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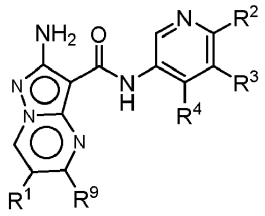
(54) Title — **PYRAZOLO[1,5-A]PYRIMIDINES USEFUL AS INHIBITORS OF ATR KINASE FOR THE TREATMENT OF CANCER DISEASES**

(56) References Cited:
WO-A1-2010/071837
WO-A1-2012/138938

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

Patentkrav

1. Forbindelse som har formelen I:



I

eller et farmasøytisk akseptabelt salt derav, hvori:

R^1 uavhengig velges fra $-C(J^1)_2CN$, halogen, $-(L)_k-W$ eller M;

R^9 uavhengig velges fra H, $-C(J^1)_2CN$, halogen, $-(L)_k-W$ eller M;

J^1 uavhengig velges fra H eller C_{1-2}-alkyl; eller

to forekomster av J^1, sammen med karbonatomet som de er festet til, danner en 3−4-leddet eventuelt substituert karbosyklisk ring;

k er 0 eller 1;

M og L er en C_{1-8}-alifatisk, hvori opptil tre metylenenheter eventuelt erstattes med -O-, -NR-, -C(O)- eller $-S(O)_n-$, hver M og L^1 eventuelt substitueres med 0−3 forekomster av J^{LM};

J^{LM} uavhengig velges fra halogen, -CN eller en C_{1-4}-alifatisk kjede hvori opptil to metylenenheter av den alifatiske kjeden eventuelt erstattes med -O-, -NR-, -C(O)- eller $-S(O)_n-$;

W uavhengig velges fra en 3−7-leddet helt mettet, delvis umettet eller aromatisk monosyklisk ring som har 0−3 heteroatomer valgt fra oksygen, nitrogen eller svovel; eller en 7−12-leddet helt mettet, delvis umettet eller aromatisk bisyklisk ring som har 0−5 heteroatomer valgt fra oksygen, nitrogen eller svovel;

hvori W eventuelt substitueres med 0−5 forekomster av J^W;

J^W uavhengig velges fra -CN, halogen, $-CF_3$; et C_{1-4}-alifatisk hvori opptil to metylenenheter eventuelt erstattes med -O-, -NR-, -C(O)- eller $-S(O)_n-$; eller en 3−6-

leddet ikke-aromatisk ring som har 0−2 heteroatomer valgt fra oksygen, nitrogen eller svovel;

R^2 uavhengig velges fra H; halogen; -CN; NH_2; et C_{1-2}-alkyl eventuelt substituert med 0−3 forekomster av fluor; eller en C_{1-3}-alifatisk kjede hvori opptil to metylenenheter av den alifatiske kjeden eventuelt erstattes med -O-, -NR-, -C(O)- eller -$S(O)_n$;

R^3 uavhengig velges fra H; halogen; C_{1-4}-alkyl eventuelt substituert med 1−3 forekomster av halogen; C_{3-4}-sykloalkyl; 3−4-leddet heterosyklyl; -CN; eller en C_{1-3}-alifatisk kjede hvori opptil to metylenenheter av den alifatiske kjeden eventuelt erstattes med -O-, -NR-, -C(O)- eller -$S(O)_n$;

R^4 uavhengig velges fra Q^1 eller en C_{1-10}-alifatisk kjede hvori opptil fire metylenheter av den alifatiske kjeden eventuelt erstattes med -O-, -NR-, -C(O)- eller -$S(O)_n$-; hver R^4 eventuelt substitueres med 0−5 forekomster av J^Q; eller

R^3 og $R^{4,}$, tatt sammen med atomene som de er bundet til, danner en 5−6-leddet aromatisk eller ikke-aromatisk ring som har 0−2 heteroatomer valgt fra oksygen, nitrogen eller svovel; idet ringen som dannes av R^3 og R^4 eventuelt substitueres med 0−3 forekomster av J^Z;

Q^1 uavhengig velges fra en 3−7-leddet helt mettet, delvis umettet eller aromatisk monosyklisk ring, den 3−7-leddede ringen har 0−3 heteroatomer valgt fra oksygen, nitrogen eller svovel; eller en 7−12-leddet helt mettet, delvis umettet eller aromatisk bisyklisk ring som har 0−5 heteroatomer valgt fra oksygen, nitrogen eller svovel;

J^Z uavhengig velges fra C_{1-6}-alifatisk, =O, halogen eller →O;

J^Q uavhengig velges fra -CN; halogen; =O; Q^2; eller en C_{1-8}-alifatisk kjede hvori opptil tre metylenenheter av den alifatiske kjeden eventuelt erstattes med -O-, -NR-, -C(O)- eller -$S(O)_n$-; hver forekomst av J^Q eventuelt substitueres med 0−3 forekomster av J^R; eller

to forekomster av J^Q på det samme atomet, tatt sammen med atomet de er bundet til, danner en 3−6-leddet ring som har 0−2 heteroatomer valgt fra oksygen, nitrogen eller svovel; hvori ringen dannet av to forekomster av J^Q eventuelt substitueres med 0−3 forekomster av J^X; eller

to forekomster av J^Q, sammen med Q^1, danner et 6−10-leddet mettet eller delvis umettet broforbundet ringsystem;

Q^2 uavhengig velges fra en 3−7-leddet helt mettet, delvis umettet eller aromatisk monosyklisk ring som har 0−3 heteroatomer valgt fra oksygen, nitrogen eller svovel; eller en 7−12-leddet helt mettet, delvis umettet eller aromatisk bisyklisk ring som har 0−5 heteroatomer valgt fra oksygen, nitrogen eller svovel;

J^R uavhengig velges fra -CN; halogen; =O; →O; Q^3; eller en C_{1-6}-alifatisk kjede hvori opptil tre metylenheter av den alifatiske kjeden eventuelt erstattes med -O-, -NR-, -C(O)- eller -$S(O)_n$-; hver J^R eventuelt substitueres med 0−3 forekomster av J^T; eller

to forekomster av J^R på det samme atomet, sammen med atomet som de er bundet til, danner en 3−6-leddet ring som har 0−2 heteroatomer valgt fra oksygen, nitrogen eller svovel; hvori ringen dannet av to forekomster av J^R eventuelt substitueres med 0−3 forekomster av J^X; eller

to forekomster av J^R, sammen med Q^2, danner et 6−10-leddet mettet eller delvis umettet broforbundet ringsystem;

Q^3 er en 3−7-leddet helt mettet, delvis umettet eller aromatisk monosyklisk ring som har 0−3 heteroatomer valgt fra oksygen, nitrogen eller svovel; eller en 7−12-leddet helt mettet, delvis umettet eller aromatisk bisyklisk ring som har 0−5 heteroatomer valgt fra oksygen, nitrogen eller svovel;

J^X uavhengig velges fra -CN; =O; halogen; eller en C_{1-4}-alifatisk kjede hvori opptil to metylenenheter av den alifatiske kjeden eventuelt erstattes med -O-, -NR-, -C(O)- eller -$S(O)_n$-;

J^T uavhengig velges fra halogen, -CN; →O; =O; -OH; en C_{1-6}-alifatisk kjede hvori opptil to metylenenheter av den alifatiske kjeden eventuelt erstattes med -O-, -NR-, -C(O)- eller -$S(O)_n$-; eller en 3−6-leddet ikke-aromatisk ring som har 0−2 heteroatomer valgt fra oksygen, nitrogen eller svovel; hver forekomst av J^T eventuelt substitueres med 0−3 forekomster av J^M; eller

to forekomster av J^T på det samme atomet, sammen med atomet som de er bundet til, danner en 3−6-leddet ring som har 0−2 heteroatomer valgt fra oksygen, nitrogen eller svovel; eller

to forekomster av J^T, sammen med Q^3, danner et 6−10-leddet mettet eller delvis umettet broforbundet ringsystem;

J^M uavhengig velges fra halogen eller C_{1-6}-alifatisk;

n er 0, 1 eller 2; og
R uavhengig velges fra H eller C_{1-4}-alifatisk.

2. Forbindelsen ifølge krav 1,
hvori (I) R^9 er H; eller:
hvori (II) R^9 er M; eventuelt hvori M er en C_{1-8}-alifatisk hvori opptil tre metylenenheter eventuelt erstattes med -O- eller -NR-; eventuelt dertil hvori M er C_{1-4}-alkyl, -(C_{1-4}-alkyl)O(C_{1-3}-alifatisk), -(C_{1-3}-alkyl)OH, -O(C_{1-4}-alkyl)N(C_{1-2}-alkyl)$_2$, -NH(C_{1-4}-alkyl) eller -(C_{1-4}-alkyl)NH(C_{1-4}-alkyl); eventuelt dertil hvori M er C_{1-4}-alkyl.

3. Forbindelsen ifølge et hvilket som helst av kravene 1−2, hvori R^9 er -$(L^1)_k$-W; eventuelt:
hvori (I) k er 0; eller:
hvori (II) k er 1; eventuelt hvori L er en C_{1-8}-alifatisk, hvori opptil tre metylenenheter eventuelt erstattes med -O- eller -NR-; eventuelt dertil hvori L er -O-, -O(C_{1-4}-alifatisk)- eller -NR(C_{1-3}-alkyl)-.

4. Forbindelsen ifølge krav 3,
hvori (I) W er en 3−7-leddet helt mettet, delvis umettet eller aromatisk monosyklisk ring som har 0−3 heteroatomer valgt fra oksygen, nitrogen eller svovel; eventuelt hvori W er et 3−7-leddet heterosyklyl, eventuelt dertil hvori W uavhengig velges fra pyrrolidinyl, piperidinyl, piperazinyl, oksetanyl eller azetidinyl; eller:
hvori (II) W er en 7−12-leddet helt mettet, delvis umettet eller aromatisk bisyklisk ring som har 0−5 heteroatomer valgt fra oksygen, nitrogen eller svovel.

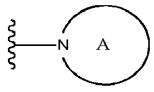
5. Forbindelsen ifølge krav 3 eller krav 4,
hvori (I) J^W velges fra C_{1-3}-alkyl eller CF_3; eller:
hvori (II) to forekomster av J^W på det samme atomet, sammen med atomet som de er bundet til, danner en 3−6-leddet ring som har 0−2 heteroatomer valgt fra oksygen, nitrogen eller svovel; eventuelt hvori ringen dannet av de to forekomstene av J^W på det samme atomet er oksetanyl.

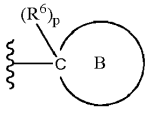
6. Forbindelsene ifølge et hvilket som helst av kravene 1 til 5,
hvori (I) R^1 er fluor; eller:
hvori (II) R^1 er $-CH_2CN$, $-C(CH_3)_2CN$ eller $-CH(C_{1-2}\text{-alkyl})CN$; eller:
hvori (III) R^1 er klor.

7. Forbindelsen ifølge et hvilket som helst av kravene 1 til 6, hvori R^2 uavhengig velges fra $-CF_3$, $-NH(C_{1-2}\text{-alkyl})$, klor eller H; eventuelt:
hvori (I) R^2 er H; eller:
hvori (II) R^2 er -klor.

8. Forbindelsen ifølge et hvilket som helst av kravene 1 til 7, hvori R^3 velges uavhengig fra H, klor, fluor, CHF_2, -CN, syklopropyl eller C_{1-4}-alkyl; eventuelt:
hvori R^3 uavhengig velges fra H, klor eller fluor; eventuelt dertil:
hvori (I) R^3 er H; eller:
hvori (II) R^3 er klor; eller:
hvori (III) R^3 er fluor.

9. Forbindelsen ifølge et hvilket som helst av kravene 1 til 8, hvori R^4 uavhengig velges fra:

-O-; 

; 

;

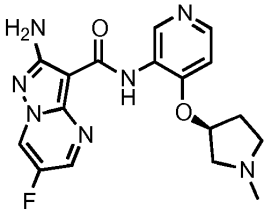
eller $-CH_2\text{-}R^7$, hvori:
-O- substitueres med én J^Q;
ring A uavhengig velges fra en 3−7-leddet helt mettet, delvis umettet eller aromatisk monosyklisk heterosyklisk ring som har 1−3 heteroatomer valgt fra oksygen, nitrogen eller svovel; eller en 7−12-leddet helt mettet, delvis umettet eller aromatisk bisyklisk ring som har 1−5 heteroatomer valgt fra oksygen, nitrogen eller svovel;
ring B uavhengig velges fra en 3−7-leddet helt mettet, delvis umettet eller aromatisk monosyklisk ring som har 0−3 heteroatomer valgt fra oksygen, nitrogen eller svovel; eller en 7−12-leddet helt mettet, delvis umettet eller aromatisk bisyklisk ring som har 0−5 heteroatomer valgt fra oksygen, nitrogen eller svovel;

R^6 er H;
R^7 uavhengig velges fra H eller en C_{1-8}-alifatisk kjede hvori opptil tre metylenenheter av den alifatiske kjeden eventuelt erstattes med -O-, -NR-, -S-, -C(O)- eller -$S(O)_n$-; og
p er 0 eller 1.

