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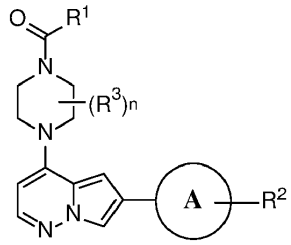
(54) Title **INHIBITORS OF ACTIVIN RECEPTOR-LIKE KINASE**

(56) References Cited: WO-A1-2014/138088

Patentkrav

1. Forbindelse av formel (I):



(I),

eller et farmasøytisk akseptabelt salt derav, hvori:

ring A er fenyl eller heteroaryl, hvori ring A eventuelt substitueres med 1, 2 eller 3 substituenter uavhengig valgt fra halogen, =O, cyano, -OR^c, -NR^dR^e, -$S(O)_kR^c$, -$NR^cS(O)_2R^c$, -$S(O)_2NR^dR^e$, -$C(=O)OR^c$, -$OC(=O)OR^c$, -$OC(=O)R^c$, -$OC(=S)OR^c$, -$C(=S)OR^c$, -$O(C=S)R^c$, -$C(=O)NR^dR^e$, -$NR^cC(=O)R^c$, -$C(=S)NR^dR^e$, -$NR^cC(=S)R^c$, -$NR^c(C=O)OR^c$, -$O(C=O)NR^dR^e$, -$NR^c(C=S)OR^c$, -$O(C=S)NR^dR^e$, -$NR^c(C=O)NR^dR^e$, -$NR^c(C=S)NR^dR^e$, -$C(=S)R^c$, -$C(=O)R^c$, C_1-C_6 alkyl, C_1-C_6 halogenalkyl, C_1-C_6-heteroalkyl, karbosyklyl, (C_1-C_6-alkylen)-karbosyklyl, (C_1-C_6-heteroalkylen)-karbosyklyl, heterosyklyl, (C_1-C_6-alkylen)-heterosyklyl, (C_1-C_6-heteroalkylen)-heterosyklyl, aryl, (C_1-C_6-alkylen)-aryl, (C_1-C_6-heteroalkylen)-aryl, heteroaryl, (C_1-C_6-alkylen)-heteroaryl og (C_1-C_6-heteroalkylen)-heteroaryl, hvori hvert av alkylet, alkylenet, heteroalkylet, heteroalkylenet, karbosyklylet, heterosyklylet, arylet og heteroarylet eventuelt substitueres med ett eller flere halogen, OR^c, -NOa, cyano, -$NR^cC(=O)R^c$, -NR^dR^e, -$S(O)_kR^c$, -$C(=O)OR^c$, -$C(=O)NR^dR^e$, -$C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl eller C_1-C_6-heteroalkyl i tillegg til R^2;

R^1 velges fra NH(C_1-C_6-alkyl), N(C_1-C_6-alkyl)$_2$, C_1-C_6-alkyl, -O-C_1-C_6-alkyl, -C(O)-C_1-C_4-alkyl, karbosyklyl, heterosyklyl, -O-(C_0-C_4-alkylen)-karbosyklyl, -O-(C_0-C_4-alkylen)-heterosyklyl, -NH-(C_0-C_4-alkylen)-karbosyklyl, -NH-aryl, -NH-O-(C_1-C_4-alkyl), -S-heterosyklyl, -S-(C_0-C_3-alkylen)-(O-holdig heterosyklyl), og -NH-(C_0-C_4-alkylen)-heterosyklyl, hvori hver alkyl-, alkylen-, karbosyklyl-, aryl- og heterosyklyldel av R^1 eventuelt substitueres med 1, 2, 3 eller 4 substituenter

uavhengig valgt fra deuterium, halogen, =O, cyano, -OR^c, -NR^dR^e, -$S(O)_kR^c$, -$NR^cS(O)_2R^c$, -$S(O)_2NR^dR^e$, -$C(=O)OR^c$, -$OC(=O)OR^c$, -$OC(=O)R^c$, -$OC(=S)OR^c$, -$C(=S)OR^c$, -$O(C=S)R^c$, -$C(=O)NR^dR^e$, -$NR^cC(=O)R^c$, -$C(=S)NR^dR^e$, -$NR^cC(=S)R^c$, -$NR^c(C=O)OR^c$, -$O(C=O)NR^dR^e$, -$NR^c(C=S)OR^c$, -$O(C=S)NR^dR^e$, -$NR^c(C=O)NR^dR^e$, -$NR^c(C=S)NR^dR^e$, -$C(=S)R^c$, -$C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl,

C_1-C_6-heteroalkyl, karbosyklyl, (C_1-C_6-alkylen)-karbosyklyl, (C_1-C_6-heteroalkylen)-karbosyklyl, heterosyklyl, (C_1-C_6-alkylen)-heterosyklyl, (C_1-C_6-heteroalkylen)-heterosyklyl, aryl, (C_1-C_6-alkylen)-aryl, (C_1-C_6-heteroalkylen)-aryl, heteroaryl, (C_1-C_6-alkylen)-heteroaryl og (C_1-C_6-heteroalkylen)-heteroaryl, hvori hvert av alkylet, alkylenet, heteroalkylet, heteroalkylenet, karbosyklylet, heterosyklylet, arylet og heteroarylet eventuelt substitueres med ett eller flere halogen, OR^c, -NO_2, cyano, -$NR^cC(=O)R^c$, -NR^dR^e, -$S(O)_kR^c$, -$C(=O)OR^c$, -$C(=O)NR^dR^e$, -$C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl eller C_1-C_6-heteroalkyl; eller

R^1 tas sammen med ett R^3 for å danne en mettet ring sammensmeltet til piperazinringen i formel (I), og hvori ringen dannet med R^1 og R^3 eventuelt substitueres med 1, 2 eller 3 substituenter uavhengig valgt fra halogen, =O, cyano, -OR^c, -NR^dR^e, -$S(O)_kR^c$, -$NR^cS(O)_2R^c$, -$S(O)_2NR^dR^e$, -$C(=O)OR^c$, -$OC(=O)OR^c$, -$OC(=O)R^c$, -$OC(=S)OR^c$, -$C(=S)OR^c$, -$O(C=S)R^c$, -$C(=O)NR^dR^e$, -$NR^cC(=O)R^c$, -$C(=S)NR^dR^e$, -$NR^cC(=S)R^c$, -$NR^c(C=O)OR^c$, -$O(C=O)NR^dR^e$, -$NR^c(C=S)OR^c$, -$O(C=S)NR^dR^e$, -$NR^c(C=O)NR^dR^e$, -$NR^c(C=S)NR^dR^e$, -$C(=S)R^c$, -$C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl, C_1-C_6-heteroalkyl, karbosyklyl,

(C_1-C_6-alkylen)-karbosyklyl, (C_1-C_6-heteroalkylen)-karbosyklyl, heterosyklyl, (C_1-C_6-alkylen)-heterosyklyl, (C_1-C_6-heteroalkylen)-heterosyklyl, aryl, (C_1-C_6-alkylen)-aryl, (C_1-C_6-heteroalkylen)-aryl, heteroaryl, (C_1-C_6-alkylen)-heteroaryl og (C_1-C_6-heteroalkylen)-heteroaryl, hvori hvert av alkylet, alkylenet, heteroalkylet, heteroalkylenet, karbosyklylet, heterosyklylet, arylet og heteroarylet eventuelt substitueres med ett eller flere av halogen, OR^c, -NO_2, cyano, -$NR^cC(=O)R^c$, -NR^dR^e, -$S(O)_kR^c$, -$C(=O)OR^c$, -$C(=O)NR^dR^e$, -$C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl eller C_1-C_6-heteroalkyl;

R^2 velges fra halogen, C_1-C_6-alkyl, heterosyklyl, sykloalkyl, -NH-(C_0-C_4-alkylen)-

heterosyklyl, -(C_1-C_4-alkylen)-heterosyklyl, -(C_1-C_4-alkylen)-NH-heterosyklyl og -O-(C_0-C_4-alkylen)-heterosyklyl, hvori en hvilken som helst heterosyklyl-, sykloalkyl-, alkyl- eller alkylendel av R^2 eventuelt substitueres med 1, 2, 3 eller 4 substituenter uavhengig valgt fra halogen, =O, cyano, -OR^c, -NR^dR^e, -$S(O)_kR^c$, -$NR^cS(O)_2R^c$, -$S(O)_2NR^dR^e$, -$C(=O)OR^c$, -$OC(=O)OR^c$, -$OC(=O)R^c$, -$OC(=S)OR^c$, -$C(=S)OR^c$, -$O(C=S)R^c$, -$C(=O)NR^dR^e$, -$NR^cC(=O)R^c$, -$C(=S)NR^dR^e$, -$NR^cC(=S)R^c$, -$NR^c(C=O)OR^c$, -$O(C=O)NR^dR^e$, -$NR^c(C=S)OR^c$, -$O(C=S)NR^dR^e$, -$NR^c(C=O)NR^dR^e$, -$NR^c(C=S)NR^dR^e$, -$C(=S)R^c$, -$C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl, C_1-C_6-heteroalkyl, karbosyklyl, (C_1-C_6-alkylen)-karbosyklyl, (C_1-C_6-heteroalkylen)-karbosyklyl, heterosyklyl, (C_1-C_6-alkylen)-heterosyklyl, (C_1-C_6-heteroalkylen)-heterosyklyl, aryl, (C_1-C_6-alkylen)-aryl, (C_1-C_6-heteroalkylen)-aryl, heteroaryl, (C_1-C_6-alkylen)-heteroaryl og (C_1-C_6-heteroalkylen)-heteroaryl, hvori hvert av alkylet, alkylenet, heteroalkylet, heteroalkylenet, karbosyklylet, heterosyklylet, arylet og heteroarylet eventuelt substitueres med ett eller flere av halogen, OR^c, -NOa, cyano, -$NR^cC(=O)R^c$, -NR^dR^e, -$S(O)_kR^c$, -$C(=O)OR^c$, -$C(=O)NR^dR^e$, -$C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl eller C_1-C_6-heteroalkyl; eller R^2 tas sammen med et hvilket som helst ringatom i ring A for å danne et sykloalkyl eller mettet heterosyklylring som sammensmeltes til ring A, og hvori ring dannet av R^2 og ringatomet i ring A eventuelt substitueres med 1, 2 eller 3 substituenter uavhengig valgt fra halogen, =O, cyano, -OR^c, -NR^dR^e, -$S(O)_kR^c$, -$NR^cS(O)_2R^c$, -$S(O)_2NR^dR^e$, -$C(=O)OR^c$, -$OC(=O)OR^c$, -$OC(=O)R^c$, -$OC(=S)OR^c$, -$C(=S)OR^c$, -$O(C=S)R^c$, -$C(=O)NR^dR^e$, -$NR^cC(=O)R^c$, -$C(=S)NR^dR^e$, -$NR^cC(=S)R^c$, -$NR^c(C=O)OR^c$, -$O(C=O)NR^dR^e$, -$NR^c(C=S)OR^c$, -$O(C=S)NR^dR^e$, -$NR^c(C=O)NR^dR^e$, -$NR^c(C=S)NR^dR^e$, -$C(=S)R^c$, -$C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl, C_1-C_6-heteroalkyl, karbosyklyl, (C_1-C_6-alkylen)-karbosyklyl, (C_1-C_6-heteroalkylen)-karbosyklyl, heterosyklyl, (C_1-C_6-alkylen)-heterosyklyl, (C_1-C_6-heteroalkylen)-heterosyklyl, aryl, (C_1-C_6-alkylen)-aryl, (C_1-C_6-heteroalkylen)-aryl, heteroaryl, (C_1-C_6-alkylen)-heteroaryl og (C_1-C_6-heteroalkylen)-heteroaryl, hvori hvert av alkylet, alkylenet, heteroalkylet, heteroalkylenet, karbosyklylet, heterosyklylet, arylet og heteroarylet eventuelt substitueres med ett eller flere av halogen, OR^c, -NO_2, cyano, -$NR^cC(=O)R^c$, -NR^dR^e, -$S(O)_kR^c$, -$C(=O)OR^c$, -

$C(=O)NR^dR^e$, $-C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl eller C_1-C_6-heteroalkyl; eller

R^2 tas sammen med et hvilket som helst mettet ringatom i ring A for å danne et sykloalkyl eller mettet heterosyklylring som sammensmeltes, spirosammensmeltes eller brodannes til ring A, og hvori ringen dannet av R^2 og ringatomet i ring A eventuelt substitueres med 1, 2 eller 3 substituenter uavhengig valgt fra halogen, =O, cyano, $-OR^c$, $-NR^dR^e$, $-S(O)_kR^c$, $-NR^cS(O)_2R^c$, $-S(O)_2NR^dR^e$, $-C(=O)OR^c$, $-OC(=O)OR^c$, $-OC(=O)R^c$, $-OC(=S)OR^c$, $-C(=S)OR^c$, $-O(C=S)R^c$, $-C(=O)NR^dR^e$, $-NR^cC(=O)R^c$, $-C(=S)NR^dR^e$, $-NR^cC(=S)R^c$, $-NR^c(C=O)OR^c$, $-O(C=O)NR^dR^e$, $-NR^c(C=S)OR^c$, $-O(C=S)NR^dR^e$, $-NR^c(C=O)NR^dR^e$, $-NR^c(C=S)NR^dR^e$, $-C(=S)R^c$, $-C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl, C_1-C_6-heteroalkyl, karbosyklyl,

(C_1-C_6-alkylen)-karbosyklyl, (C_1-C_6-heteroalkylen)-karbosyklyl, heterosyklyl, (C_1-C_6-alkylen)-heterosyklyl, (C_1-C_6-heteroalkylen)-heterosyklyl, aryl, (C_1-C_6-alkylen)-aryl, (C_1-C_6-heteroalkylen)-aryl, heteroaryl, (C_1-C_6-alkylen)-heteroaryl og (C_1-C_6-heteroalkylen)-heteroaryl, hvori hvert av alkylet, alkylenet, heteroalkylet, heteroalkylenet, karbosyklylet, heterosyklylet, arylet og heteroarylet eventuelt substitueres med ett eller flere av halogen, OR^c, $-NO_2$, cyano, $-NR^cC(=O)R^c$, $-NR^dR^e$, $-S(O)_kR^c$, $-C(=O)OR^c$, $-C(=O)NR^dR^e$, $-C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl eller C_1-C_6-heteroalkyl;

hver R^3 velges uavhengig fra C_1-C_4-alkyl og C_1-C_4-halogenalkyl;

hver R^c velges fra hydrogen, hydroksy, C_1-C_6-alkyl, C_1-C_6-heteroalkyl, karbosyklyl, (C_1-C_6-alkylen)-karbosyklyl, (C_1-C_6-heteroalkylen)-karbosyklyl, heterosyklyl, (C_1-C_6-alkylen)-heterosyklyl, (C_1-C_6-heteroalkylen)-heterosyklyl, aryl, (C_1-C_6-alkylen)-aryl, (C_1-C_6-heteroalkylen)-aryl, heteroaryl, (C_1-C_6-alkylen)-heteroaryl eller (C_1-C_6-heteroalkylen)-heteroaryl, hver av disse substitueres eventuelt med ett eller flere av halogen, hydroksy, C_1-C_6-alkyl, C_1-C_6-halogenalkyl, C_1-C_6-heteroalkyl, karbosyklyl, heterosyklyl, aryl eller heteroaryl;

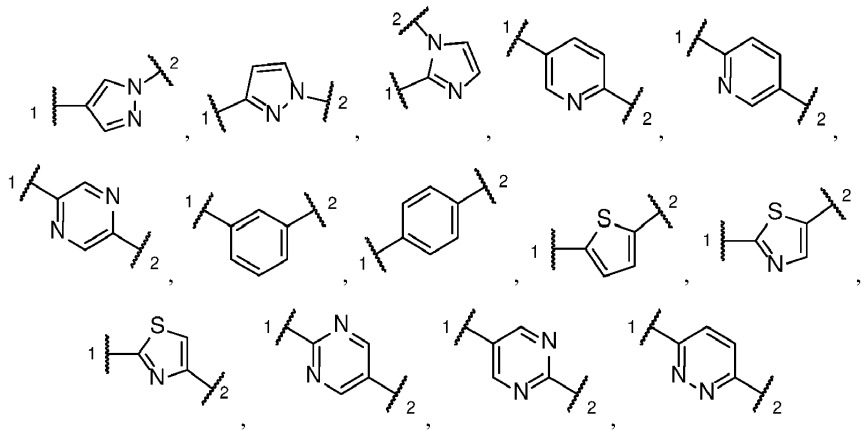
hver R^d og R^e velges uavhengig fra hydrogen, C_1-C_6-alkyl eller C_1-C_6-heteroalkyl;

hver k er uavhengig 0, 1 eller 2; og

n er 0, 1, 2 eller 3.

2. Forbindelsen ifølge krav 1 eller et farmasøytisk akseptabelt salt derav, hvori n er 0; eller n er 1 og R^3 velges fra metyl, etyl og $-CHF_2$.

3. Forbindelsen ifølge krav 1 eller krav 2 eller et farmasøytisk akseptabelt salt derav, hvori ring A velges fra:



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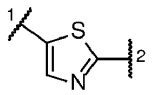


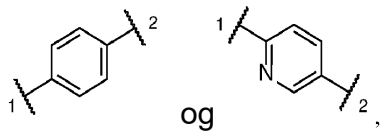
hvori:

"1" representerer en del av ring A bundet til en pyrrolo[1,2-b]pyridazindel;

"2" representerer en del av ring A bundet til R^2; og

ring A substitueres eventuelt med 1, 2 eller 3 substituenter uavhengig valgt fra halogen, =O, cyano, $-OR^c$, $-NR^dR^e$, $-S(O)_kR^c$, $-NR^cS(O)_2R^c$, $-S(O)_2NR^dR^e$, $-C(=O)OR^c$, $-OC(=O)OR^c$, $-OC(=O)R^c$, $-OC(=S)OR^c$, $-C(=S)OR^c$, $-O(C=S)R^c$, $-C(=O)NR^dR^e$, $-NR^cC(=O)R^c$, $-C(=S)NR^dR^e$, $-NR^cC(=S)R^c$, $-NR^c(C=O)OR^c$, $-O(C=O)NR^dR^e$, $-NR^c(C=S)OR^c$, $-O(C=S)NR^dR^e$, $-NR^c(C=O)NR^dR^e$, $-NR^c(C=S)NR^dR^e$, $-C(=S)R^c$, $-C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl, C_1-C_6-heteroalkyl, karbosyklyl, (C_1-C_6-alkylen)-karbosyklyl, (C_1-C_6-heteroalkylen)-karbosyklyl, heterosyklyl, (C_1-C_6-alkylen)-heterosyklyl, (C_1-C_6-heteroalkylen)-heterosyklyl, aryl, (C_1-C_6-alkylen)-aryl, (C_1-C_6-heteroalkylen)-aryl, heteroaryl, (C_1-C_6-alkylen)-heteroaryl og (C_1-C_6-heteroalkylen)-heteroaryl, hvori hvert av alkylet, alkylenet, heteroalkylet, heteroalkylenet, karbosyklylet, heterosyklylet, arylet og heteroarylet eventuelt substitueres med ett eller flere av halogen, OR^c, $-NO_2$,

cyano, -$NR^cC(=O)R^c$, -NR^dR^e, -$S(O)_kR^c$, -$C(=O)OR^c$, -$C(=O)NR^dR^e$, -$C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl eller C_1-C_6-heteroalkyl i tillegg til R^2, eventuelt hvori ring A velges fra



og/eller

hvori ring A eventuelt substitueres med 1 eller 2 substituenter i tillegg til R^2, hvori hver valgfrie substituent uavhengig velges fra cyano, halogen, metyl og -$OCHF_2$.

4. Forbindelsen ifølge et hvilket som helst av kravene 1–3 eller et farmasøytisk akseptabelt salt derav, hvori R^1 velges fra -C(O)-(C_1-C_3-alkyl), C_1-C_3-alkyl, -O-(C_1-C_5-alkyl), -NH(C_1-C_5-alkyl), -N(C_1-C_4-alkyl)$_2$, -NH-(C_3-C_6-sykloalkyl), C_3-C_6-sykloalkyl, -O-(C_3-C_6-sykloalkyl), -O-(C_1-C_3-alkylen)-(C_3-C_6-sykloalkyl), -(C_1-C_3-alkylen)-(C_3-C_6-sykloalkyl), -O-(C_0-C_3-alkylen)-(O-holdig heterosyklyl), -NH-(C_0-C_3-alkylen)-(O-holdig heterosyklyl), et O-holdig heterosyklyl, et N-holdig heterosyklyl, -O-(C_0-C_3-alkylen)-(N-holdig heterosyklyl), -S-(C_0-C_3-alkylen)-(O-holdig heterosyklyl), - NH-O-(C_1-C_3-alkyl), og -NH-fenyl, hvori en hvilken som helst alkyl-, sykloalkyl-, fenyl- eller heterosyklyldel av R^1 eventuelt substitueres med 1, 2 eller 3 substituenter uavhengig valgt fra deuterium, halogen, cyano, acetyl, C_1-C_4-alkyl, C_1-C_4-halogenalkyl, -O-C_1-C_4-alkyl, -C_1-C_4-alkylen-O-C_1-C_4-alkyl, heteroaryl, fenyl, sykloalkyl, -COOH, og hydroksy, hvori hvert av heteroarylet, fenylet og sykloalkylet eventuelt substitueres med ett eller flere av halogen, OR^c, -NO_2, cyano, -$NR^cC(=O)R^c$, -NR^dR^e, -$S(O)_kR^c$, -$C(=O)OR^c$, -$C(=O)NR^dR^e$, -$C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl eller C_1-C_6-heteroalkyl; eller R^1 tas sammen med et hvilket som helst ringatom i piperazindelen av formel (I) for å danne en karbosyklyl- eller heterosyklylring sammensmeltet til piperazindelen,

og/eller

hvori R^1 velges fra 1-(3-klorfenyl)syklopropyl, 1-(3-fluorfenyl)syklopropyl, 1-acetylsyklopropyl, 1-syklopropylsyklopropyl, 1-difluormetylsyklopropyl, 1-fluorsyklopropyl, 1-metylpropylaminol-pyridin-3-ylsyklopropyl, 1-tiazol-2-ylsyklopropyl, 1-tien-2-ylsyklopropyl, 1-trifluormetylsyklopropyl, 2-(4-klorfenyl)syklopropyl, 2,2,2-trifluoretoksy, 2,2-difluorsyklopropyl, 2,2-dimetylsyklopropyl, 2-cyanosyklopropyl, 2-cyanoetyl, 2-

cyanoetylamino2-syklobutylsyklopropyl, 2-fluorsyklopropyl, 2-fluoretoksy, 2-hydroksyetylamino, 2-metoksyetoksy, 2-metylsyklopropyl, 2-oksa-6-azaspiro[3.3]heptan-6-yl, 3,3-difluorsyklobutyl, 3-cyanoazetidin-1-yl, 3-cyanosyklobutyl, 3-fluorsyklobutyl, 3-hydroksy-3-metylsyklobutyl, 3-hydroksy-3-trifluormetylsyklobutyl, 3-hydroksyazetidin-1-yl, 3-hydroksysyklobutyl, 3-metoksyazetidin-1-yl, 3-metoksymetylazetidin-1-yl, 3-fenyl-3-hydroksysyklobutyl, 4-cyanosykloheksyl, 4-cyanoypiperidin-1-yl, 4-hydroksy-4-metylsykloheksyl, 4-hydroksysykloheksyl, 4-hydroksypiperidin-1-yl, 4-metylsykloheksyl, acetyl, azetidin-1-yl, syklobutoksy, syklobutyl, syklobutylamino, syklopentylamino, syklopropyl, syklopropylmetyl, dietylamino, etoksy, etyl, etylamino, isobutoksy, isopropoksy, isopropyl, isopropylamino, metoksymetyl, N-etyl-N-metylamino, pentylamino, piperidin-1-yl, propylamino, propyloksypyrrolidin-1-yl, og t-butylamino, t-butoksy, 2,2-dimetylpropoksy, 2,2-difluoretoksy, N-(2,2-dimetylpropyl)amino, N-(1,2-dimetylpropyl)amino, 2,2,2-trifluoretylamino, N-(metoksymetyl)amino, oksetan-3-yloksy, oksetan-3-yl, oksetan-3-ylamino, oksetan-3-ylmetoksy, N-(oksetan-3-ylmetyl)amino, tetrahydrofuran-3-yloksy, tetrahydropyran-4-yloksy, 3-cyanosyklobutoksy, 1,3-dihydroksypropan-2-yloksy, 1-acetylazetidin-3-yloksy, 1-hydroksy-2-hydroksykarbonyletan-2-yloksy, 1-metyl-2-fluoretoksy, 2,2-difluoretylamino, 2-cyanoetan-1-yloksy, 2-fluoretylamino, 2-fluorfenylamino, 2-fluorpropoksy, 2-metyloksetan-3-yloksy, 3-cyano-oksetan-3-yloksy, 3-deutero-oksetan-3-yloksy, 6-oksa-1-azaspiro[3.3]heptan-1-yl, syklopropoksy, etoksyamino, oksetan-3-yltio, perdeuteroetoksy, fenylamino, tetrahydrofuran-2-yloksy og tetrahydrofuran-3-yl eller

R^1 tas sammen med et ringatom i piperazindelen for å danne et 6-oksoheksahydropyrrolo[1,2-a]pyrazin-2-yl eller 2-etyl-3-oksoheksahydroimidazo[1,5-a]pyrazin-7-yl.

5. Forbindelsen ifølge et hvilket som helst av kravene 1–4 eller et farmasøytisk akseptabelt salt derav, hvori R^2 velges fra halogen, sykloalkyl, heterosyklyl, -O-(C_0-C_4-alkylen)-(heterosyklyl), -(C_1-C_3-alkylen)-heterosyklyl, -(C_1-C_3-alkylen)-NH-(C_1-C_3-alkyl), -(hydroksysubstituert C_1-C_3-alkylen)-NH-(C_1-C_3-alkyl), C_1-C_4-alkyl substituert med både hydroksy og ett eller flere av amino, C_1-C_4-alkylamino eller di-C_1-C_4-alkylaminocyanosubstituert C_1-C_4-alkyl, hydroksy, -$S(O)_2$-C_1-C_4-alkyl og -(aminosubstituert C_1-C_3-alkylen)-heterosyklyl, eller R^2 tas sammen med et ringatom i ring

