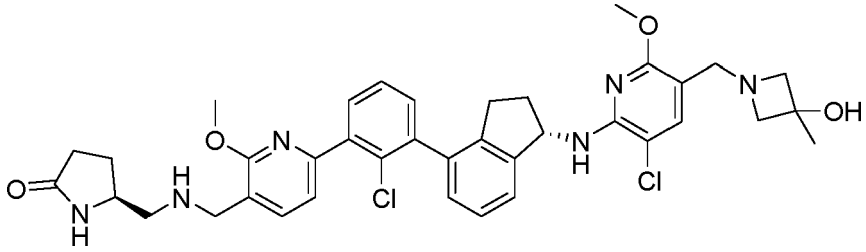
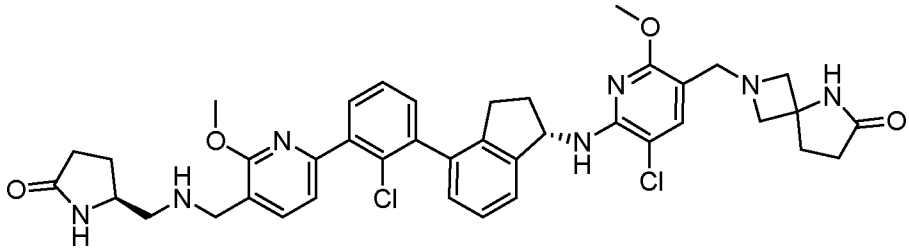
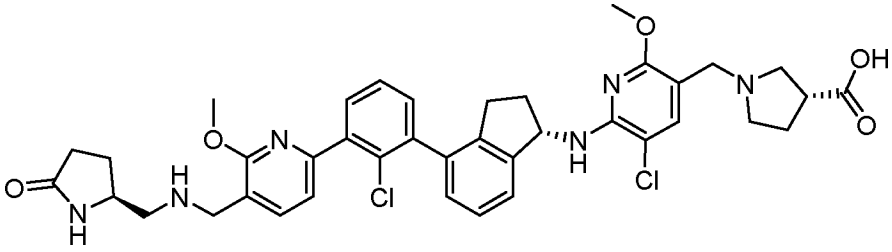
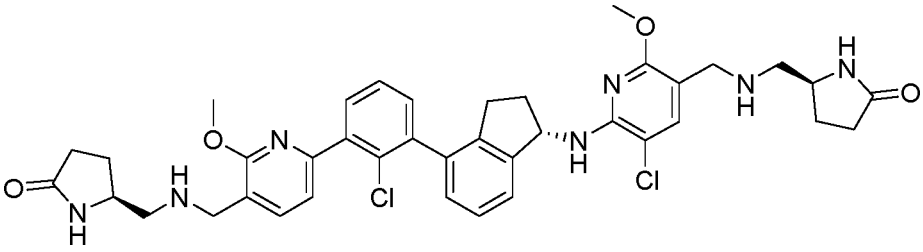
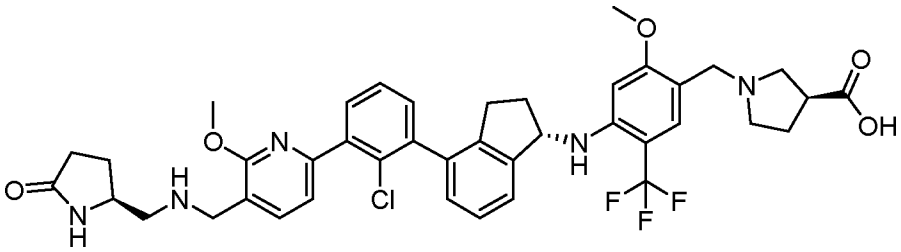
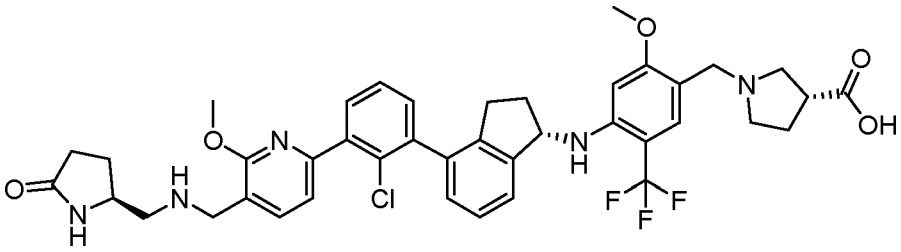
hvor hver cykloalkyl, aryl, heteroaryl eller heterocyklyl er valgfritt substituert med 1 til 4 grupper uavhengig valgt fra okso, -NO_2, -N_3, -OR^a, halo, cyano, -C_{1-6}-alkyl, -C_{1-6}-haloalkyl, -C_{2-6}-alkenyl, -C_{2-6}-alkynyl, -O-C_{1-6}-haloalkyl, NR^aR^b, -$C(O)R^a$, -$C(O)OR^a$, -OC_{1-6}-alkylCN, -$C(O)NR^aR^b$, -$NR^aC(O)R^a$, $NR^aC(O)OR^a$, -$C(O)N(R^a)OR^b$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$NR^aS(O)_2R^b$, -$NR^aS(O)_2NR^aR^b$, -$C(O)NR^aS(O)_2NR^aR^b$, -C_{3-8}-cykloalkyl, heteroaryl og -C_{1-6}-alkyl-C_{3-8}-cykloalkyl.

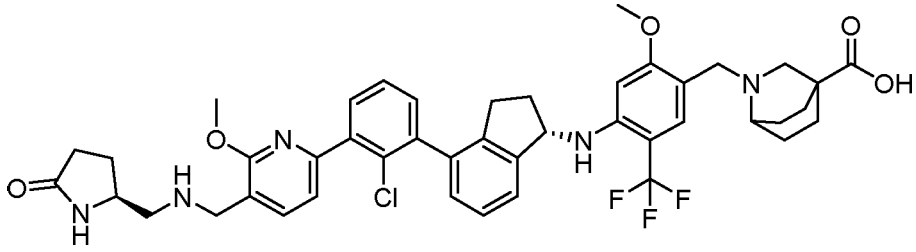
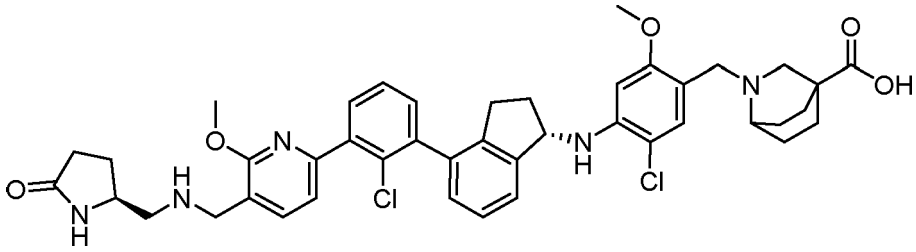
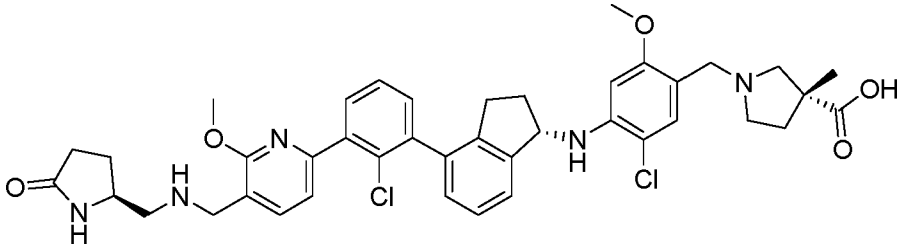
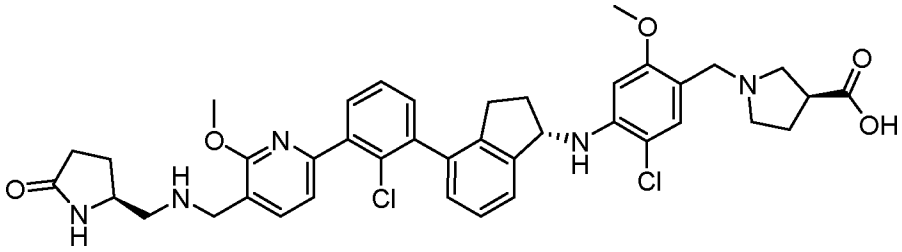
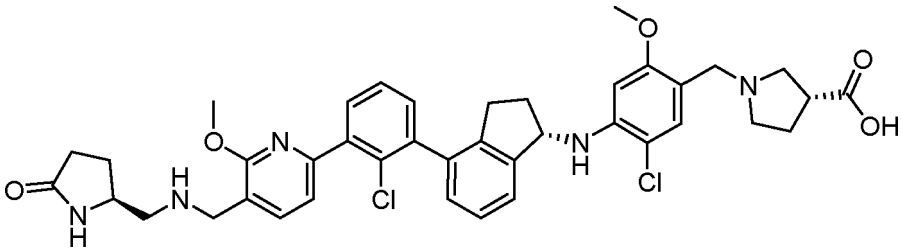
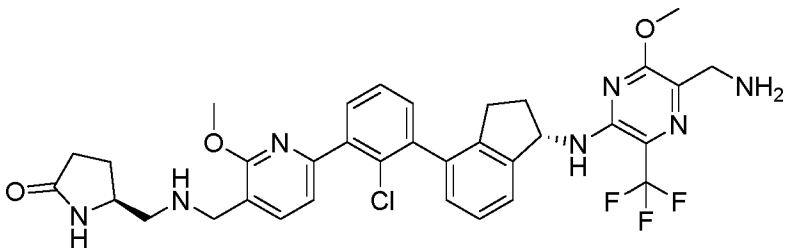
8. Forbindelse ifølge et hvilket som helst av kravene 1 til 7, hvor R^1 og R^2 er slått sammen for å danne en heterocyklyl valgfritt substituert med 1 til 3 grupper uavhengig valgt fra okso, -C_{1-6}-alkyl, -C_{3-8}-cykloalkyl, -C_{2-6}-alkenyl, -C_{2-6}-alkynyl, -OR^a, -$C(O)OR^a$, -C_{1-6}-cyanoalkyl, -C_{1-6}-alkylOR^a, -C_{1-6}-haloalkyl, -C_{1-3}-alkylC_{3-8}-cykloalkyl, -$C(O)R^a$, -C_{1-6}-alkyl$C(O)R^a$, -C_{1-6}-alkyl$C(O)OR^a$, -NR^aR^b, -C_{1-6}-alkylNR^aR^b, -$C(O)NR^aR^b$, -C_{1-6}-alkyl$C(O)NR^aR^b$, -$S(O)_2R^a$, -C_{1-6}-alkyl$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)N{=}S(O)R^aNR^aR^b$, -$C(O)N{=}S(O)R^aNR^aC(O)R^b$ og -C_{1-6}-alkyl$S(O)_2NR^aR^b$.