10. Forbindelsen ifølge krav 9, hvori R^4 er -O-: eventuelt:
hvori (I) J^Q uavhengig velges fra -(C_{1-4}-alkyl), -(C_{1-4}-alkyl)N(C_{1-4}-alkyl)$_2$, -(C_{1-3}-alkyl)O(C_{1-2}-alkyl)N(C_{1-3}-alkyl)$_2$, (C_{1-4}-alkyl)OH, -(C_{1-4}-alkyl)NH_2 eller -(C_{1-4}-alkyl)O(C_{1-4}-alkyl); eller:
hvori (II) J^Q er Q^2; eventuelt:
hvori (i) Q^2 er en 3−7-leddet helt mettet, delvis umettet eller aromatisk monosyklisk ring som har 0−3 heteroatomer valgt fra oksygen, svovel eller nitrogen; eventuelt: hvori Q^2 uavhengig velges fra et 5−6-leddet aryl, et 5−6-leddet heteroaryl, et 4−6-leddet sykloalifatisk eller et 3−7-leddet heterosyklyl; eventuelt dertil:
hvori (a) Q^2 uavhengig velges fra et 4−7-leddet sykloalifatisk eller et 3−7-leddet heterosyklyl; eventuelt hvori Q^2 er et 3−7-leddet heterosyklyl; eventuelt dertil: hvori Q^2 uavhengig velges fra pyrrolidinyl, piperidinyl, azepanyl, pyrazolidinyl, isoksazolidinyl, oksazolidinyl, tiazolidinyl, imidazolidinyl, piperazinyl, morfolinyl, tiomorfolinyl, 1,3-oksazinanyl, 1,3-tiazinanyl, dihydropyridinyl, dihydroimidazolyl, 1,3-tetrahydropyrimidinyl, dihydropyrimidinyl, 1,4-diazepanyl, 1,4-oksazepanyl, 1,4-tiazepanyl, tetrahydrotiopyranyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl og oksetanyl; eventuelt dertil hvori Q^2 uavhengig velges fra tetrahydrotiopyranyl, pyrrolidinyl, piperidinyl, piperazinyl, tetrahydrofuranyl, tetrahydropyranyl eller azetidinyl; eller:
hvori (b) Q^2 er et 5−6-leddet heteroaryl; eventuelt hvori Q^2 uavhengig velges fra imidazolyl, pyrrolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyrazolyl, 1,2,3-triazolyl eller 1,2,4-triazolyl; eventuelt dertil hvori Q^2 er pyridinyl; eller:
hvori (c) Q^2 er et 4−6-leddet sykloalifatisk; eventuelt hvori Q^2 uavhengig velges fra syklobutyl eller sykloheksyl; eller:
hvori (d) Q^2 er fenyl; eller:
hvori (ii) Q^2 er et 7−12-leddet helt mettet, delvis umettet eller aromatisk bisyklisk ring som har 0−5 heteroatomer valgt fra oksygen, nitrogen eller svovel; eventuelt hvori Q^2 er 6,7-

dihydro-5H-pyrrolo[1,2-a]imidazol.

11. Forbindelsen ifølge et hvilket som helst av kravene 9 og 10 uavhengig valgt fra:



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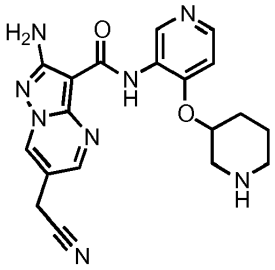

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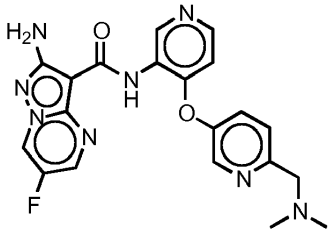

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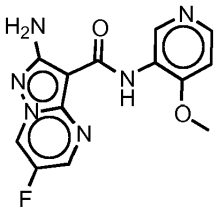

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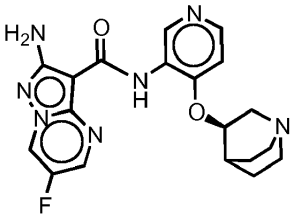
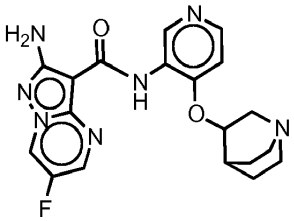
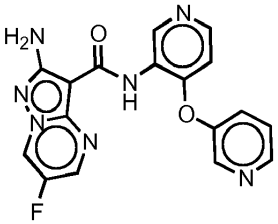


I-O-5



I-O-6



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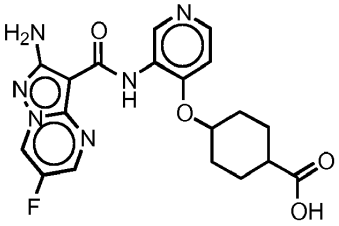

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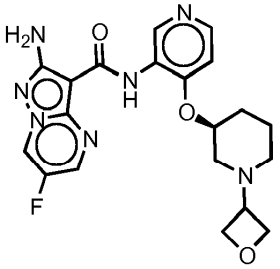

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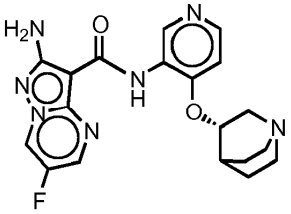

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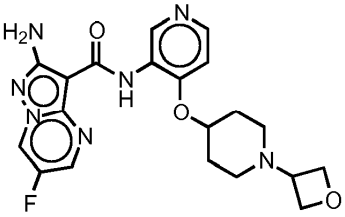
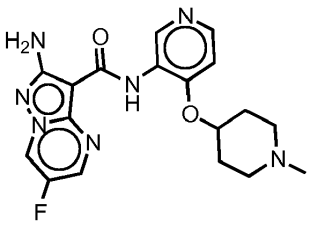
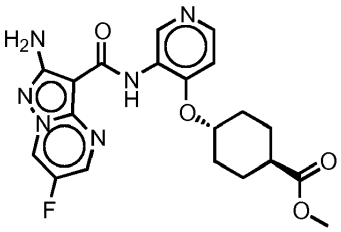


I-O-11



I-O-12



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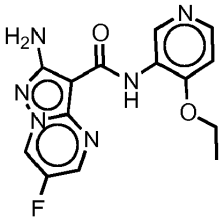

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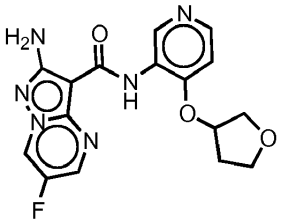

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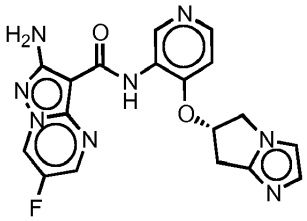

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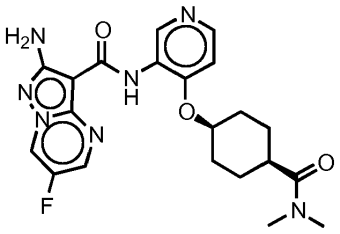

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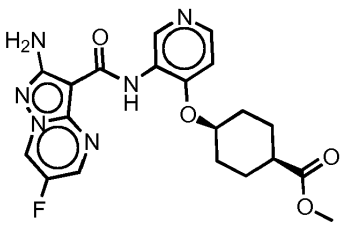

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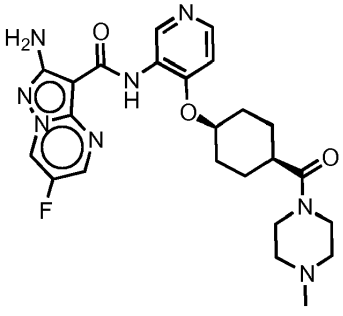

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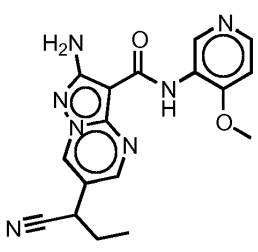

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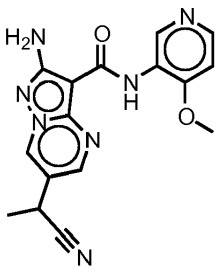

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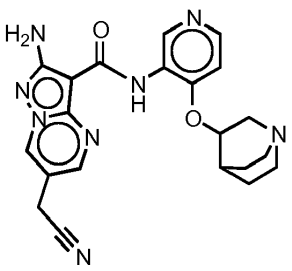

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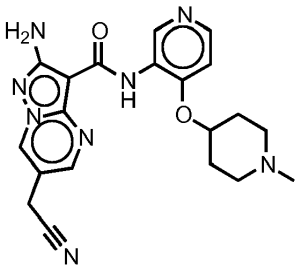

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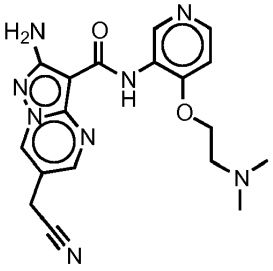

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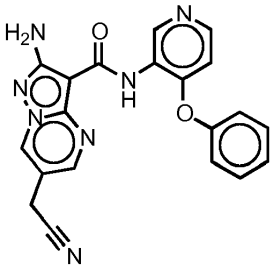

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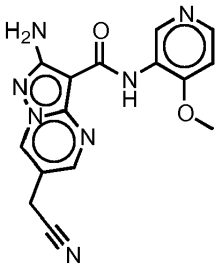

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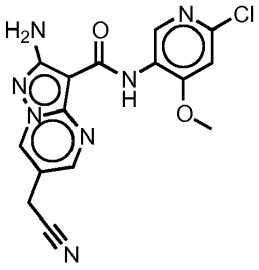

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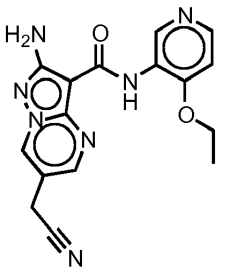

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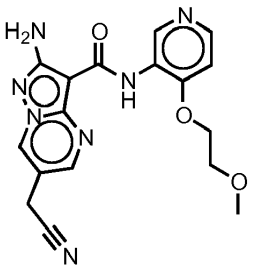

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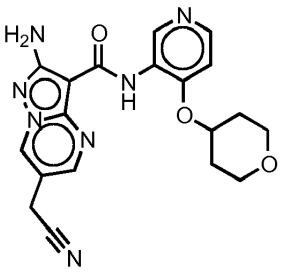

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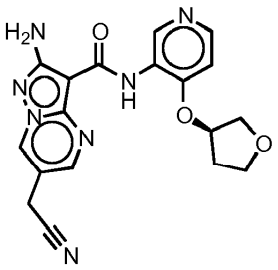

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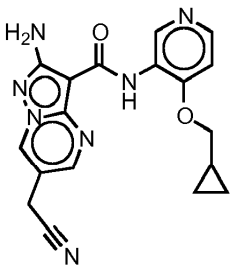

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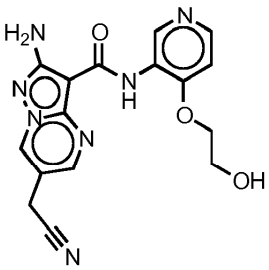

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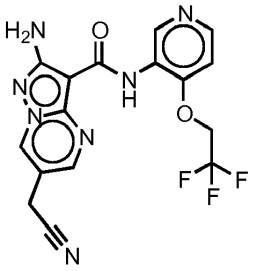

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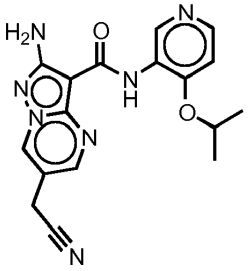

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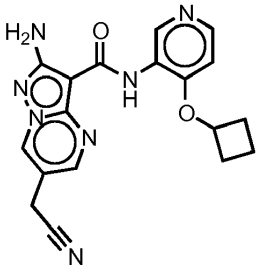

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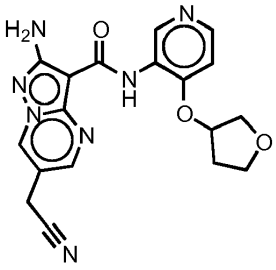

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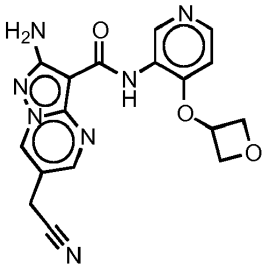

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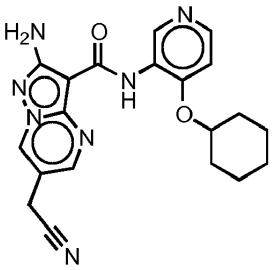

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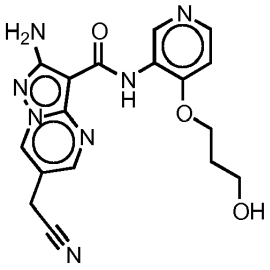