A for å danne et heterosyklyl eller et karbosyklyl som sammensmeltes til ring A, hvori et hvilket som helst heterosyklyl eller karbosyklyl eventuelt substitueres med 1, 2 eller 3 substituenter uavhengig valgt fra halogen, cyano, hydroksy, $-NH_2$, $-NH(C_1-C_4\text{-alkyl})$, $-NH-C(O)-O-(C_1-C_4\text{-alkyl})$, =O, $-C(O)-C_1-C_4\text{-alkyl}$, $-C_1-C_4\text{-alkyl}$, deuterert $C_1-C_4\text{-alkyl}$, $-C_1-C_4\text{-halogenalkyl}$, hydroksysubstituert $-C_1-C_4\text{-alkyl}$, $-O-C_1-C_4\text{-alkyl}$, $-O-C_1-C_4\text{-halogenalkyl}$, $-(C_1-C_4\text{-alkylen})-O-(C_1-C_4\text{-alkyl})$, -(aminosubstituert $C_1-C_4\text{-alkylen})-O-(C_1-C_4\text{-alkyl})$, $-(C_1-C_4\text{-alkylen})-O-(C_1-C_4\text{-halogenalkyl})$, $-C(O)-O-C_1-C_4\text{-alkyl}$, -COOH, C_3-C_6-sykloalkyl, heterosyklyl og -NH-heterosyklyl, hvori hvert heterosyklyl eventuelt substitueres med ett eller flere av halogen, OR^c, $-NO_2$, cyano, $-NR^cC(=O)R^c$, $-NR^dR^e$, $-S(O)_kR^c$, $-C(=O)OR^c$, $-C(=O)NR^dR^e$, $-C(=O)R^c$, C_1-C_6-alkyl, C_1-C_6-halogenalkyl eller C_1-C_6-heteroalkyl ,

og/eller

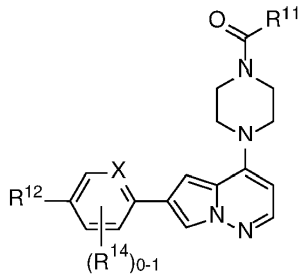
hvori R^2 velges fra 1-(1-hydroksypropan-2-yl)-4-metoksypiperidin-4-yl, 1-(3-difluormetoksy)propan-2-yl-4-metoksypiperidin-4-yl, 1-(3-metoksy)propan-2-yl-4-metoksypiperidin-4-yl, 1-(oksetan-3-yl)-4-metoksypiperidin-4-yl, 1-(oksetan-3-yl)piperidin-4-yl, 1-(propan-2-yl)piperidin-3-yl, 1-(propan-2-yl)piperidin-4-yl, 1-(pyrrolidin-1-yl)etan-1-yl, 1,2,3,6-tetrahydropyridin-4-yl, 1,4-diazabisyklo[4.2.0]oktan-4-yl, 1-acetylpiperidin-4-yl, 1-syklobutylpiperidin-3-yl, 1-etyl-3,3-difluorpiperidin-4-yl, 1-etyl-3-fluorpiperidin-4-yl, 1-etyl-3-hydroksyazetidin-3-yl, 1-etyl-4-fluorpyrrolidin-3-yl, 1-etylazetidin-3-yl, 1-etylazetidin-3-yloksy, 1-etylpiperidin-3-yl, 1-etylpiperidin-3-yloksy, 1-etylpiperidin-4-yl, 1-etylpiperidin-4-yloksy, 1-etylpyrrolidin-3-yl, 1-etylpyrrolidin-3-ylmetoksy, 1-etylpyrrolidin-3-yloksy, 1H-pyrrolidin-2-yl, 1-hydroksy-2-aminoprop-2-yl, 1-isopropyl-1,2,3,6-tetrahydropyridin-4-yl, 1-isopropyl-2-metylpyrrolidin-2-yl, 1-isopropyl-3,4-dimetylpiperazin-3-yl, 1-isopropyl-3-etoksypiperidin-3-yl, 1-isopropyl-3-fluorpiperidin-3-yl, 1-isopropyl-3-hydroksyazetidin-3-yl, 1-isopropyl-3-hydroksypiperidin-3-yl, 1-isopropyl-3-hydroksypyrrolidin-3-yl, 1-isopropyl-3-metoksyazetidin-3-yl, 1-isopropyl-3-metoksypiperidin-3-yl, 1-isopropyl-3-metoksypyrrolidin-3-yl, 1-isopropyl-3-metylpiperazin-3-yl, 1-isopropyl-4-cyanopiperidin-4-yl, 1-isopropyl-4-etoksypiperidin-4-yl, 1-isopropyl-4-fluorpiperidin-4-yl, 1-isopropyl-4-fluorpyrrolidin-3-yl, 1-isopropyl-4-hydroksypiperidin-3-yl, 1-isopropyl-4-hydroksypiperidin-4-yl, 1-isopropyl-4-

metoksypiperidin-4-yl, 1-isopropyl-4-metylpiperazin-3-yl, 1-isopropyl-4-metylpiperidin-4-yl, 1-isopropyl-4-trifluormetylpiperidin-4-yl, 1-isopropyl-5-metylpyrrolidin-3-yl, 1-isopropylazetidin-2-ylmetoksy, 1-isopropylazetidin-3-yl, 1-isopropylazetidin-3-ylmetoksy, 1-isopropylazetidin-3-yloksy, 1-isopropylpiperazin-3-yl, 1-isopropylpiperazin-4-yl, 1-isopropylpiperidin-2-yl, 1-isopropylpiperidin-3-yl, 1-isopropylpiperidin-4-yl, 1-isopropylpyrrolidin-2-yl, 1-isopropylpyrrolidin-3-yl, 1-metyl-1-cyanoetyl, 1-sek-butylpiperidin-4-yl, 1-t-butoksykarbonyl-4-aminopiperidin-4-yl, 2-(isopropylamino)-3-hydroksypropan-2-yl, 2-(isopropylamino)-propan-2-yl, 2,3,5,6-tetrahydroimidazo[2,1-b]tiazol-6-yl, 2,6-diazaspiro[3.3]heptan-2-yl, 2,6-diazaspiro[3.4]oktan-2-yl, 2,6-diazaspiro[3.4]oktan-6-yl, 2,7-diazaspiro[4.4]nonan-2-yl, 2-difluormetylpiperazin-1-yl, 2-isopropyl-2,6-diazaspiro[3.3]heptan-6-yl, 2-metyl-1H-pyrrolidin-2-yl, 2-oksa-5,8-diazaspiro[3.5]nonan-8-yl, 2-okso-4-etylpiperazin-1-yl, 2-oksopiperazin-1-yl, 2-trifluormetylpiperazin-1-yl, 3,3-difluorpiperidin-4-yl, 3,3-dimetyl-4-etylpiperazin-1-yl, 3-aminopyrrolidin-1-yl, 3-fluorpiperidin-3-yl, 3-fluorpiperidin-4-yl, 3-hydroksyazetidin-3-yl, 3-hydroksykinuklidin-3-yl, 3-metyl-4-etylpiperazin-1-yl, 3-metylpiperazin-1-yl, 3-trifluormetylpiperazin-1-yl, 4-(1,1,2,2,2-pentadeuteroetyl)piperazin-1-yl, 4-(2,2-difluoretyl)piperazin-1-yl, 4-(2-hydroksyetyl)piperazin-1-yl, 4-(2-metoksyetyl)piperazin-1-yl, 4-(metoksykarbonylamino)piperidin-4-yl, 4-(oksetan-3-yl)piperazin-1-yl, 4,5-dihydro-1H-imidazol-2-yl, 4,5-dihydro-1H-imidazol-2-ylamino, 4-aminopiperidin-1-yl, 4-cyanopiperidin-4-yl, 4-etoksypiperidin-4-yl, 4-etylmorfolin-2-yl, 4-etylpiperazin-1-yl, 4-etylpiperazin-1-yletoksy, 4-fluorpiperidin-4-yl, 4-fluorpyrrolidin-3-yl, 4-hydroksy-tetrahydro-2H-pyran-4-yl, 4-isopropylmorfolin-3-yl, 4-isopropylpiperazin-1-yl, 4-metoksypiperidin-4-yl, 4-metylpiperazin-1-yl, 4-metylpiperidin-4-yl, 5,5-difluorpiperidin-3-yl, 5-etyl-2,5-diazabisyklo[2.2.1]heptan-2-yl, 6-etyl-2,6-diazaspiro[3.3]heptan-2-yl, 6-isopropyl-2,6-diazaspiro[3.3]heptan-2-yl, 6-metylmorfolin-2-yl, azetidin-2-ylmetoksy, azetidin-3-yl, brom, syklopentyl, heksahydropyrazino[2,1-c][1,4]oksazin-8(1H)-yl, heksahydropyrrolo[1,2-a]pyrazin-2(1H)-yl, morfolin-2-yl, morfolin-3-yl, oktahydro-2H-pyrido[1,2-a]pyrazin-2-yl, piperazin-1-yl, piperazin-1-yletoksy, piperidin-4-yl, piperidin-2-yl, piperidin-3-

yl, piperidin-3-yloksy, piperidin-4-yloksy, pyrrolidin-2-yl, pyrrolidin-3-yl, pyrrolidin-3-ylmetoksy, pyrrolidin-3-yloksy, kinuklidin-4-yl, tetrahydro-2H-pyran-4-yl, 1-(1-fluorpropan-2-yl)-4-etoksypiperidin-4-yl, 1-(1-fluorpropan-2-yl)-4-metoksypiperidin-4-yl, 1-(2-fluorpropyl)-4-etoksypiperidin-4-yl, 1-(2-fluorpropyl)-4-etoksypiperidin-4-yl, 1-(3-(difluormetoksy)propan-2-yl)-4-metoksypiperidin-4-yl, 1-(oksetan-3-yl)-4-etoksypiperidin-4-yl, 1-(tetrahydrofuran-2-yl)-1-aminometyl, 1-amino-2-hydroksy-2-metylpropyl, 1-amino-2-metoksyetyl, 1-azabisyklo[2.2.1]heptan-4-yl, 1-syklopropyl-4-etoksypiperidin-4-yl, 1-dietylamino-2-hydroksyetyl, 1-etylamino-2-hydroksyetyl, 1-isopropyl-4-difluormetoksypiperidin-3-yl, 1-isopropyl-4-difluormetoksypiperidin-4-yl, 1-isopropyl-4-hydroksymetylpiperidin-4-yl, 1-isopropyl-4-metoksykarbonylpiperidin-4-yl, 1-isopropyl-4-(metoksymetyl)piperidin-4-yl, 1-isopropyl-4-metoksypiperidin-4-yl, 1-metyl-1-isopropylamino-2-hydroksyetyl, 2,2,5,5-tetrametyl-4-hydroksypiperidin-4-yl, 2,2-dimetyl-4-metoksypiperidin-4-yl, 2-amino-1-hydroksyetyl, 2-amino-3-hydroksypropyl, 2-azaspiro[3.3]heptan-6-yl, 2-hydroksy-1-aminoetyl, 2-hydroksy-1-isopropylaminoetyl, 2-hydroksyetylaminometyl, 3-amino-oksetan-3-yl, 3-etoksypiperidin-3-yl, 3-metoksypiperidin-3-yl, 4-amino-tetrahydropyran-4-yl, 4-etoksytetrahydropyran-4-yl, 4-hydroksykarbonylpiperidin-4-yl, 4-hydroksymetylpiperidin-4-yl, 4-metoksykarbonylpiperidin-4-yl, 4-metoksytetrahydropyran-4-yl, 4-trifluormetylpiperidin-4-yl, etylsulfonyl og oksetan-3-ylaminometyl, eller

R^2 tas sammen med ring A for å danne 3'H-spiro[azetidin-3,1'-isobenzofuran]-5'-yl, 6-isopropyl-4,5,6,7-tetrahydrotieno[2,3-c]pyridin-2-yl, 4,5,6,7-tetrahydrotiazolo[4,5-c]pyridin-2-yl, 4,5,6,7-tetrahydrotiazolo[5,4-c]pyridin-2-yl, 5,6,7,8-tetrahydroimidazo[1,5-a]pyrazin-3-yl, 7-metyl-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazin-3-yl, 4,5,6,7-tetrahydrotieno[2,3-c]pyridin-2-yl, 5-isopropyl-4,5,6,7-tetrahydrotiazolo[5,4-c]pyridin-2-yl, 1-amino-2,3-dihydro-1H-inden-5-yl eller 1-(isopropylamino)-2,3-dihydro-1H-inden-5-yl.

6. Forbindelsen ifølge krav 1 eller et farmasøytisk akseptabelt salt derav, hvori forbindelsen er en forbindelse av formel (II):



(II),

hvori:

X er C(R^{13}) eller N;

R^{11} velges fra -NH-(C_3-C_4-sykloalkyl); -NH-C_1-C_3-alkyl; -O-C_3-C_4-sykloalkyl; -O-C_1-C_3-alkyl eventuelt substituert med én eller flere substituenter valgt fra fluor, hydroksy, cyano og deuterium; og -O-(O-holdig heterosyklus);

R^{12} velges fra:

piperidin-3-yl eventuelt 3-substituert med C_1-C_3-alkoksy, fluor, C_1-C_3-alkyl eller cyano; og

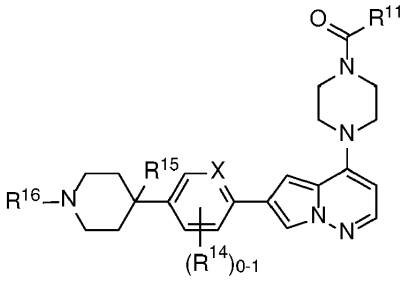
piperidin-4-yl eventuelt 4-substituert med C_1-C_3-alkoksy, fluor, C_1-C_3-alkyl, cyano, hvori R^{12} i tillegg eventuelt 1-substitueres med C_1-C_5-alkyl eventuelt substituert med ett eller flere hydroksy og/eller ett eller flere -NH_2;

R^{13} velges fra hydrogen, cyano og fluor; og

R^{14} er fluor.

7. Forbindelsen ifølge krav 6 eller et farmasøytisk akseptabelt salt derav, hvori forbindelsen er:

(A) en forbindelse av formel (IIa):



(IIa),

eller et farmasøytisk akseptabelt salt derav, hvori:

X er C(R^{13}) eller N;

R^{11} velges fra: -NH-(C_3-C_4-sykloalkyl); -NH-C_1-C_3-alkyl; -O-C_3-C_4-sykloalkyl; -O-(C_1-C_3-alkyl) eventuelt substituert med én eller flere substituenter valgt fra fluor, hydroksy, cyano og deuterium; og -O-(O-holdig heterosyklus);

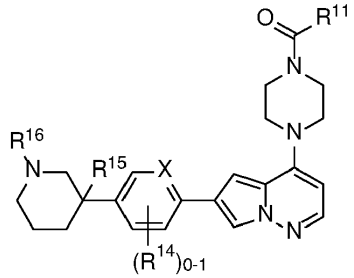
R^{13} velges fra hydrogen, cyano og fluor;

R^{14} er fluor;

R^{15} velges fra hydrogen, C_1-C_3-alkoksy, fluor, C_1-C_3-alkyl og cyano; og

R^{16} er hydrogen eller C_1-C_5-alkyl eventuelt substituert med én eller flere hydroksy og/eller én eller flere -NH_2; eller

(B) en forbindelse av formel (IIb):



(IIb),

eller et farmasøytisk akseptabelt salt derav, hvori:

X er C(R^{13}) eller N;

R^{11} velges fra: -NH-(C_3-C_4-sykloalkyl); -NH-C_1-C_3-alkyl; -O-C_3-C_4-sykloalkyl; -O-(C_1-C_3-alkyl) eventuelt substituert med én eller flere substituenter valgt fra fluor, hydroksy, cyano og deuterium; og -O-(O-holdig heterosyklus);

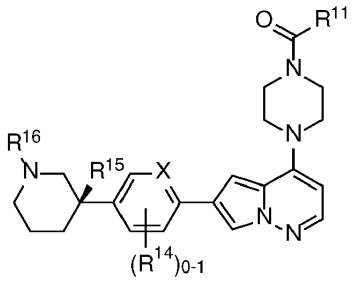
R^{13} velges fra hydrogen, cyano og fluor;

R^{14} er fluor;

R^{15} velges fra hydrogen, C_1-C_3-alkoksy, fluor, C_1-C_3-alkyl og cyano; og

R^{16} er hydrogen eller C_1-C_5-alkyl eventuelt substituert med ett eller flere hydroksy og/eller ett eller flere -NH_2,

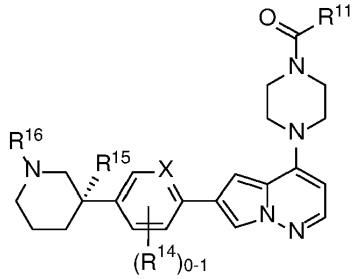
eventuelt hvori forbindelsen av formel IIb er enten en forbindelse av formel (IIb-1):



(IIb-1),

eller et farmasøytisk akseptabelt salt derav,

eller en forbindelse av formel (IIb-2):



(IIb-2),

eller et farmasøytisk akseptabelt salt derav.

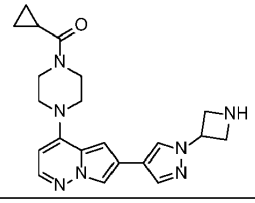
8. Forbindelsen ifølge krav 6 eller krav 7 eller et farmasøytisk akseptabelt salt derav, hvori:

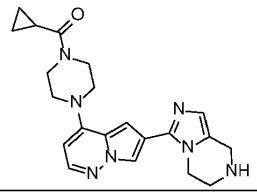
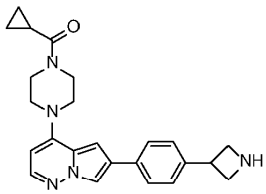
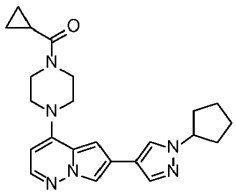
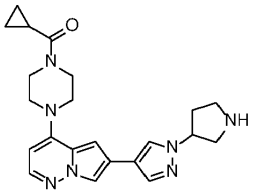
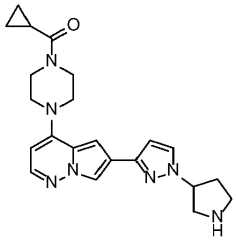
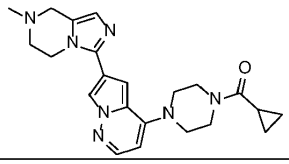
R^{14} er fraværende; eller

R^{13} er hydrogen; eller

R^{11} velges fra -NH-C_1-C_3-alkyl; -O-C_1-C_3-alkyl eventuelt substituert med én eller flere substituenter valgt fra fluor, hydroksy, cyano og deuterium; oksetan-3-yloksy og tetrahydrofuran-3-yloksy, eventuelt hvori R^{11} velges fra -OCH_2CH_3, -$NHCH(CH_3)_2$, oksetan-3-yloksy og tetrahydrofuran-3-yloksy.

9. Forbindelsen ifølge krav 1, hvori forbindelsen velges fra en hvilken som helst av de følgende forbindelsene:

#	Struktur
100	

#	Struktur
101	
102	
103	
104	
105	
106	

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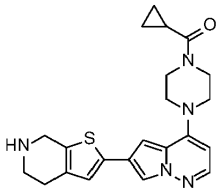
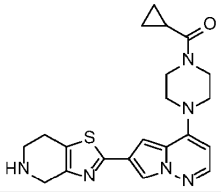
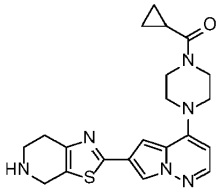
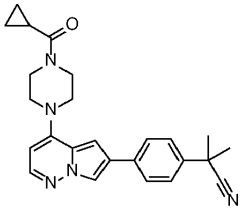
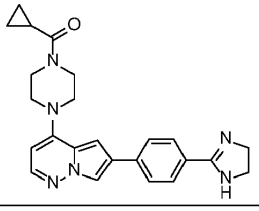
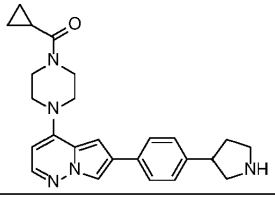
107	
108	
109	
110	
111	
112	

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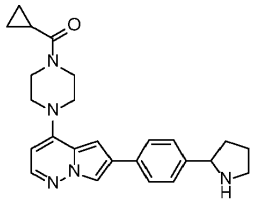
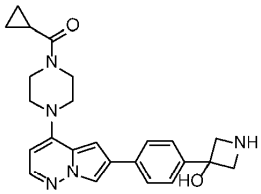
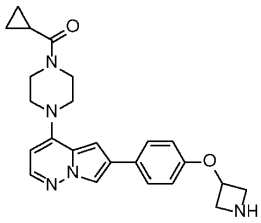
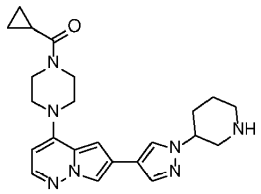
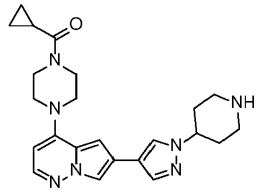
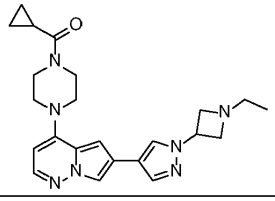
113	
114	
115	
116	
117	
118	

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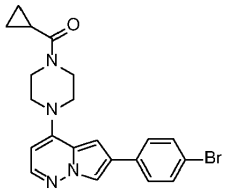
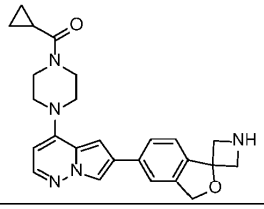
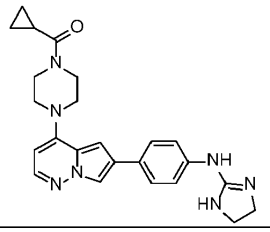
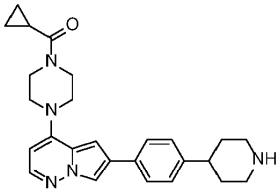
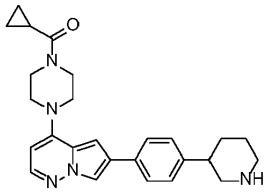
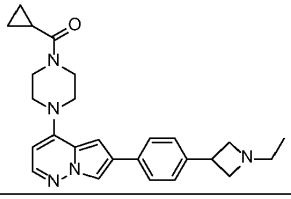
119	
120	
121	
122	
123	
124	

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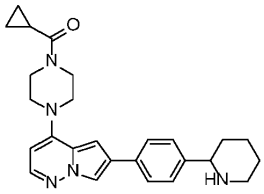
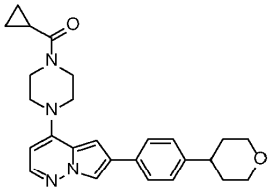
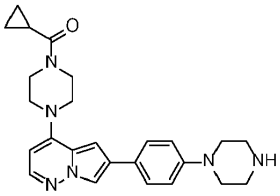
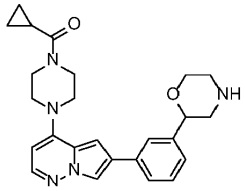
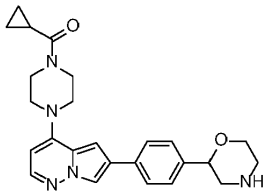
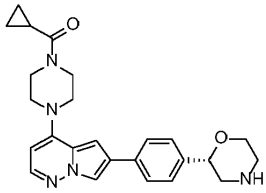
125	
126	
127	
128	
129	
130	

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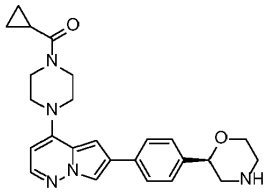
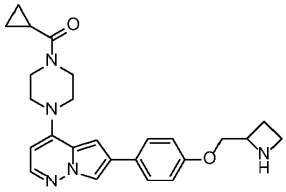
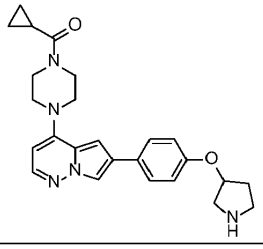
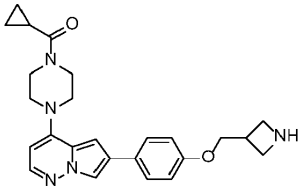
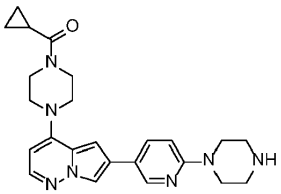
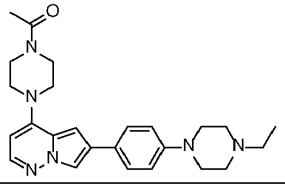
131	
132	
133	
134	
135	
136	

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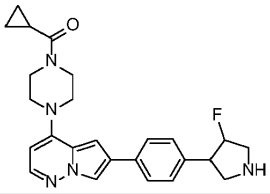
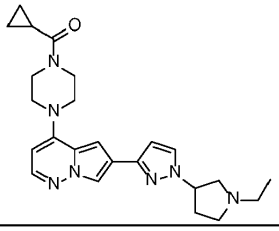
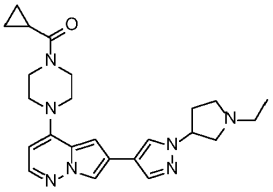
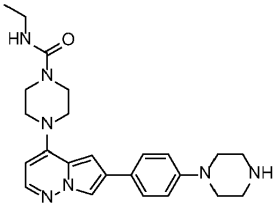
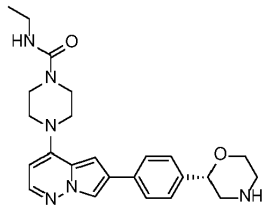
137	
138	
139	
140	
141	

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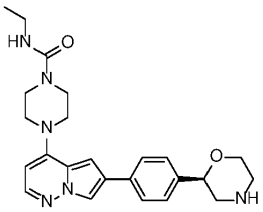
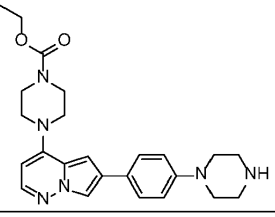
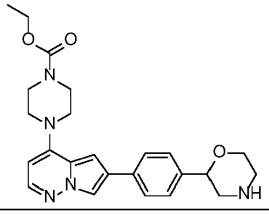
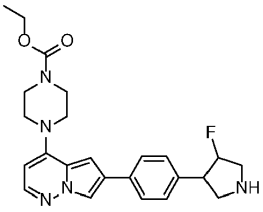
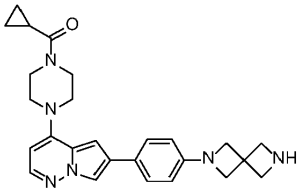
142	
143	
144	
145	
146	

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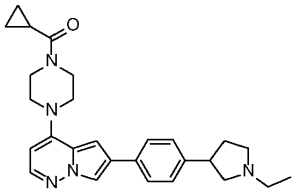
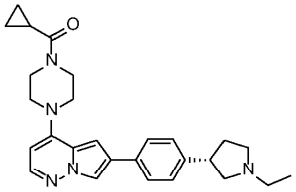
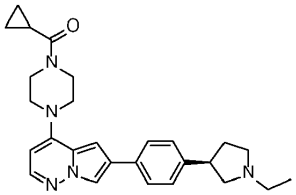
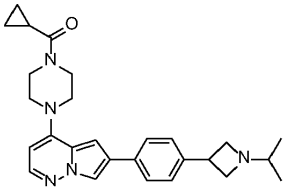
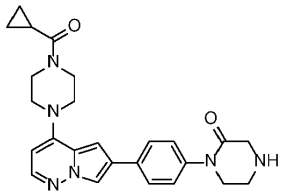
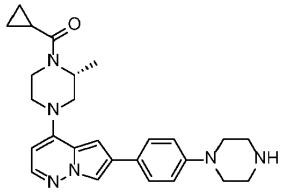
147	
148	
149	
150	
151	
152	

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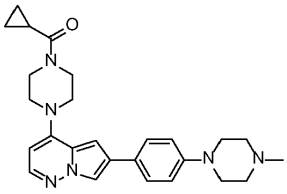
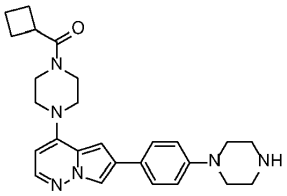
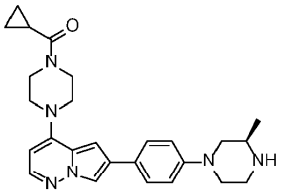
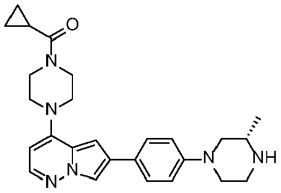
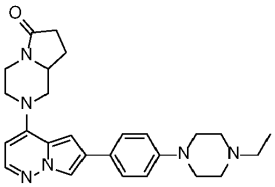
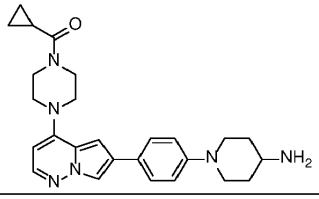
153	
154	
155	
156	
157	
158	

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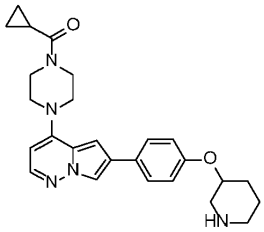
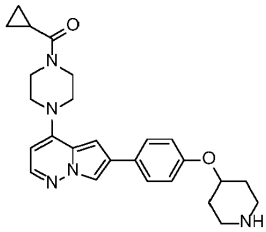
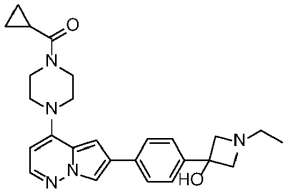
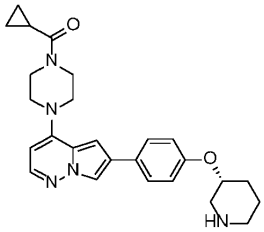
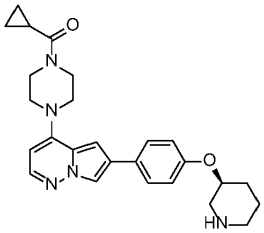
159	
160	
161	
162	
163	

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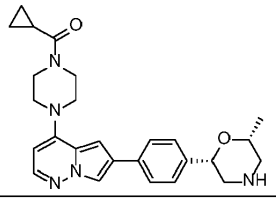
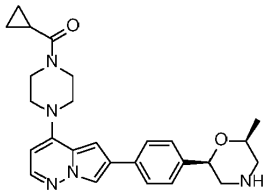
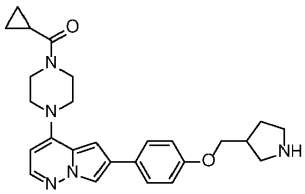
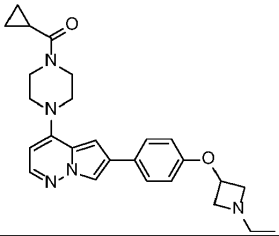
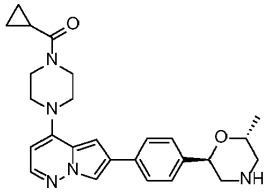
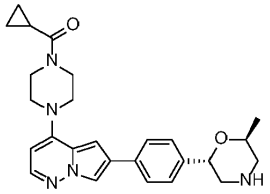
164	
165	
166	
167	
168	
169	

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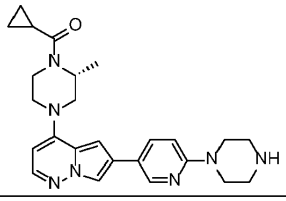
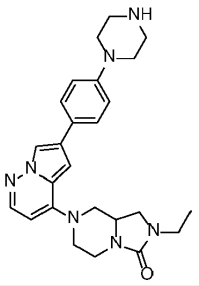
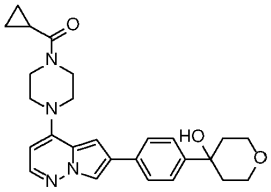
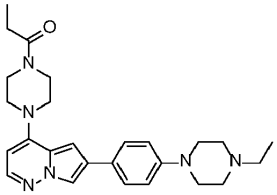
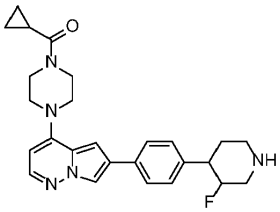
170	
171	
172	
173	
174	

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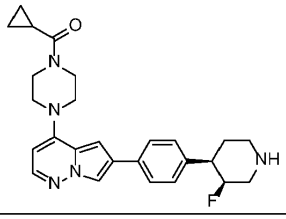
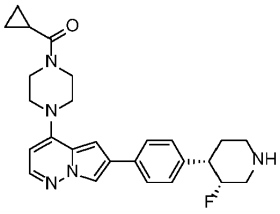
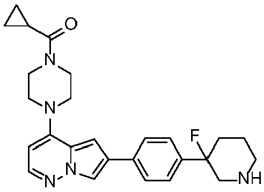
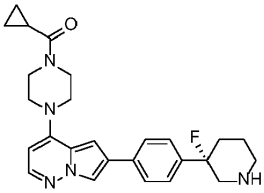
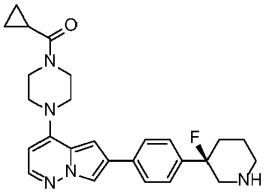
175	
176	
177	
178	
179	

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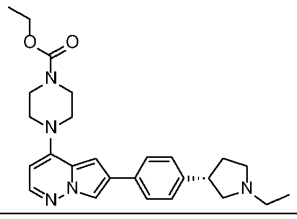
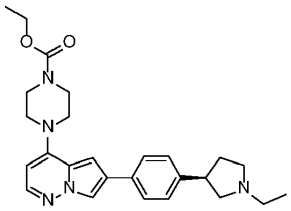
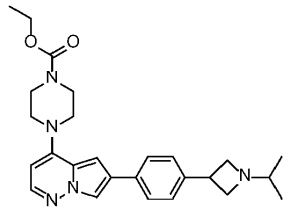
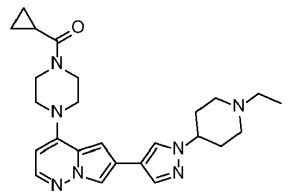
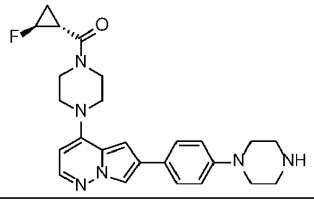
180	
181	
182	
183	
184	