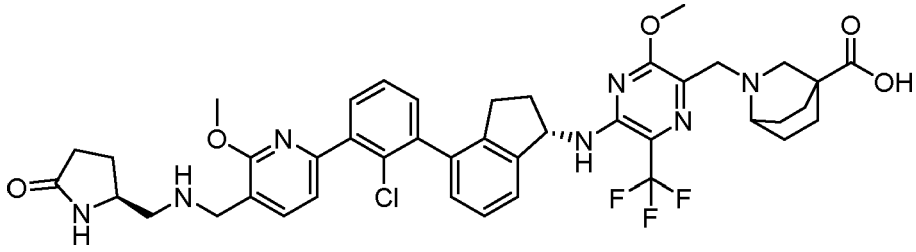
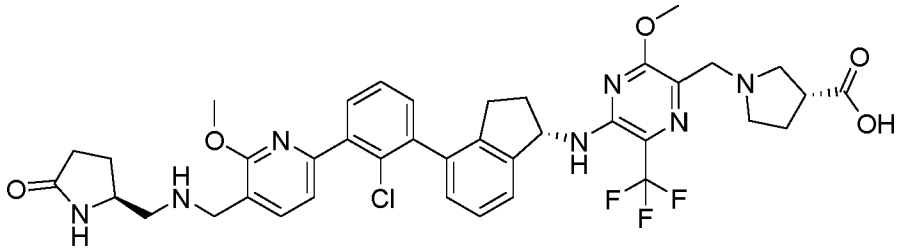
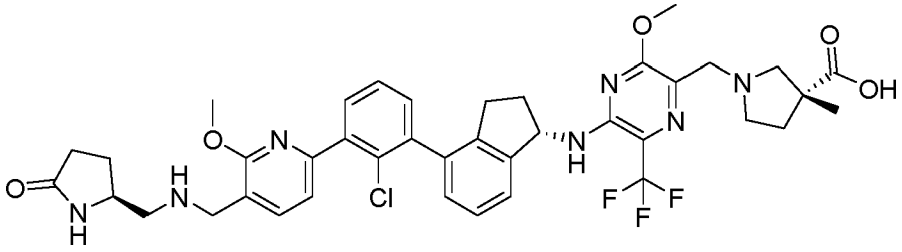
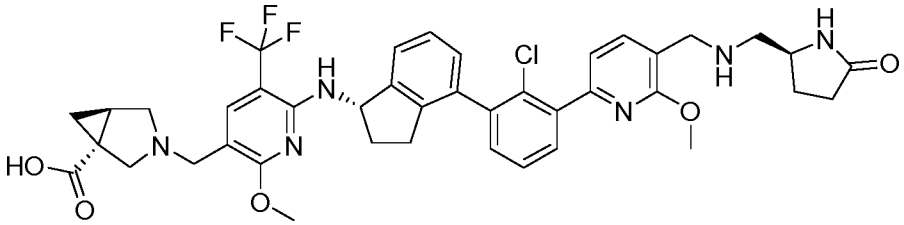
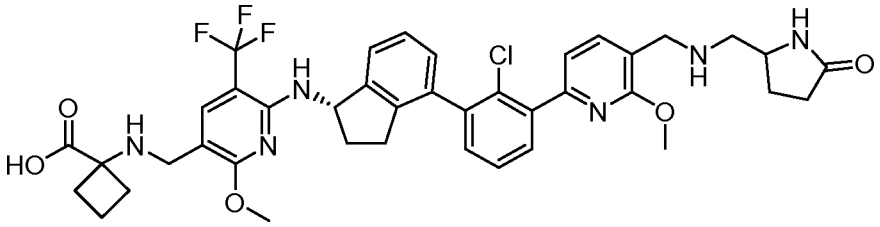
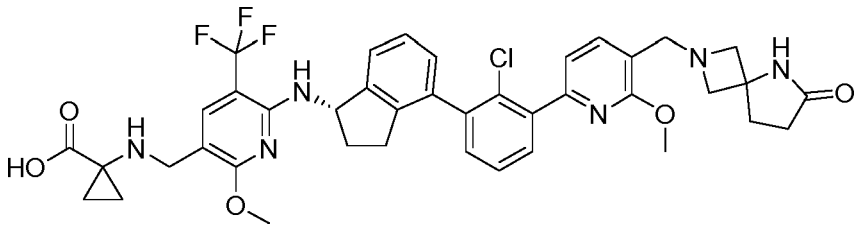
9. Forbindelse ifølge et hvilket som helst av kravene 1 til 7, hvor i det minste én av R^1 og R^2 er -C_{1-6}-alkylheteroaryl eller -C_{1-6}-alkylheterocyklyl.

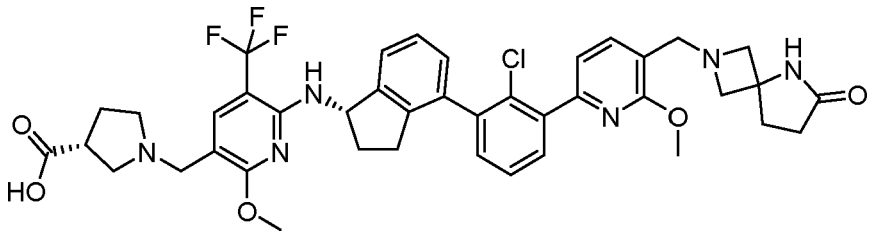
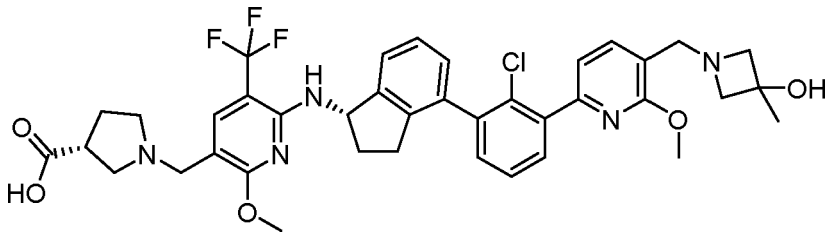
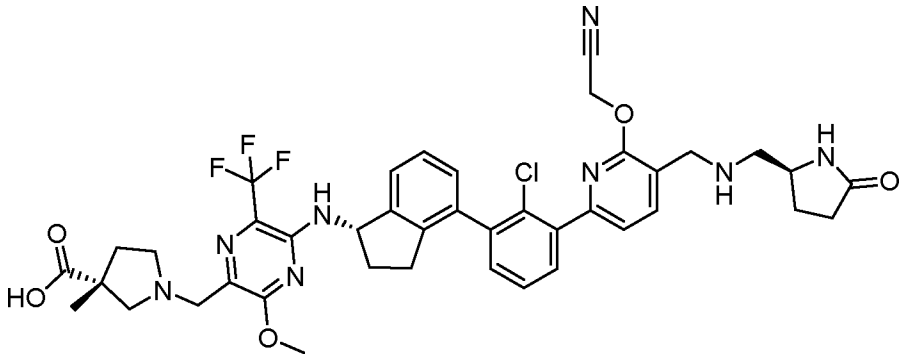
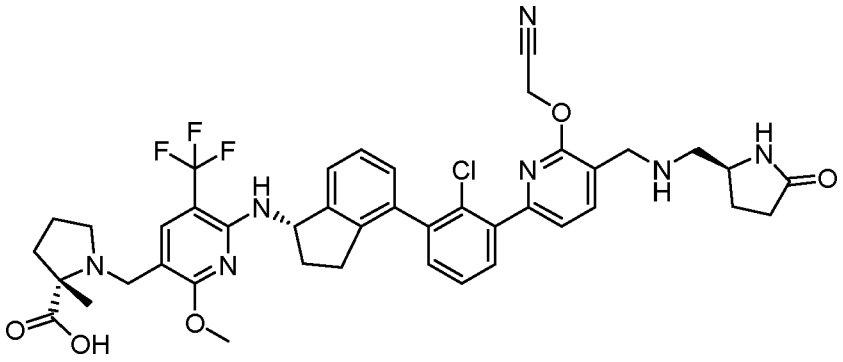
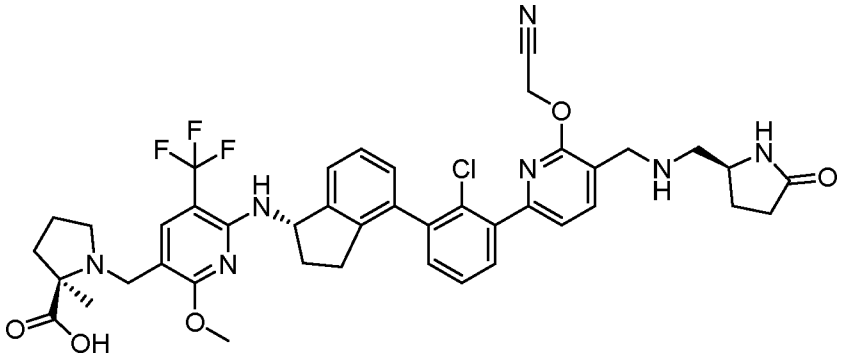
10. Forbindelse ifølge krav 1, valgt fra de følgende forbindelser A-1 til A-109, eller et farmasøytisk akseptabelt salt derav:

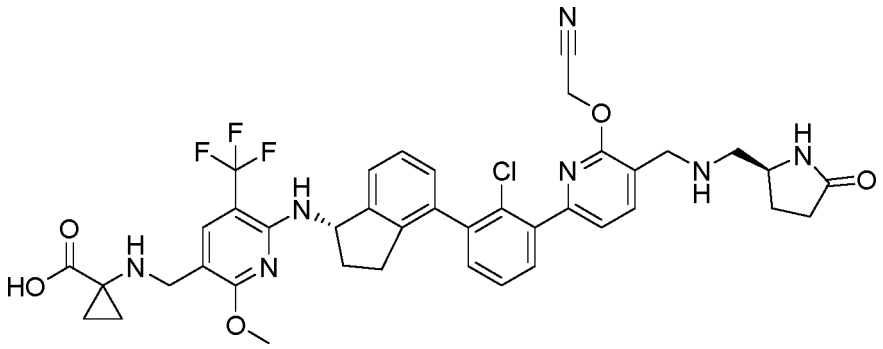
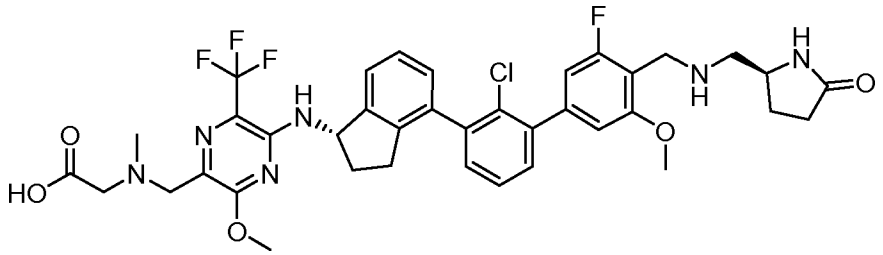
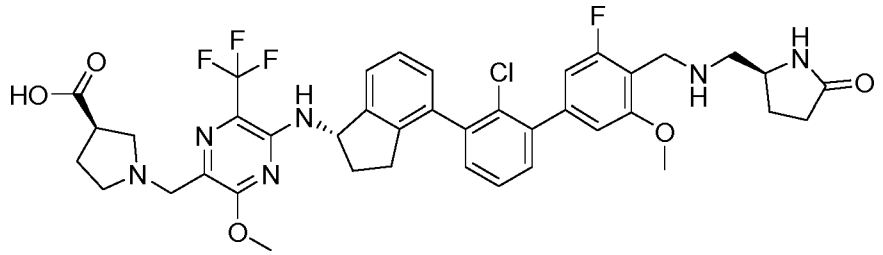
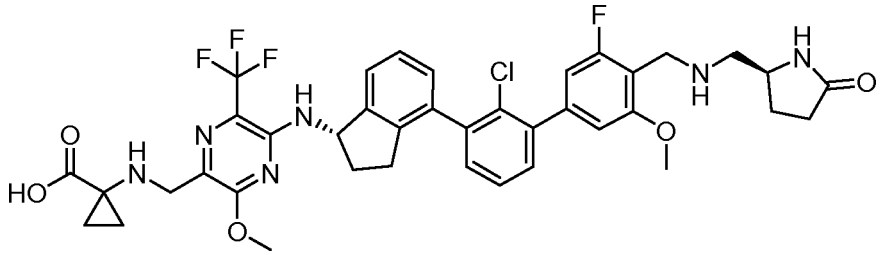
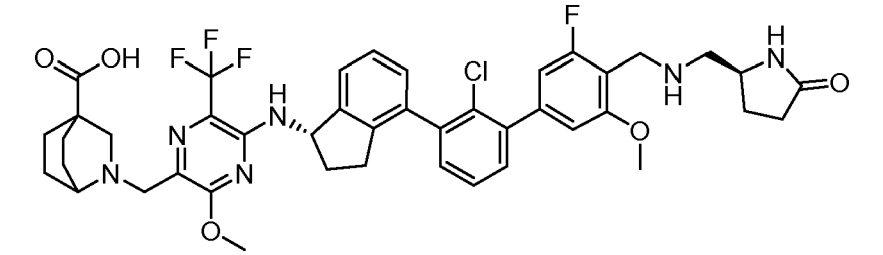
A-1	
A-2	
A-3	
A-4	
A-5	

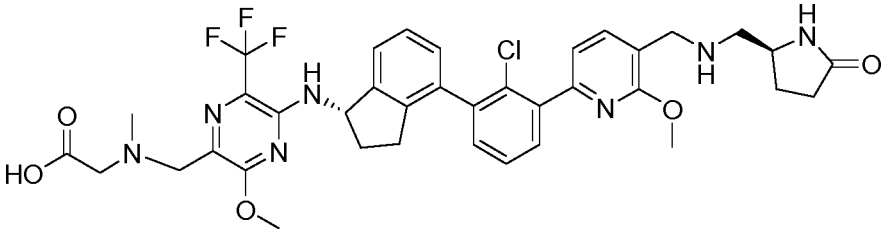
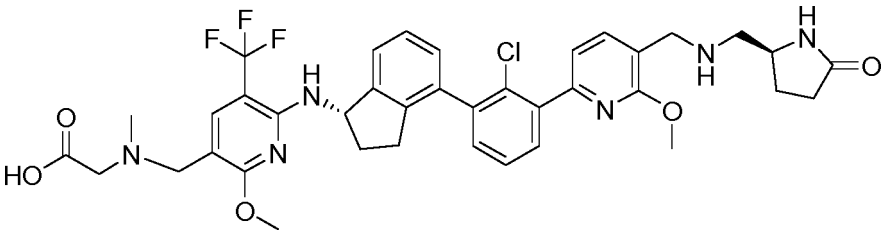
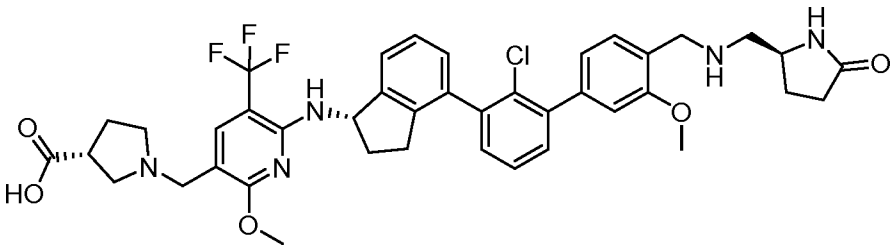
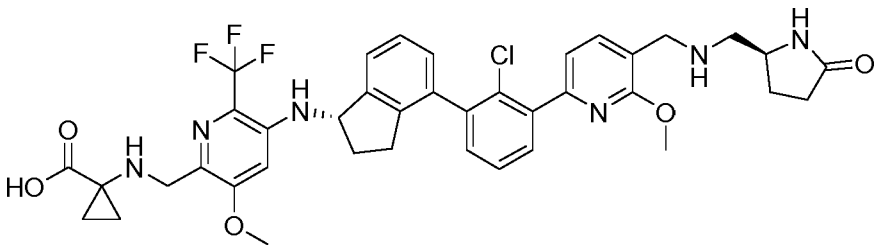
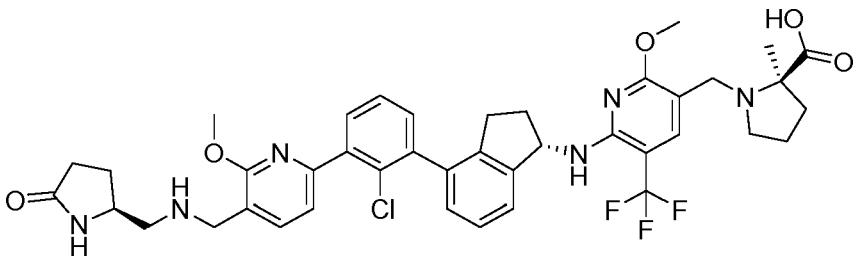
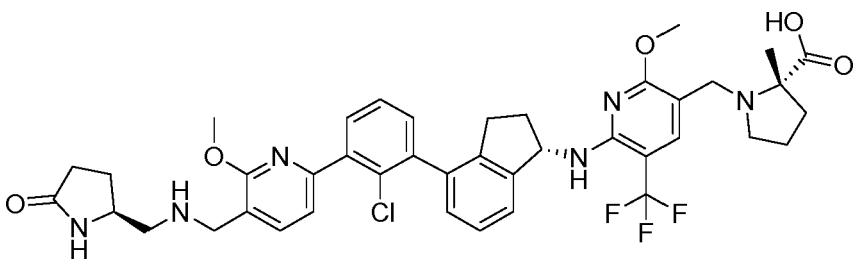
A-6	
A-7	
A-8	
A-9	
A-10	
A-11	

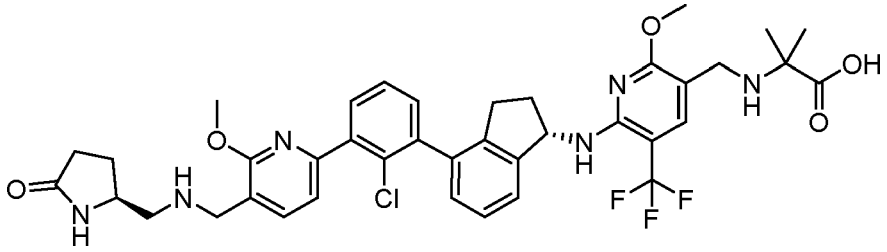
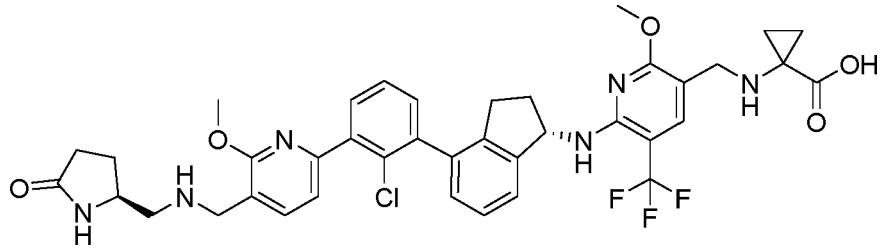
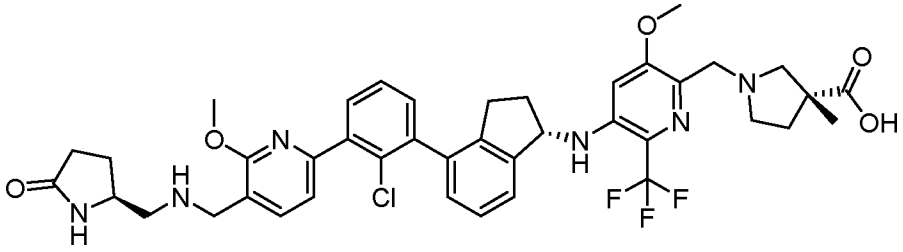
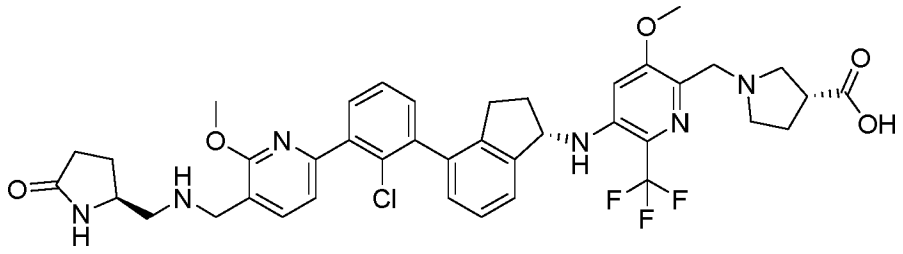
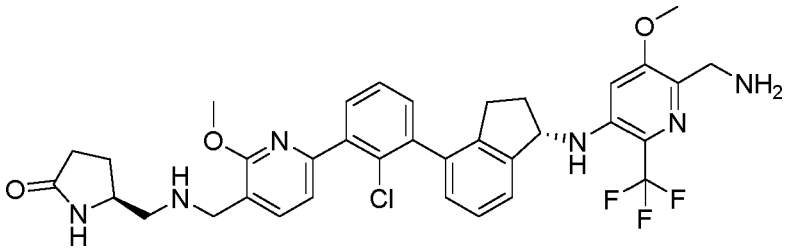
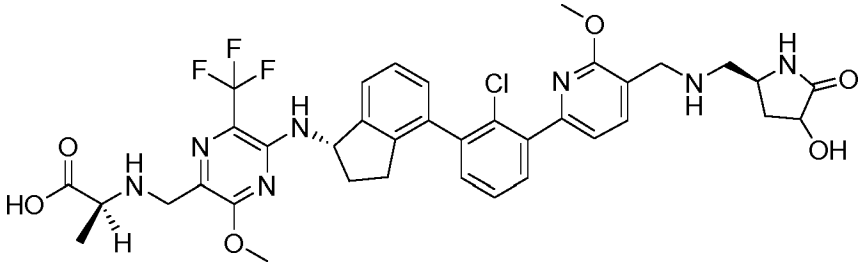
A-12	
A-13	
A-14	
A-15	
A-16	
A-17	