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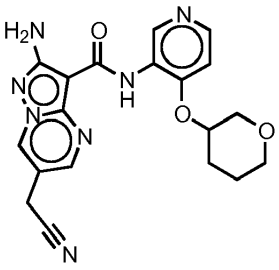

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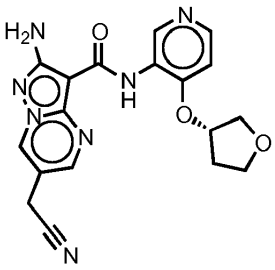

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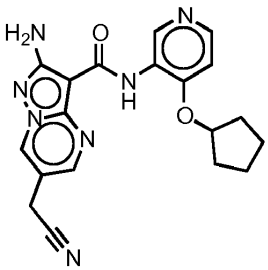

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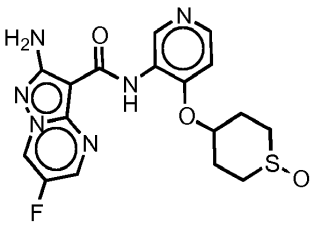

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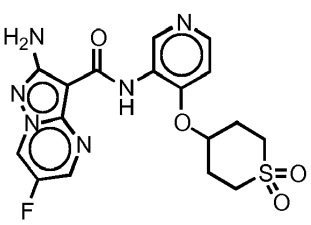

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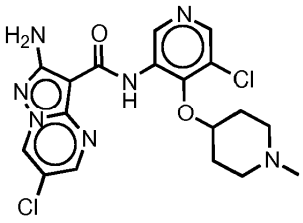

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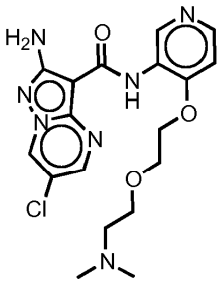

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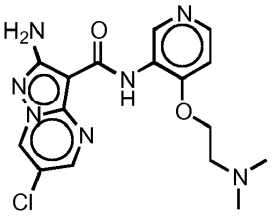

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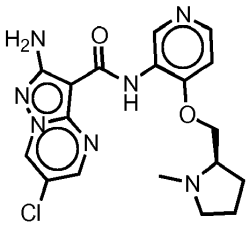

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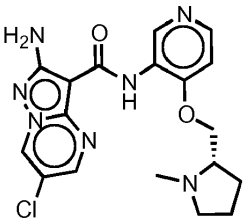

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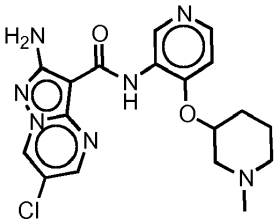

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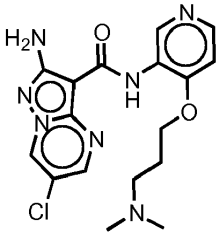

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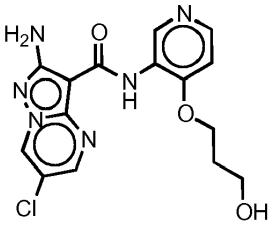

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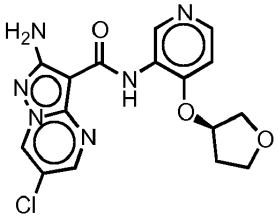

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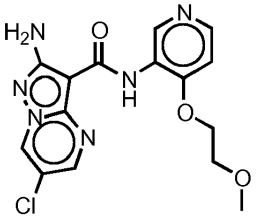

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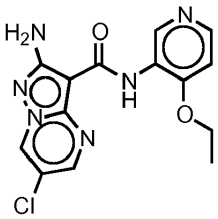

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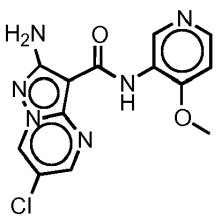

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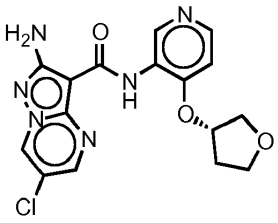

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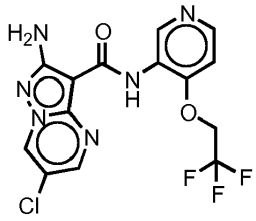

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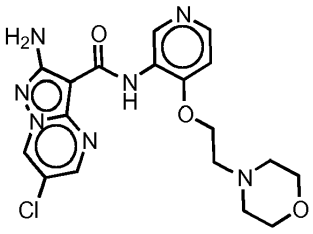

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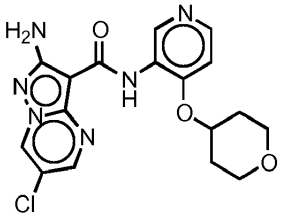

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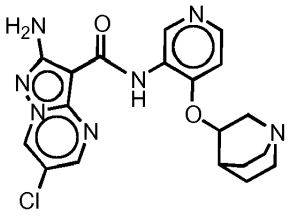

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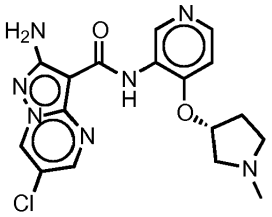

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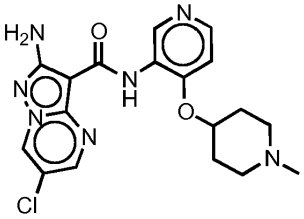

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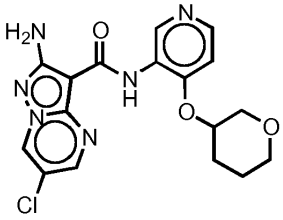

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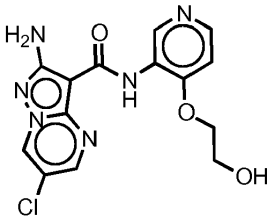

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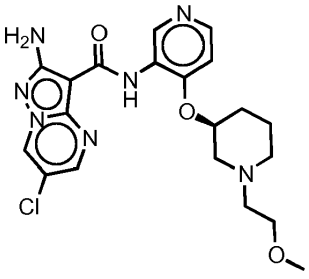

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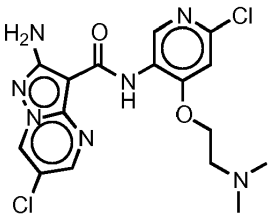

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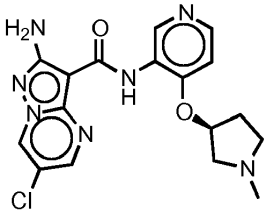
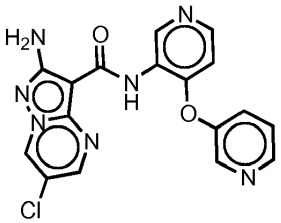
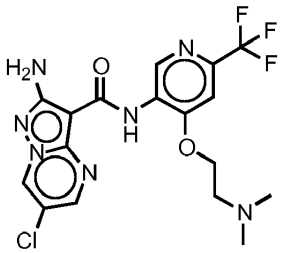


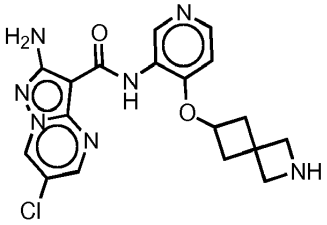
I-O-69



I-O-70



I-O-71



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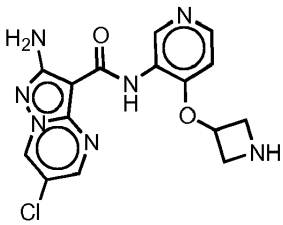

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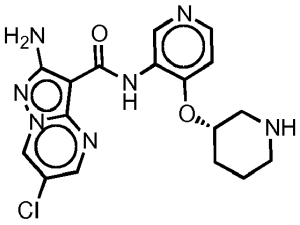
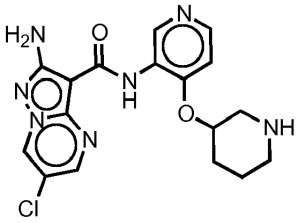
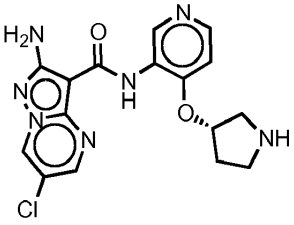


I-O74



I-O-75



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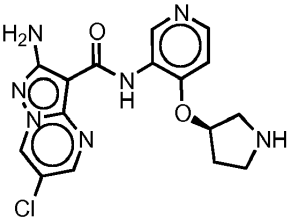

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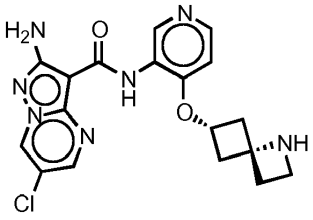

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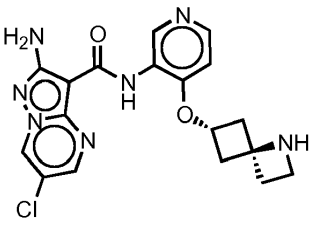
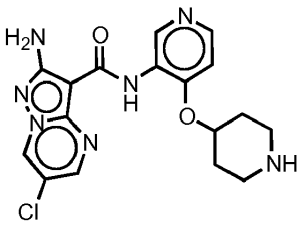
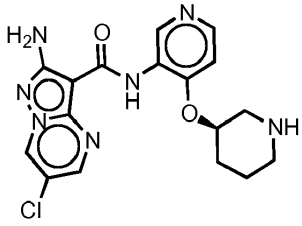


I-O-79



I-O-80



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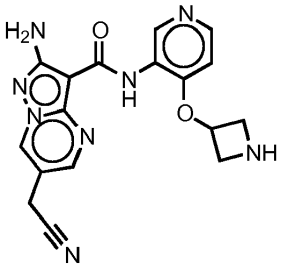
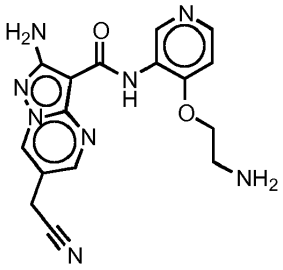


I-O-82



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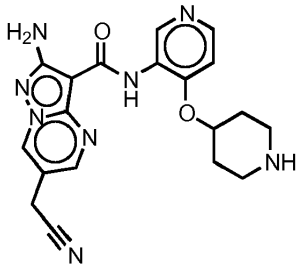

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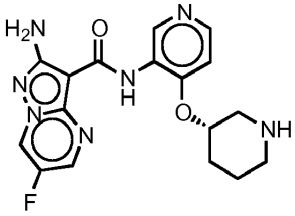

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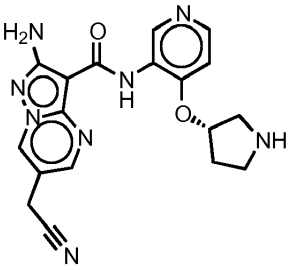
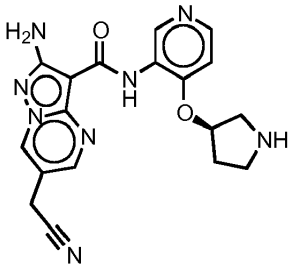
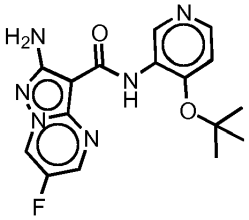


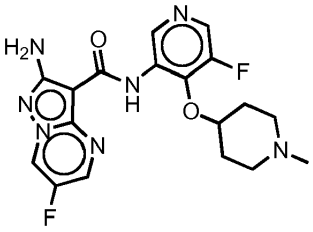
I-O-86



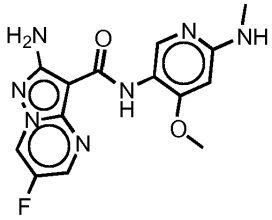
I-O-87



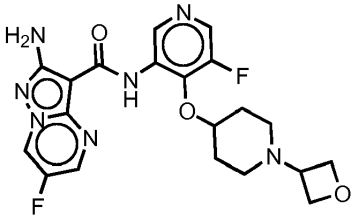
I-O-88



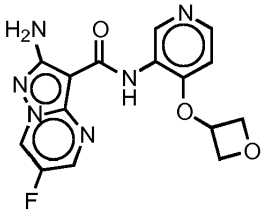
I-O-89



I-O-90

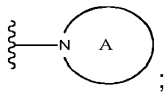


I-O-91



I-O-92.