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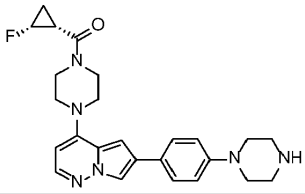
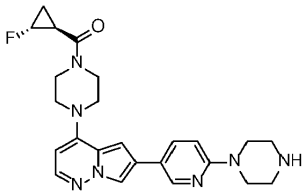
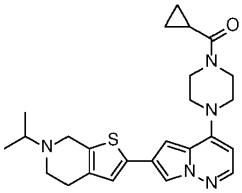
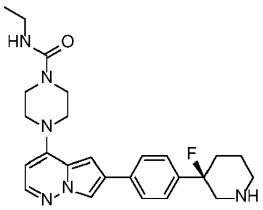
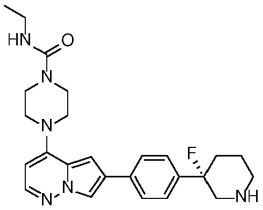
185	
186	
187	
188	
189	

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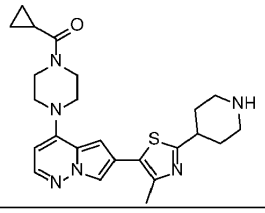
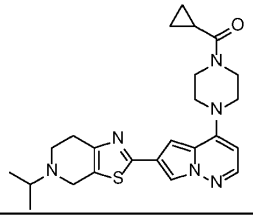
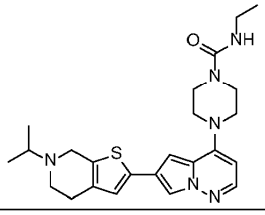
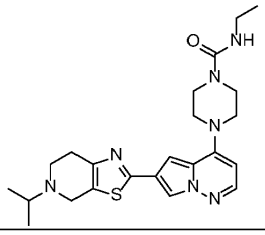
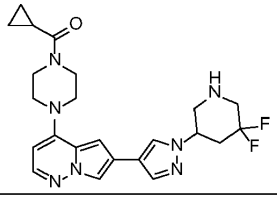
190	
191	
192	
193	
194	

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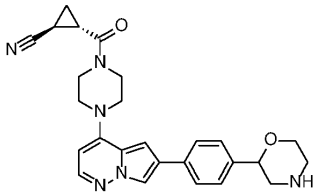
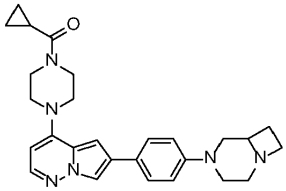
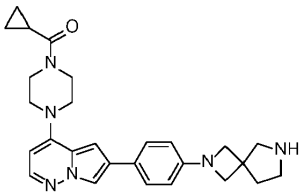
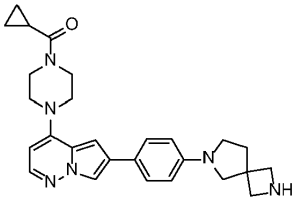
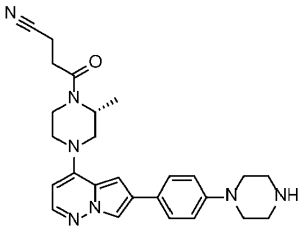
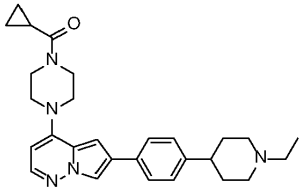
195	
196	
197	
198	
199	
200	

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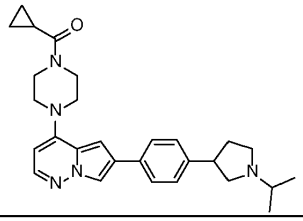
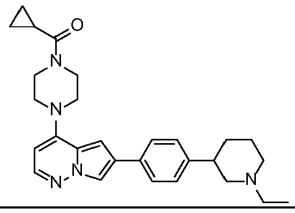
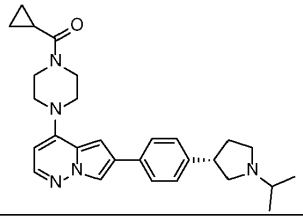
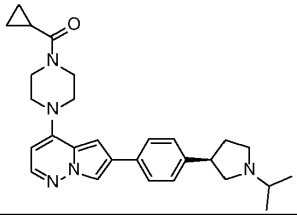
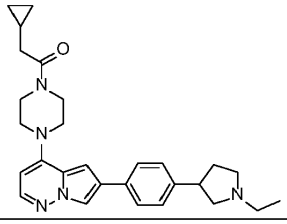
201	
202	
203	
204	
205	

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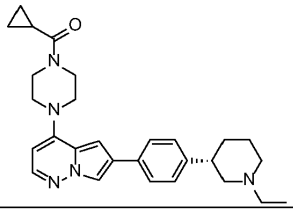
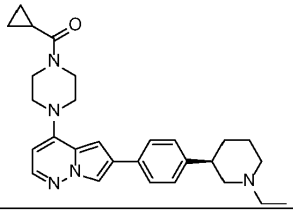
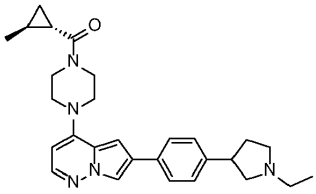
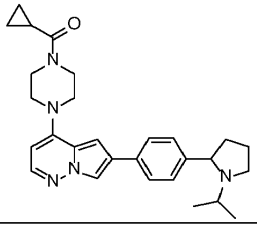
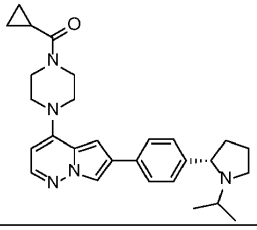
206	
207	
208	
209	
210	

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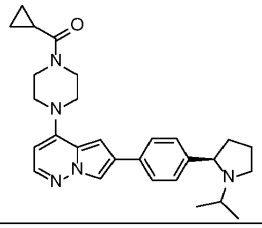
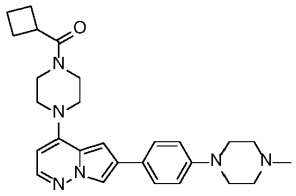
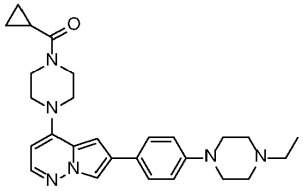
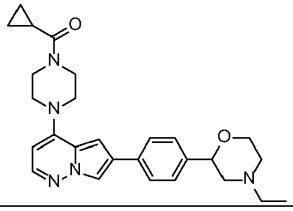
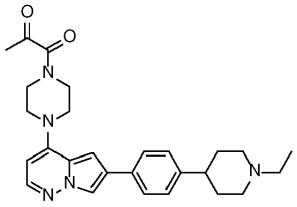
211	
212	
213	
214	
215	

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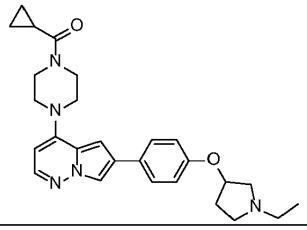
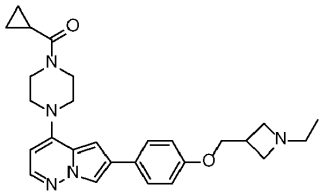
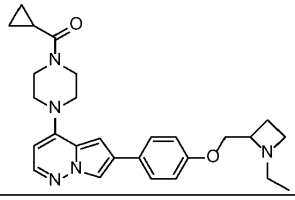
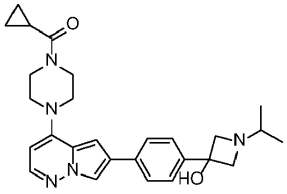
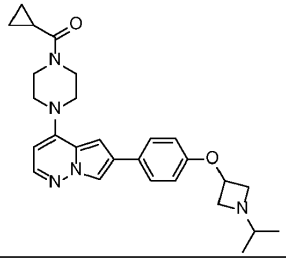
216	
217	
218	
219	
220	

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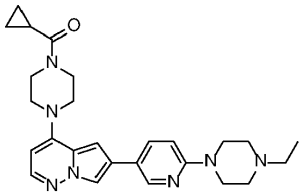
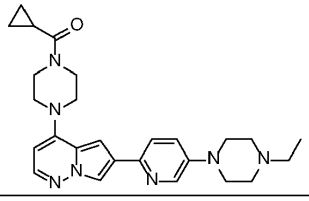
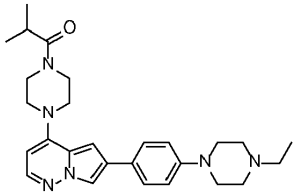
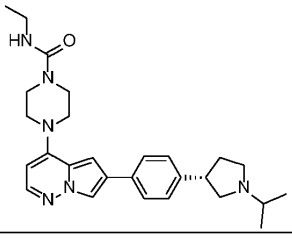
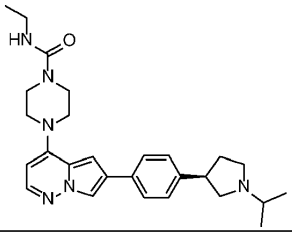
221	
222	
223	
224	
225	

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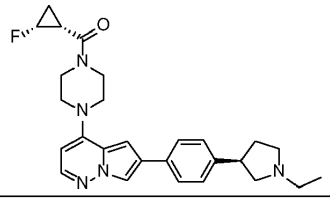
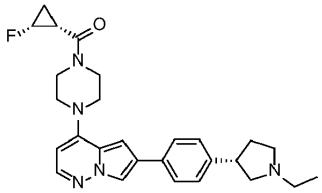
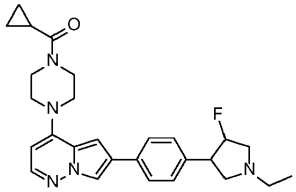
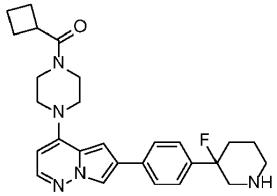
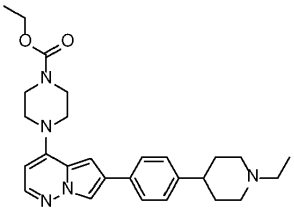
226	
227	
228	
229	
230	

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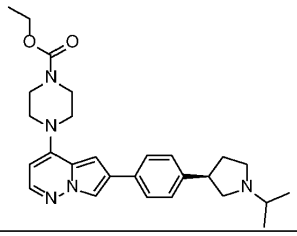
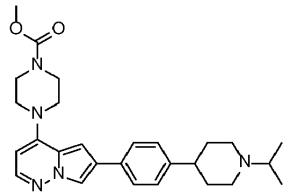
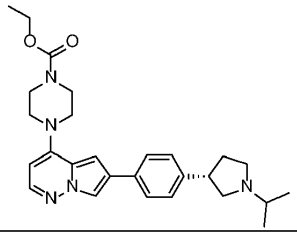
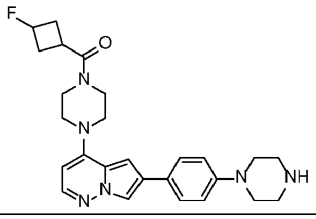
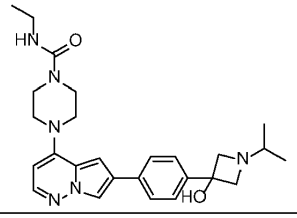
231	
232	
233	
234	
235	

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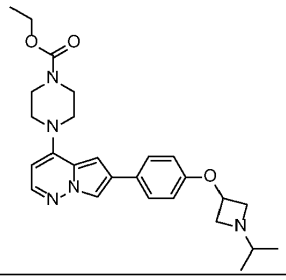
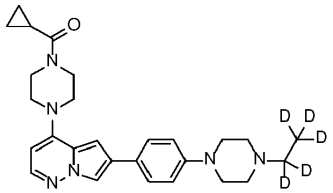
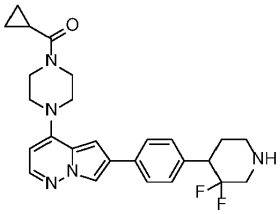
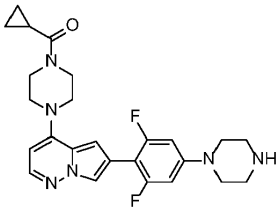
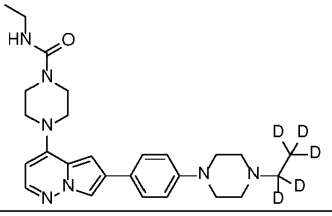
236	
237	
238	
239	
240	

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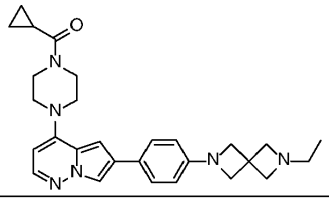
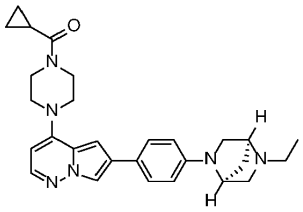
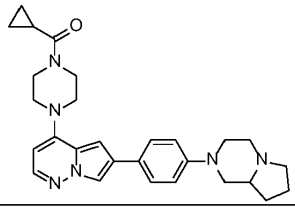
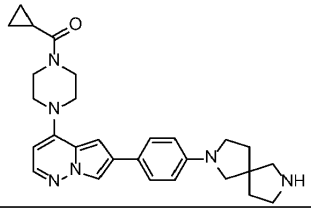
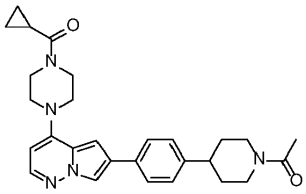
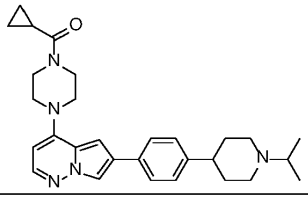
241	
242	
243	
244	
245	
246	

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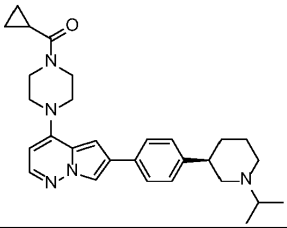
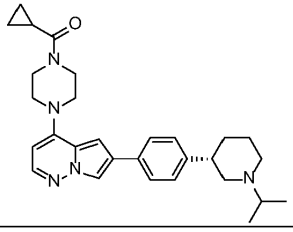
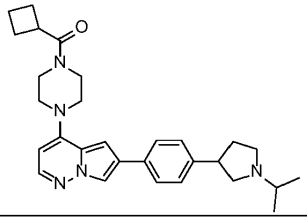
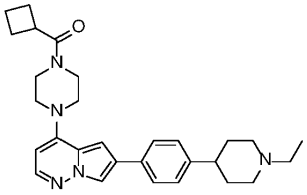
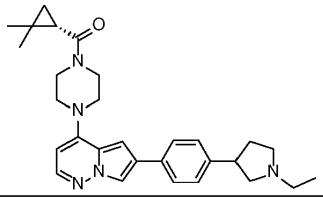
247	
248	
249	
250	
251	

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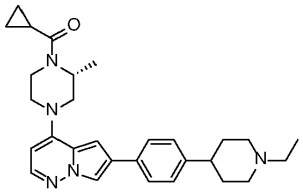
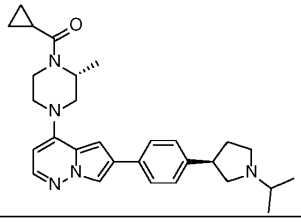
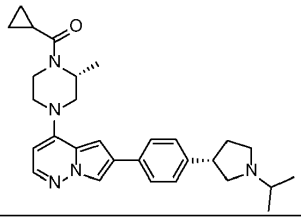
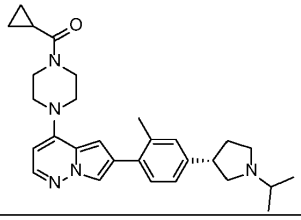
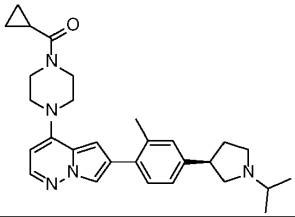
252	
253	
254	
255	
256	

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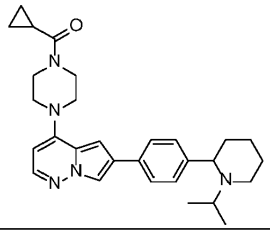
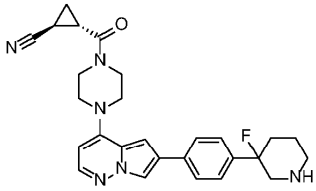
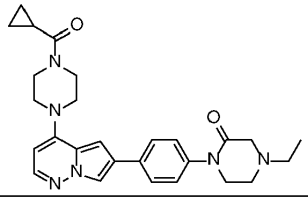
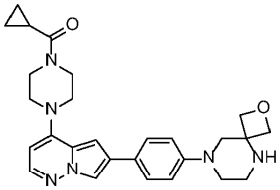
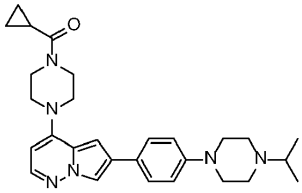
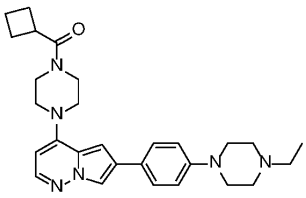
257	
258	
259	
260	
261	
262	

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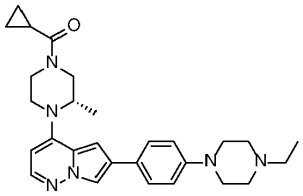
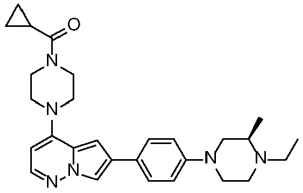
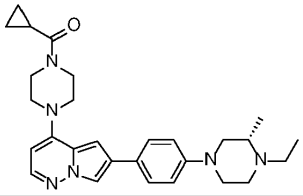
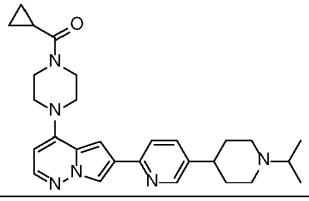
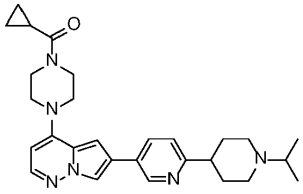
263	
264	
265	
266	
267	

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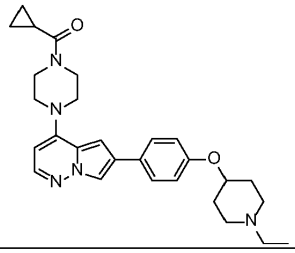
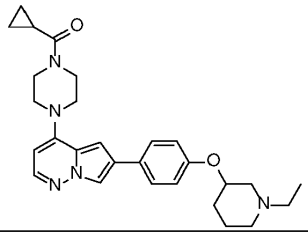
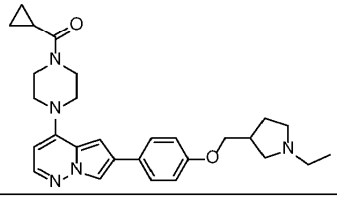
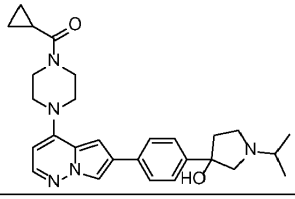
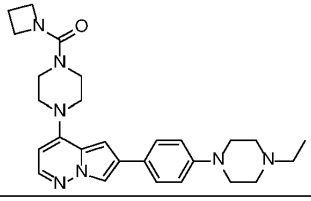
268	
269	
270	
271	
272	

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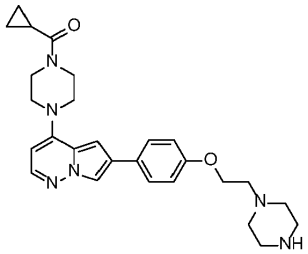
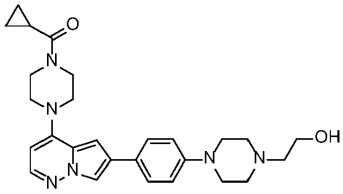
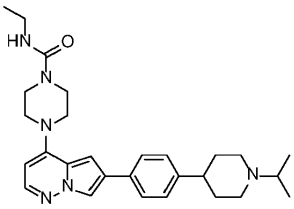
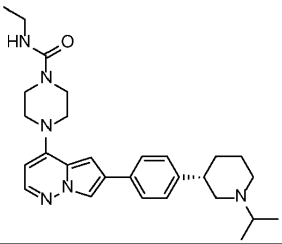
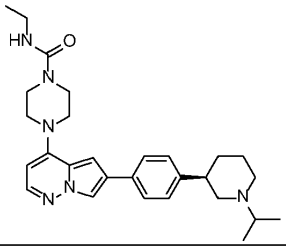
273	
274	
275	
276	
277	

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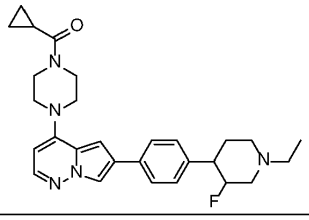
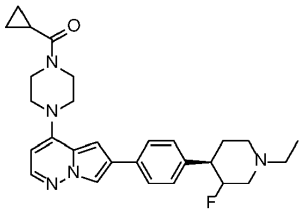
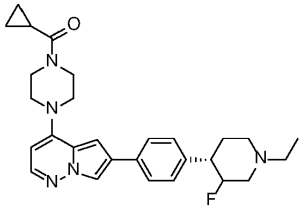
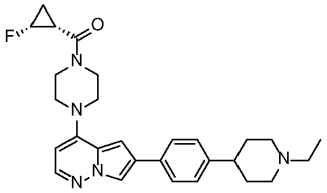
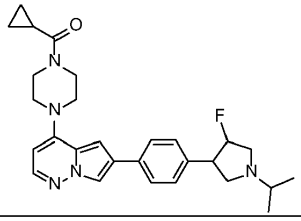
278	
279	
280	
281	
282	

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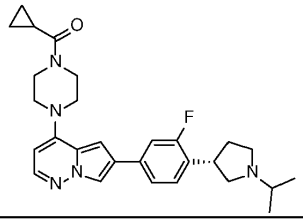
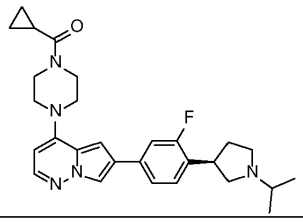
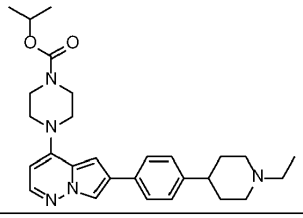
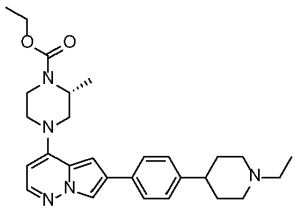
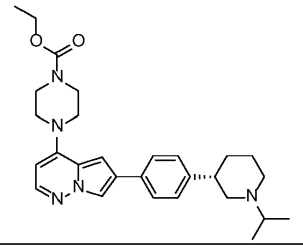
283	
284	
285	
286	
287	

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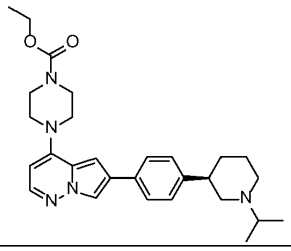
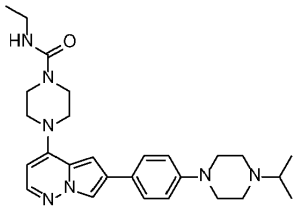
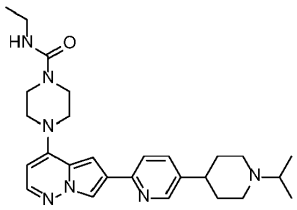
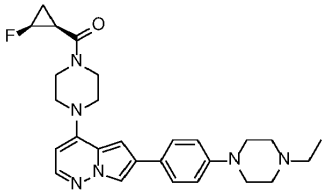
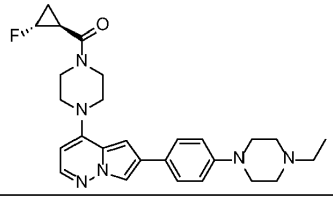
288	
289	
290	
291	
292	

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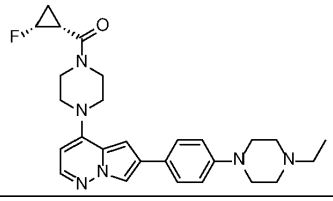
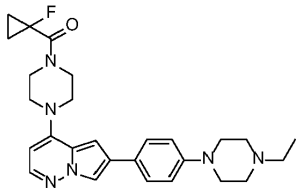
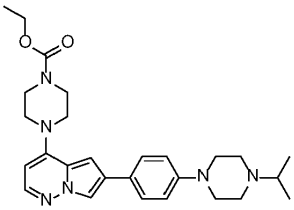
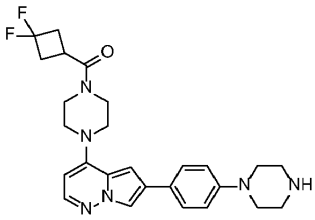
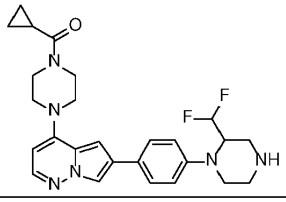
293	
294	
295	
296	
297	

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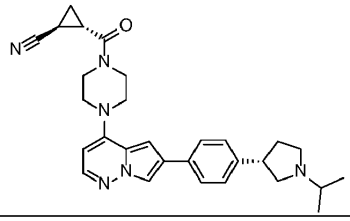
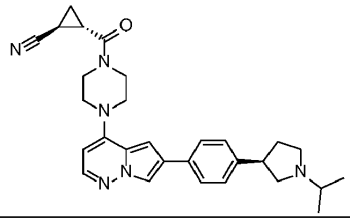
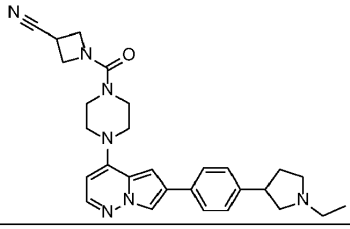
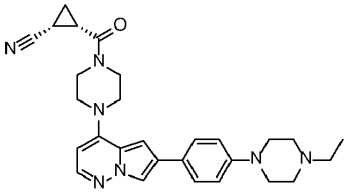
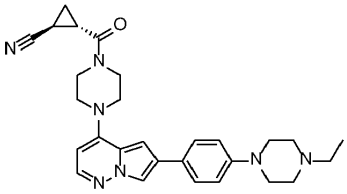
298	
299	
300	
301	
302	

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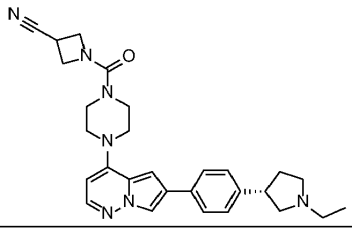
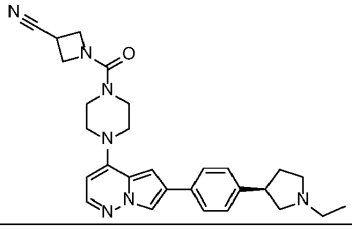
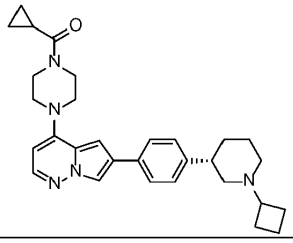
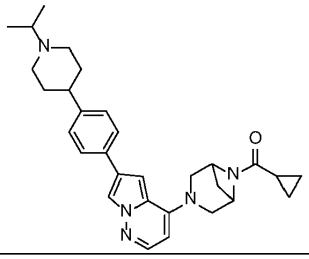
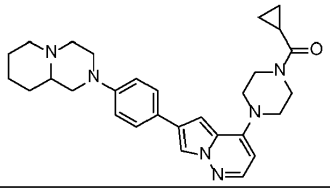
303	
304	
305	
306	
307	

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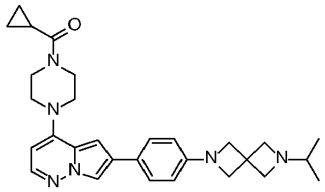
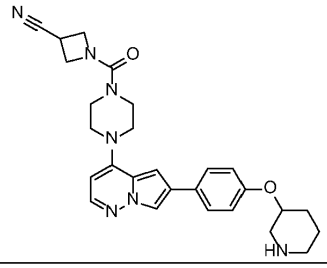
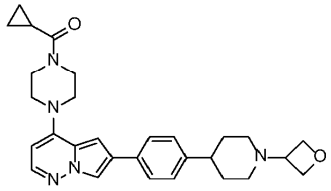
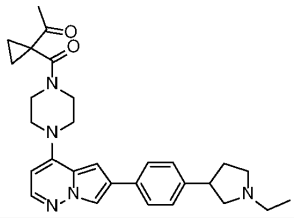
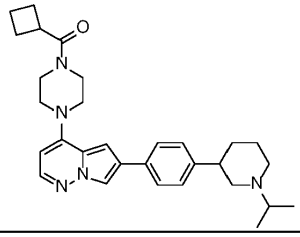
308	
309	
310	
311	
312	

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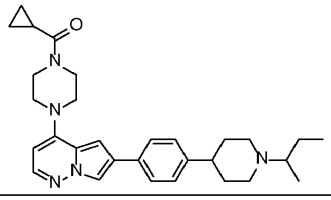
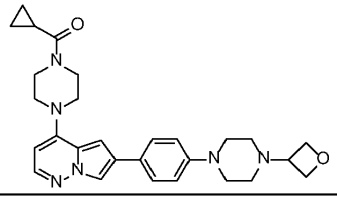
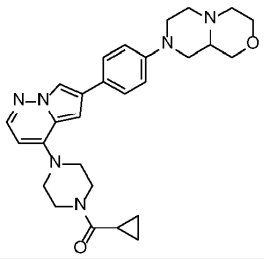
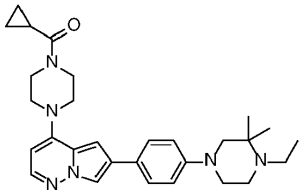
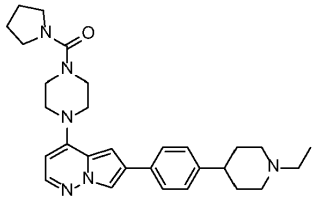
313	
314	
315	
316	
317	