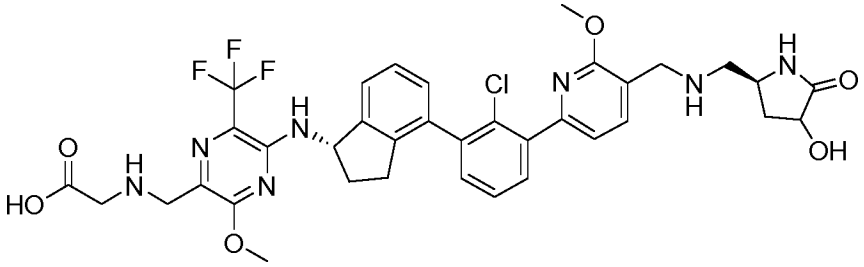
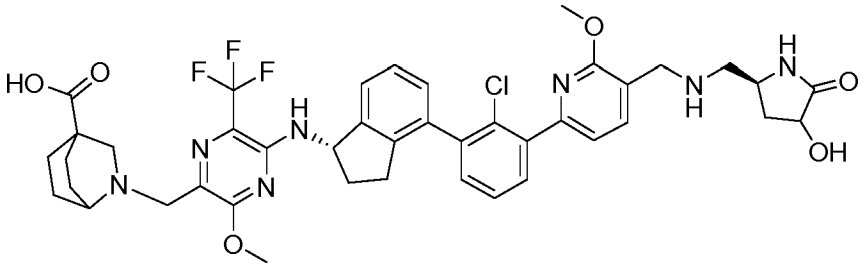
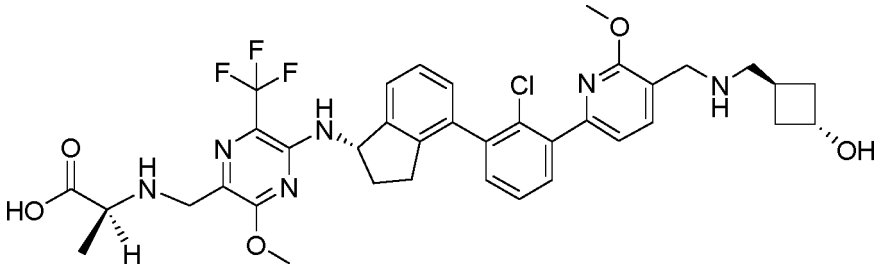
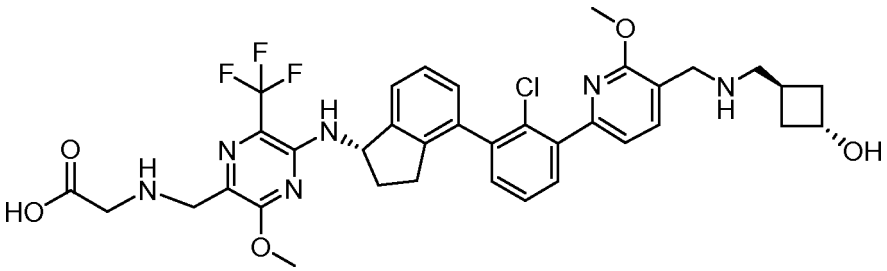
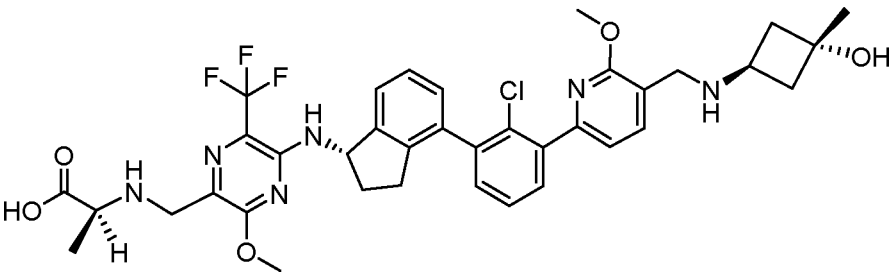
A-18	
A-19	
A-20	
A-21	
A-22	
A-23	

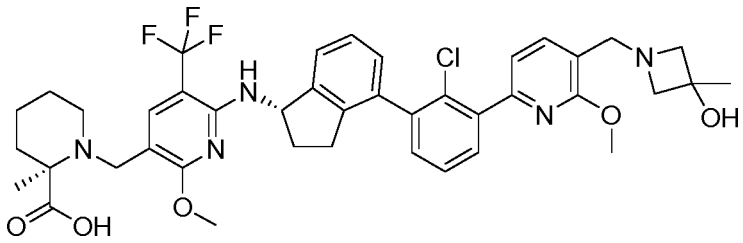
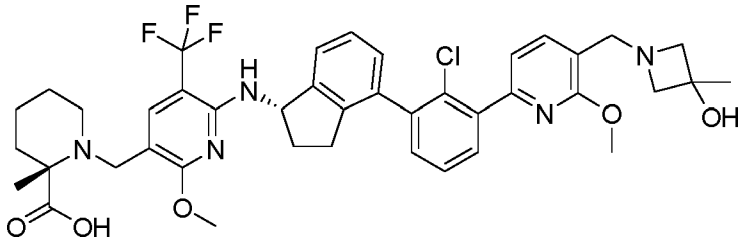
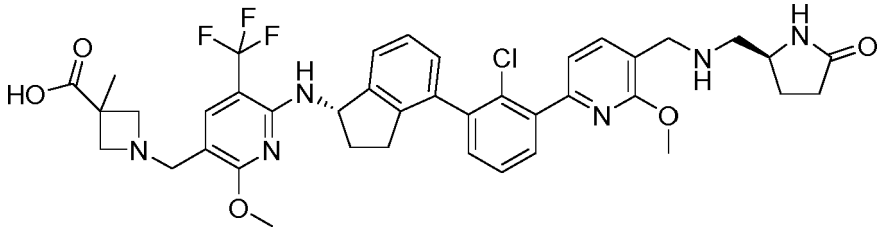
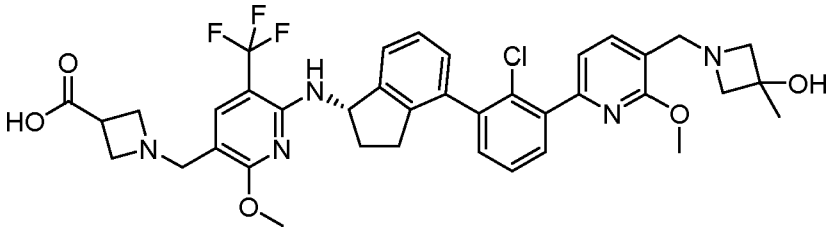
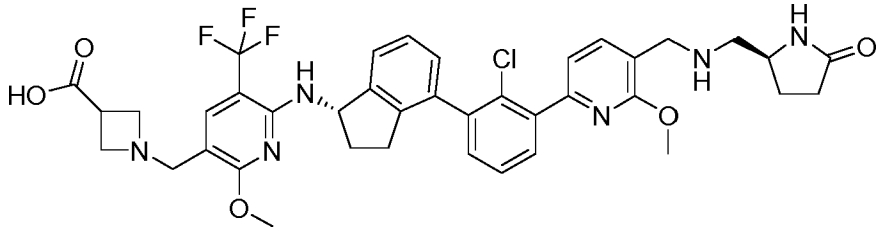
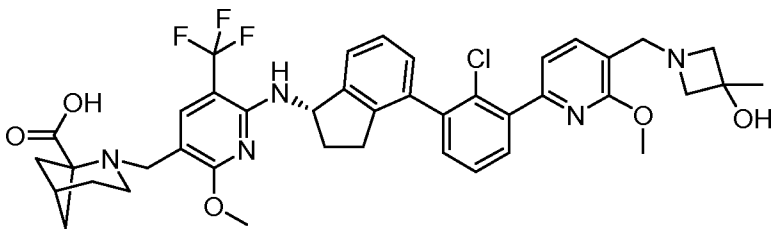
A-24	
A-25	
A-26	
A-27	
A-28	