12. Forbindelsen ifølge krav 9, hvori R^4 er:



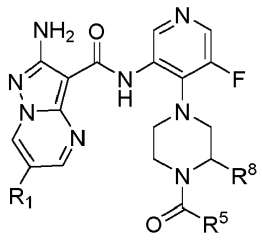
;

eventuelt hvori ring A er en 3−7-leddet helt mettet, delvis umettet eller aromatisk monosyklisk ring som har 1−3 heteroatomer valgt fra oksygen, nitrogen eller svovel; eventuelt dertil

hvori (I) ring A er et 3−7-leddet heterosyklyl; eventuelt hvori ring A uavhengig velges fra pyrrolidinyl, piperidinyl, azepanyl, pyrazolidinyl, isoksazolidinyl, oksazolidinyl, tiazolidinyl, imidazolidinyl, piperazinyl, morfolinyl, tiomorfolinyl, 1,3-oksazinanyl, 1,3-tiazinanyl, dihydropyridinyl, dihydroimidazolyl, 1,3-tetrahydropyrimidinyl, dihydropyrimidinyl, 1,4-diazepanyl, 1,4-oksazepanyl, 1,4-tiazepanyl og azetidinyl; eventuelt dertil hvori ring A uavhengig velges fra piperidinyl, piperazinyl, 1,4-diazepanyl, tiomorfolinyl, pyrrolidinyl, azepanyl, morfolinyl; eventuelt dertil hvori ring A uavhengig velges fra piperazinyl eller piperidinyl; eller:

hvori (II) ring A er et 5-leddet heteroaryl; eventuelt hvori ring A uavhengig velges fra pyrrolyl, imidazolyl, pyrazolyl, 1,2,3-triazolyl eller 1,2,4-triazolyl; eventuelt dertil hvori ring A uavhengig velges fra pyrazolyl eller imidazolyl.

13. Forbindelsen ifølge krav 9 som har formel **I-A-1:**



I-A-1
;

hvori:

R^5 velges fra C_{1-4}-alifatisk, et 3−6-leddet sykloalkyl eller et 3−6-leddet heterosyklyl som har 1−2 heteroatomer valgt fra oksygen eller svovel;

R^8 velges fra H eller C_{1-3}-alkyl; eller

R^5 og R^8, tatt sammen med atomene som de er bundet til, danner en 5−6-leddet ikke-aromatisk ring som har 1−2 heteroatomer valgt fra oksygen, nitrogen eller svovel; eventuelt:

hvori (I) R^1 er fluor; eventuelt hvori R^5 er C_{1-4}-alifatisk; eventuelt dertil hvori R^5 uavhengig velges fra metyl eller etyl; eller:

hvori (II) R^5 er et 3−6-leddet sykloalkyl; eventuelt hvori R^5 er syklopropyl; eller:

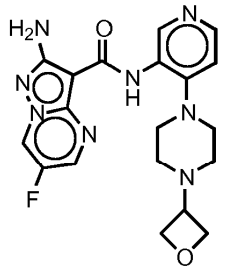
hvori (III) R^5 er et 3-6-leddet heterosyklyl som har 1−2 heteroatomer valgt fra oksygen eller svovel; eventuelt hvori R^5 er tetrahydrofuranyl eller oksytanyl; eller:

hvori (IV) R^5 og R^6, tatt sammen med atomene som de er bundet til, danner en 5−6-leddet, ikke-aromatisk ring som har 1−2 heteroatomer valgt fra oksygen, nitrogen eller svovel; eventuelt:

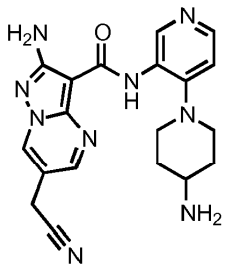
hvori (i) ringen dannet av R^5 og R^6 er en femleddet ring; eller:

hvori (ii) ringen dannet av R^5 og R^6 er en seksleddet ring.

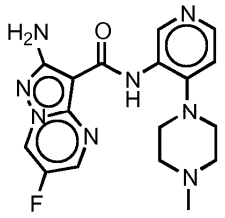
14. Forbindelsen ifølge et hvilket som helst av kravene 12 og 13, uavhengig valgt fra:



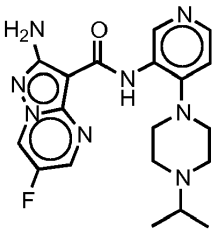
I-N-1



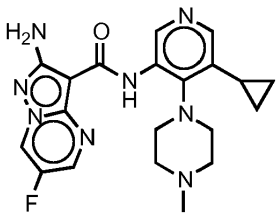
I-N-2



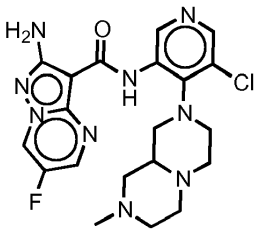
I-N-3



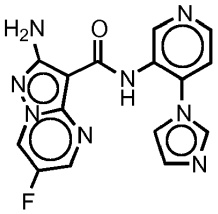
I-N-4



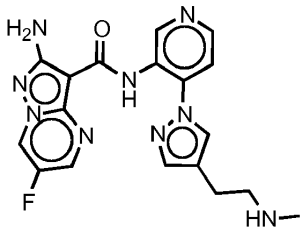
I-N-5



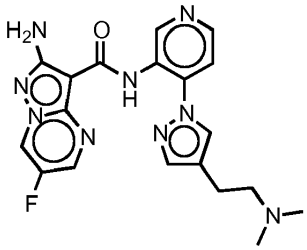
I-N-6



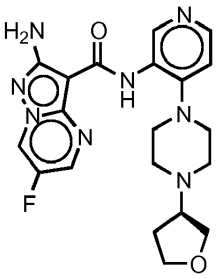
I-N-7



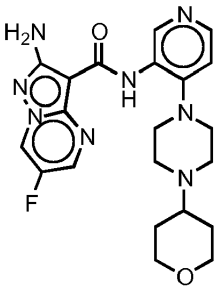
I-N-8



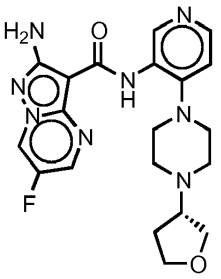
I-N-9



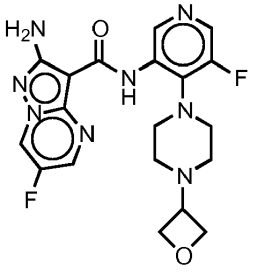
I-N-10



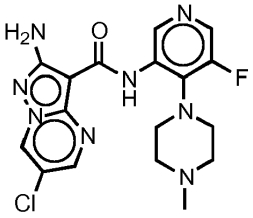
I-N-11



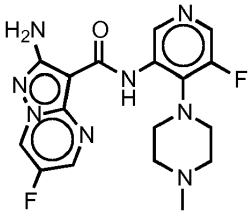
I-N-12



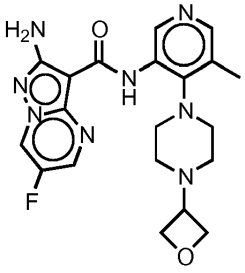
I-N-13



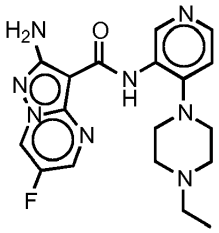
I-N-14



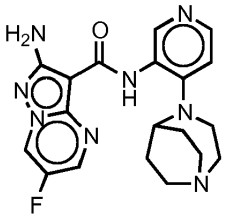
I-N-15



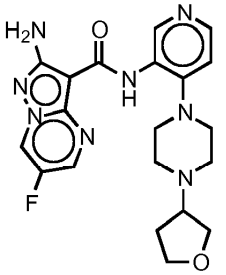
I-N-16



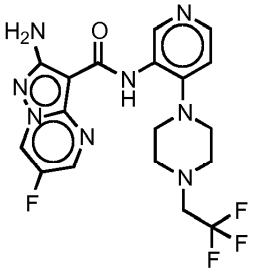
I-N-17



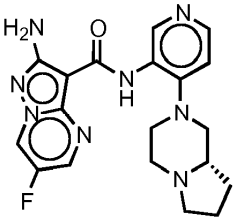
I-N-18



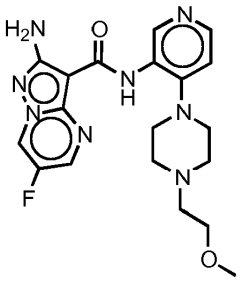
I-N-19



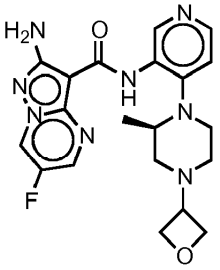
I-N-20



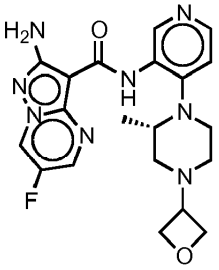
I-N-21



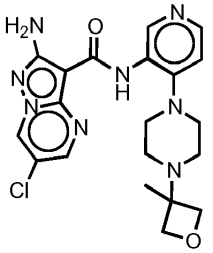
I-N-22



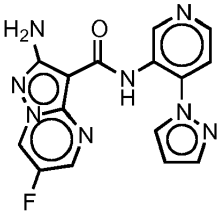
I-N-23



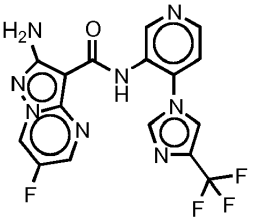
I-N-24



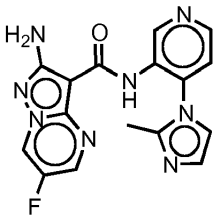
I-N-25



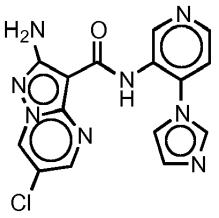
I-N-26



I-N-27



I-N-28



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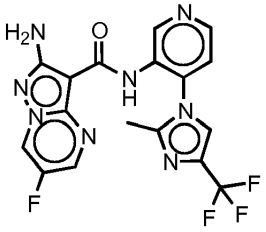

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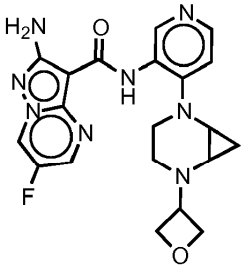

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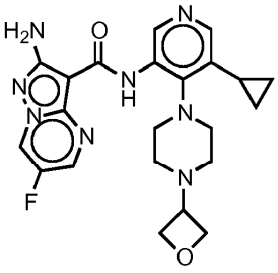

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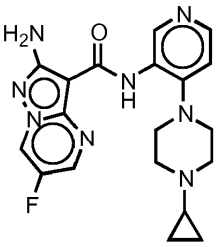

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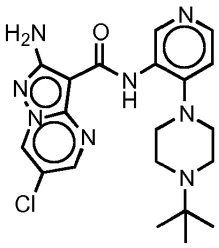

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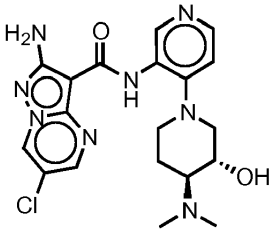

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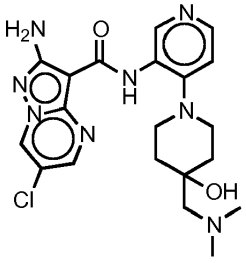

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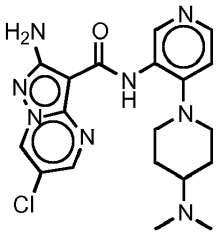

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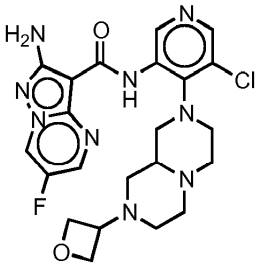

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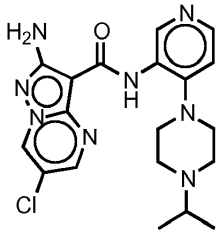

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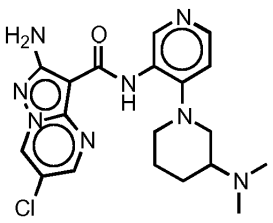

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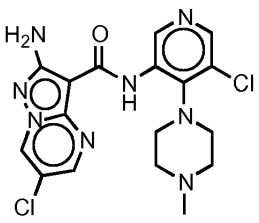

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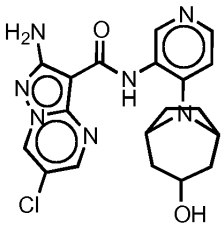

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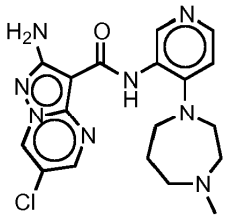

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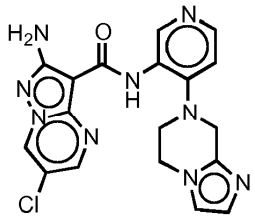

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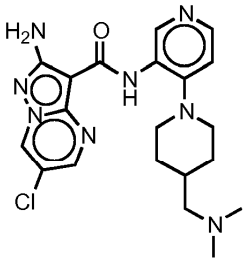

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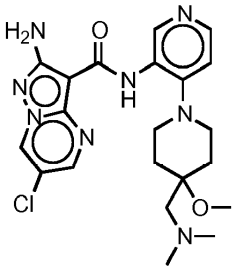

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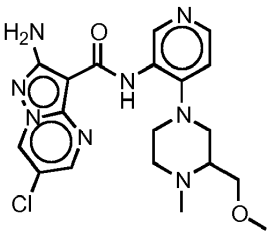