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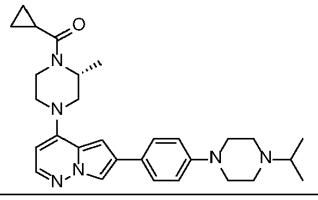
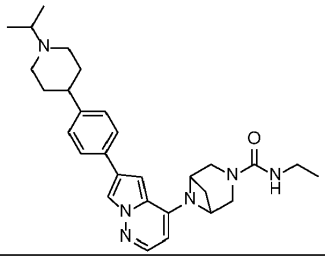
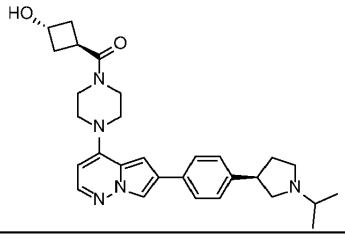
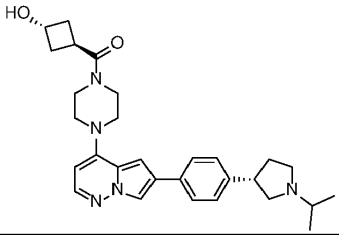
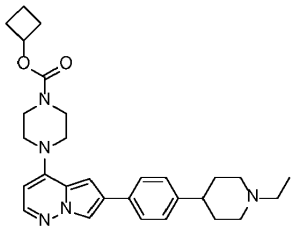
318	
319	
320	
321	
322	

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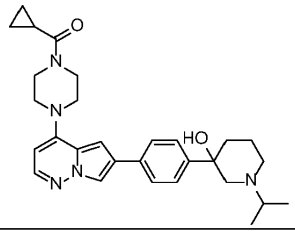
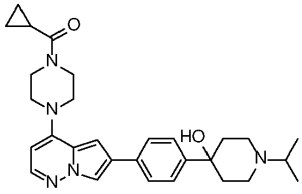
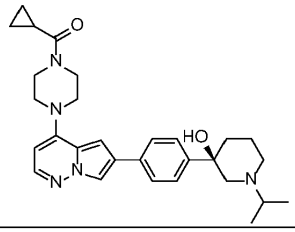
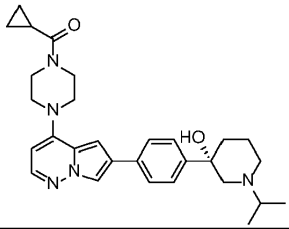
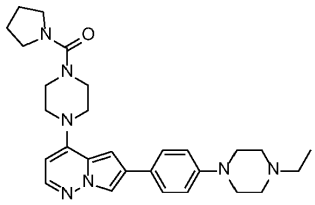
323	
324	
325	
326	
327	

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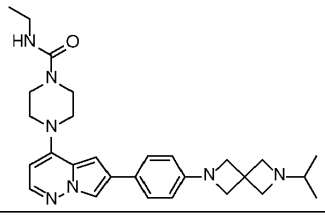
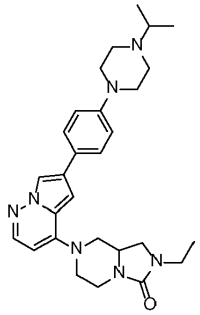
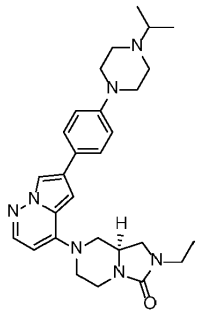
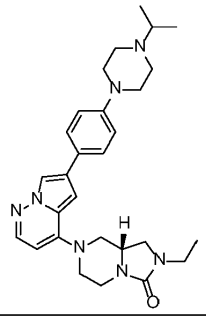
328	
329	
330	
331	

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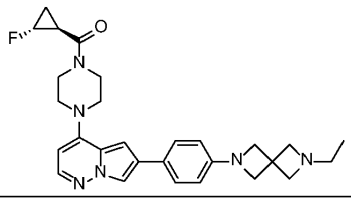
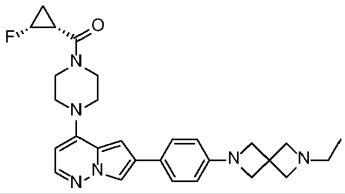
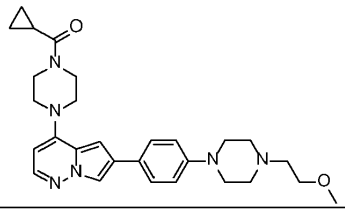
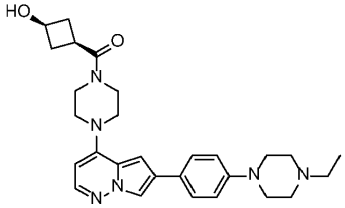
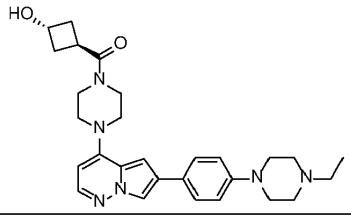
332	
333	
334	
335	
336	

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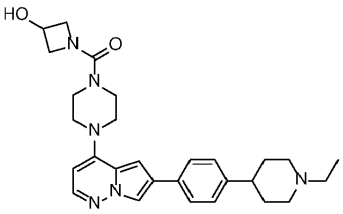
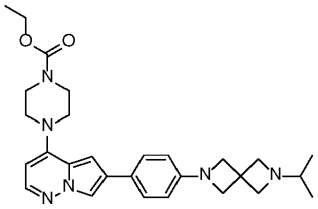
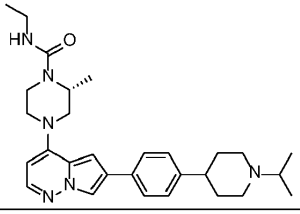
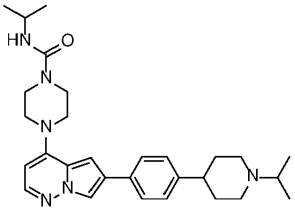
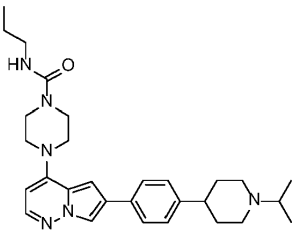
337	
338	
339	
340	
341	

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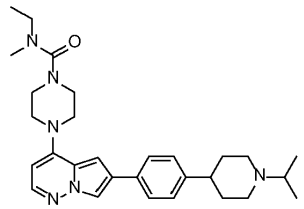
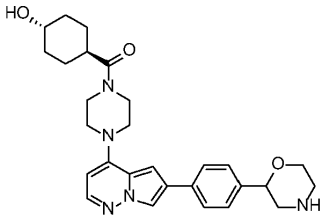
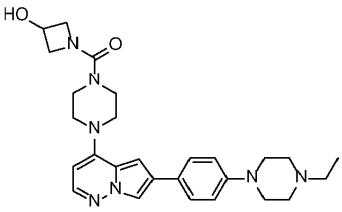
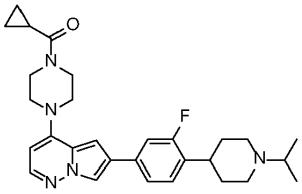
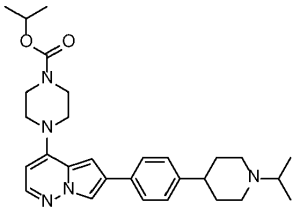
342	
343	
344	
345	
346	

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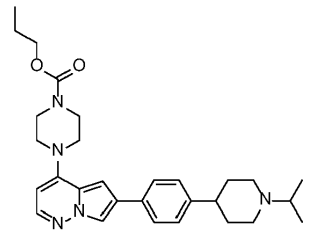
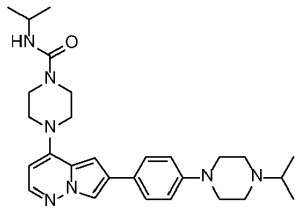
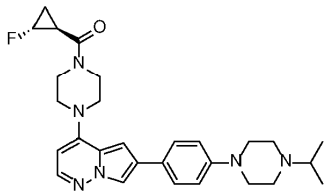
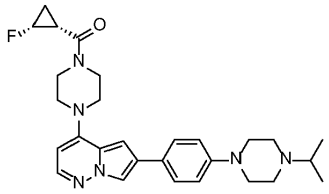
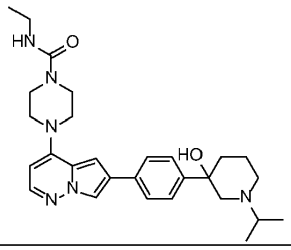
347	
348	
349	
350	
351	

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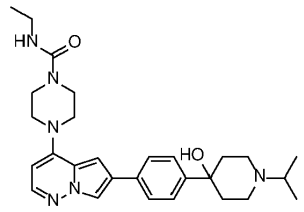
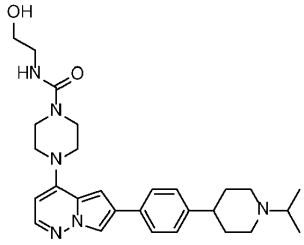
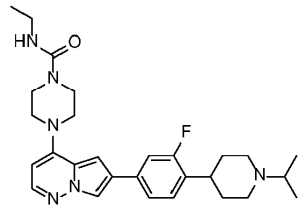
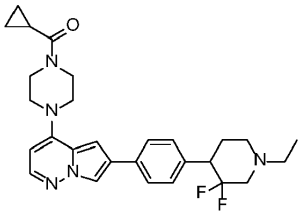
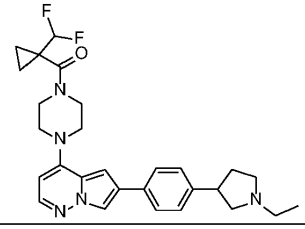
352	
353	
354	
355	
356	

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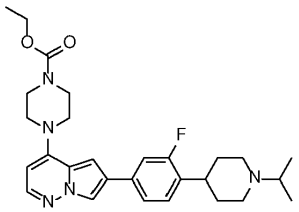
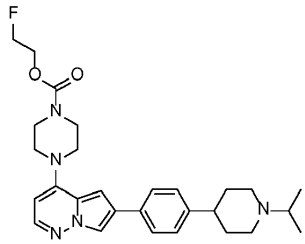
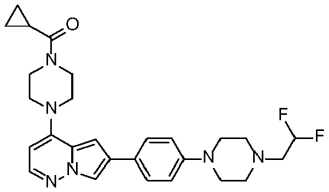
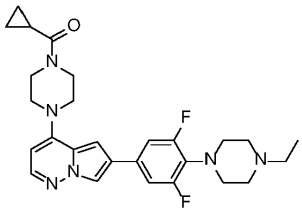
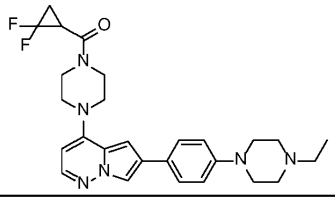
357	
358	
359	
360	
361	

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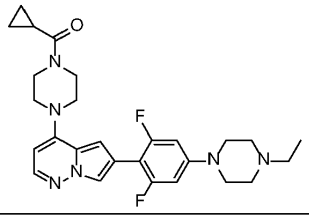
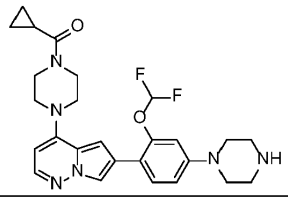
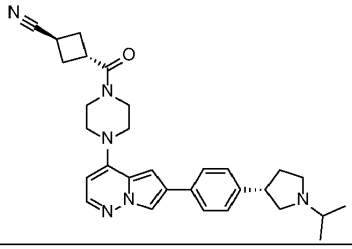
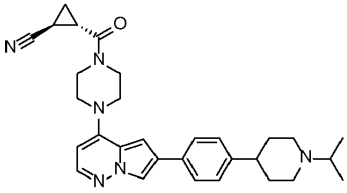
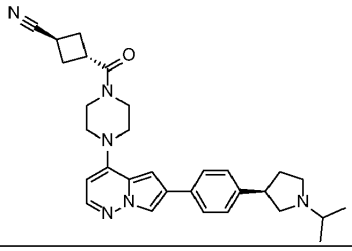
362	
363	
364	
365	
366	

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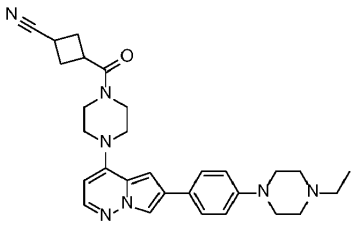
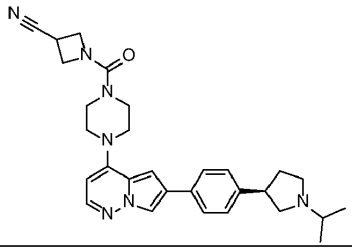
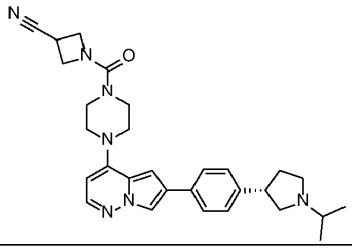
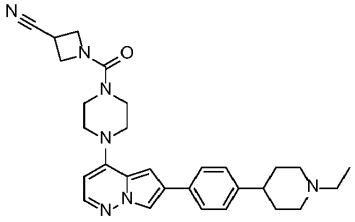
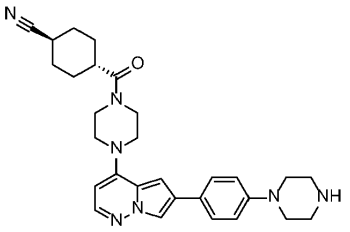
367	
368	
369	
370	
371	

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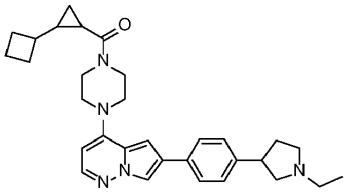
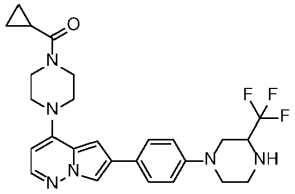
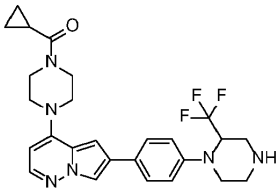
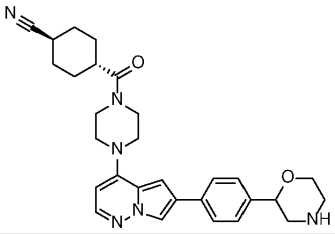
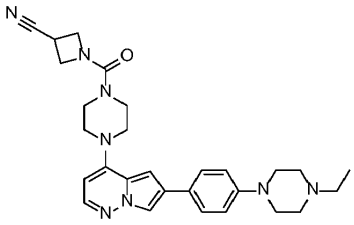
372	
373	
374	
375	
376	

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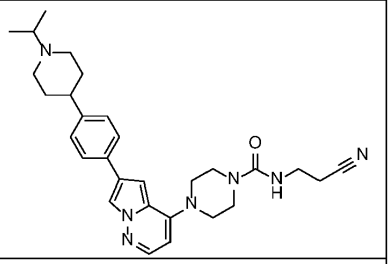
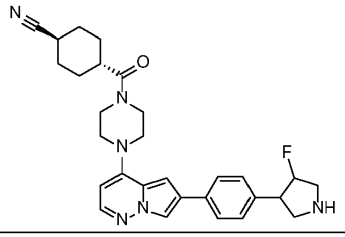
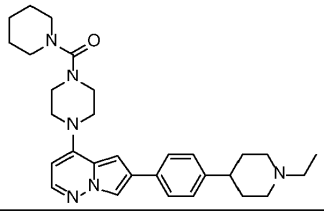
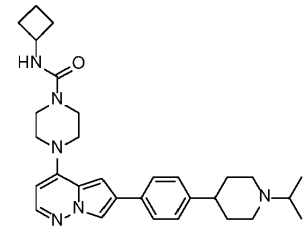
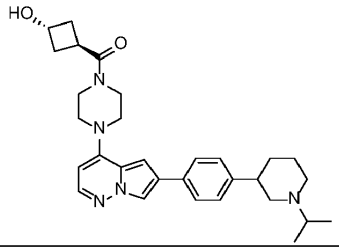
377	
378	
379	
380	
381	

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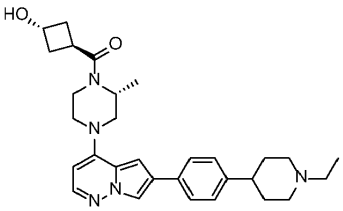
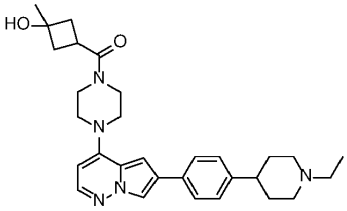
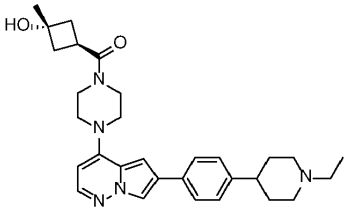
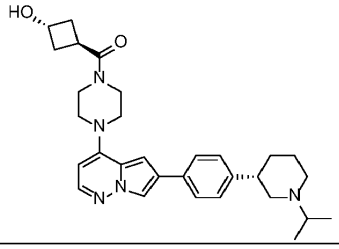
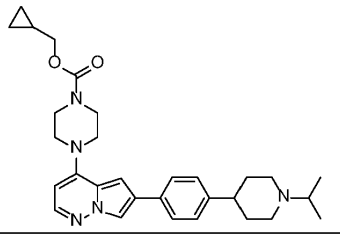
382	
383	
384	
385	
386	

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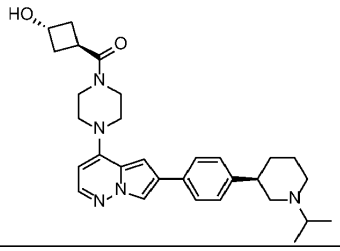
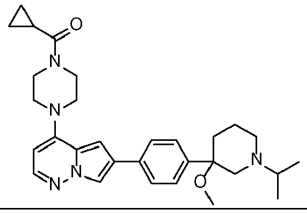
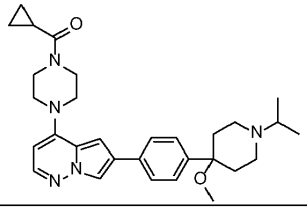
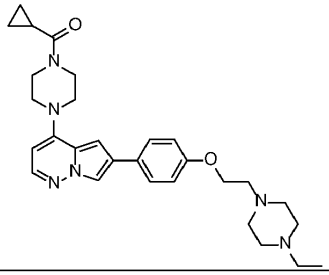
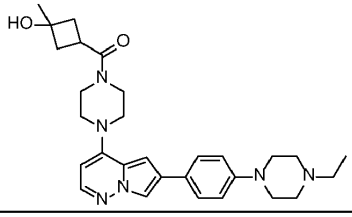
387	
388	
389	
390	
391	

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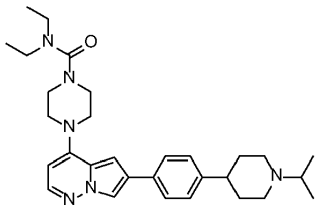
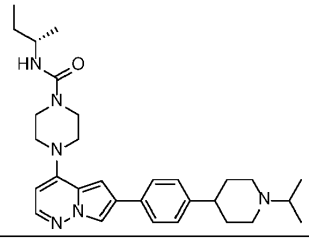
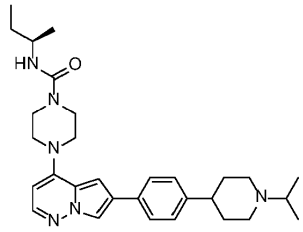
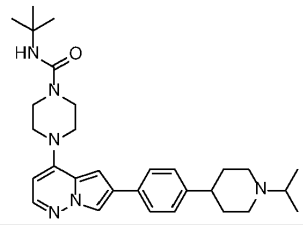
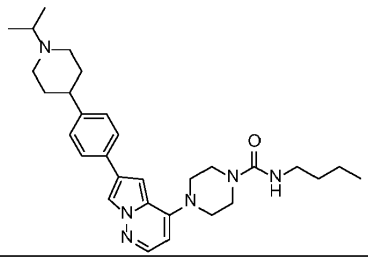
392	
393	
394	
395	
396	

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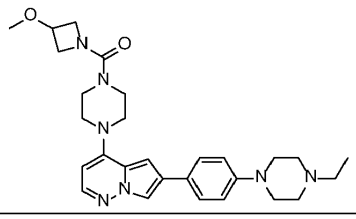
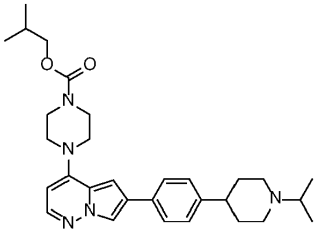
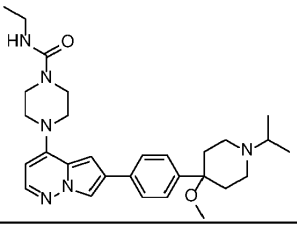
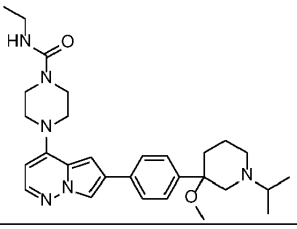
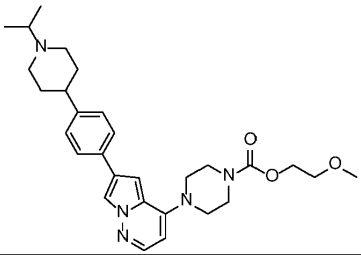
397	
398	
399	
400	
401	

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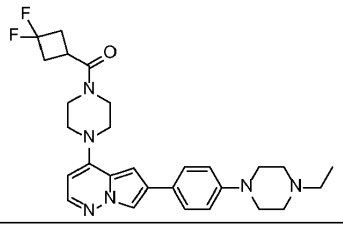
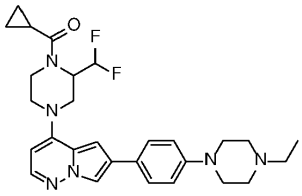
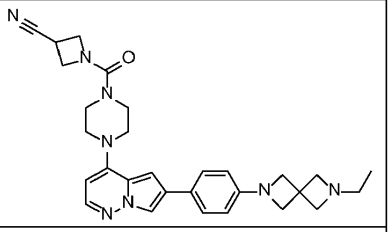
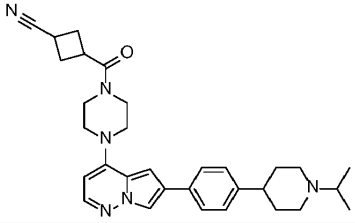
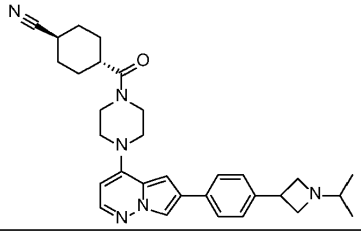
402	
403	
404	
405	
406	

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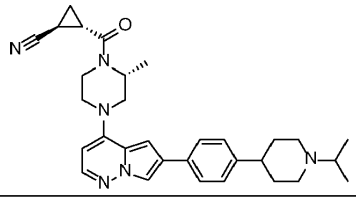
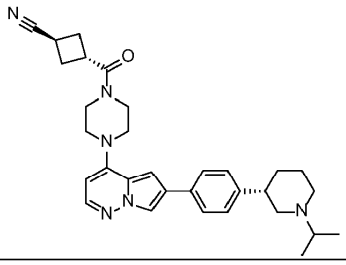
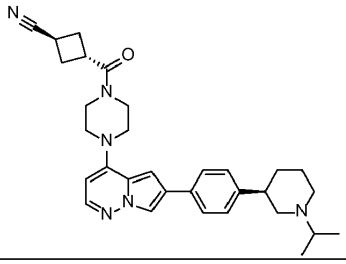
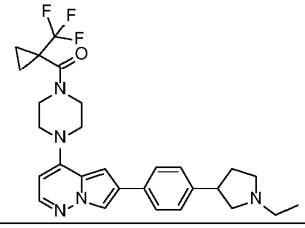
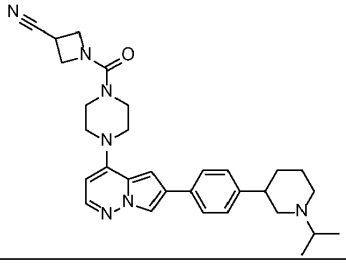
407	
408	
409	
410	
411	

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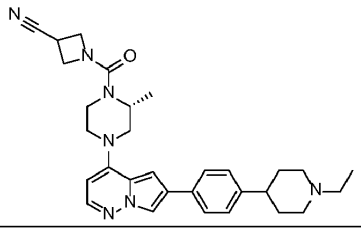
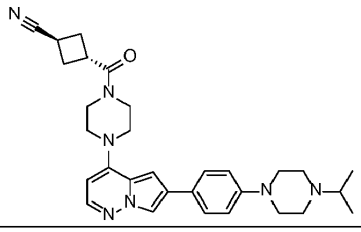
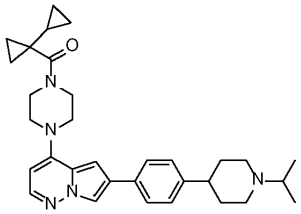
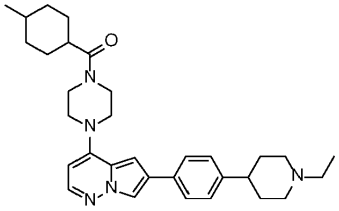
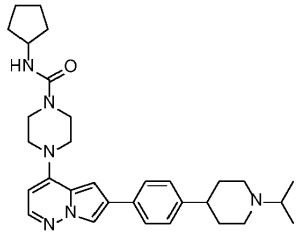
412	
413	
414	
415	
416	

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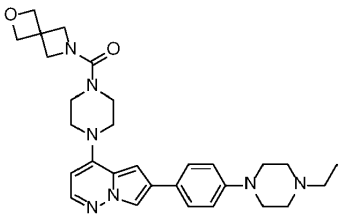
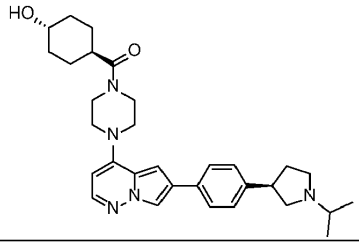
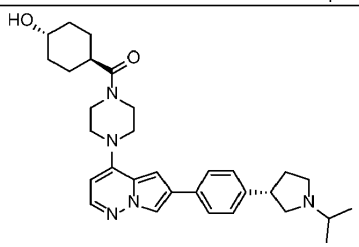
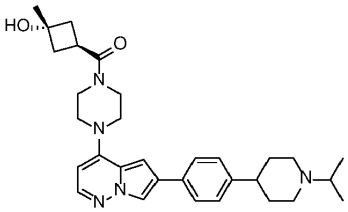
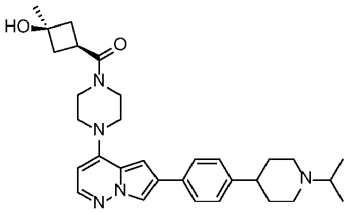
417	
418	
419	
420	
421	

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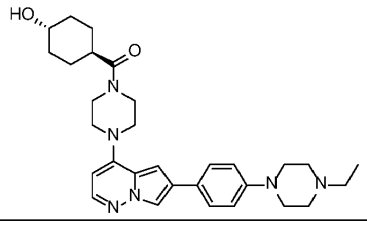
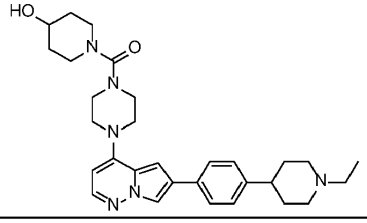
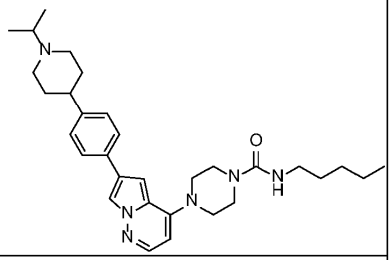
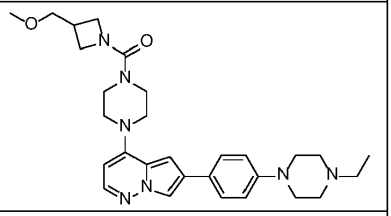
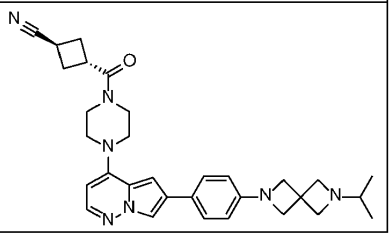
422	
423	
424	
425	
426	

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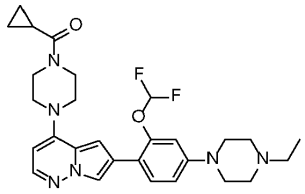
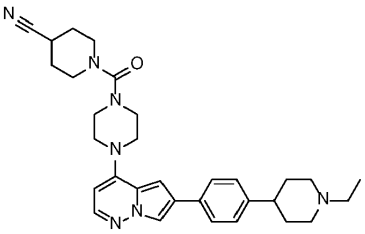
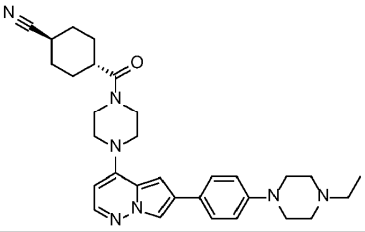
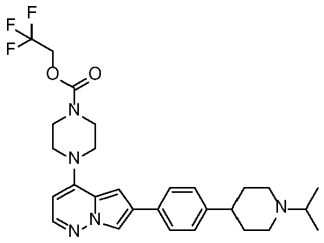
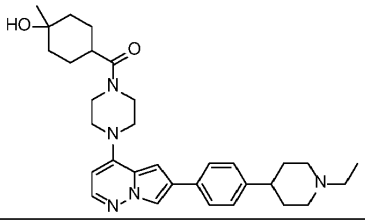
427	
428	
429	
430	
431	