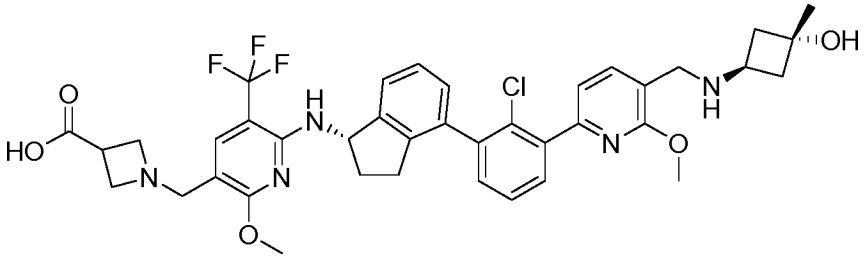
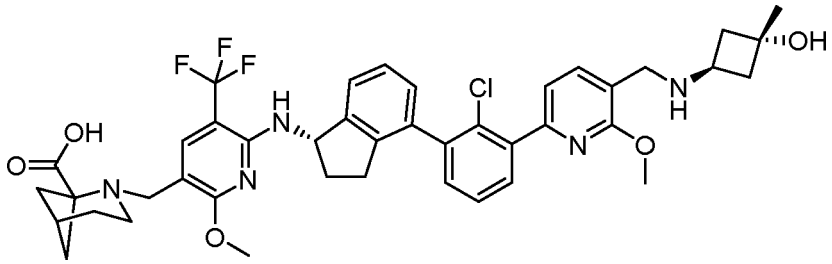
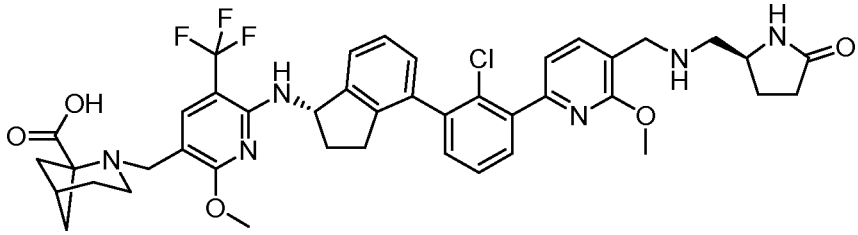
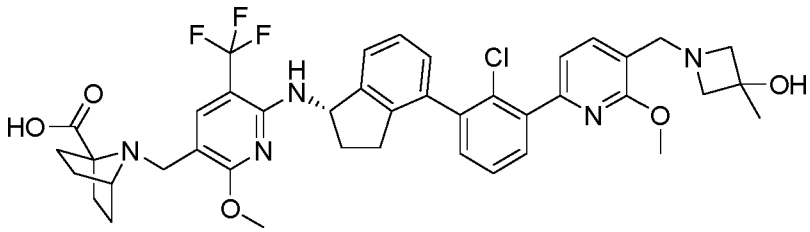
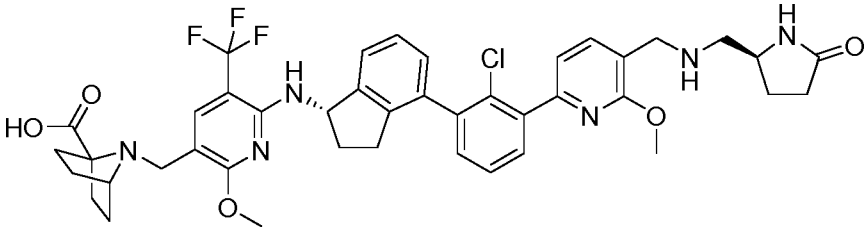
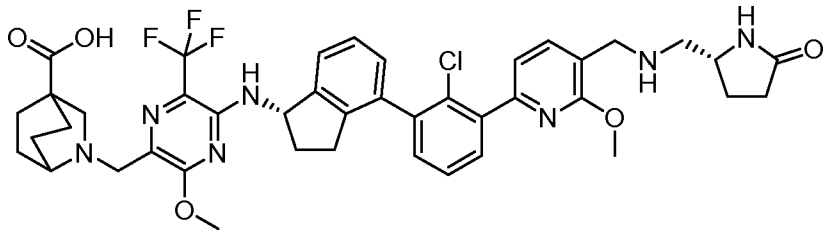
A-29	
A-30	
A-31	
A-32	
A-33	

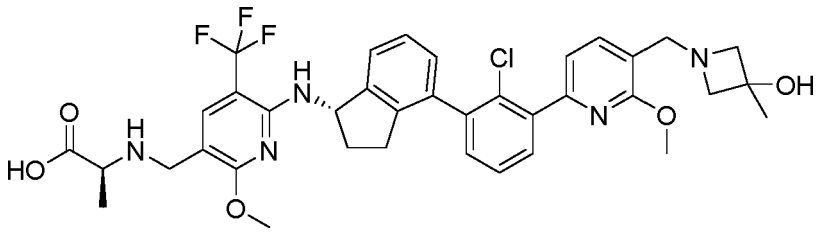
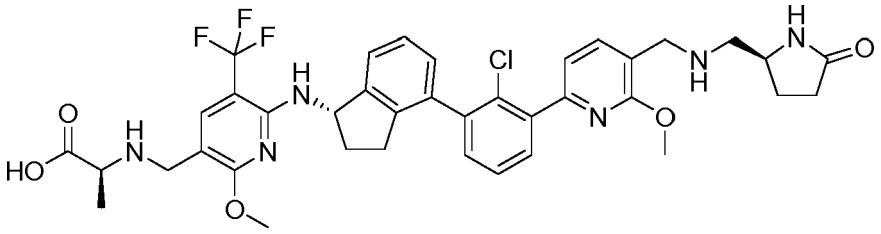
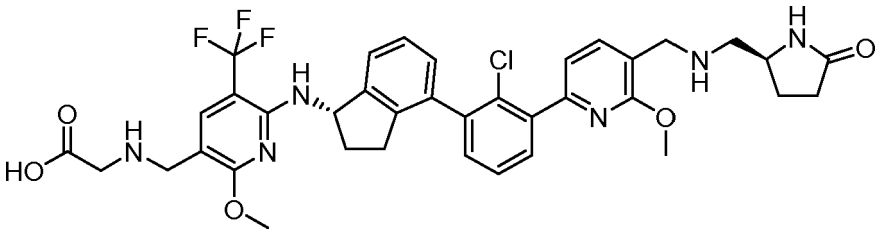
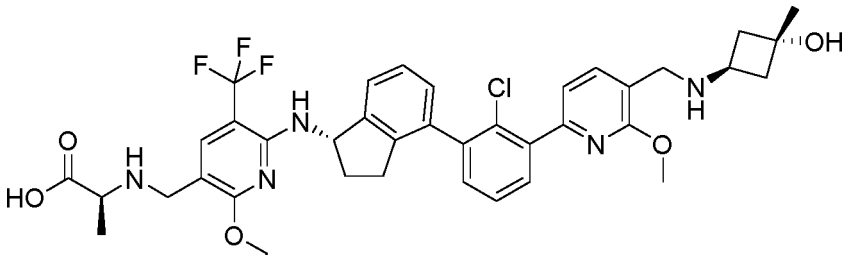
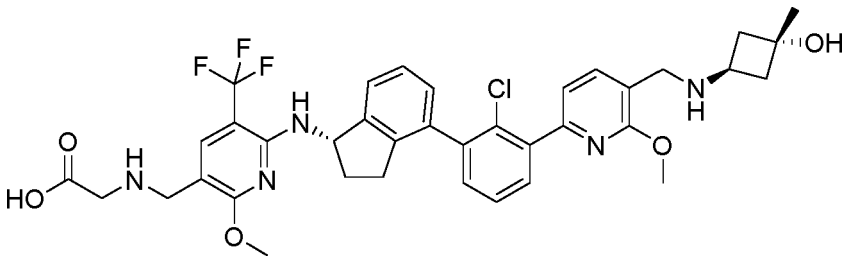
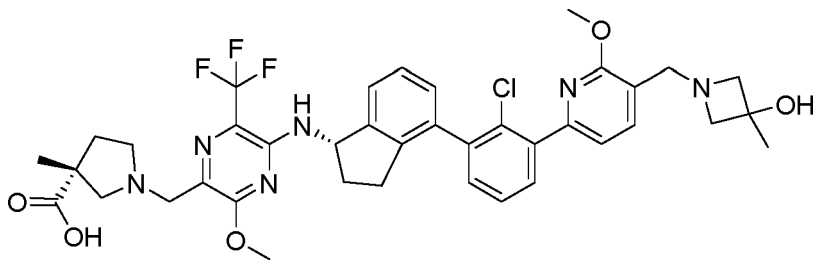
A-34	
A-35	
A-36	
A-37	
A-38	
A-39	

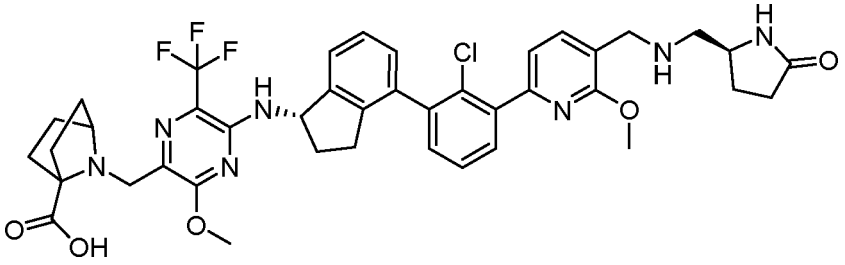
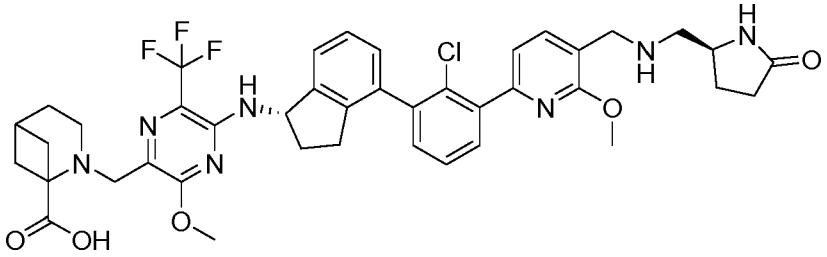
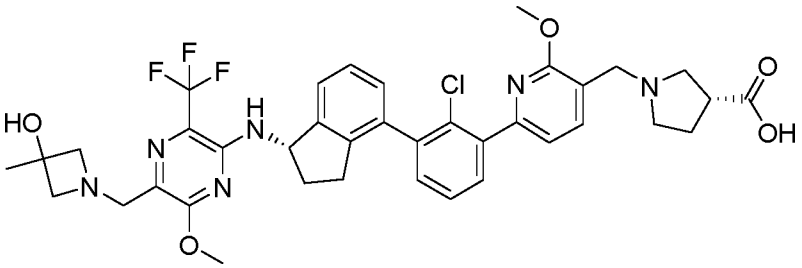
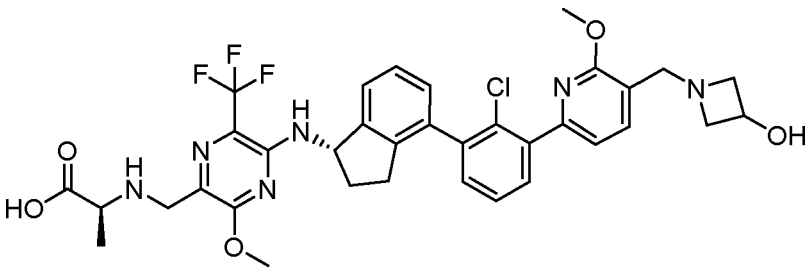
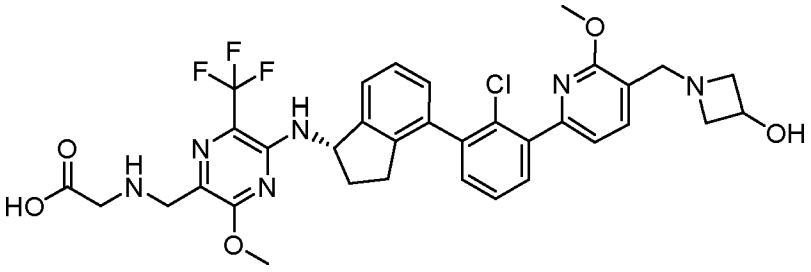
A-40	
A-41	
A-42	
A-43	
A-44	
A-45	