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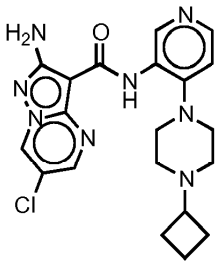

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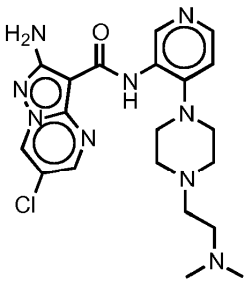

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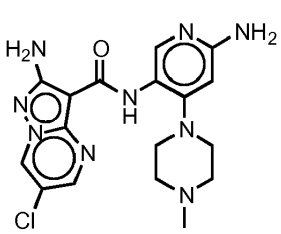
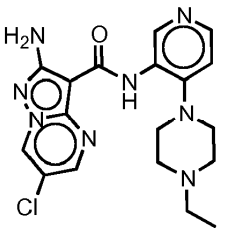


I-N-50



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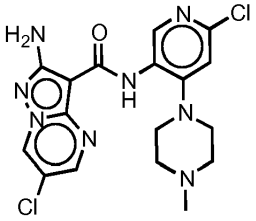

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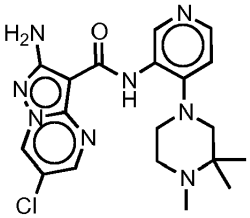

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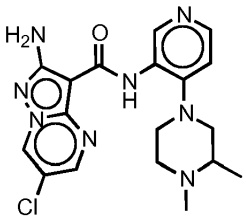

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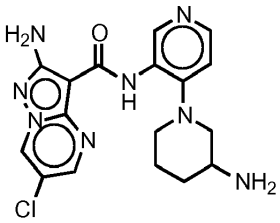

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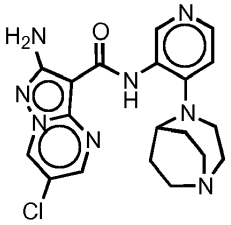
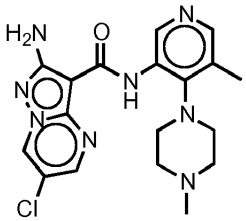


I-N-56



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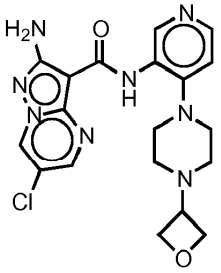

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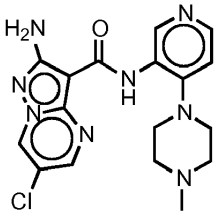

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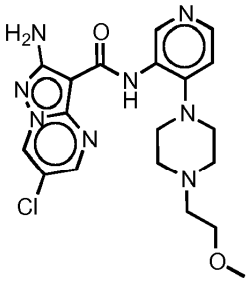

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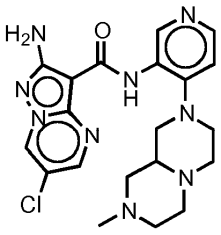
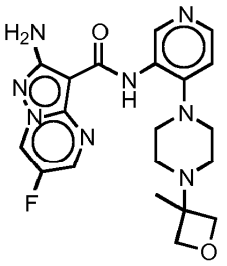
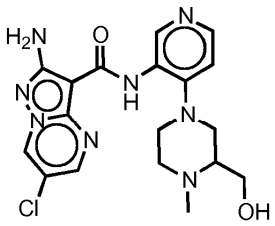


I-N-61



I-N-62



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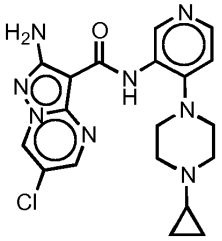

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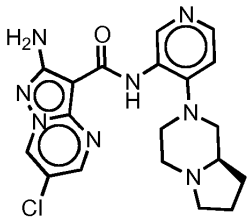

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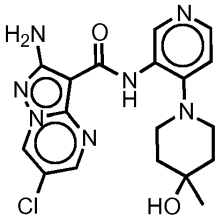
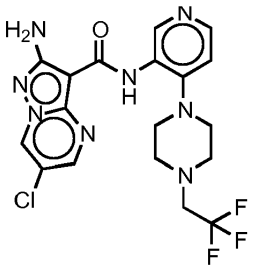
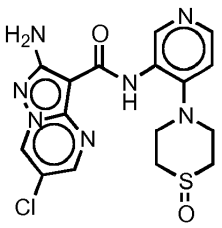


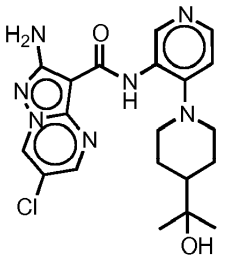
I-N-66



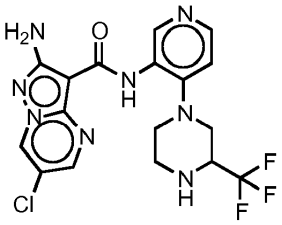
I-N-67



I-N-68



I-N-69



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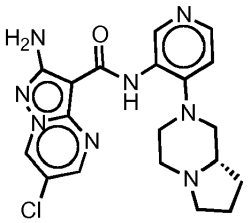

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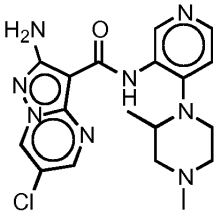
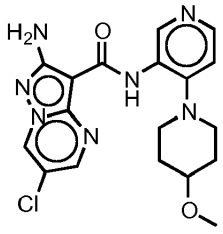
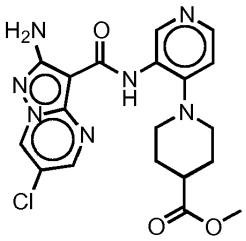


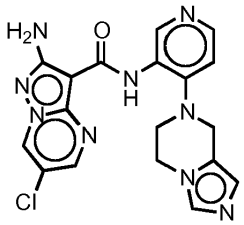
I-N-72



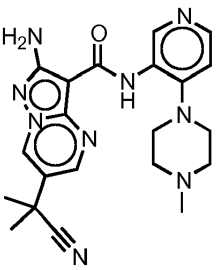
I-N-73



I-N-74



I-N-75



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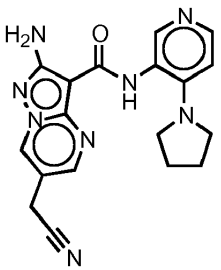
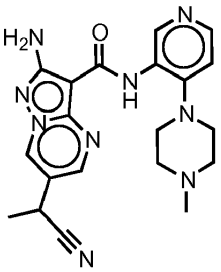
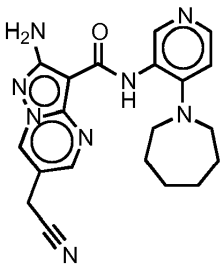


I-N-77



I-N-78



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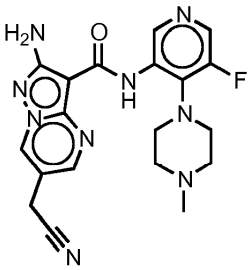

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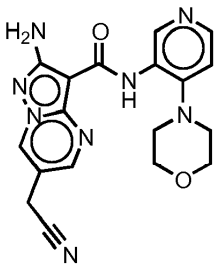
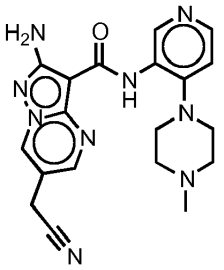
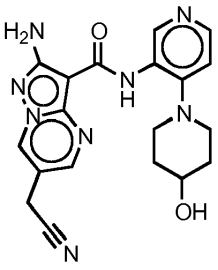


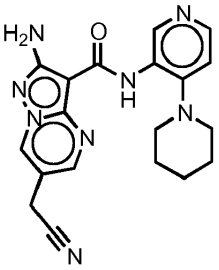
I-N-81



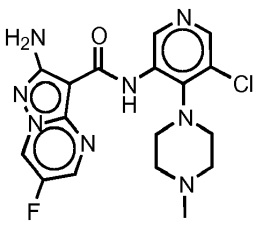
I-N-82



I-N-83



I-N-84



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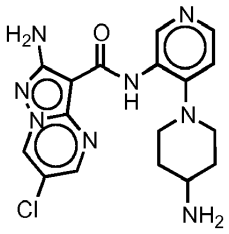

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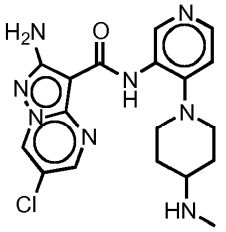
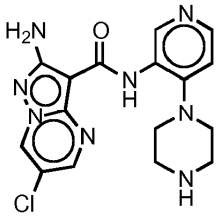


I-N-87



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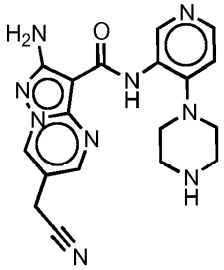

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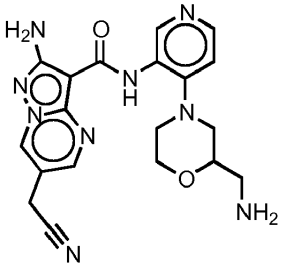

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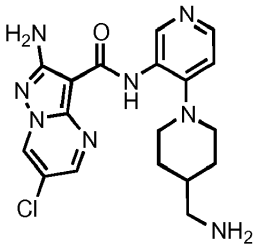

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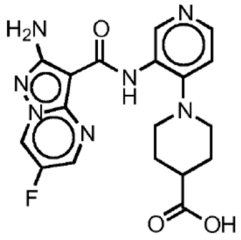

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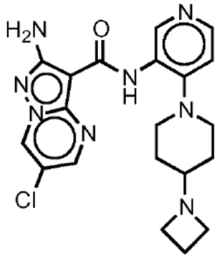

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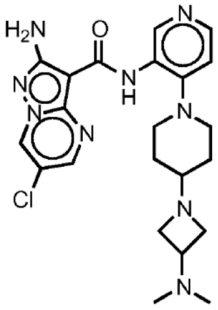

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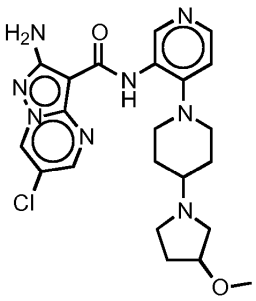

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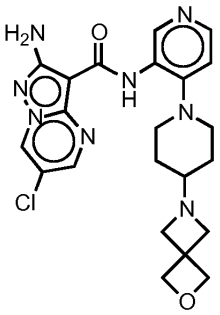

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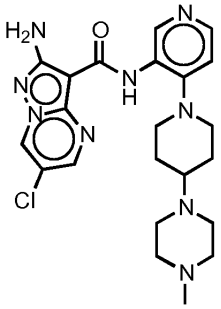

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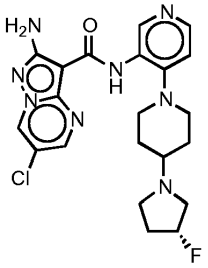

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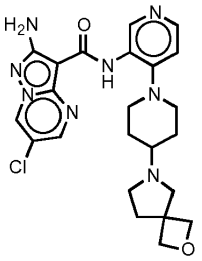

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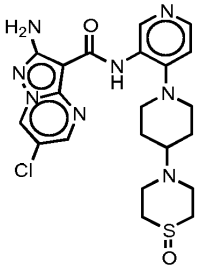

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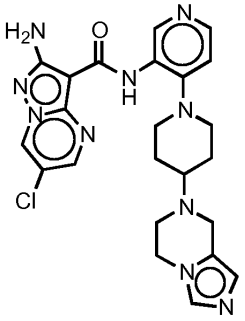

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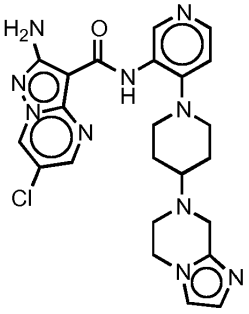

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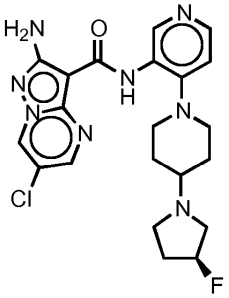

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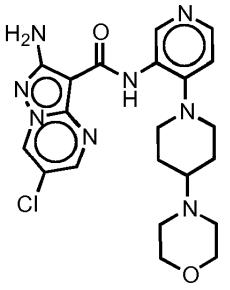

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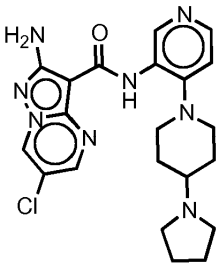

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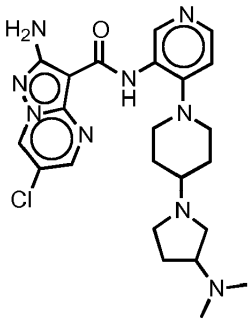