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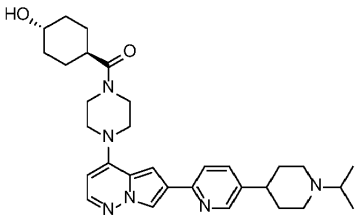
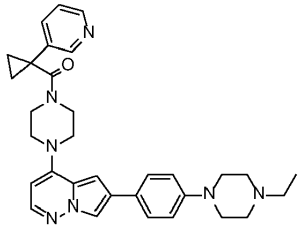
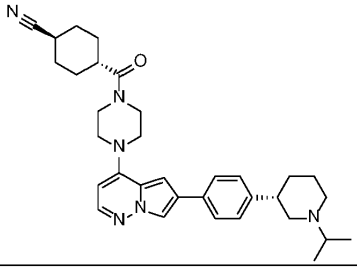
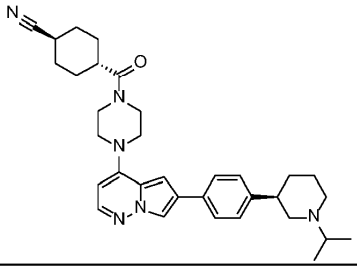
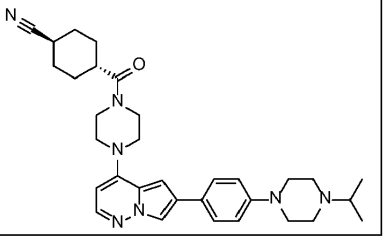
432	
433	
434	
435	
436	

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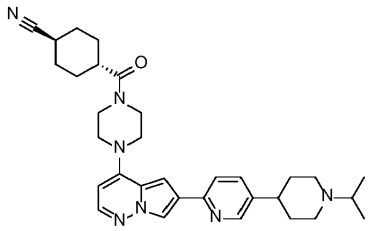
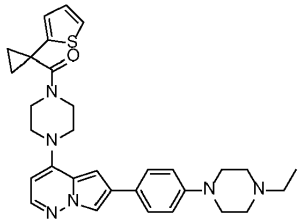
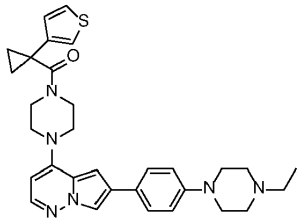
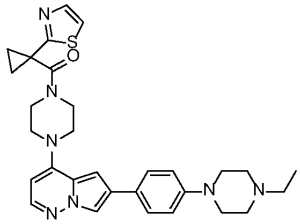
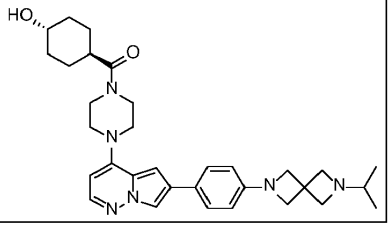
437	
438	
439	
440	
441	

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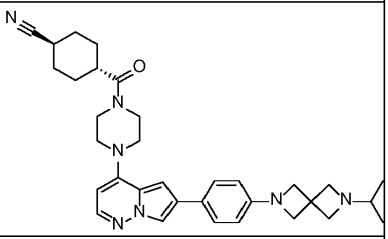
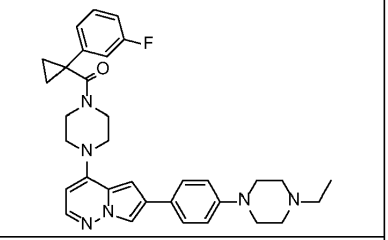
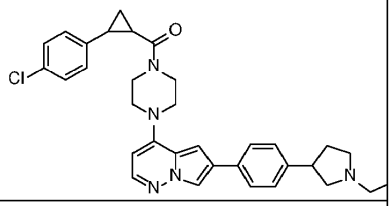
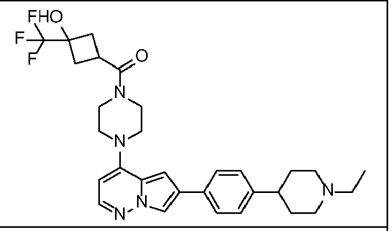
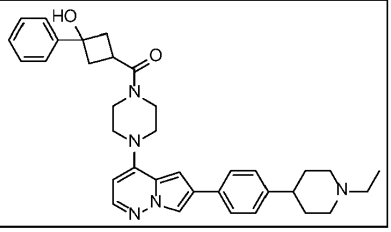
442	
443	
444	
445	
446	

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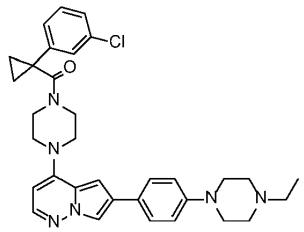
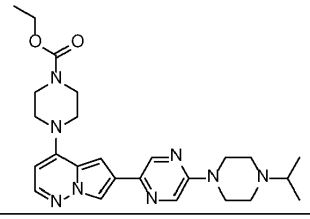
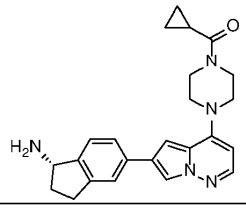
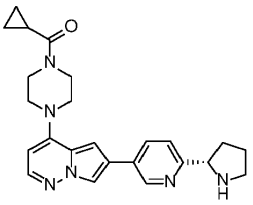
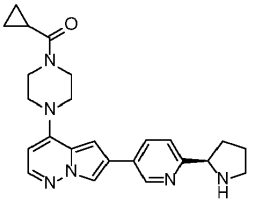
447	
448	
449	
450	
451	

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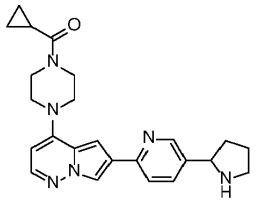
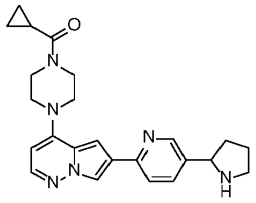
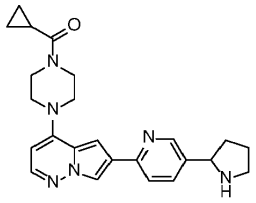
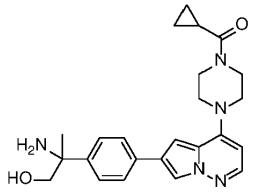
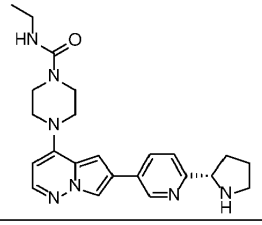
452	
453	
454	
455	
456	

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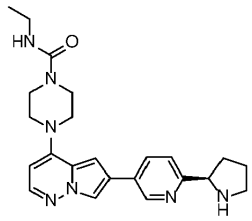
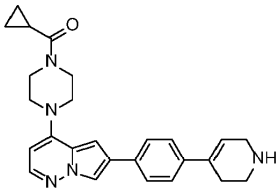
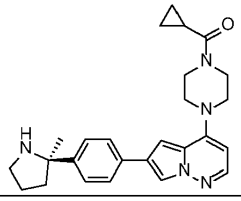
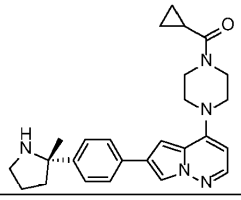
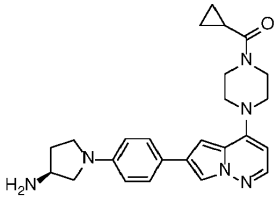
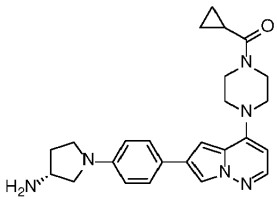
457	
458	
459	
460	
461	
462	

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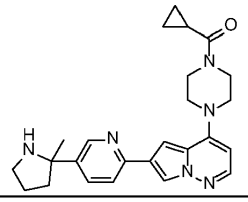
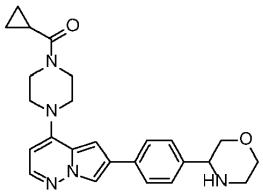
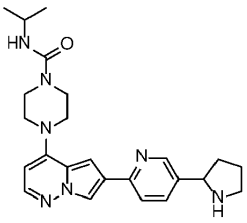
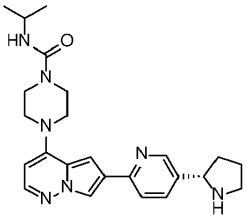
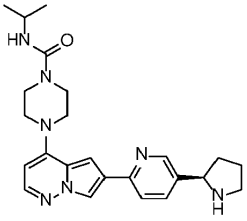
463	
464	
465	
466	
467	

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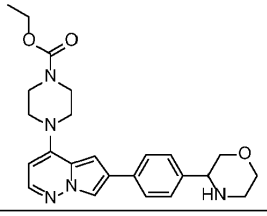
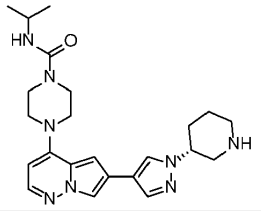
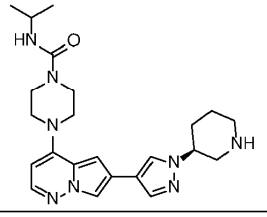
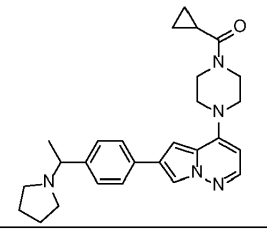
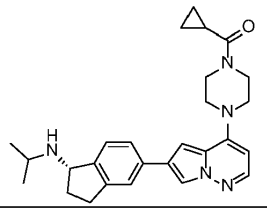
468	
469	
470	
471	
472	

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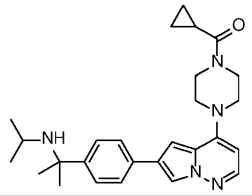
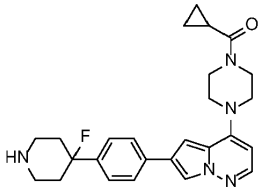
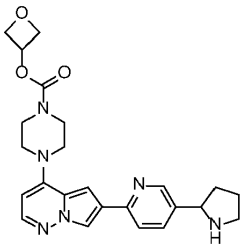
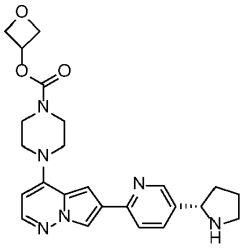
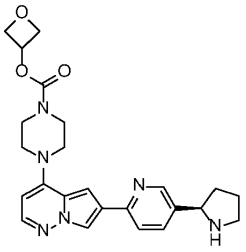
473	
474	
475	
476	
477	

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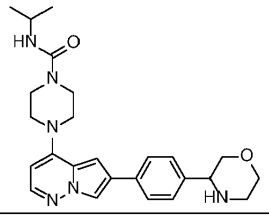
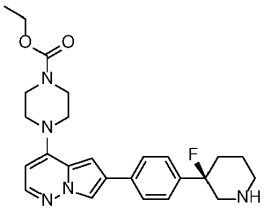
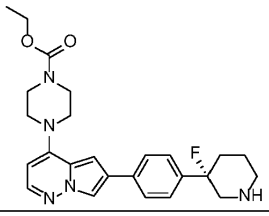
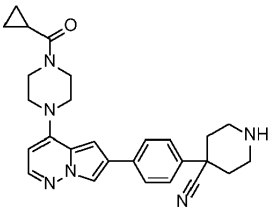
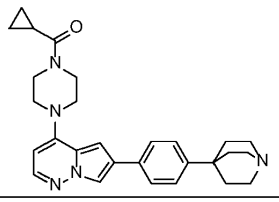
478	
479	
480	
481	
482	

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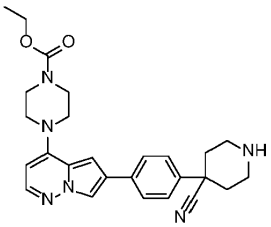
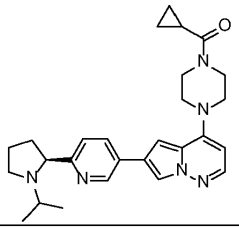
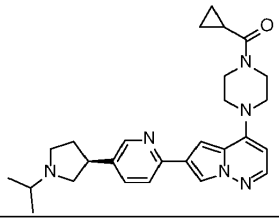
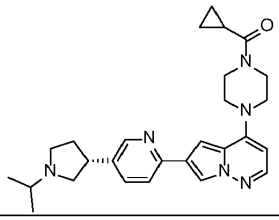
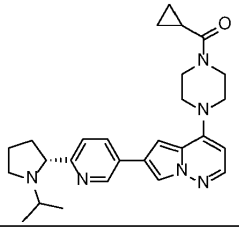
483	
484	
485	
486	
487	

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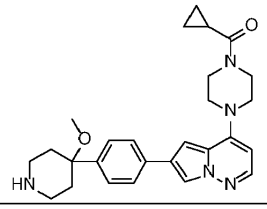
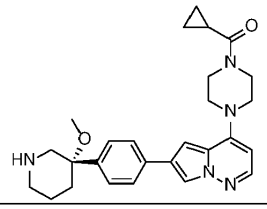
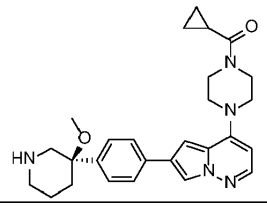
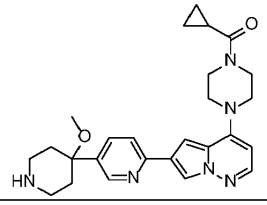
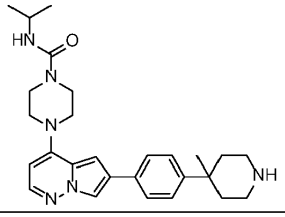
488	
489	
490	
491	
492	

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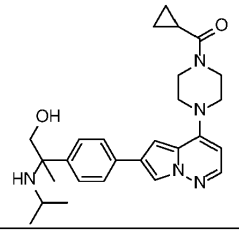
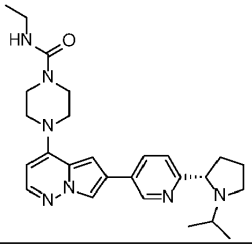
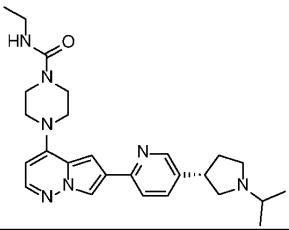
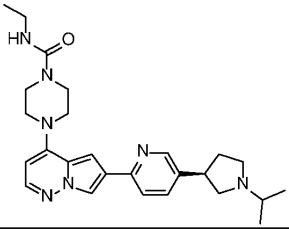
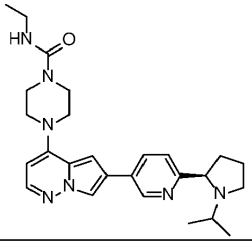
493	
494	
495	
496	
497	

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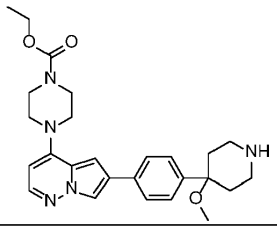
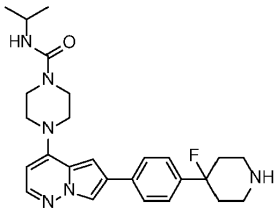
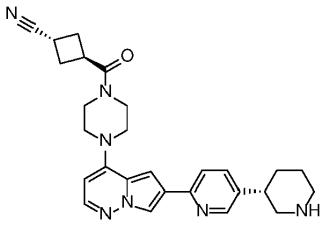
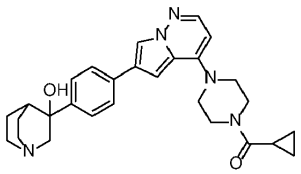
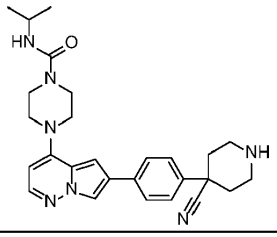
498	
499	
500	
501	
502	

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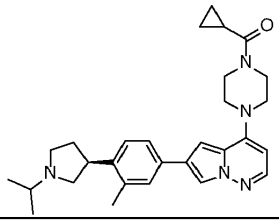
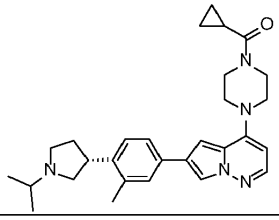
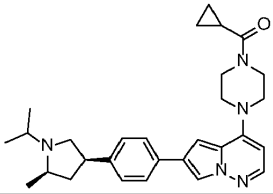
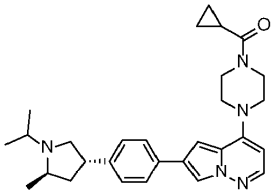
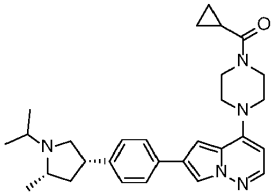
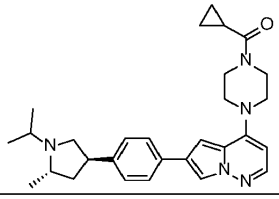
503	
504	
505	
506	
507	
508	

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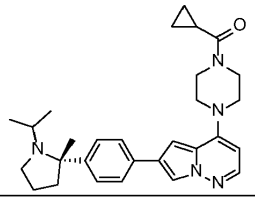
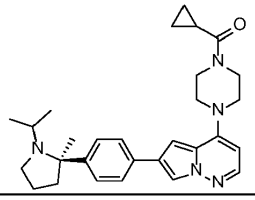
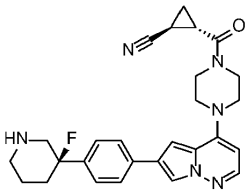
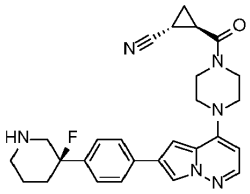
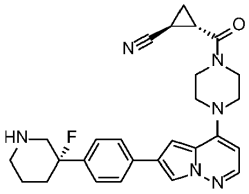
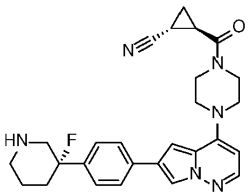
509	
510	
511	
512	
513	
514	

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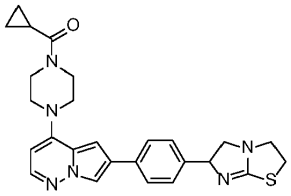
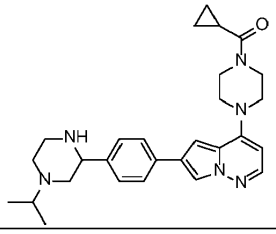
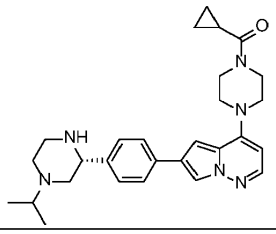
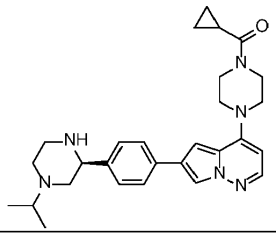
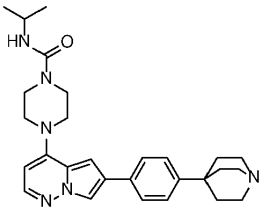
515	
516	
517	
518	
519	

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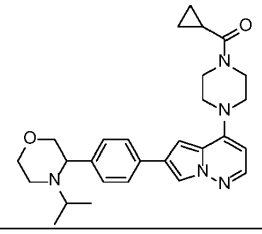
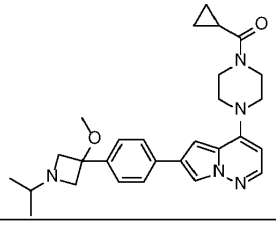
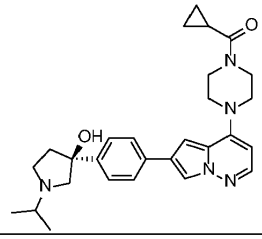
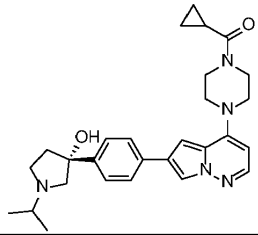
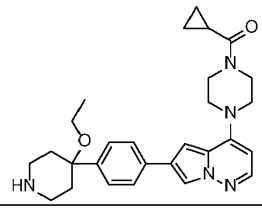
520	
521	
522	
523	
524	

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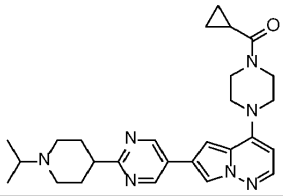
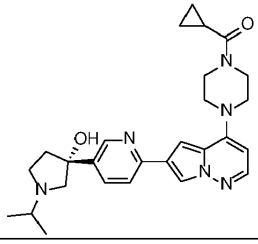
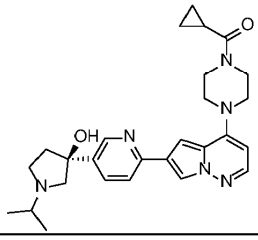
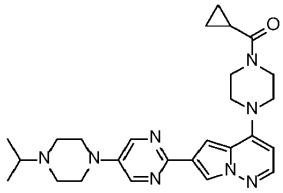
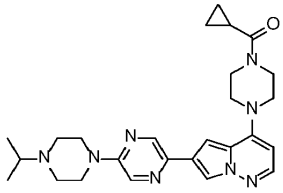
525	
526	
527	
528	
529	

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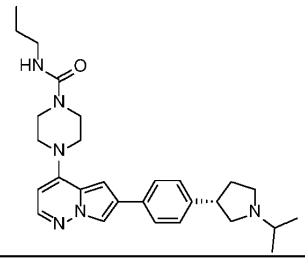
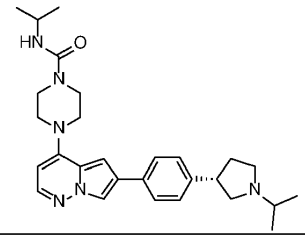
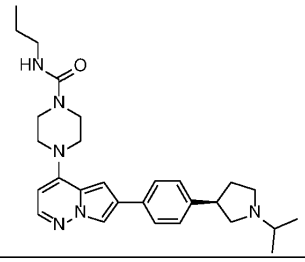
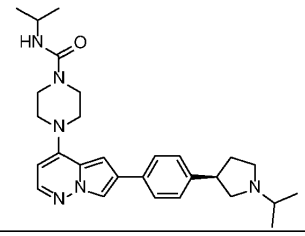
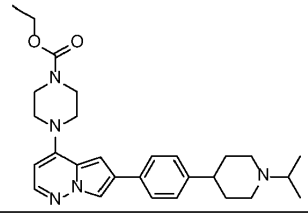
530	
531	
532	
533	
534	

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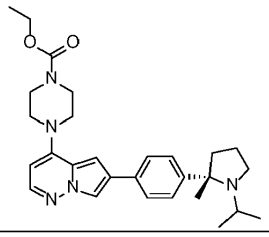
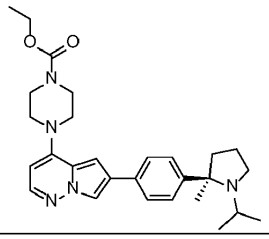
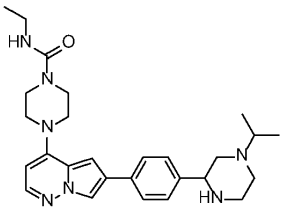
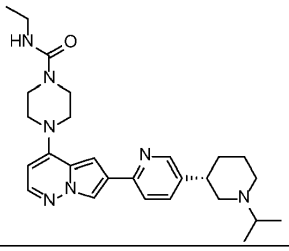
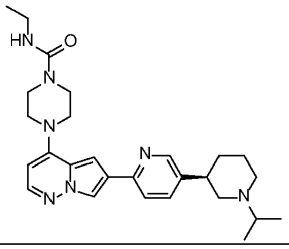
535	
536	
537	
538	
539	

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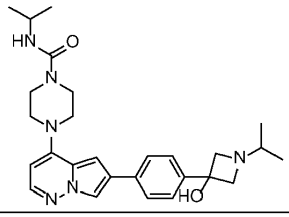
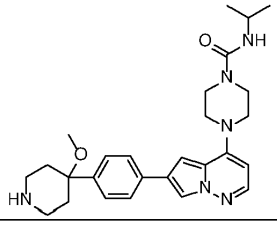
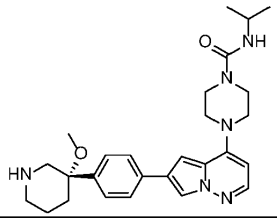
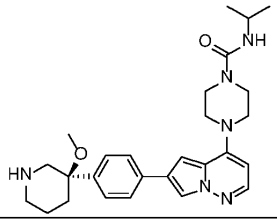
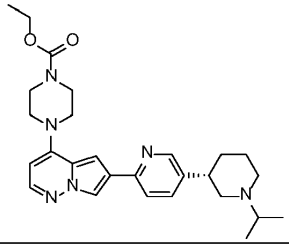
540	
541	
542	
543	
544	

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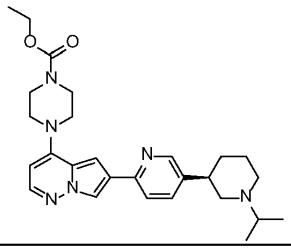
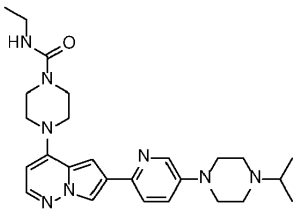
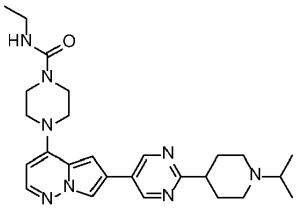
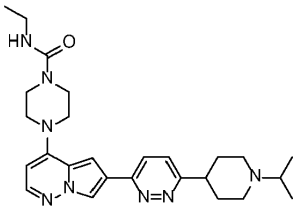
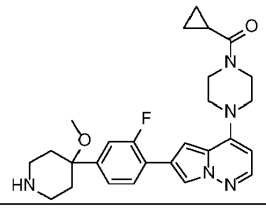
545	
546	
547	
548	
549	

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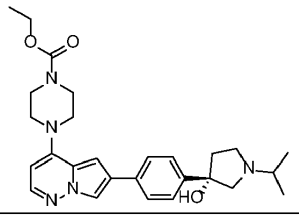
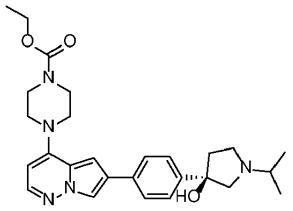
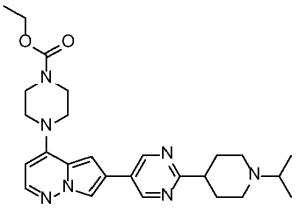
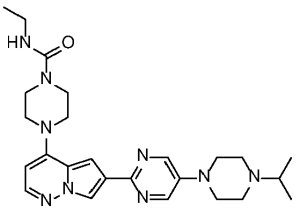
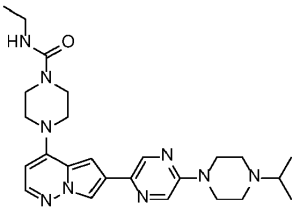
550	
551	
552	
553	
554	

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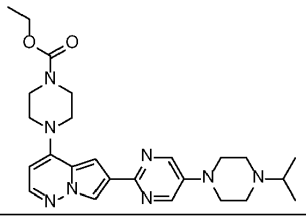
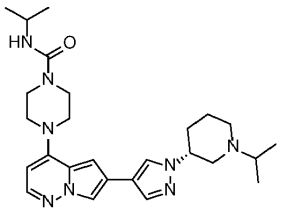
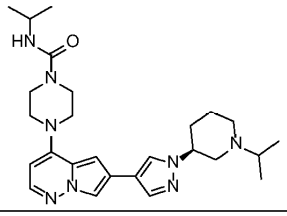
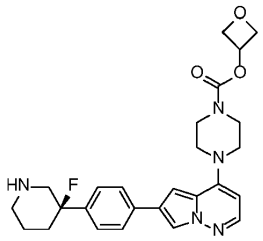
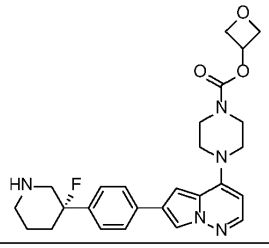
555	
556	
557	
558	
559	

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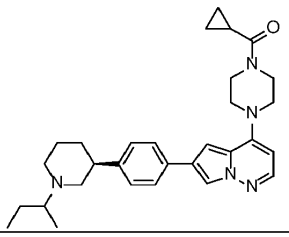
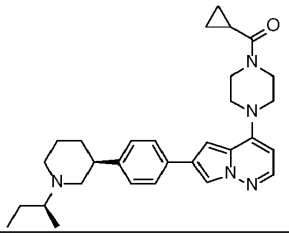
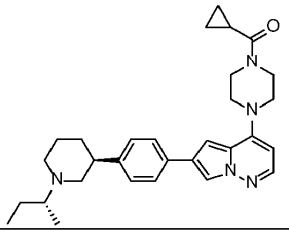
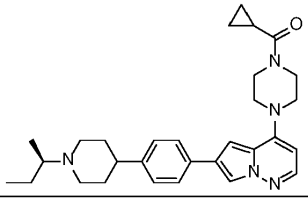
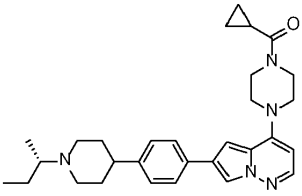
560	
561	
562	
563	
564	