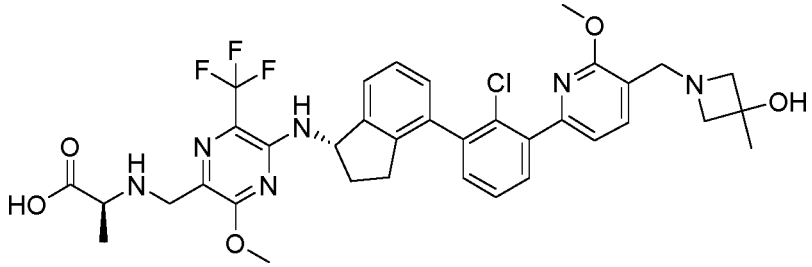
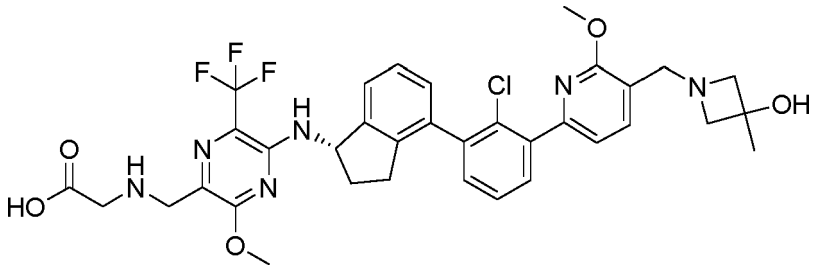
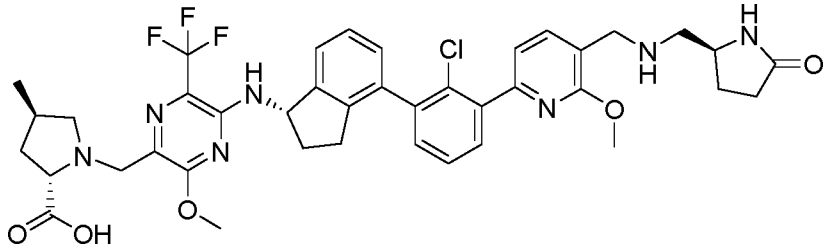
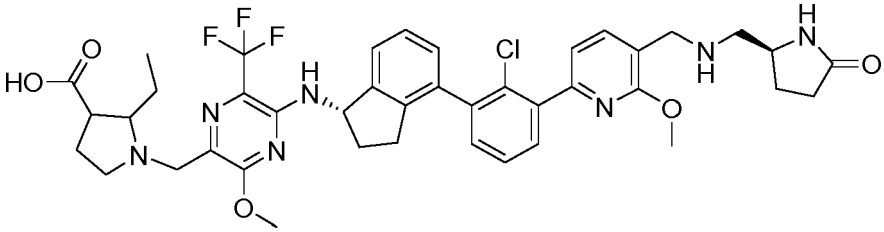
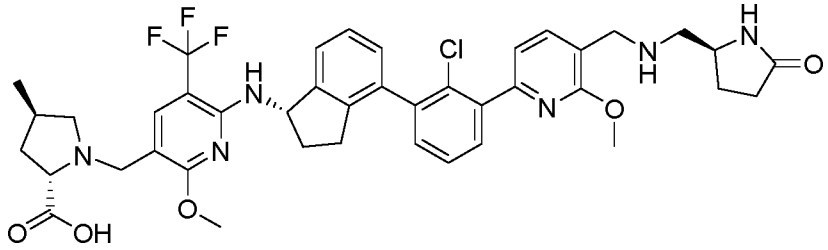
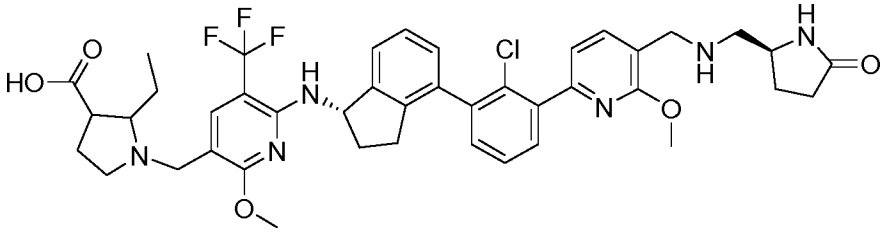
A-46	
A-47	
A-48	
A-49	
A-50	

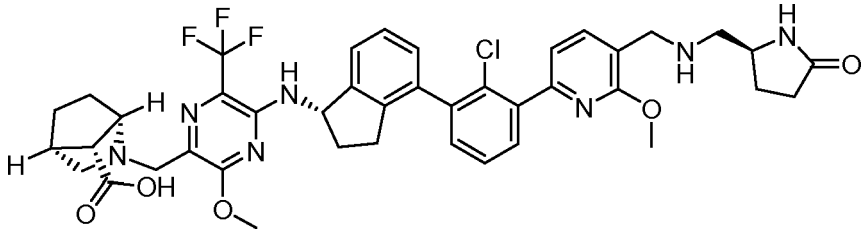
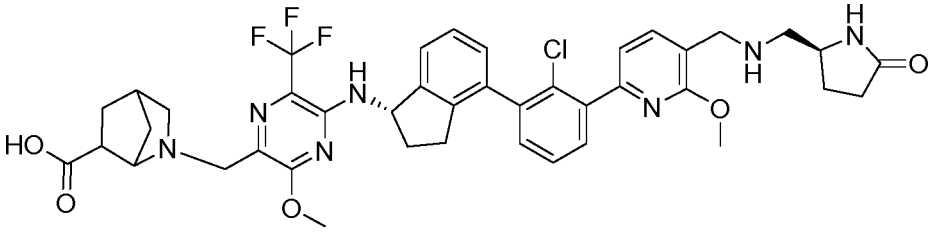
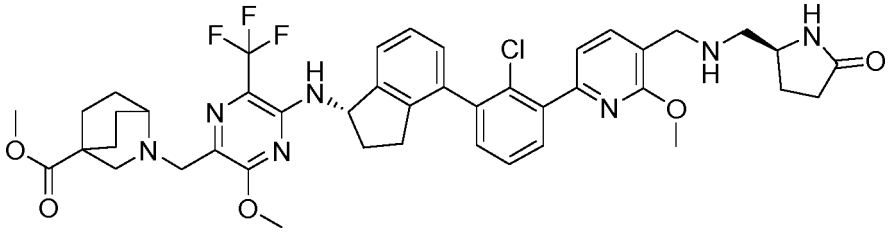
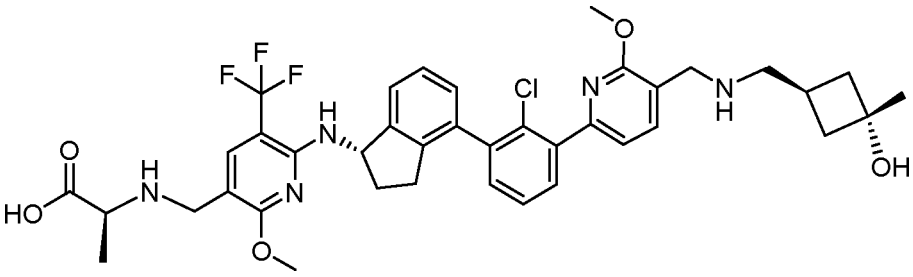
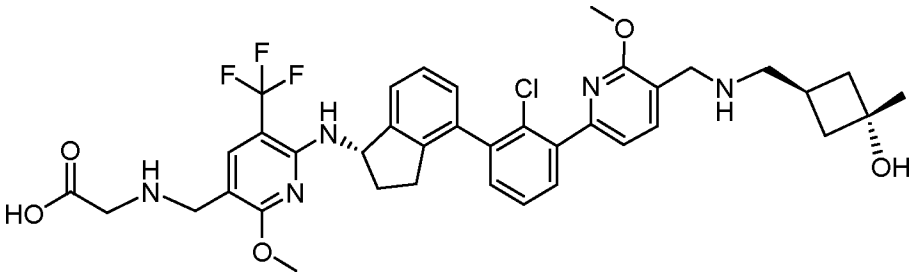
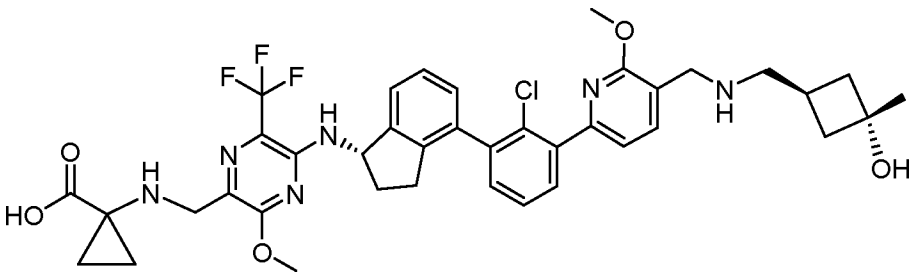
A-51	
A-52	
A-53	
A-54	
A-55	
A-56	