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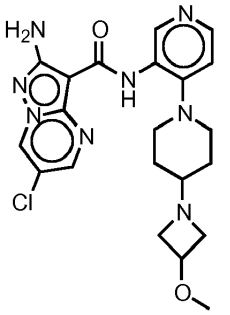

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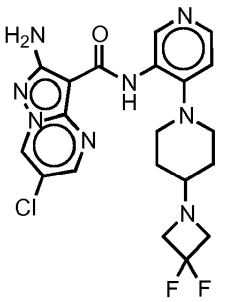

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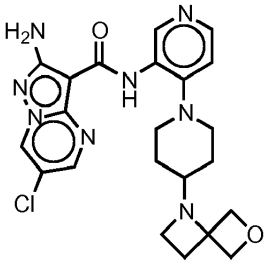

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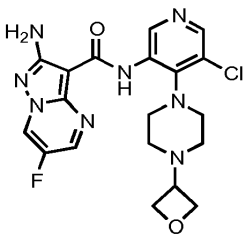

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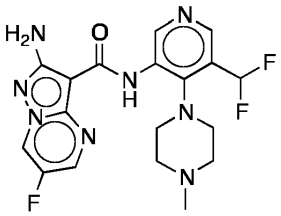

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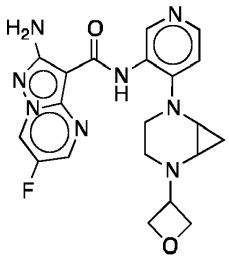

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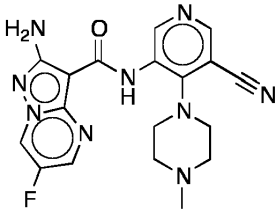

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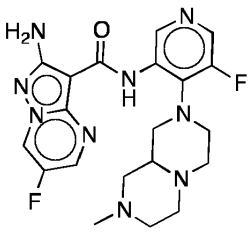

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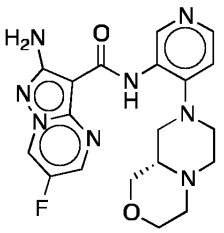

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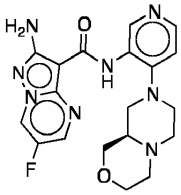

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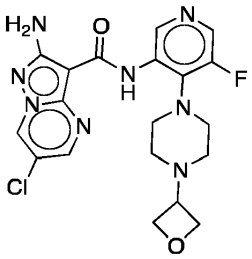

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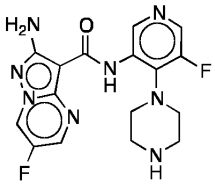

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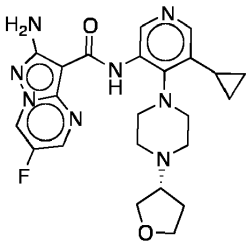

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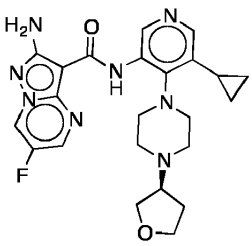

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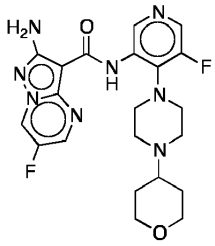

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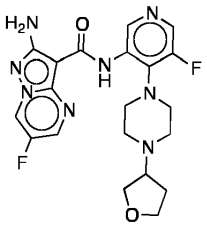

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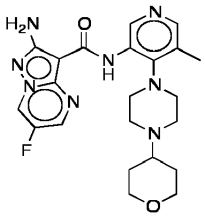

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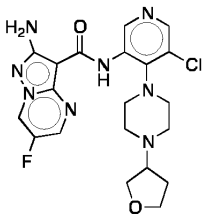

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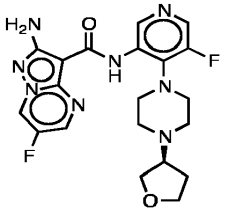

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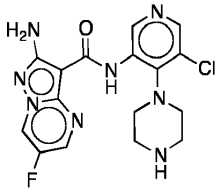

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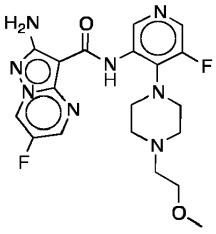

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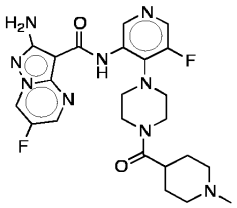

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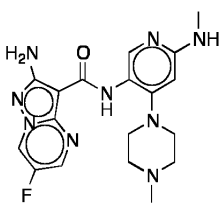

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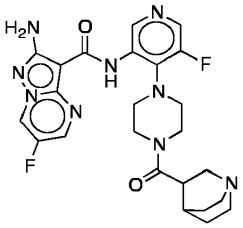

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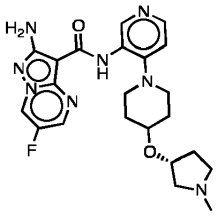

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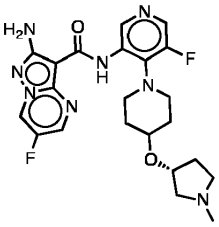

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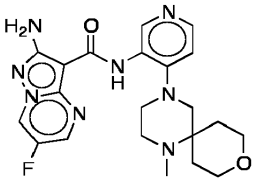

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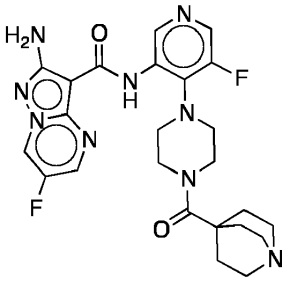

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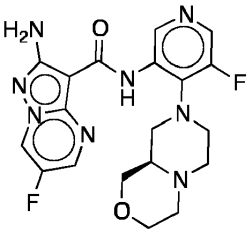

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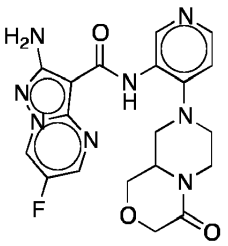
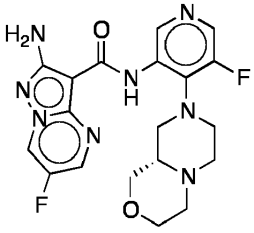


I-N-136



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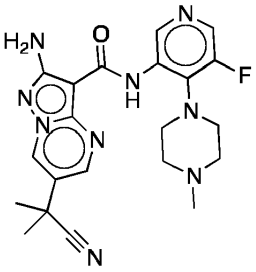
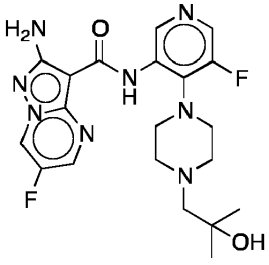


I-N-138



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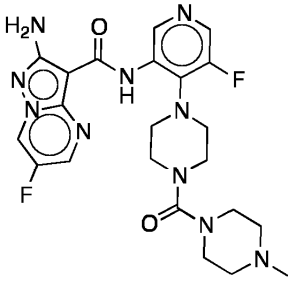

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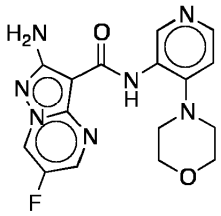

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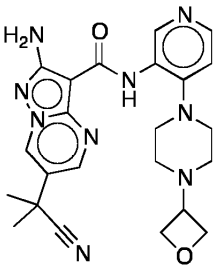
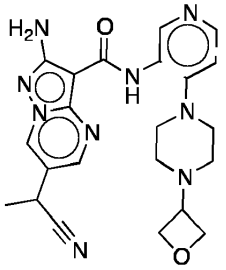


I-N-142



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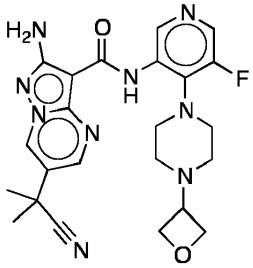

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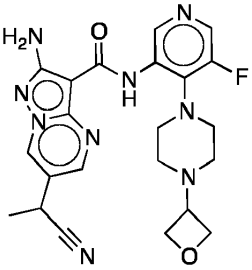

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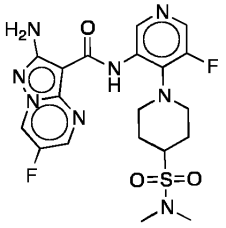

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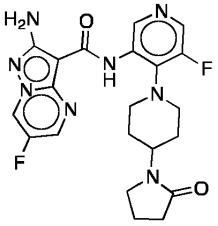

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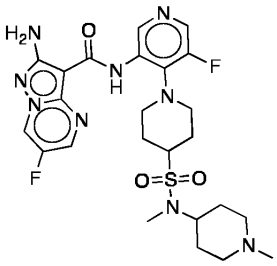

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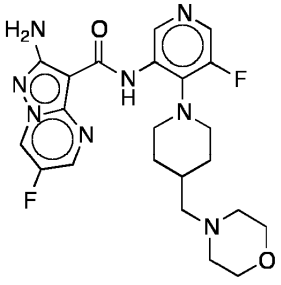
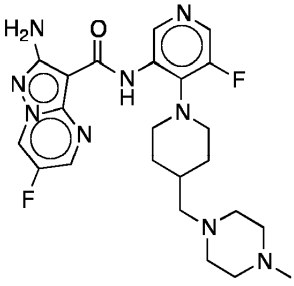


I-N-149



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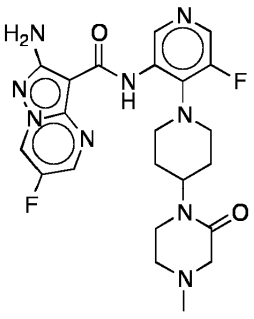

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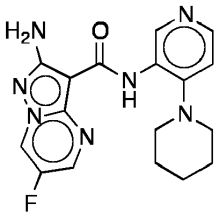

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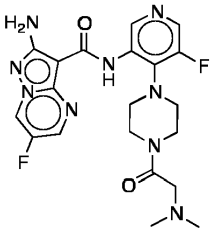

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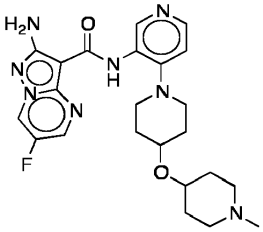

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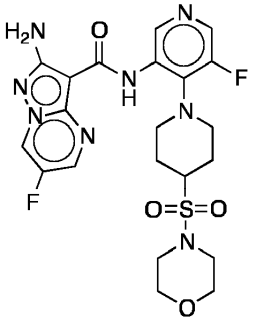

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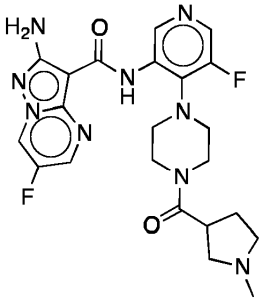

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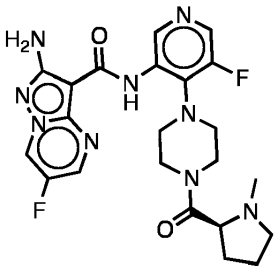

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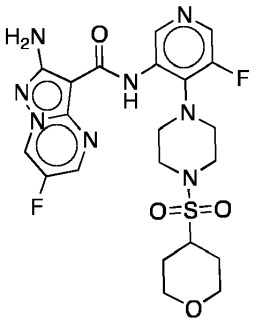

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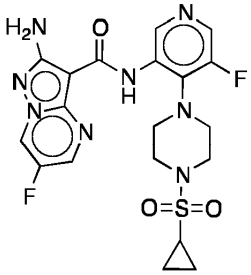

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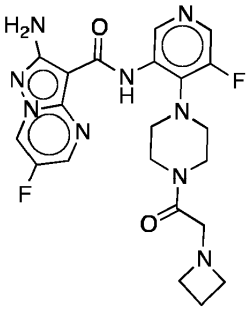

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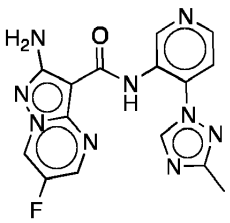

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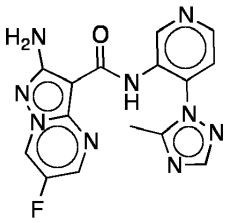

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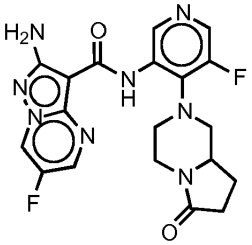
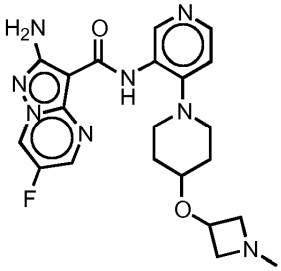


I-N-163



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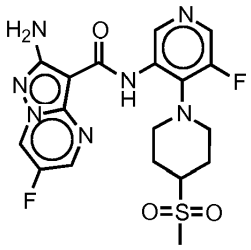