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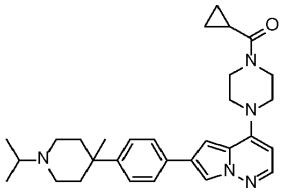
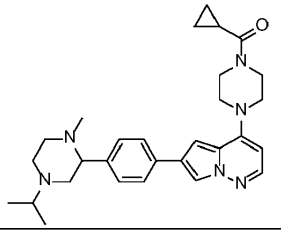
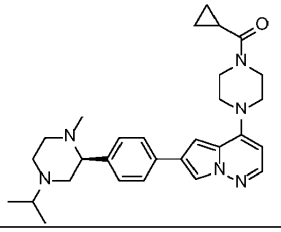
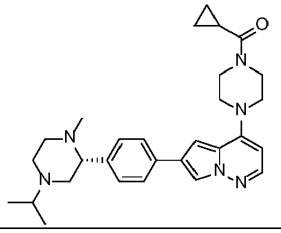
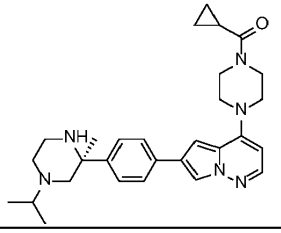
565	
566	
567	
568	
569	

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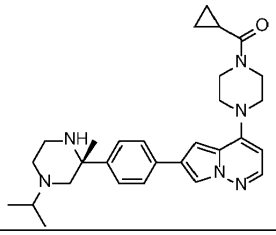
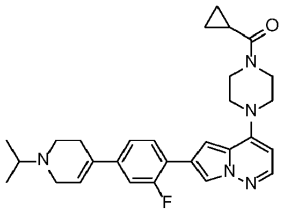
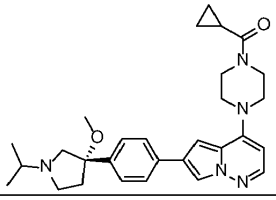
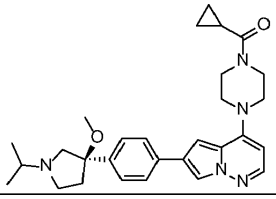
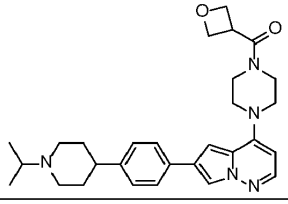
570	
571	
572	
573	
574	

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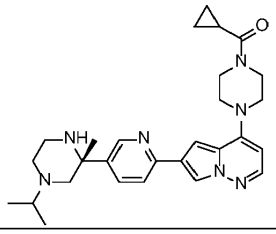
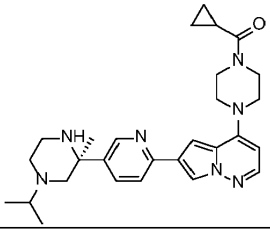
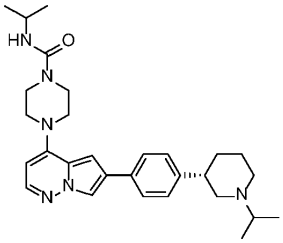
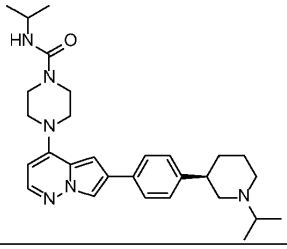
575	
576	
577	
578	

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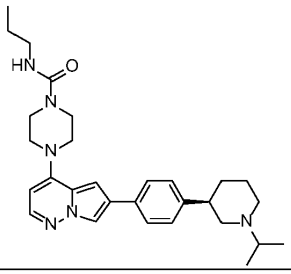
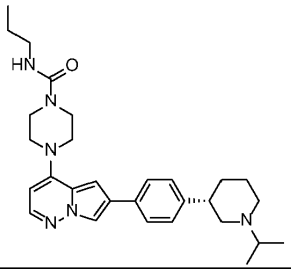
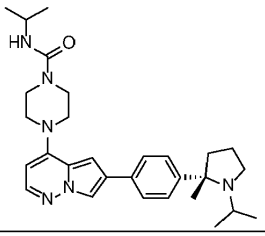
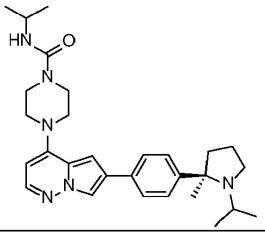
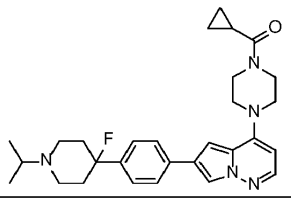
579	
580	
581	
582	
583	

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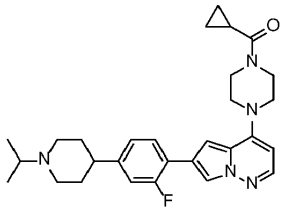
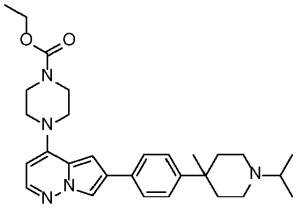
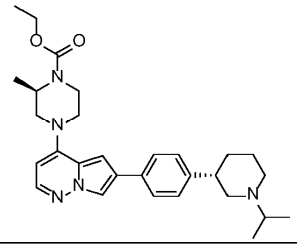
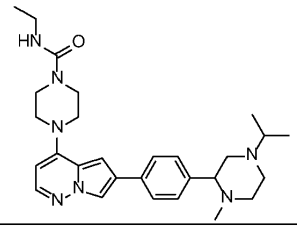
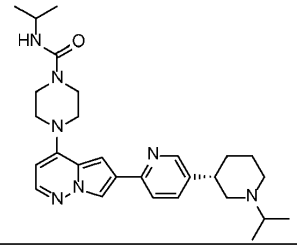
584	
585	
586	
587	
588	

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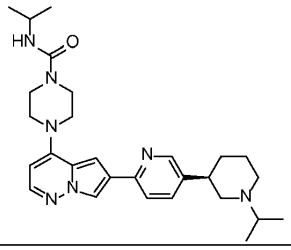
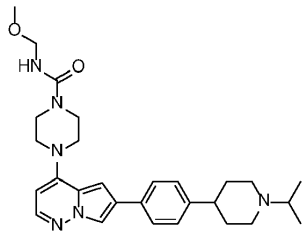
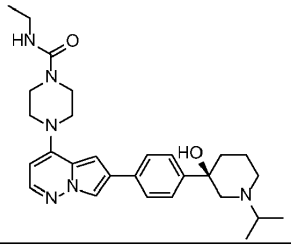
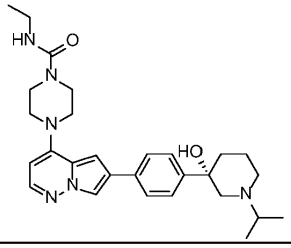
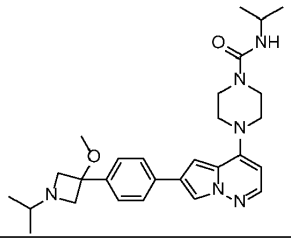
589	
590	
591	
592	
593	

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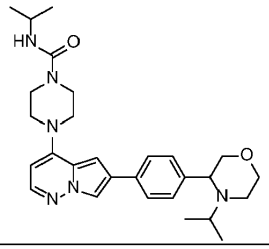
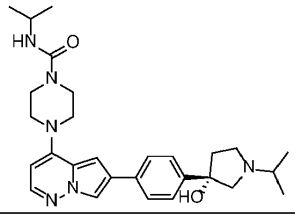
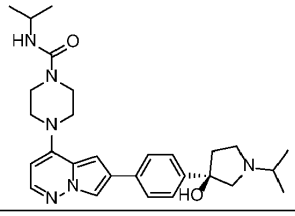
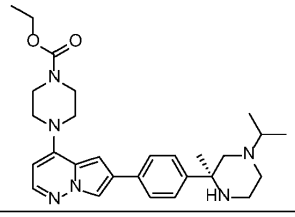
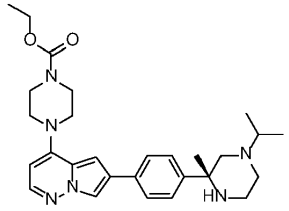
594	
595	
596	
597	
598	

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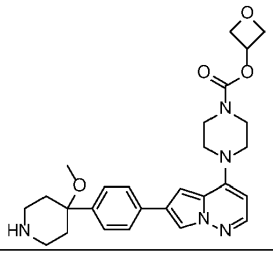
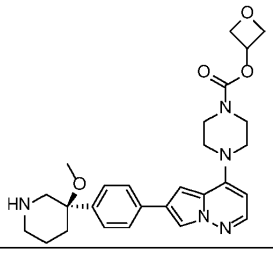
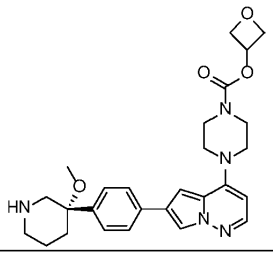
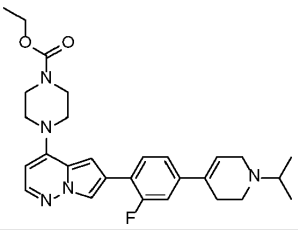
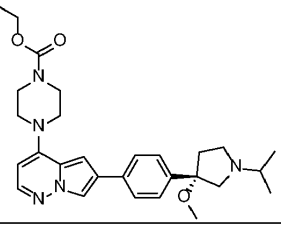
599	
600	
601	
602	
603	

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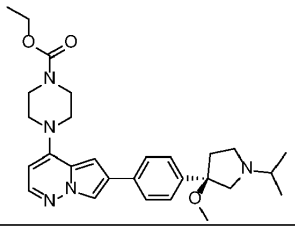
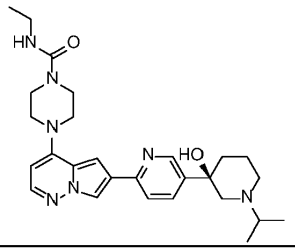
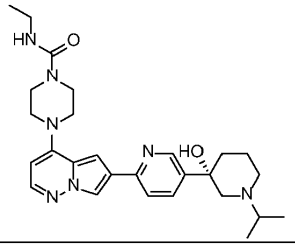
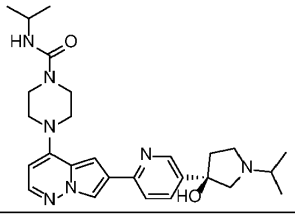
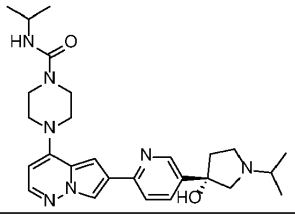
604	
605	
606	
607	
608	

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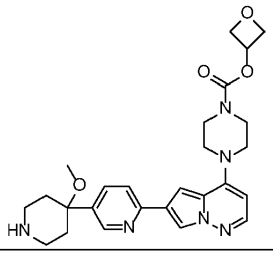
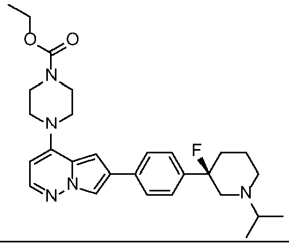
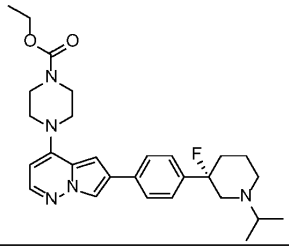
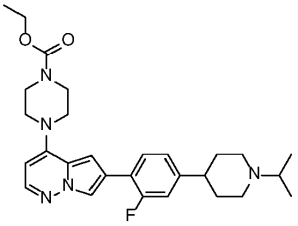
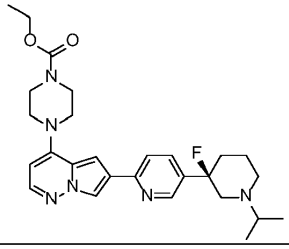
609	
610	
611	
612	
613	

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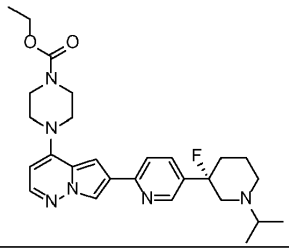
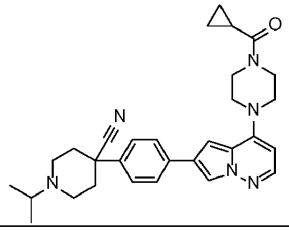
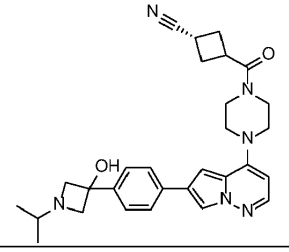
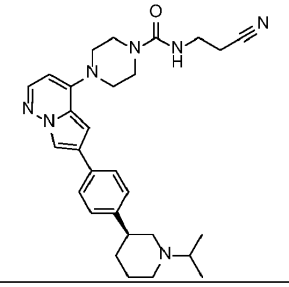
614	
615	
616	
617	

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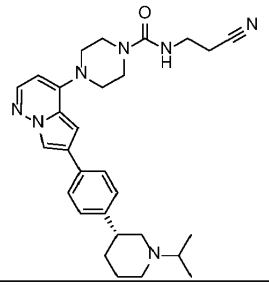
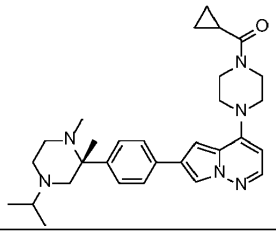
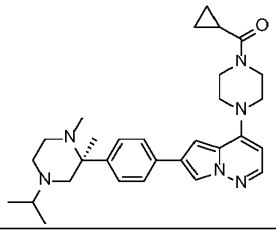
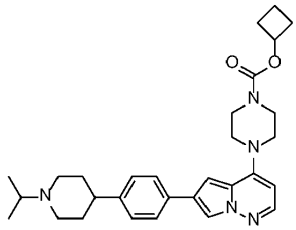
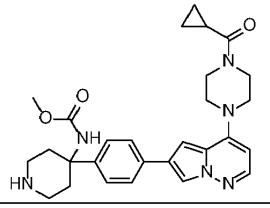
618	
619	
620	
621	
622	

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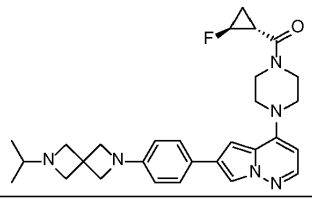
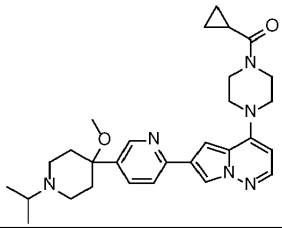
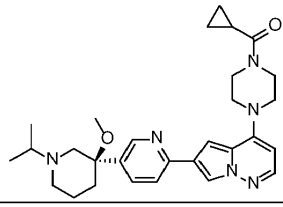
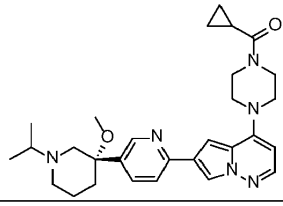
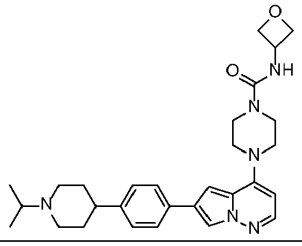
623	
624	
625	
626	
627	

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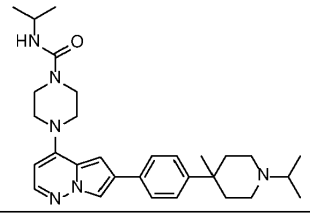
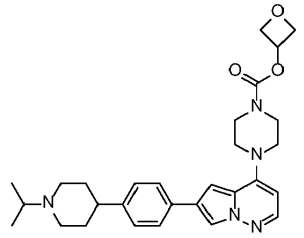
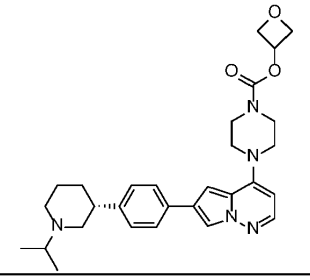
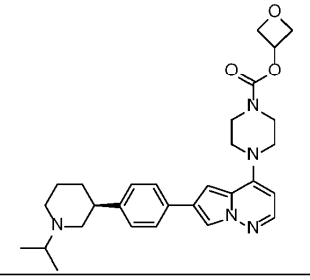
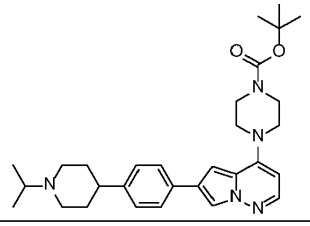
628	
629	
630	
631	
632	

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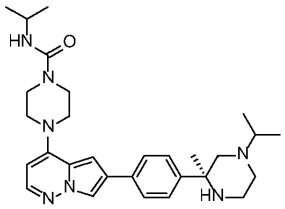
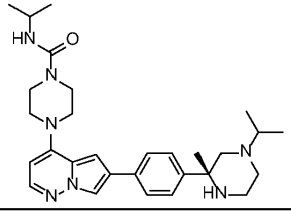
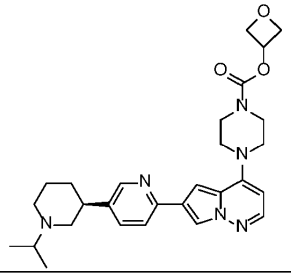
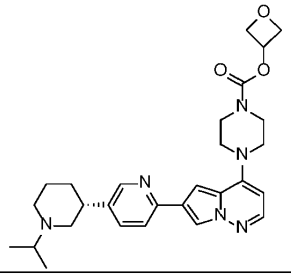
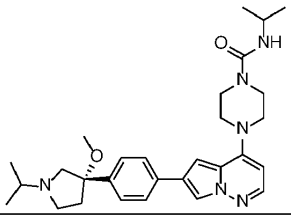
633	
634	
635	
636	
637	

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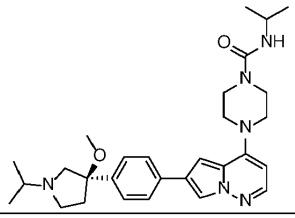
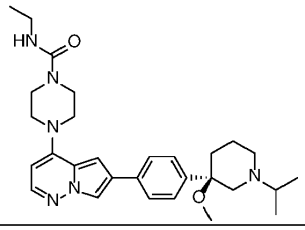
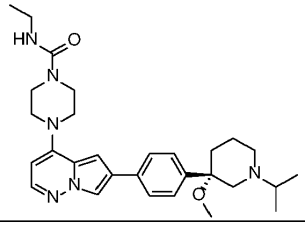
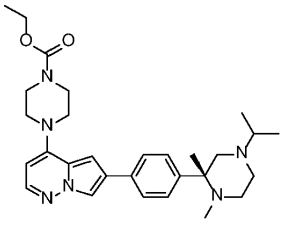
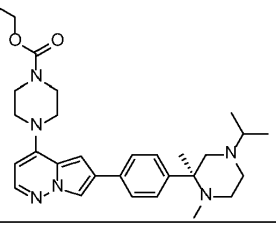
638	
639	
640	
641	
642	

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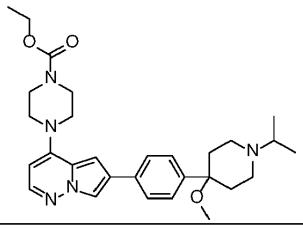
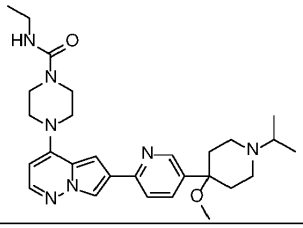
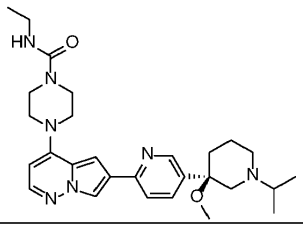
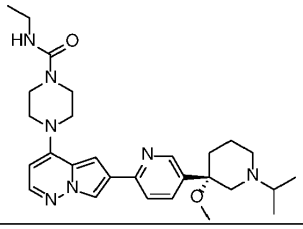
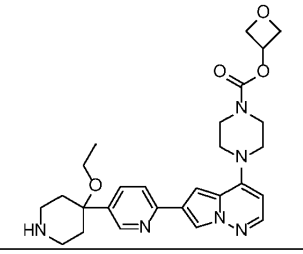
643	
644	
645	
646	
647	

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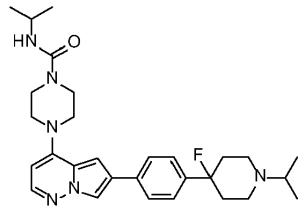
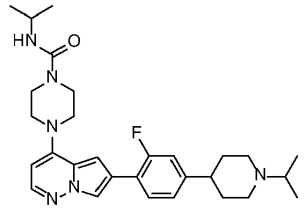
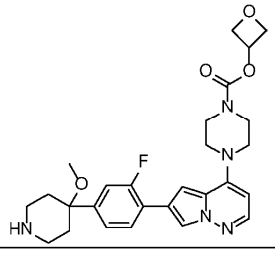
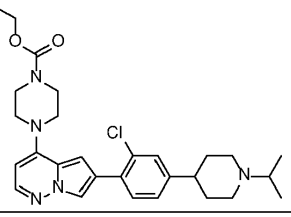
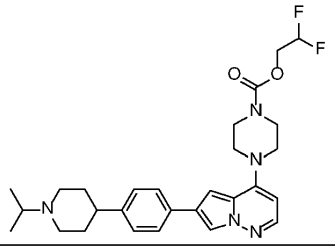
648	
649	
650	
651	
652	

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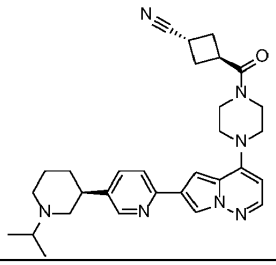
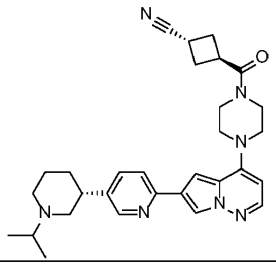
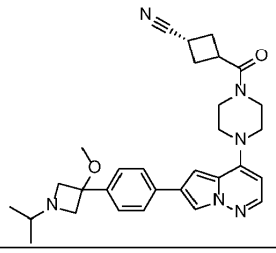
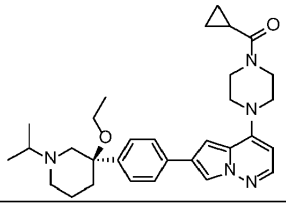
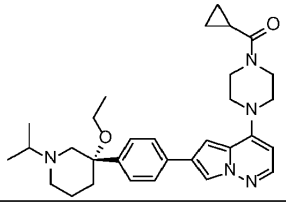
653	
654	
655	
656	
657	

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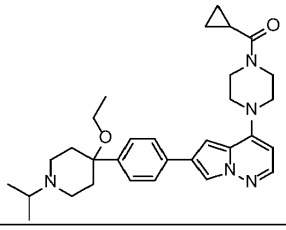
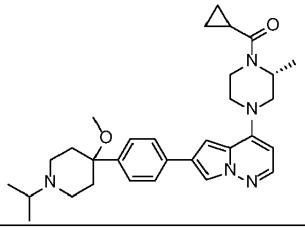
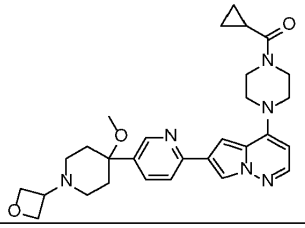
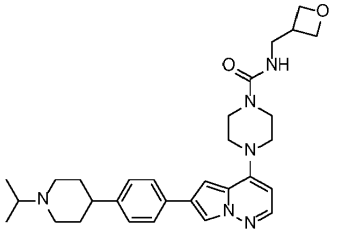
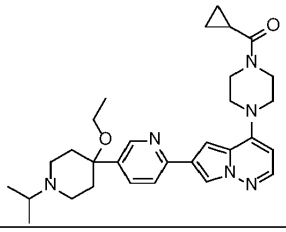
658	
659	
660	
661	
662	

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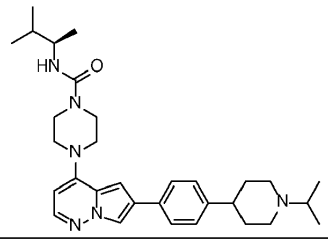
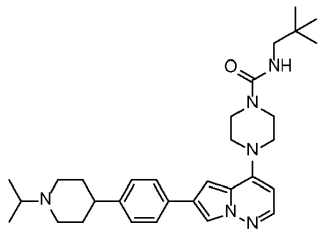
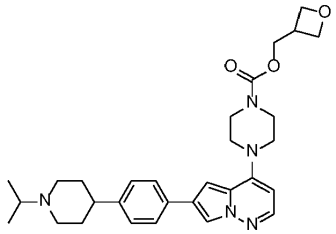
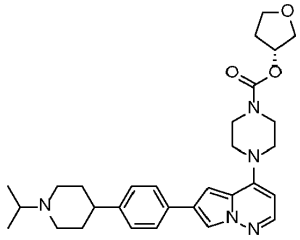
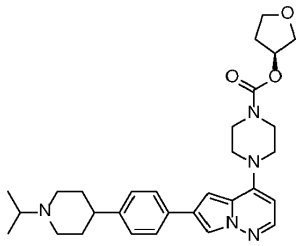
663	
664	
665	
666	
667	

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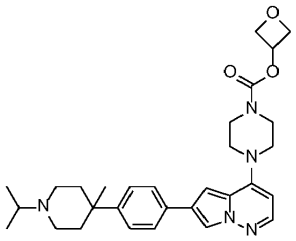
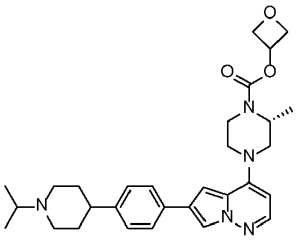
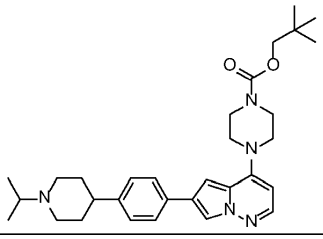
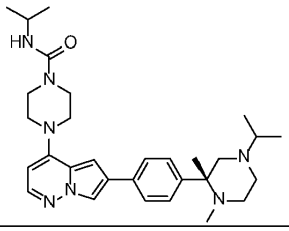
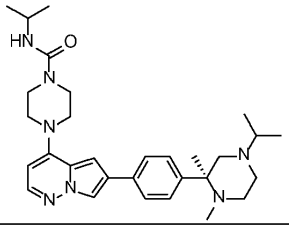
668	
669	
670	
671	
672	

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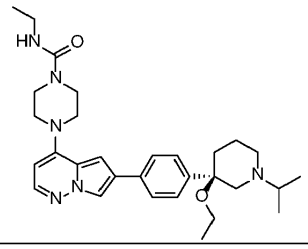
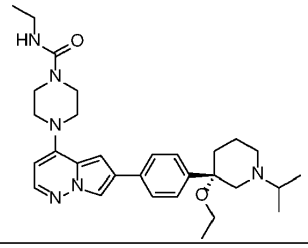
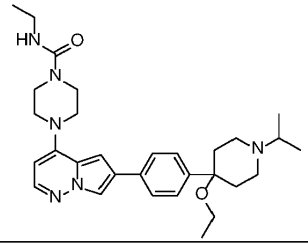
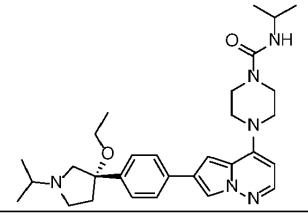
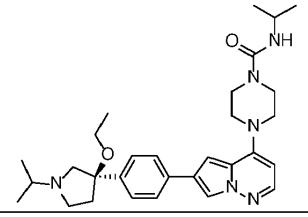
673	
674	
675	
676	
677	

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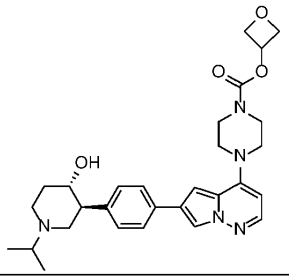
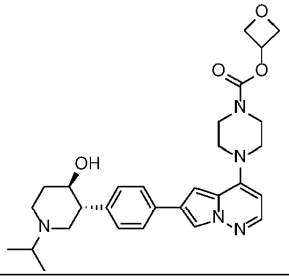
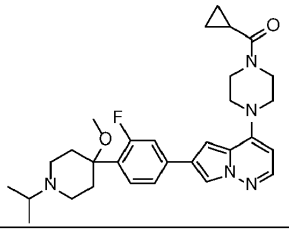
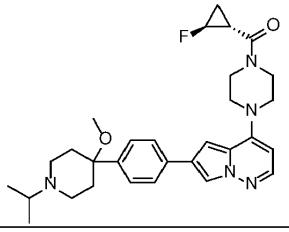
678	
679	
680	
681	

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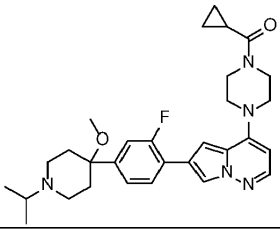
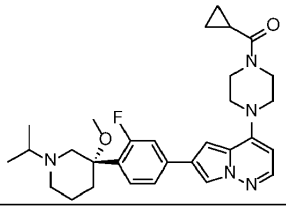
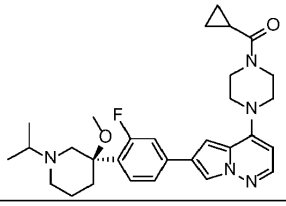
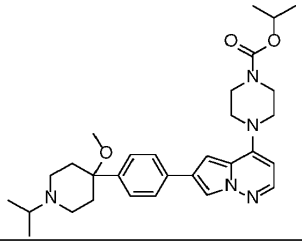
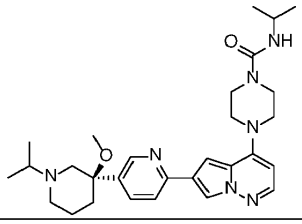
682	
683	
684	
685	
686	

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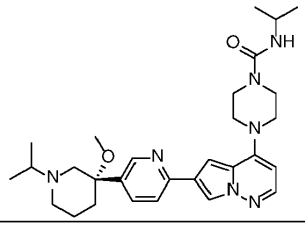
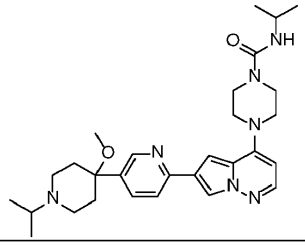
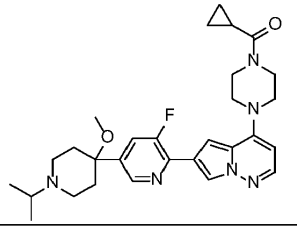
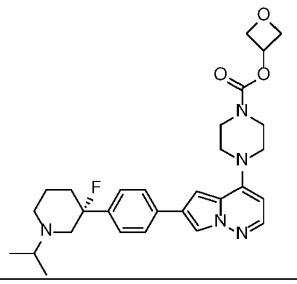
687	
688	
689	
690	