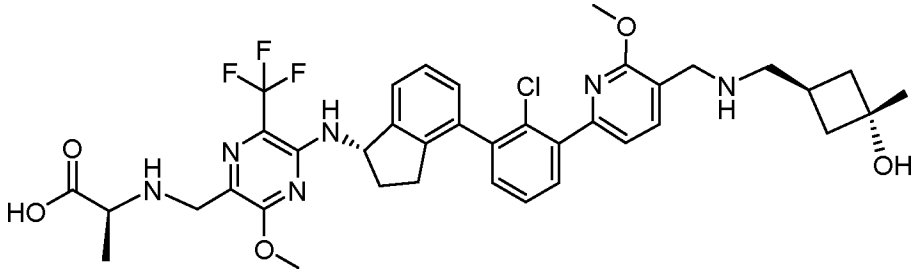
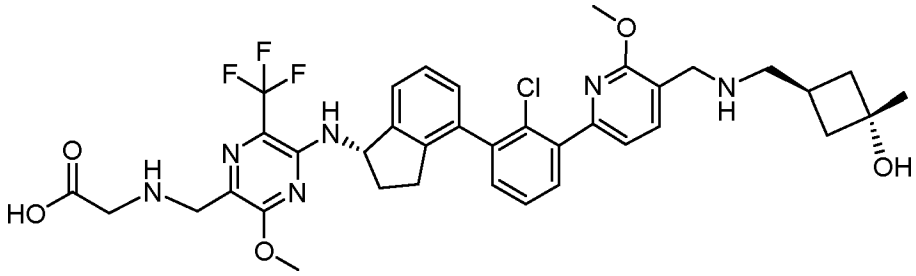
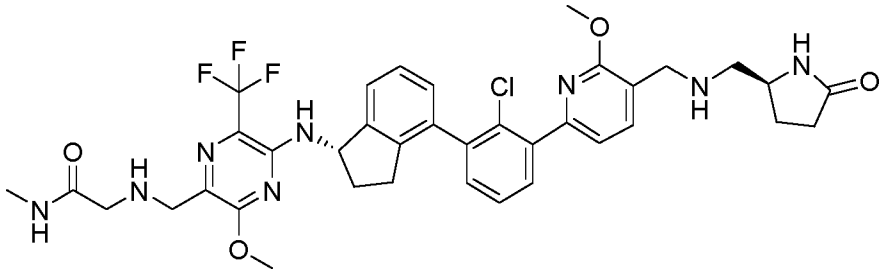
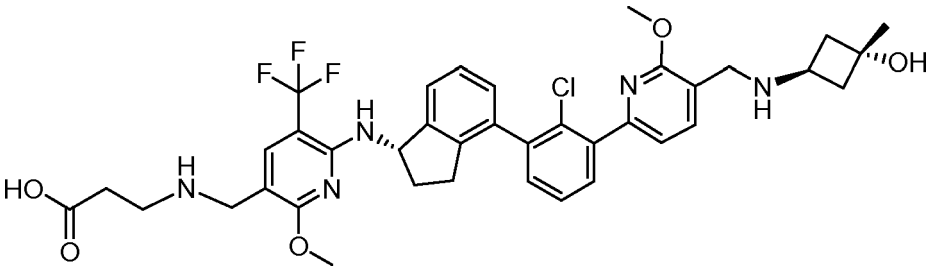
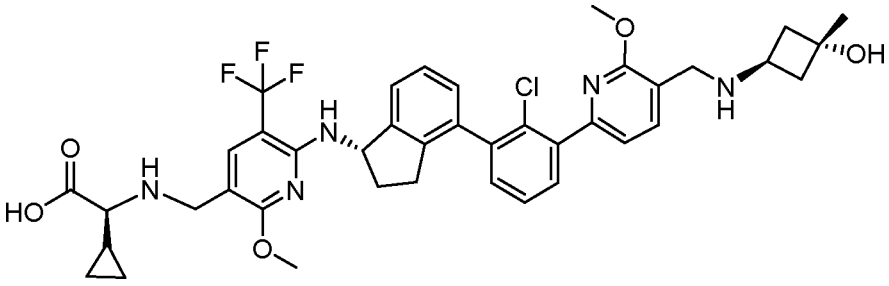
A-57	
A-58	
A-59	
A-60	
A-61	
A-62	

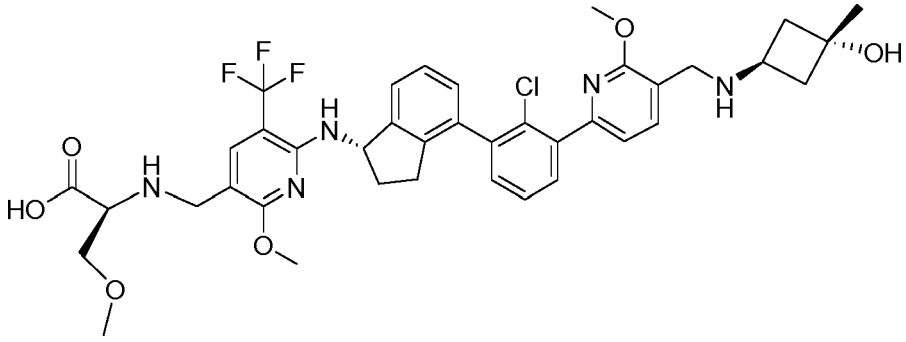
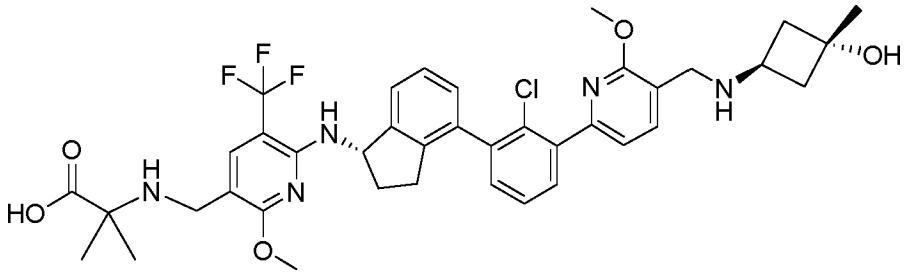
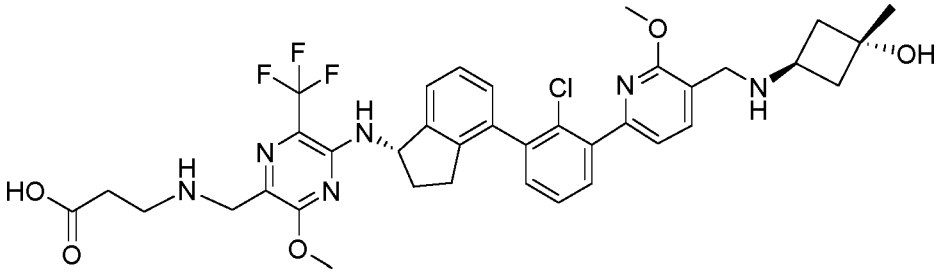
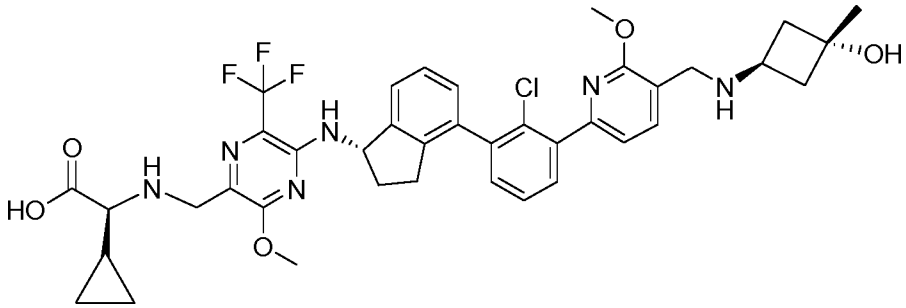
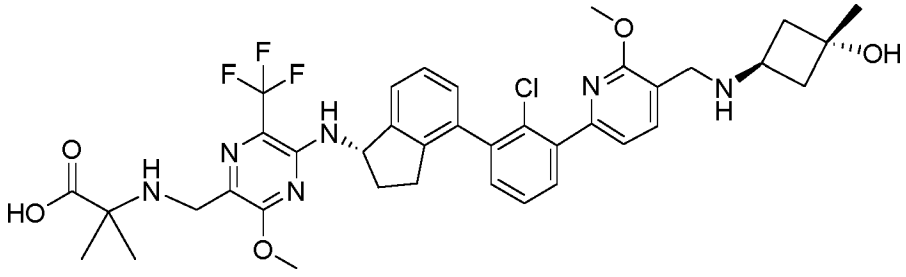
A-63	
A-64	
A-65	
A-66	
A-67	
A-68	

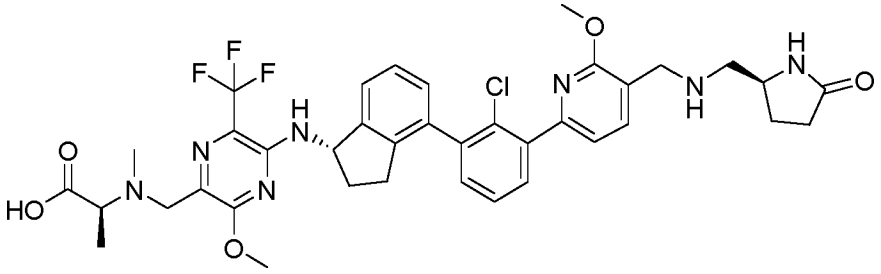
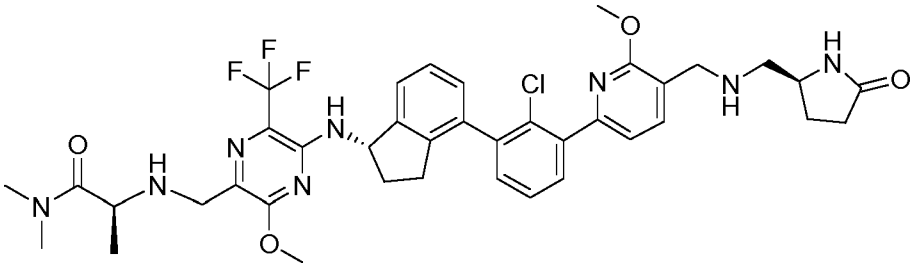
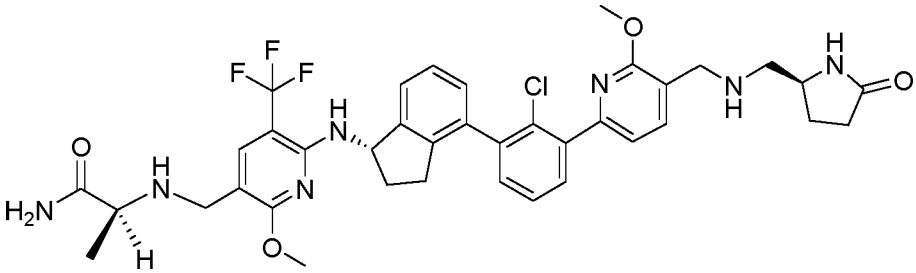
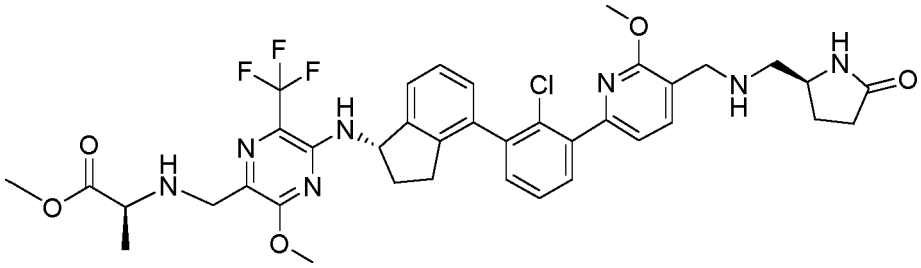
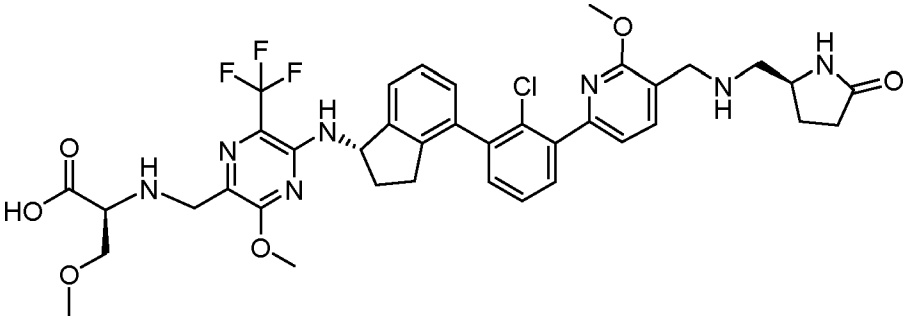
A-69	
A-70	
A-71	
A-72	
A-73	