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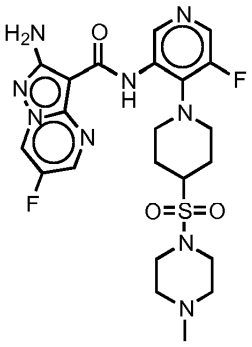
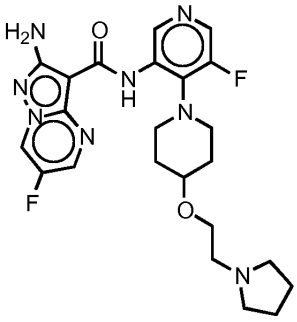


I-N-166



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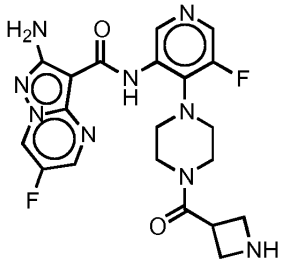

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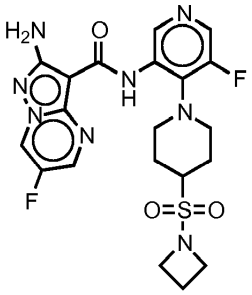

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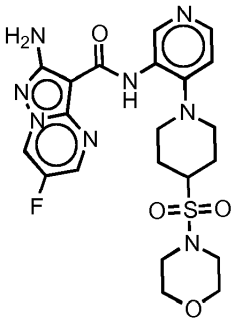

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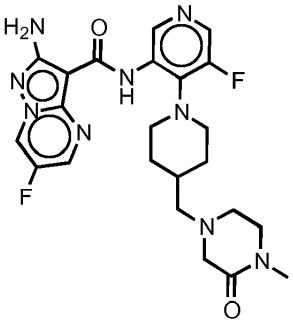

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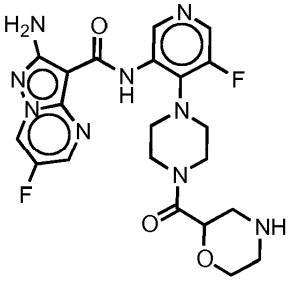

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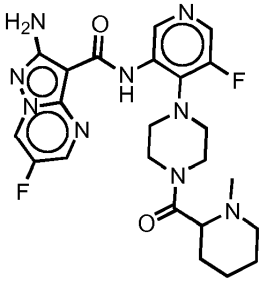

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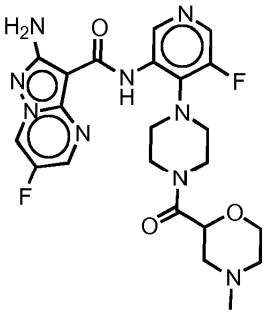

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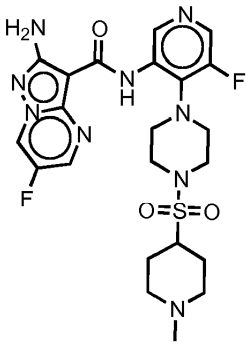

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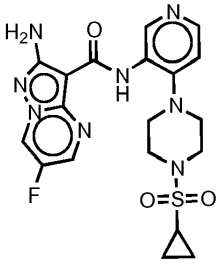

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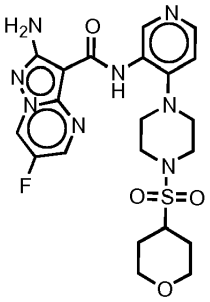
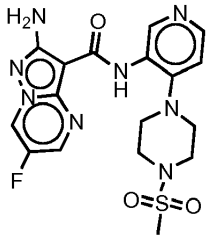
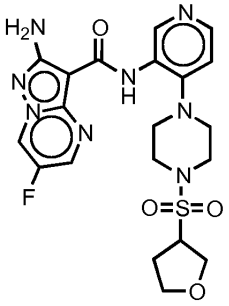


I-N-177



I-N-178



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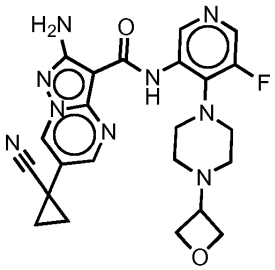

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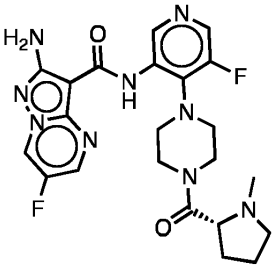
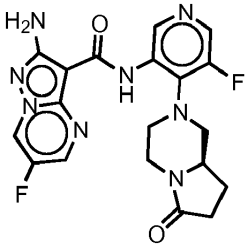
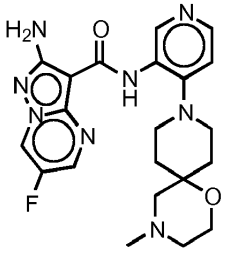


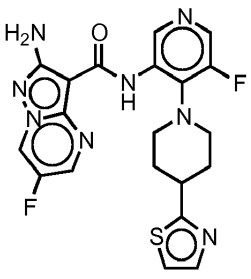
I-N-181



I-N-182



I-N-183



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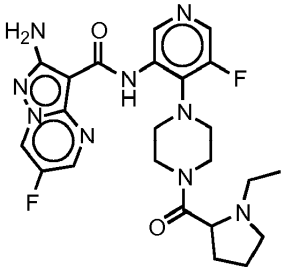

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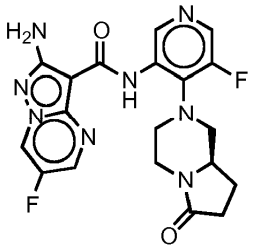
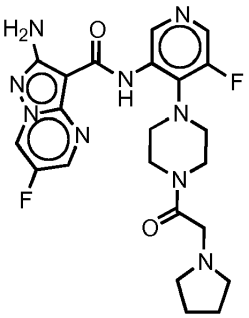
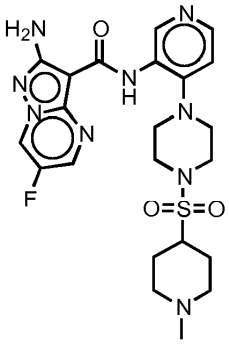


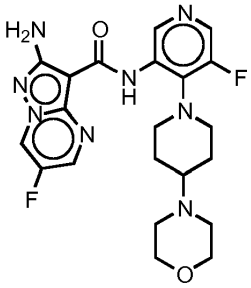
I-N-186



I-N-187



I-N-188



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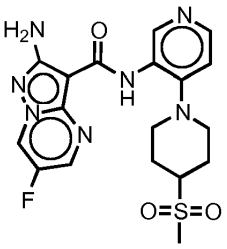
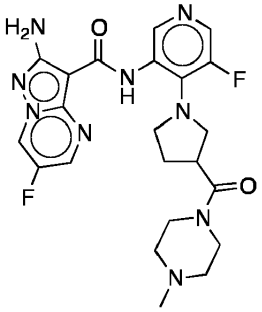
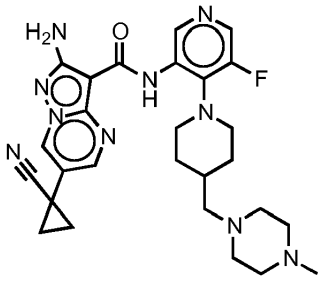


I-N-190



I-N-191



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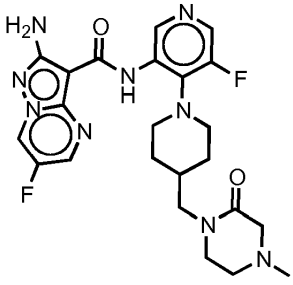
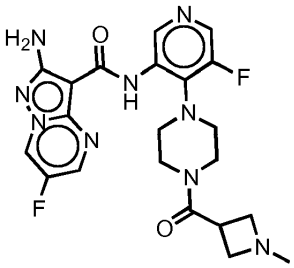
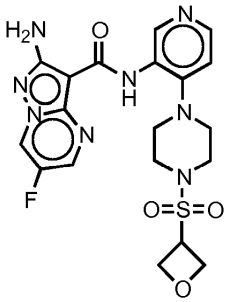


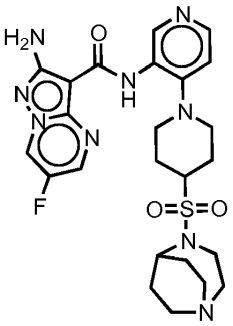
I-N-193



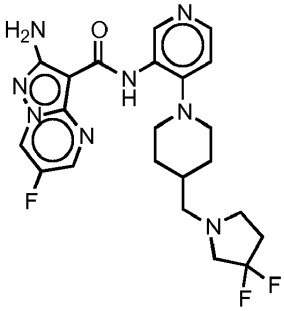
I-N-194



I-N-195



I-N-196



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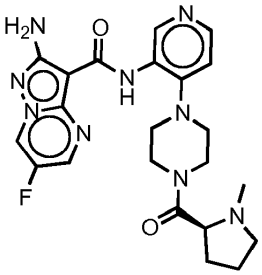
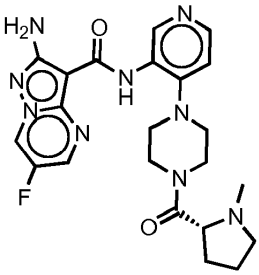
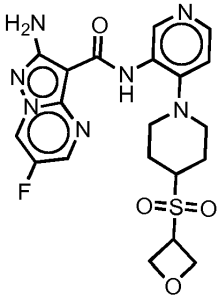


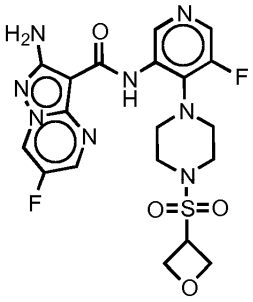
I-N-198



I-N-199



I-N-200



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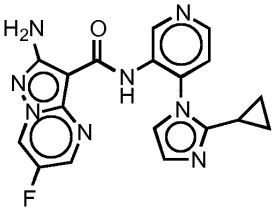

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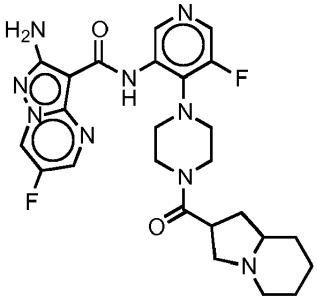

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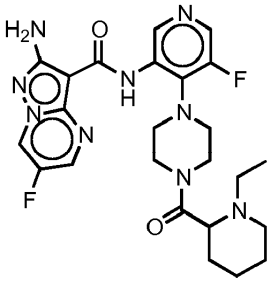

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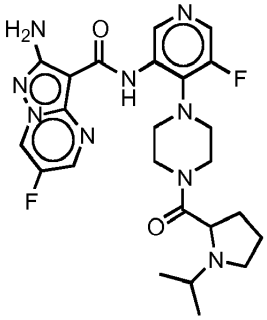

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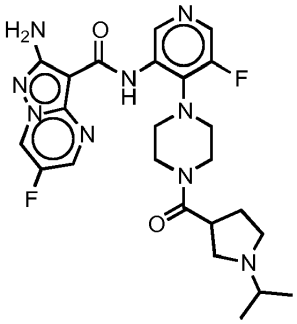

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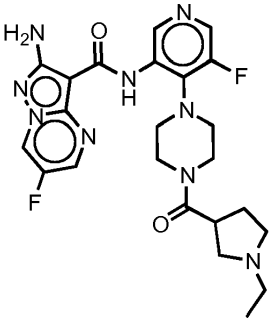

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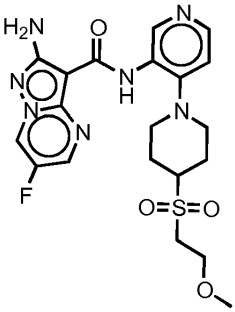

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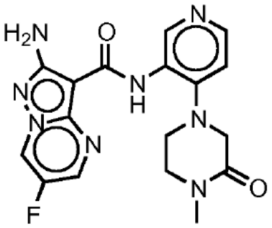

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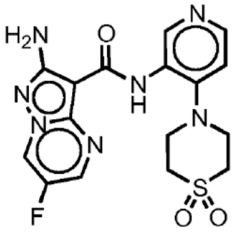

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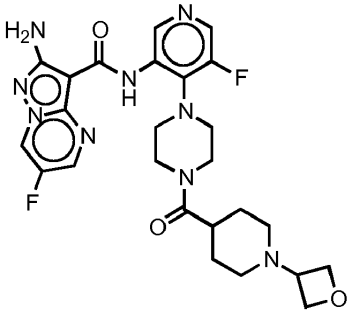

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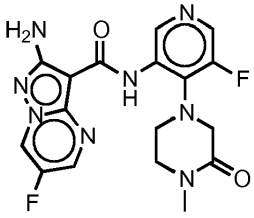

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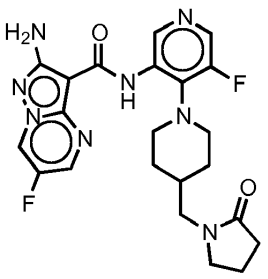