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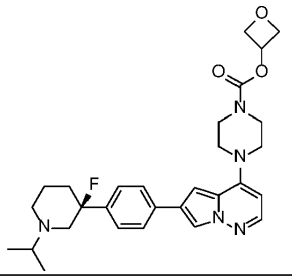
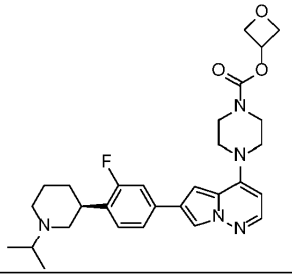
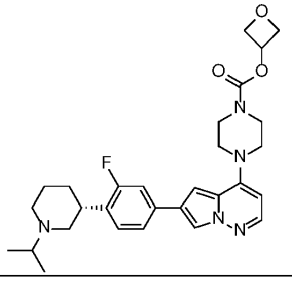
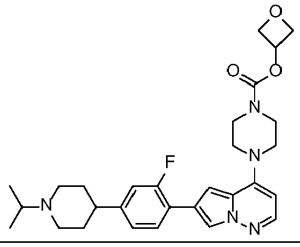
691	
692	
693	
694	

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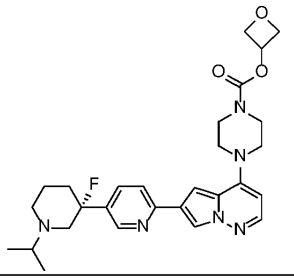
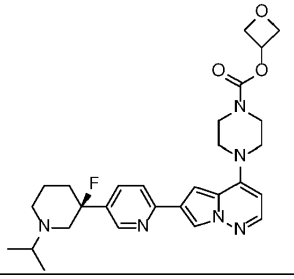
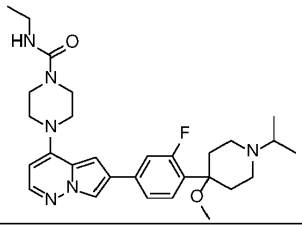
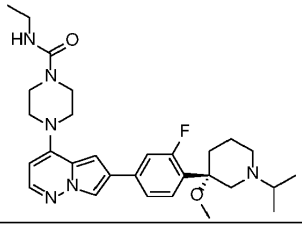
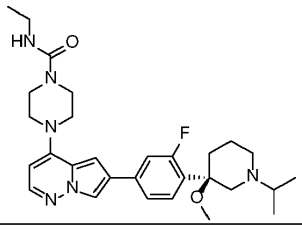
695	
696	
697	
698	
699	

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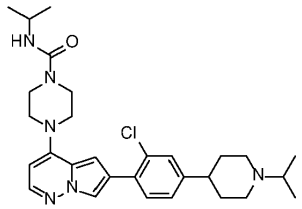
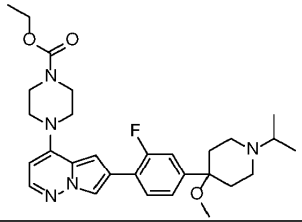
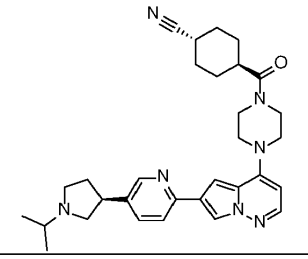
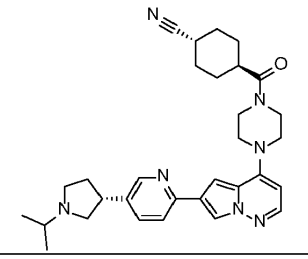
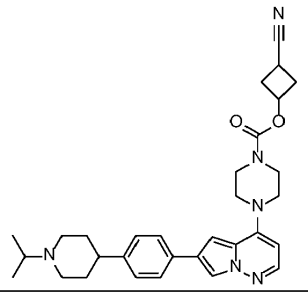
700	
701	
702	
703	
704	

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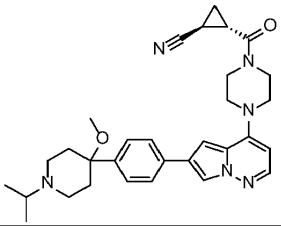
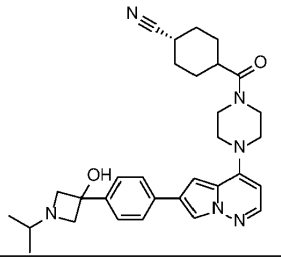
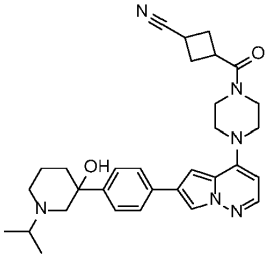
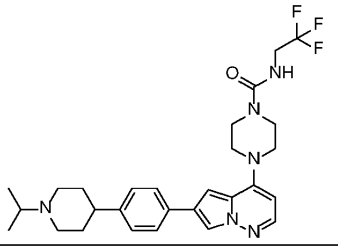
705	
706	
707	
708	

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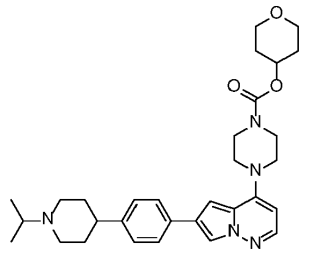
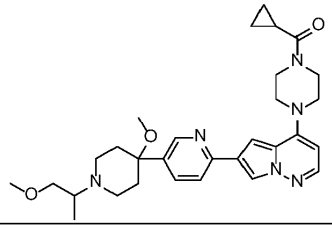
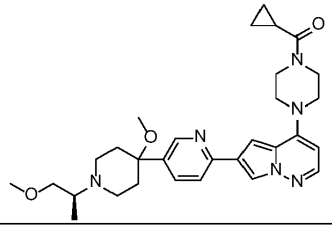
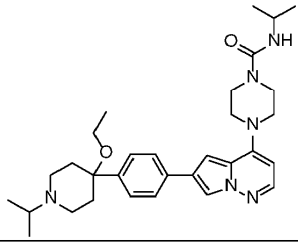
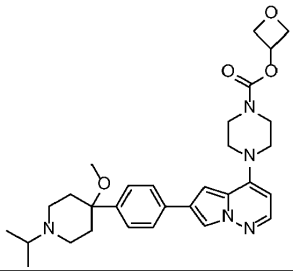
709	
710	
711	
712	
713	

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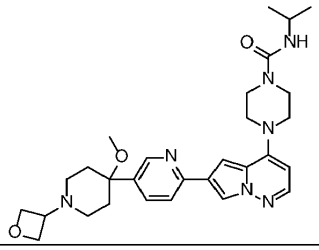
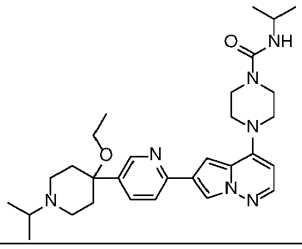
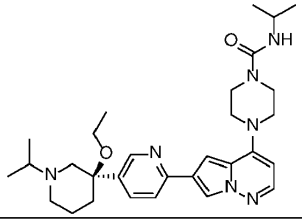
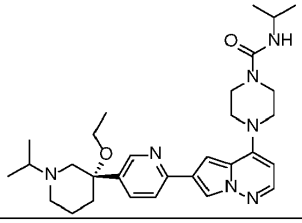
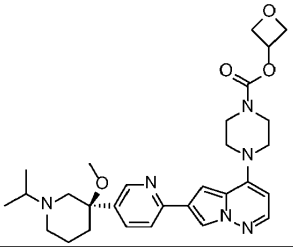
714	
715	
716	
717	
718	

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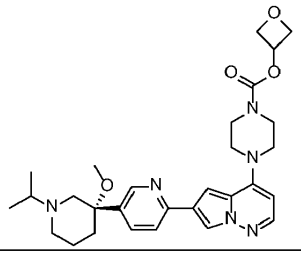
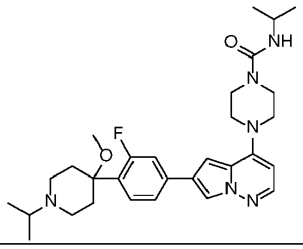
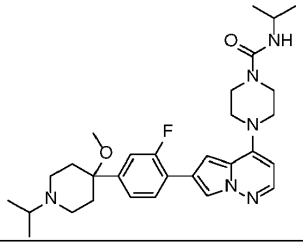
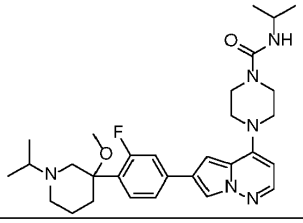
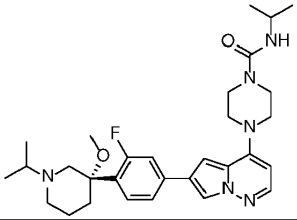
719	
720	
721	
722	
723	

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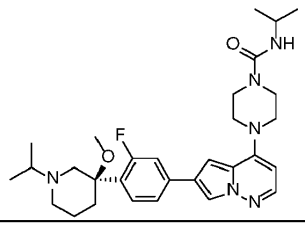
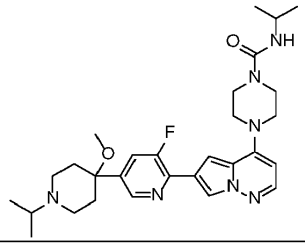
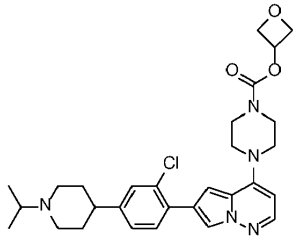
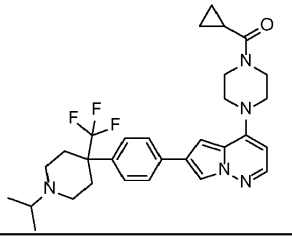
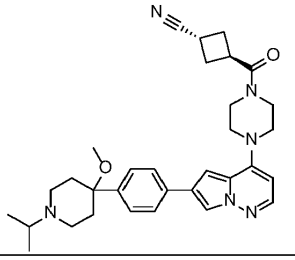
724	
725	
726	
727	
728	

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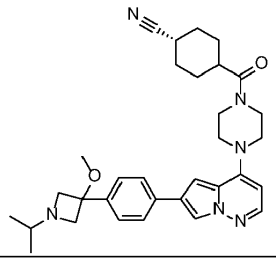
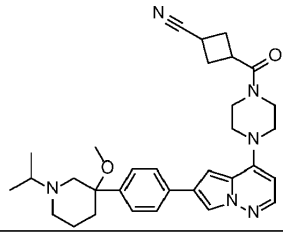
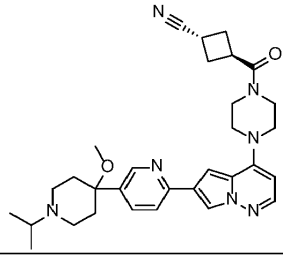
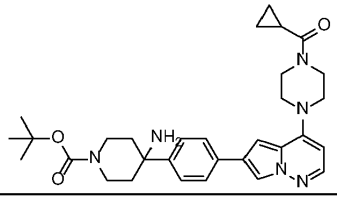
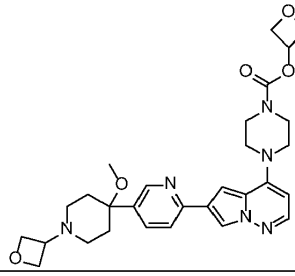
729	
730	
731	
732	
733	

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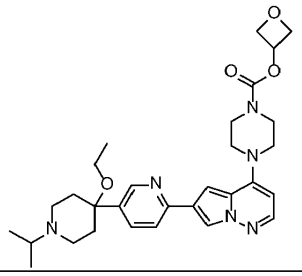
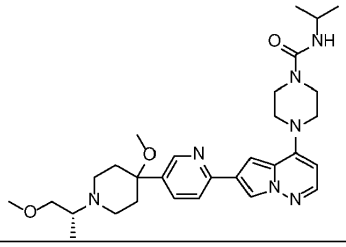
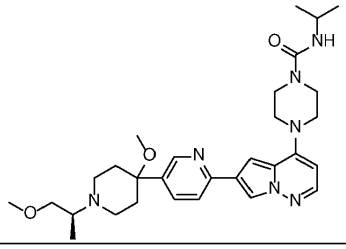
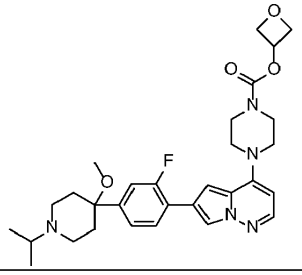
734	
735	
736	
737	

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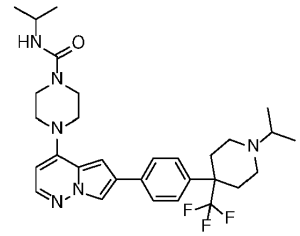
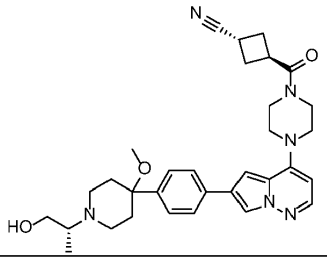
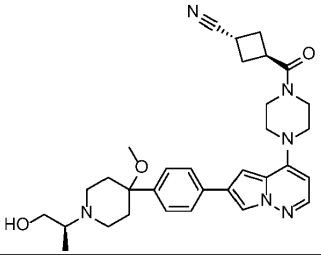
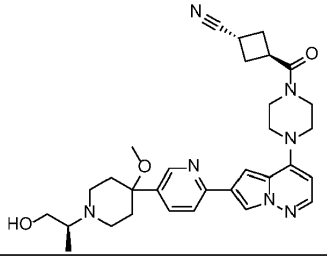
738	
739	
740	
741	

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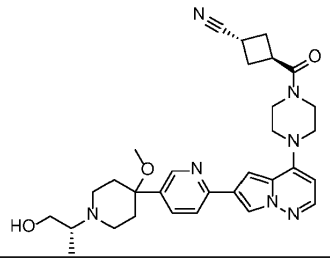
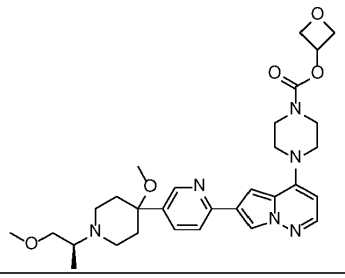
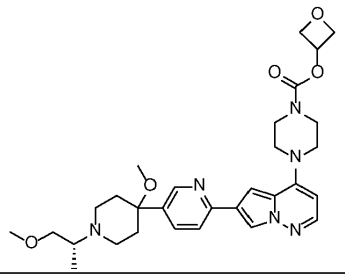
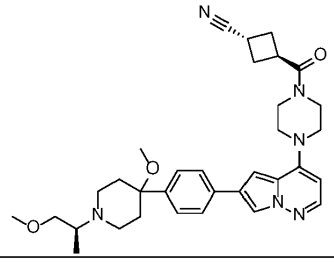
742	
743	
744	
745	

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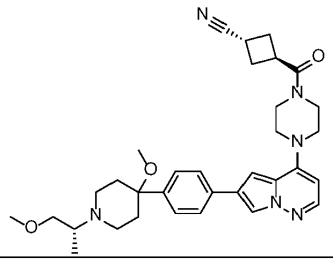
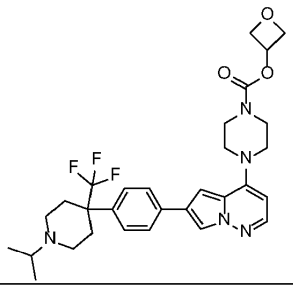
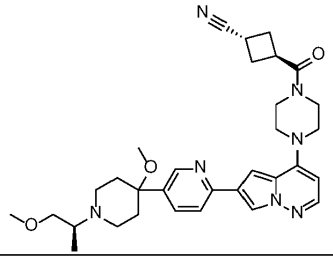
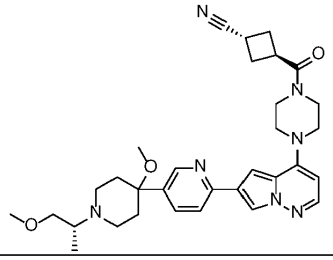
746	
747	
748	
749	

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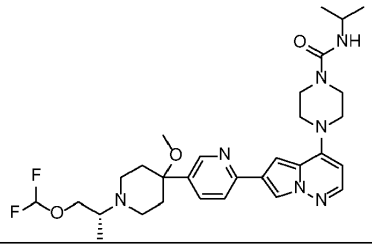
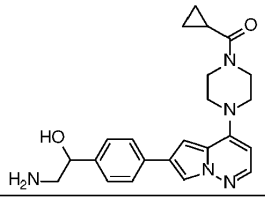
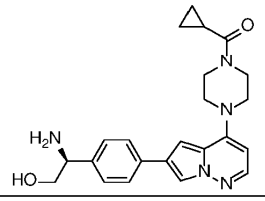
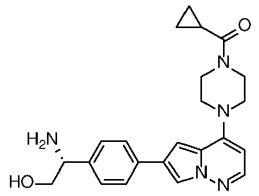
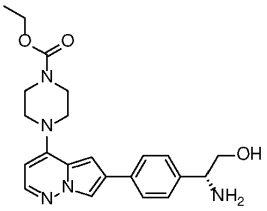
750	
751	
752	
753	
754	

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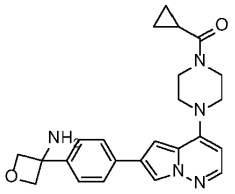
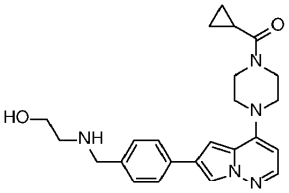
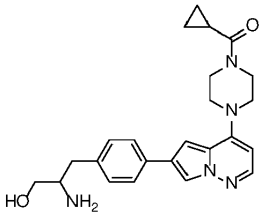
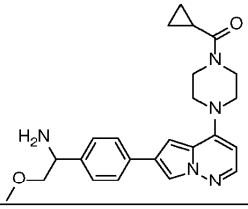
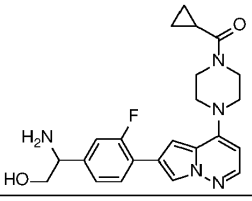
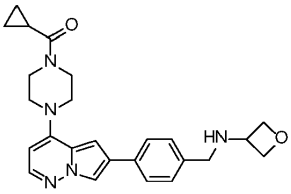
755	
756	
757	
758	
759	
760	

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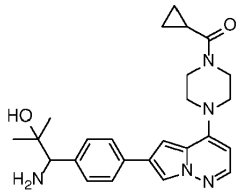
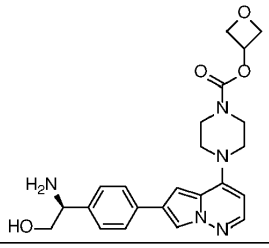
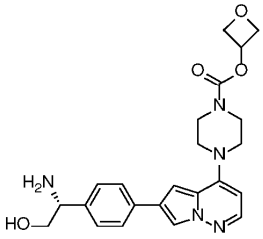
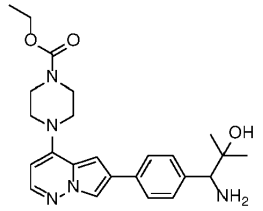
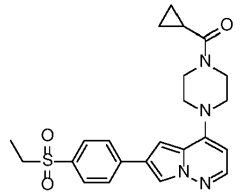
761	
762	
763	
764	
765	

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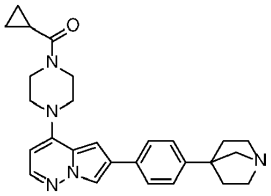
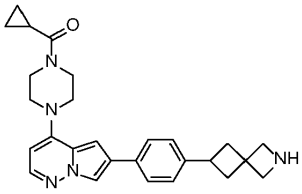
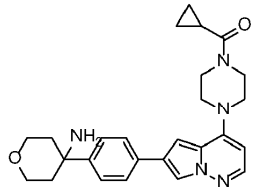
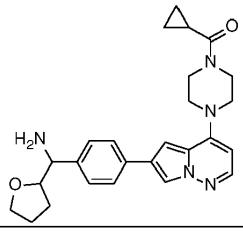
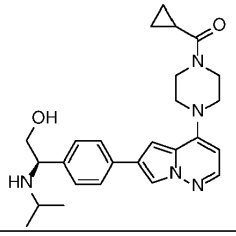
766	
767	
768	
769	
770	

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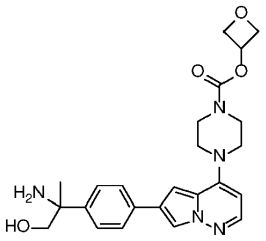
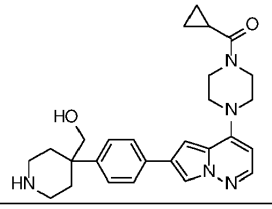
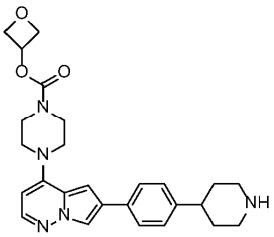
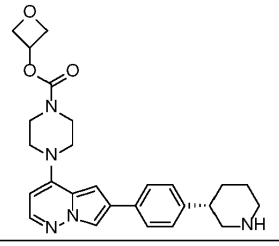
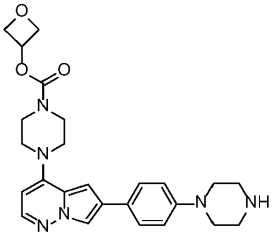
771	
772	
773	
774	
775	

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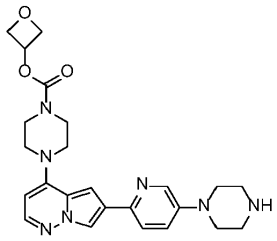
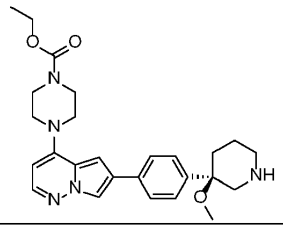
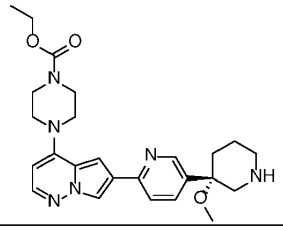
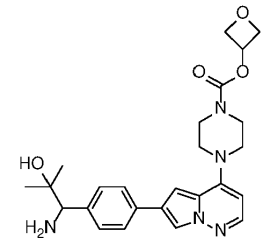
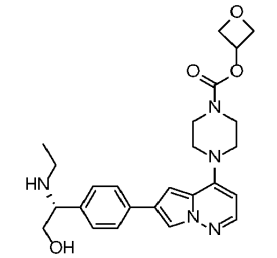
776	
777	
778	
779	
780	

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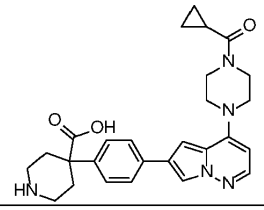
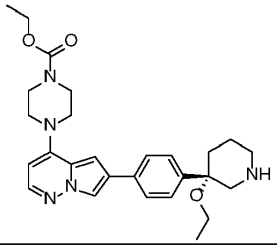
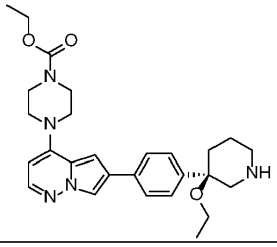
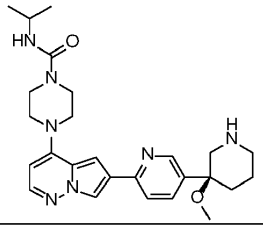
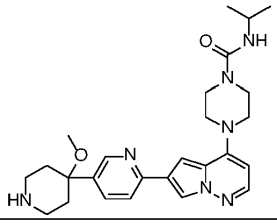
781	
782	
783	
784	
785	

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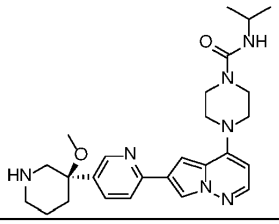
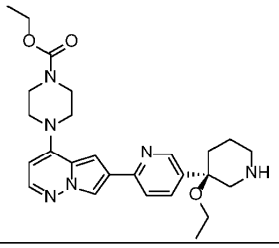
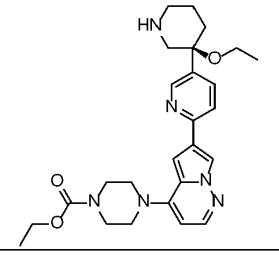
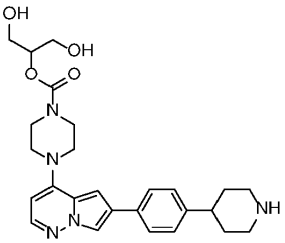
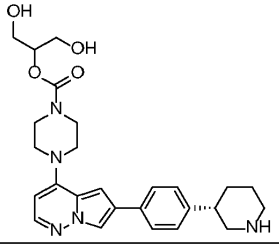
786	
787	
788	
789	
790	

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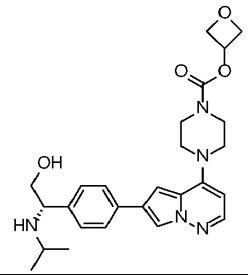
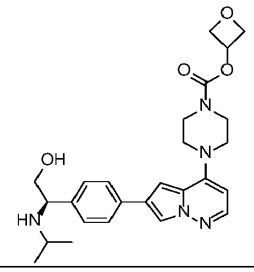
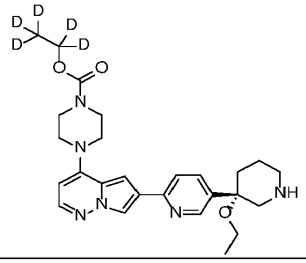
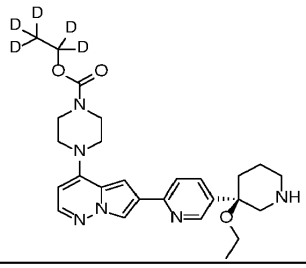
791	
792	
793	
794	

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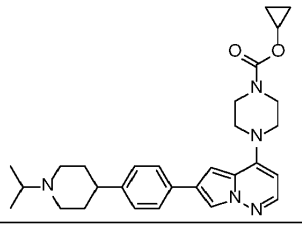
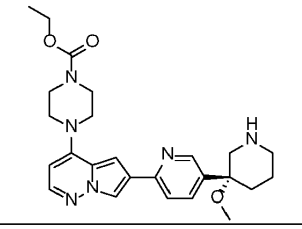
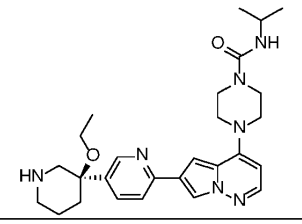
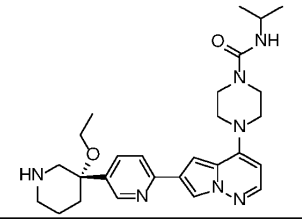
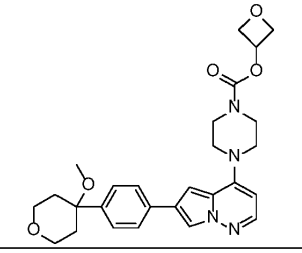
795	
796	
797	
798	
799	

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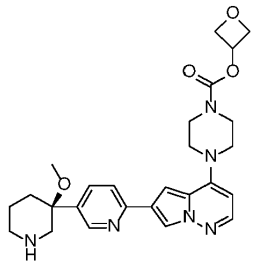
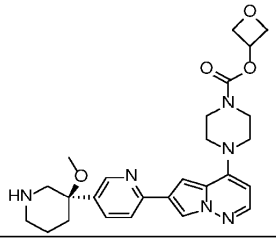
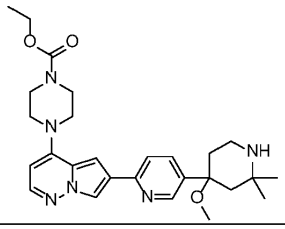
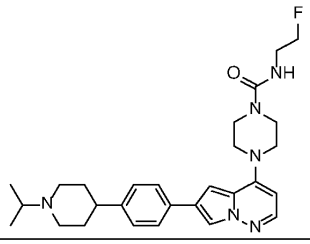
800	
801	
802	
803	

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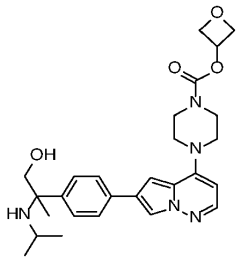
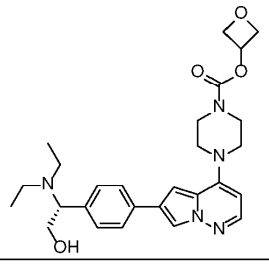
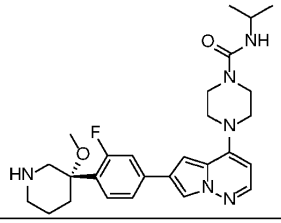
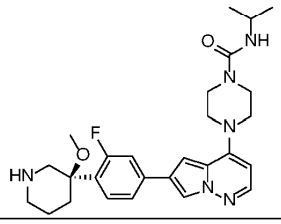
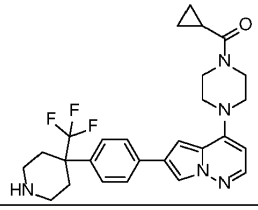
804	
805	
806	
807	
808	

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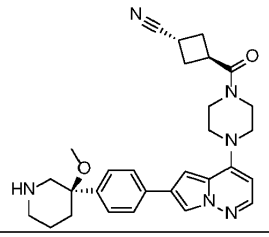
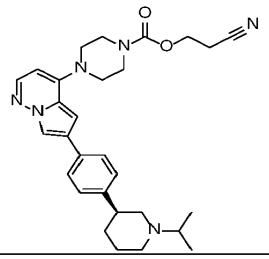
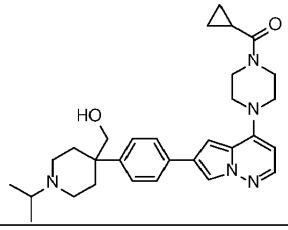
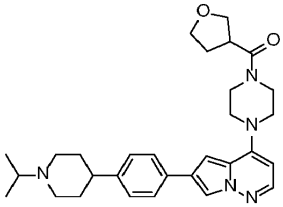
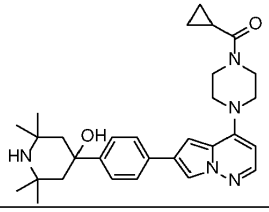
809	
810	
811	
812	
813	