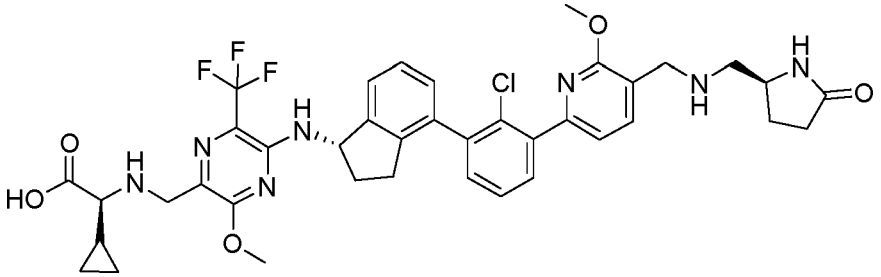
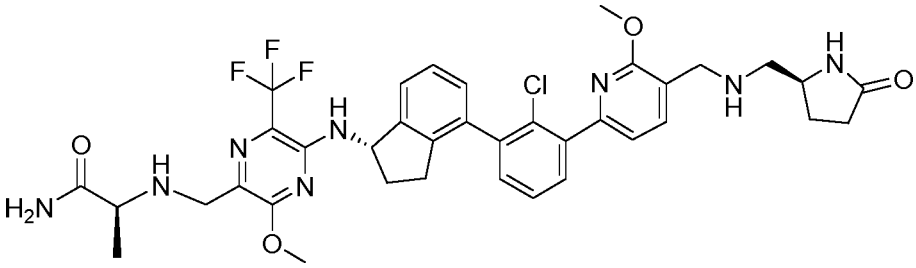
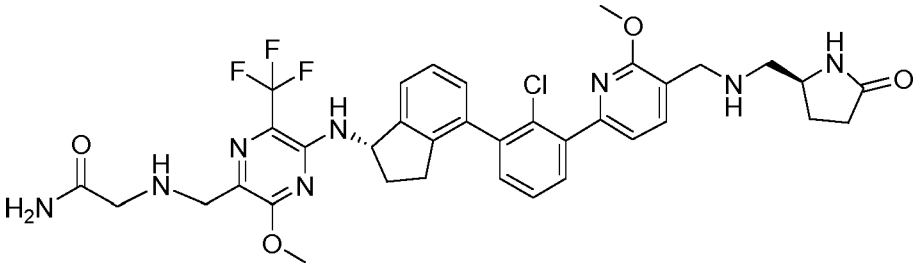
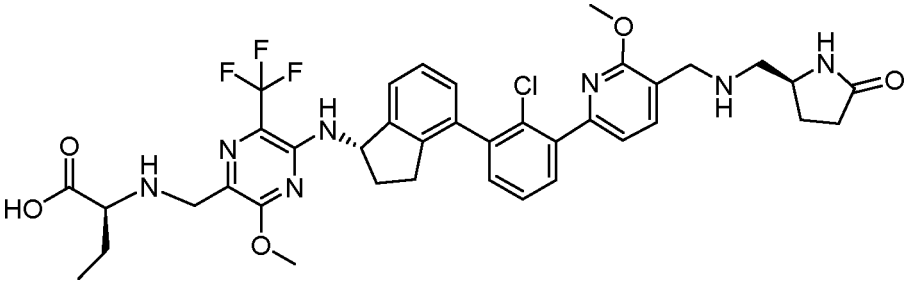
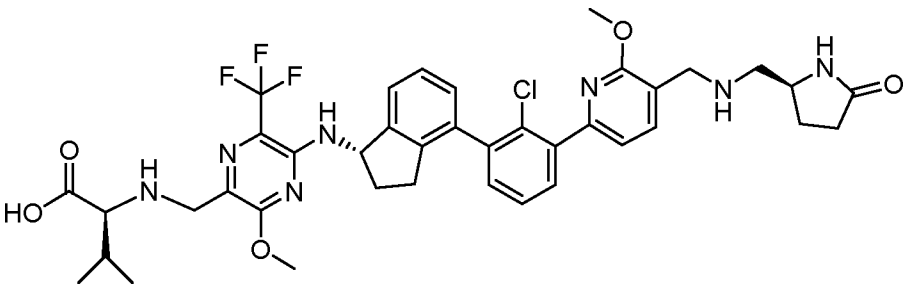
A-74	
A-75	
A-76	
A-77	
A-78	
A-79	

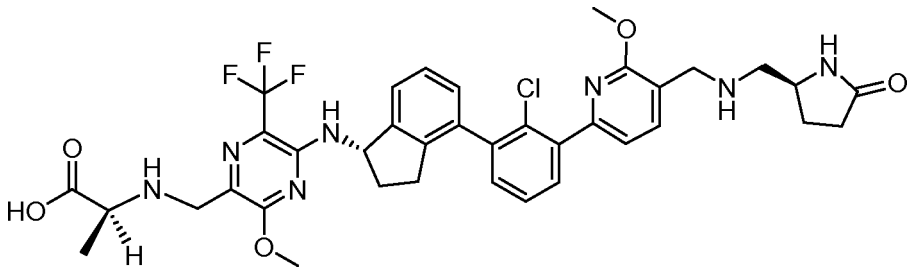
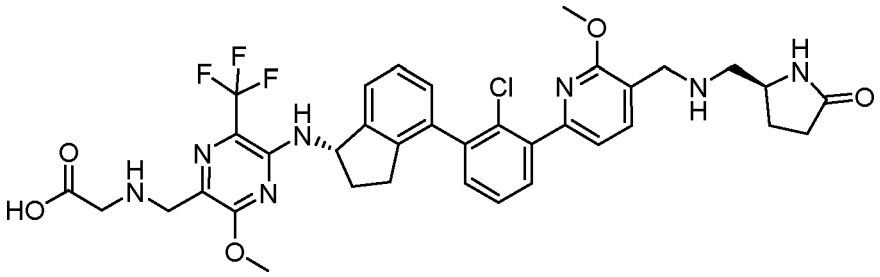
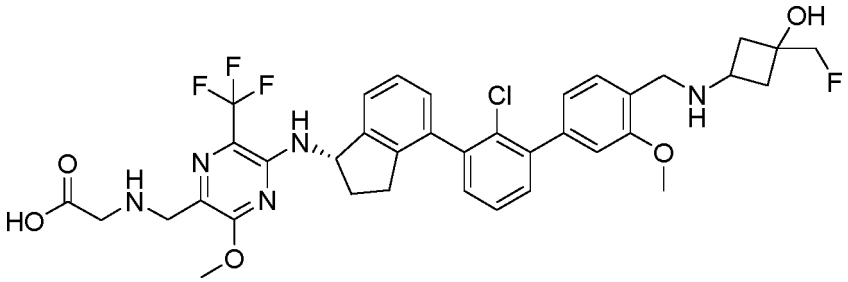
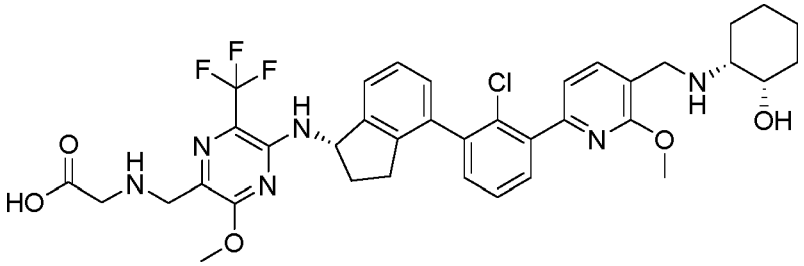
A-80	
A-81	
A-82	
A-83	
A-84	
A-85	

A-86	
A-87	
A-88	
A-89	
A-90	

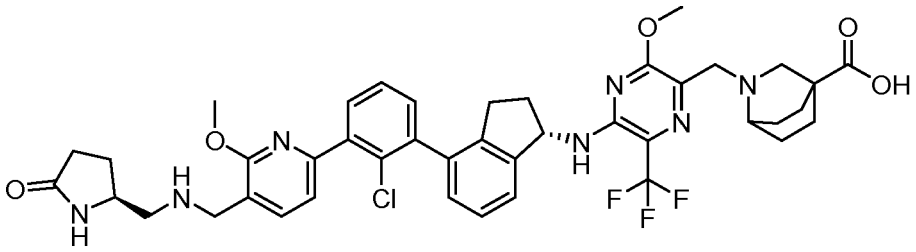
A-91	
A-92	
A-93	
A-94	
A-95	

A-96	
A-97	
A-98	
A-99	
A-100	

A-101	
A-102	
A-103	
A-104	
A-105	

A-106	
A-107	
A-108	
A-109	

11. Forbindelse ifølge krav 1, som er:



;

eller et farmasøytisk akseptabelt salt derav.

12. Farmasøytisk sammensetning omfattende en forbindelse ifølge et hvilket som helst av kravene 1-11 eller et farmasøytisk akseptabelt salt derav, og i det minste én farmasøytisk akseptabel eksipiens.

13. Farmasøytisk sammensetning ifølge krav 12, ytterligere omfattende i det minste ett ytterligere antikreftmiddel eller en terapi, valgt fra rituxan, doksorubicin, gemcitabin, nivolumab, pembrolizumab og ipilimumab, og i det minste én farmasøytisk akseptabel eksipiens.

14. Farmasøytisk sammensetning ifølge krav 12, ytterligere omfattende et ytterligere kreftmiddel, hvor det ytterligere antikreftmiddel er nivolumab, pembrolizumab, atezolizumab eller ipilimumab.