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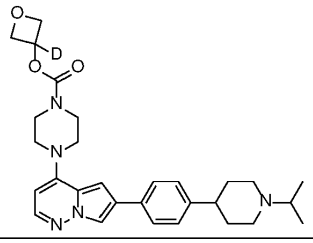
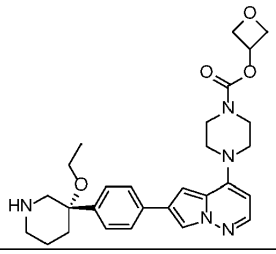
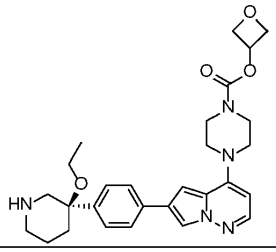
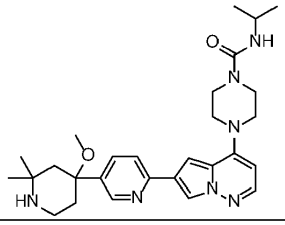
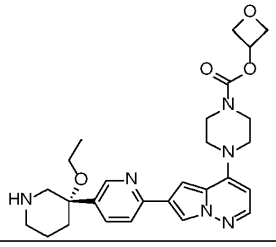
814	
815	
816	
817	
818	

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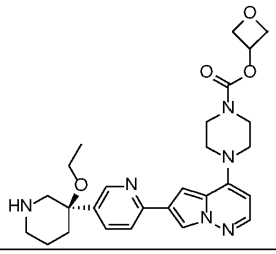
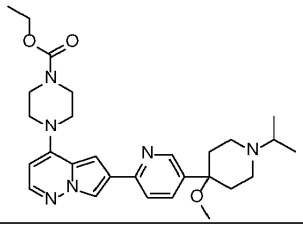
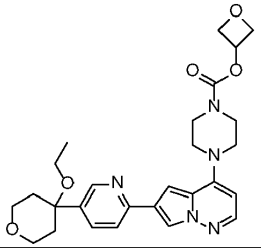
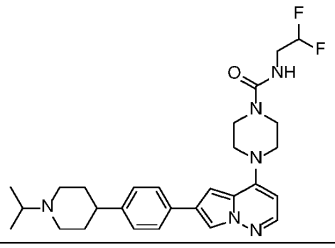
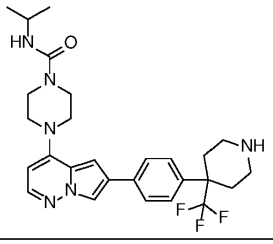
819	
820	
821	
822	
823	

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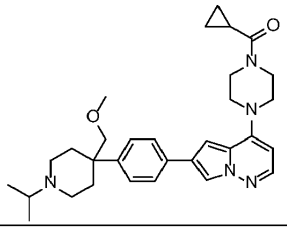
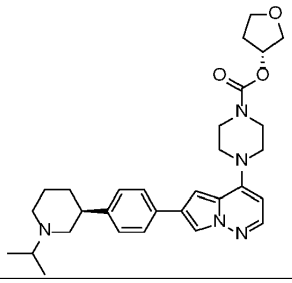
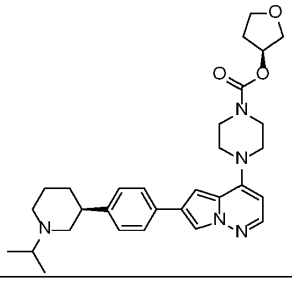
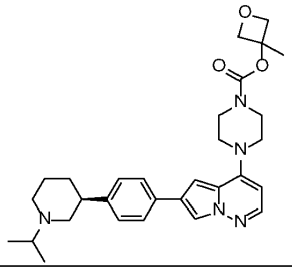
824	
825	
826	
827	

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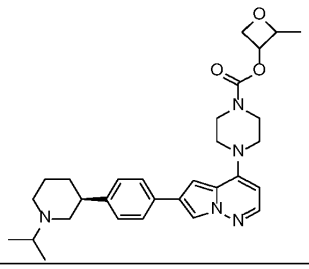
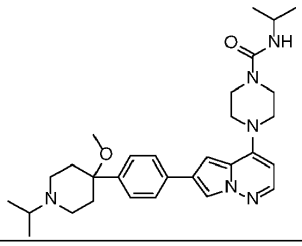
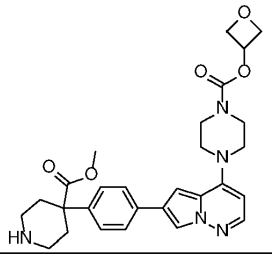
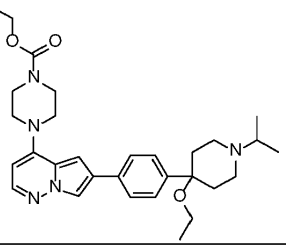
828	
829	
830	
831	

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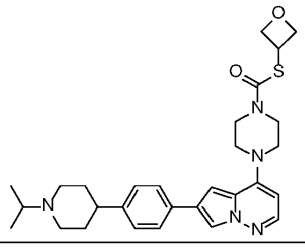
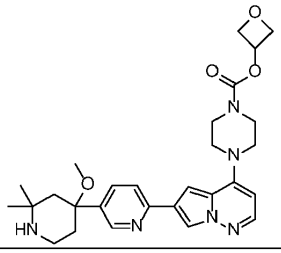
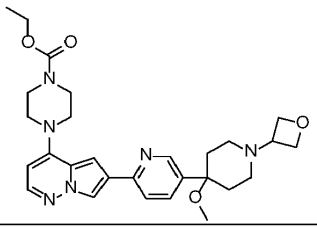
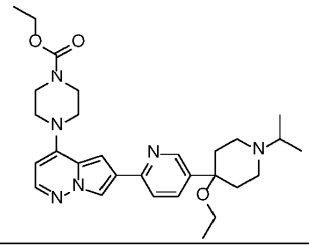
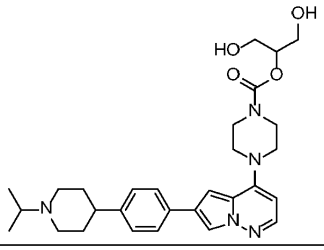
832	
833	
834	
835	
836	

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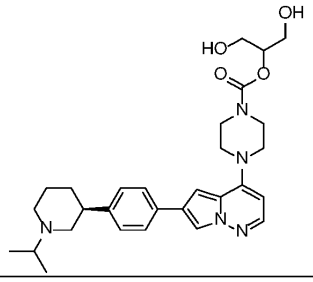
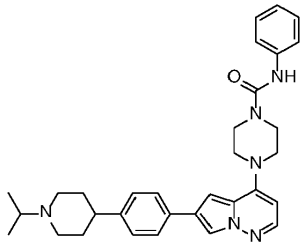
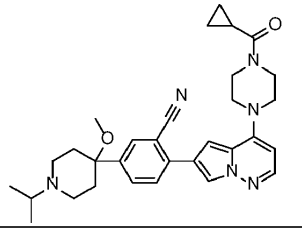
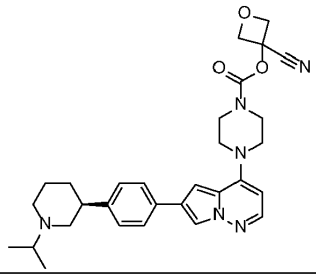
837	
838	
839	
840	

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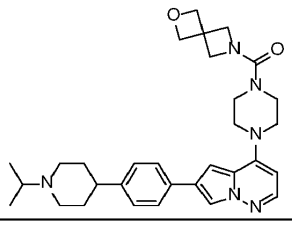
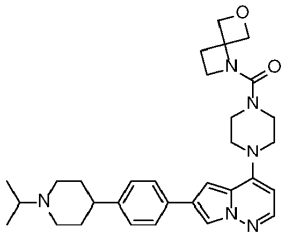
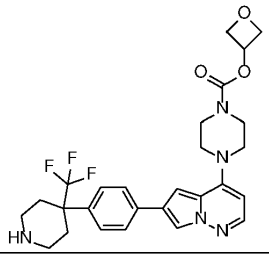
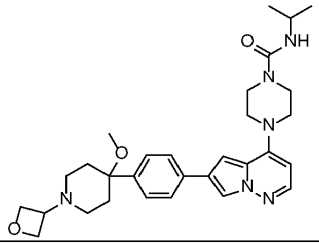
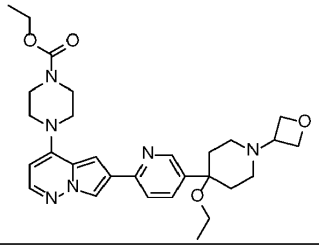
841	
842	
843	
844	
845	

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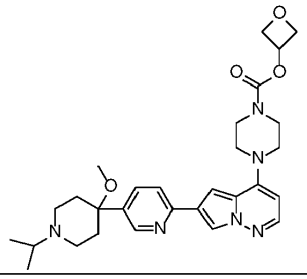
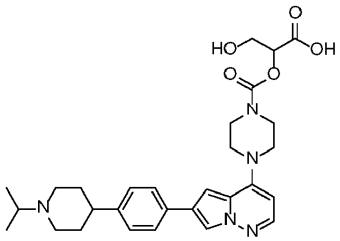
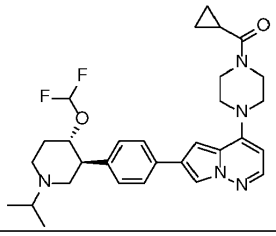
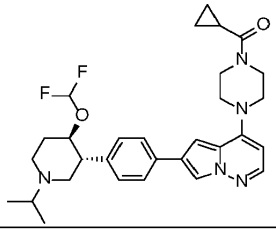
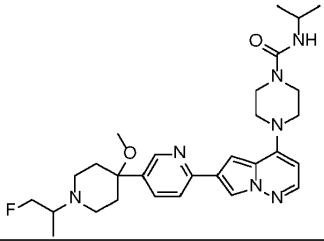
846	
847	
848	
849	
850	

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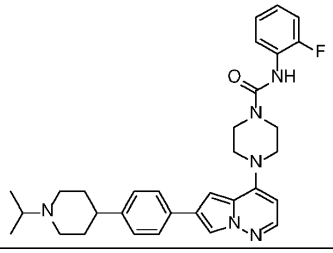
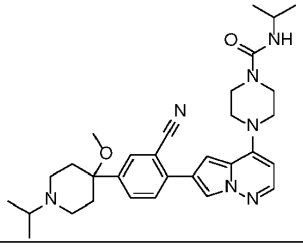
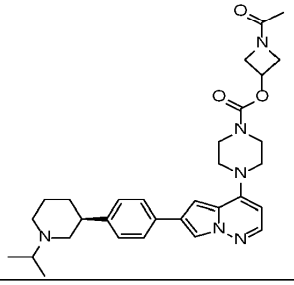
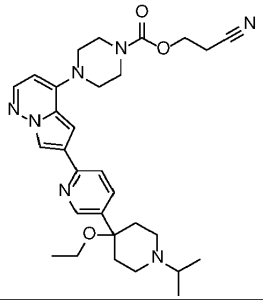
851	
852	
853	
854	

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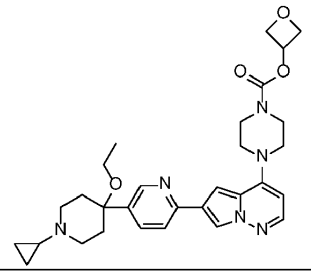
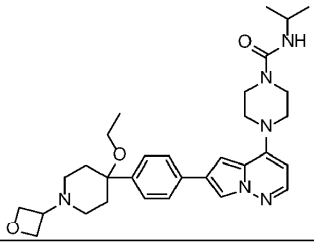
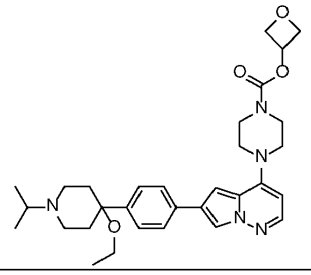
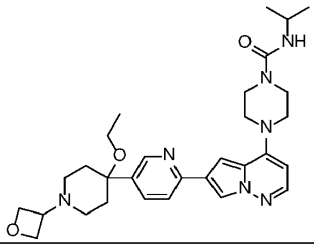
855	
856	
857	
858	

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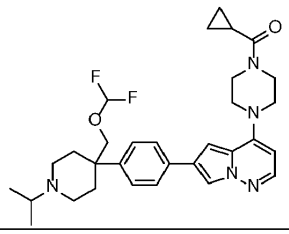
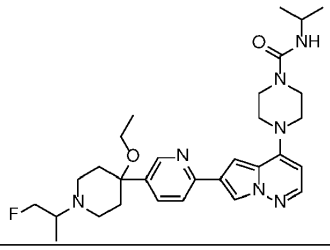
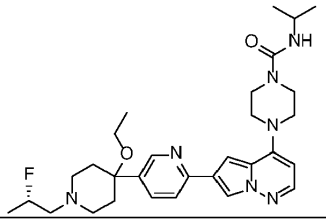
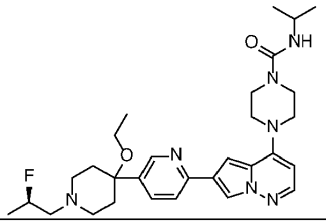
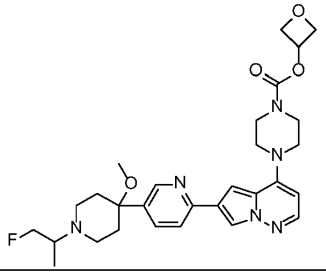
859	
860	
861	
862	
863	

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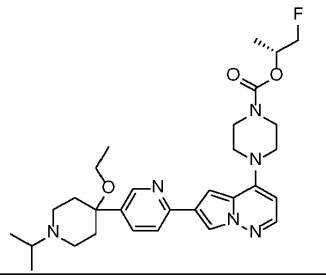
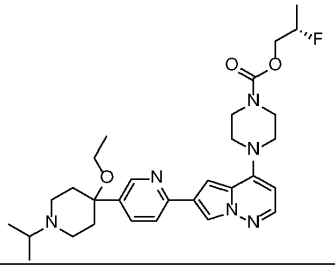
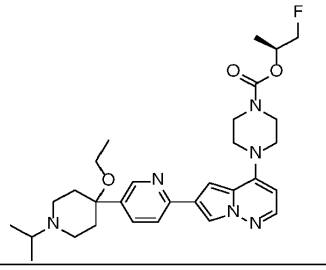
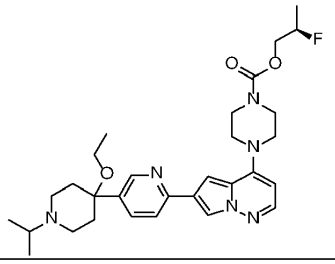
864	
865	
866	
867	

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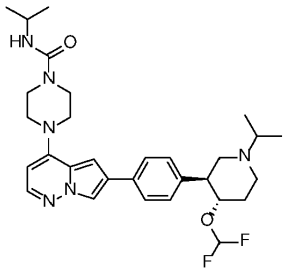
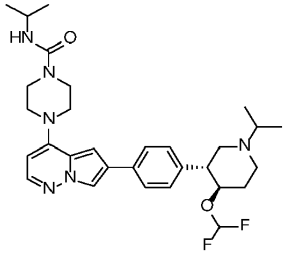
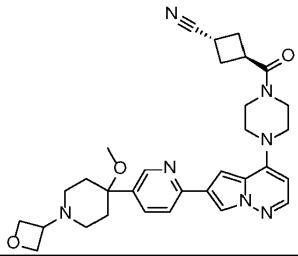
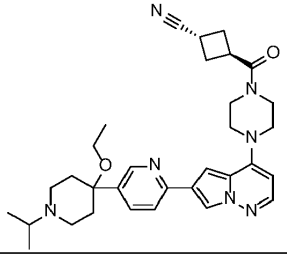
868	
869	
870	
871	

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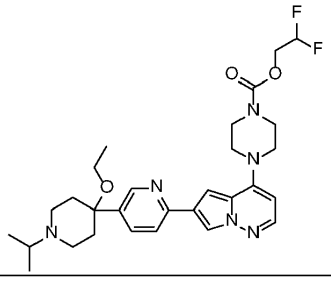
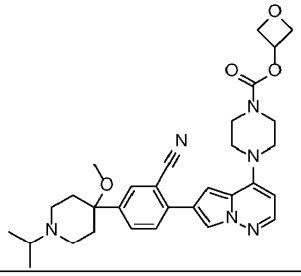
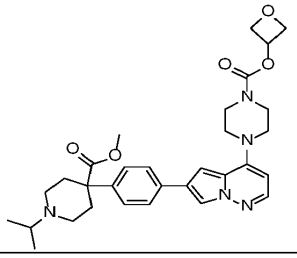
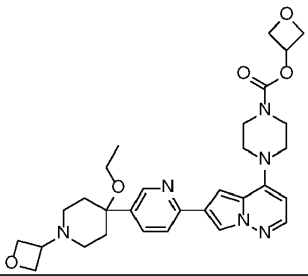
872	
873	
874	
875	

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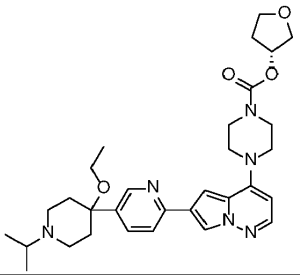
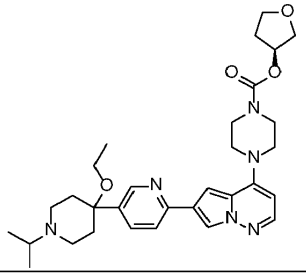
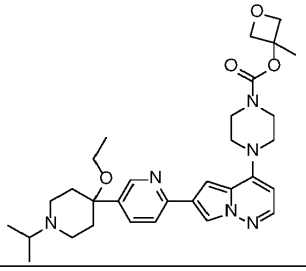
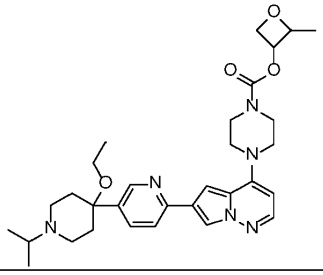
876	
877	
878	
879	

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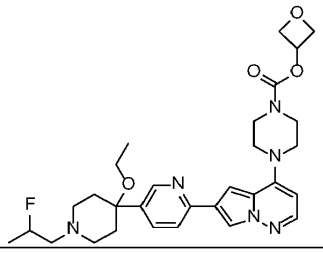
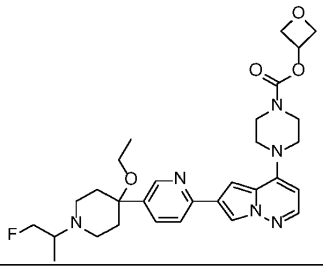
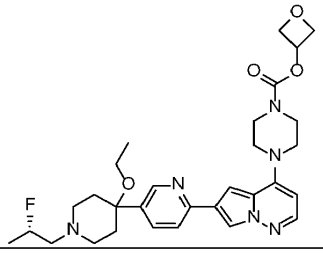
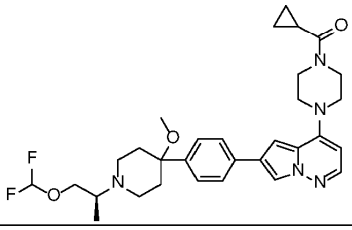
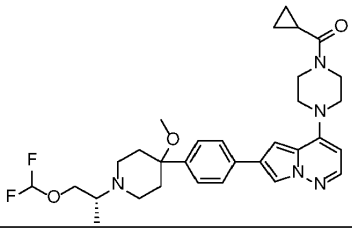
880	
881	
882	
883	
884	

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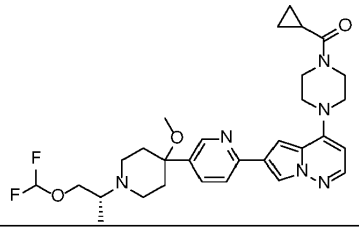
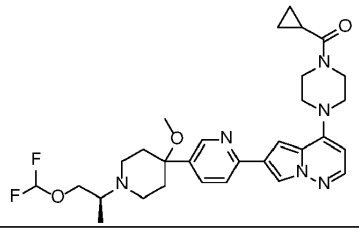
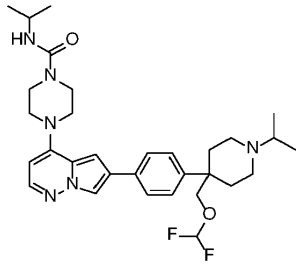
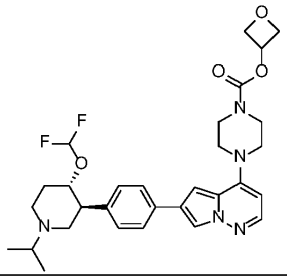
885	
886	
887	
888	

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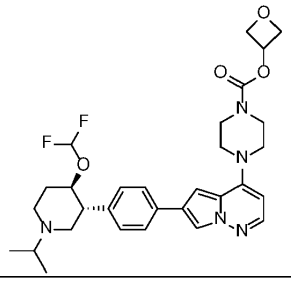
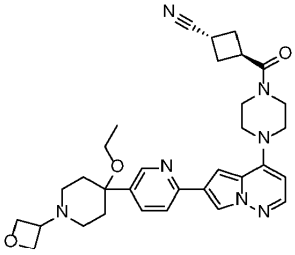
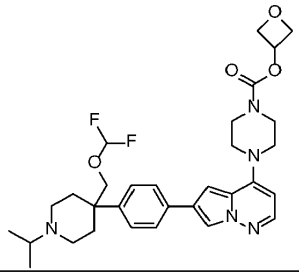
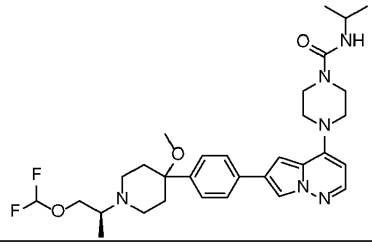
889	
890	
891	
892	

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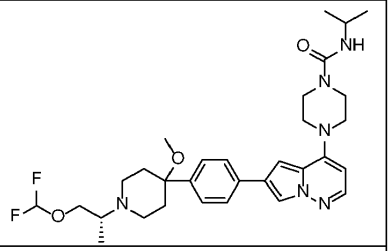
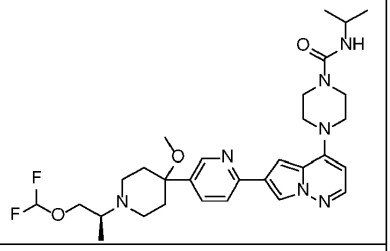
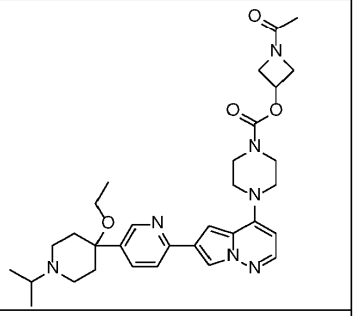
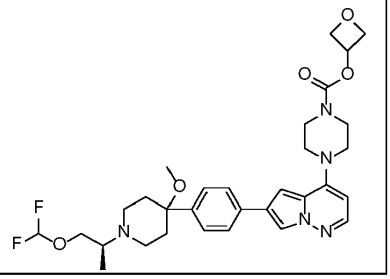
893	
894	
895	
896	

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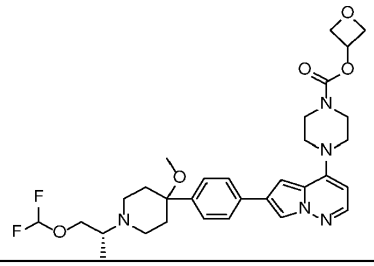
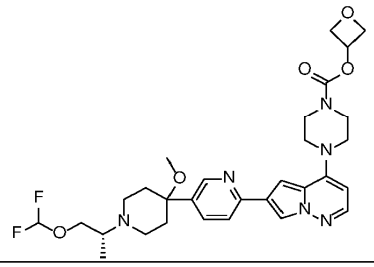
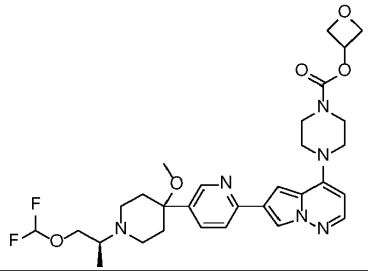
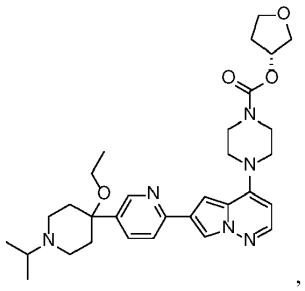
897	
898	
899	

eller et farmasøytisk akseptabelt salt derav.

10. Forbindelsen ifølge krav 1, hvori forbindelsen er av den følgende formelen:



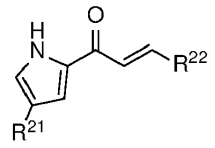
,

eller et farmasøytisk akseptabelt salt derav.

11. Farmasøytisk sammensetning, omfattende minst én forbindelse ifølge et hvilket som helst av kravene 1 til 10 eller et farmasøytisk akseptabelt salt derav, og en farmasøytisk akseptabel bærer.

12. Forbindelse som er 6-halogen-pyrrolo[1,2-b]pyridazin-4-ol, hvori halogen velges fra Cl, I og Br, spesielt 6-brompyrrolo[1,2-b]pyridazin-4-ol, forbindelsen har eventuelt en renhet på over 90 %.

13. Fremgangsmåte for å syntetisere en forbindelse ifølge krav 12, omfattende trinnet med å kombinere en forbindelse av formel C-1:



(C-1),

med en forbindelse av formel D-1:

R^{23}-O-NH_2 (D-1),

hvori:

R^{21} er klor, brom eller jod, og er fortrinnsvis brom;

R^{22} er en utgående gruppe fortrinnsvis valgt fra -N(R^{24})(R^{25}) og -OR^{24}, hvori hvert R^{24} og R^{25} er uavhengig C_1-C_4-alkyl, og er mer foretrukket -N(CH_3)$_2$; og

R^{23} er en elektrontilbaketrekkende gruppe fortrinnsvis valgt fra metylkarbonyl, t-butylkarbonyl, 4-nitrofenylkarbonyl, 4-cyanofenylkarbonyl, 4-trifluormetylfenylkarbonyl, 4-fluorfenylkarbonyl, 4-trifluormetylkarbonylfenylkarbonyl, 4-etoksykarbonylfenylkarbonyl, 4-trifluormetylsulfonylfenylkarbonyl, 2,4,6-trimetylfenylkarbonyl, 2,4,6-trimetyl-3,5-dinitrofenylkarbonyl, 2-trifluormetyl-4-nitrofenyl, 2,4-dinitrofenyl og difenylfosfinyl, og er mer foretrukket 4-nitrofenylkarbonyl.

14. Fremgangsmåten ifølge krav 13, hvori forbindelsen av formel C-1 og forbindelsen av formel D-1 løses opp i et polart løsningsmiddel, hvori det polare løsningsmidlet fortrinnsvis velges fra N-metyl-2-pyrrolidin ("NMP"), N,N-dimetylacetamid ("DMAC"), dimetylformamid ("DMF"), tetrahydrofuran ("THF"), metyltetrahydrofuran ("MeTHF"), dimetylsulfoksid ("DMSO") og syklopentylmetyleter ("CPME") og er mer foretrukket valgt fra NMP og DMAC.

15. Fremgangsmåten ifølge krav 13, hvori forbindelsen av formel C-1 behandles med en base, hvori den fortrinnsvis velges fra KOC(CH_3)$_3$, NaOC(CH_3)$_3$, LiOC(CH_3)$_3$, LiC(CH_3)$_3$, Li(CH_2)$_3$$CH_3$, LiN($C_3H_7$)$_2$, NaO$CH_3$, NaO$CH_2CH_3$, KO$CH_3$, LiO$CH_3$, LiO$CH_2CH_3$ og KOCH_2CH_3, og er foretrukket KOC(CH_3)$_3$.

16. Fremgangsmåten ifølge krav 13, hvori fremgangsmåten videre omfatter å tilsette et protoneringsmiddel, hvori protoneringsmidlet fortrinnsvis velges fra NH_4Cl, $NaHCO_3$, $KHCO_3$, $LiHCO_3$, eddiksyre, HCl, HBr og H_2SO_4, og er foretrukket NH_4Cl.

17. Forbindelse for anvendelse i en fremgangsmåte for behandling eller forbedring av fibrodysplasia ossificans progressiva hos et individ, omfattende trinnet å administrere til individet med behov derav en farmasøytisk effektiv mengde av minst én forbindelse ifølge et hvilket som helst av kravene 1 til 10 eller et farmasøytisk akseptabelt salt derav eller en farmasøytisk sammensetning ifølge krav 11,
eventuelt hvori individet har en mutasjon i et ALK2-gen som resulterer i ekspresjonen av et ALK2-enzym som har en aminosyremodifikasjon valgt fra én eller flere av L196P, PF197-8L, R202I, R206H, Q207E, R258S, R258G, G328A, G328W, G328E, G328R, G356D og R375P, for eksempel hvori ALK2-enzymet har aminosyremodifikasjonen R206H.

18. Forbindelse for anvendelse i en fremgangsmåte for behandling eller forbedring av diffus intrinsik pontin gliom hos et individ, omfattende trinnet å administrere til individet med behov derav en farmasøytisk effektiv mengde av minst én forbindelse ifølge et hvilket som helst av kravene 1 til 10 eller et farmasøytisk akseptabelt salt derav eller en farmasøytisk sammensetning ifølge krav 11,
eventuelt hvori individet har en mutasjon i et ALK2-gen som resulterer i ekspresjonen av et ALK2-enzym som har en aminosyremodifikasjon valgt fra én eller flere av R206H, G328V, G328W, G328E og G356D, for eksempel hvori ALK2-enzymet har aminosyremodifikasjonen R206H.