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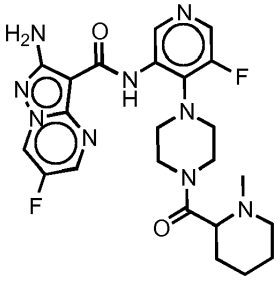

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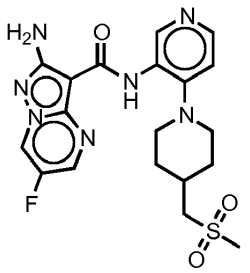

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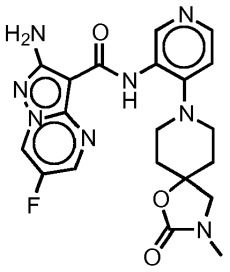

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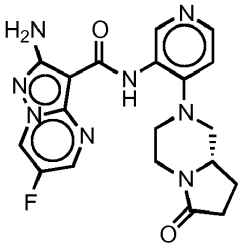

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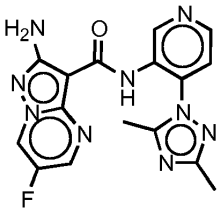

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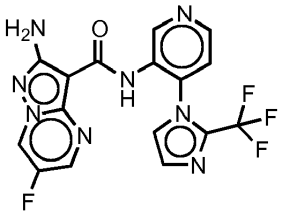

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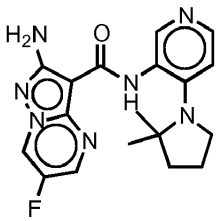

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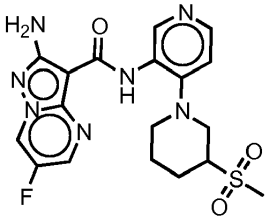

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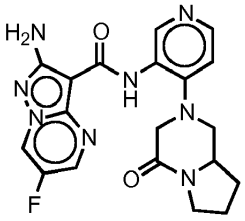

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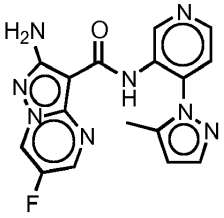

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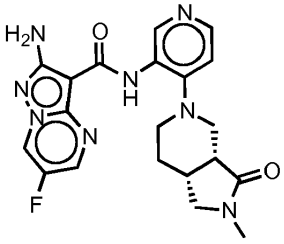

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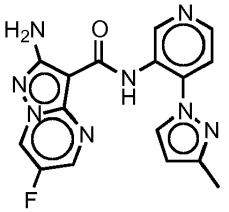

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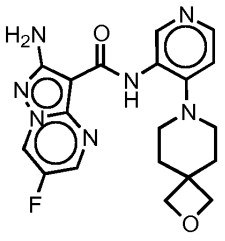

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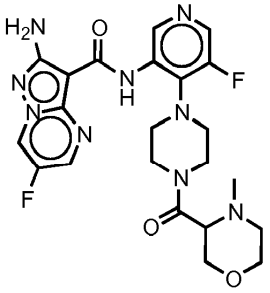

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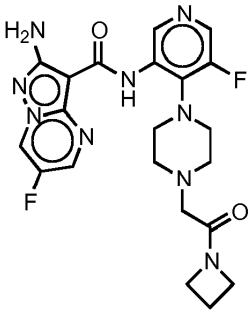

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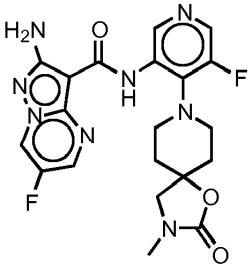

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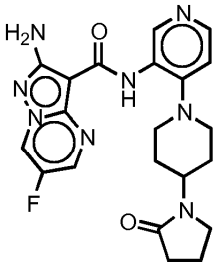

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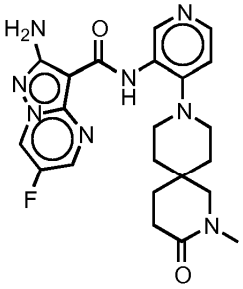

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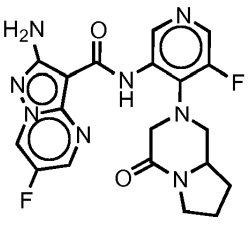

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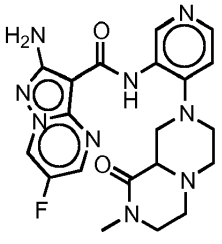

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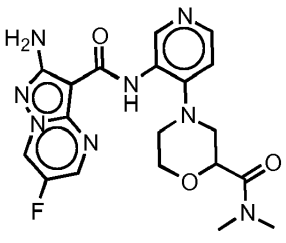

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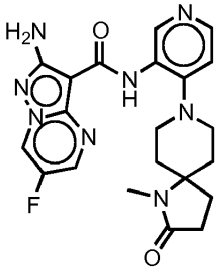

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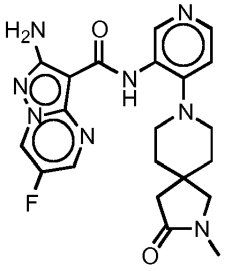

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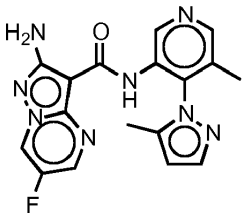

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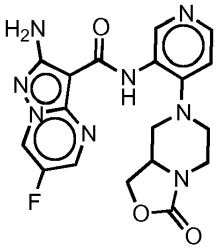

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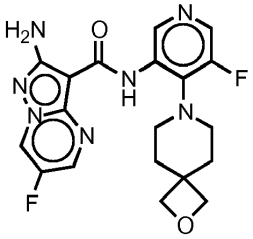

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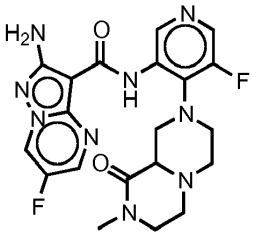

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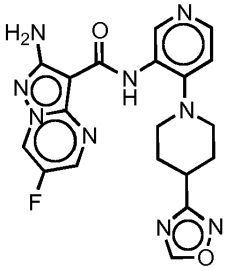

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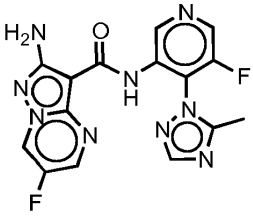

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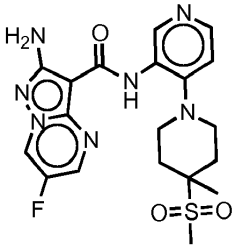

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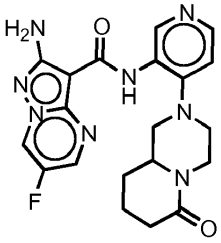

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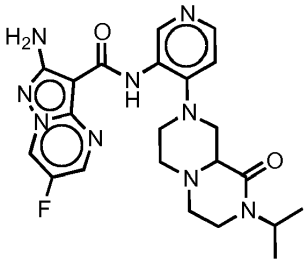

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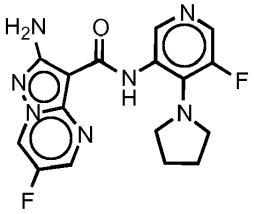

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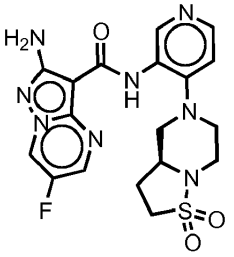

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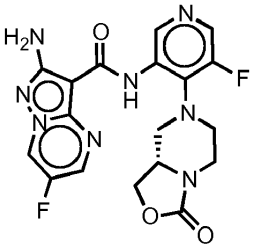

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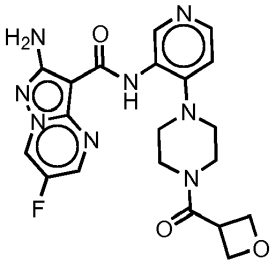

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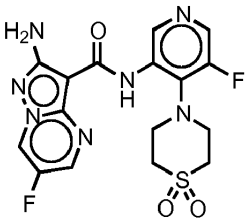

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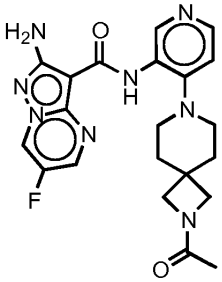

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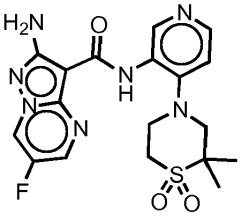

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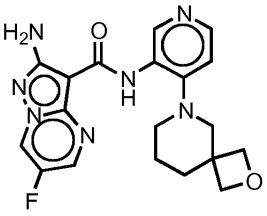

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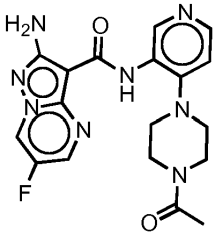

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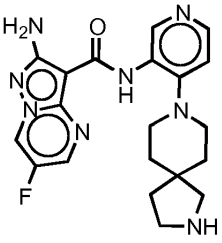

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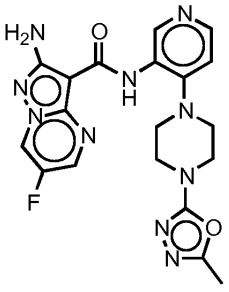

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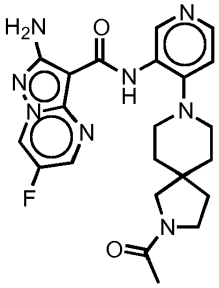
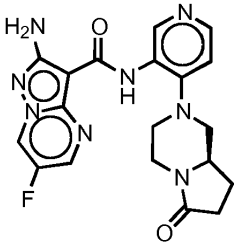
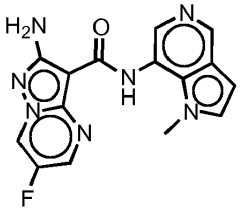


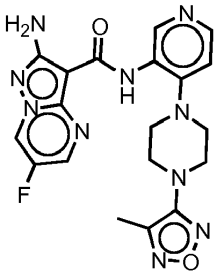
I-N-257



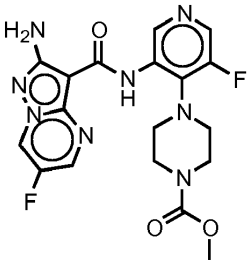
I-N-258



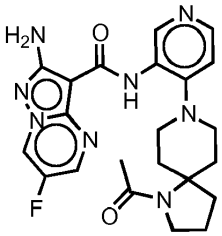
I-N-259



I-N-260



I-N-261



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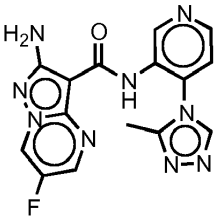
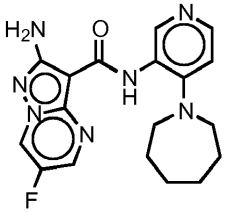


I-N-263



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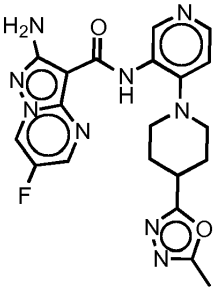
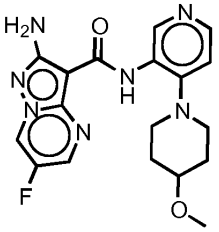


I-N-265



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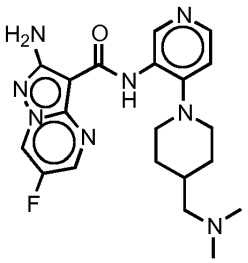

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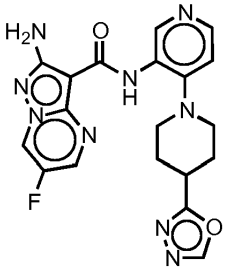
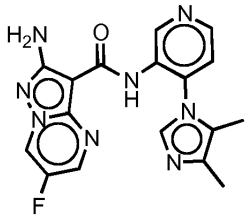
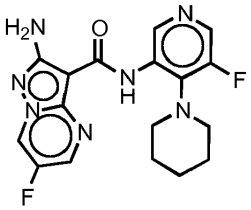


I-N-268



I-N-269



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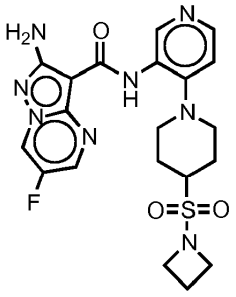

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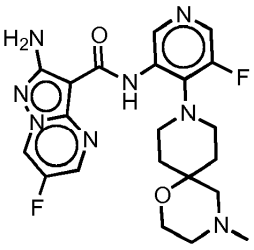

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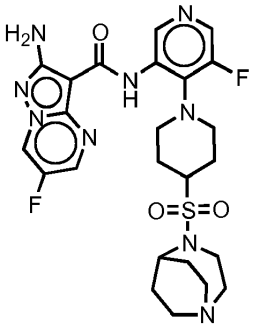
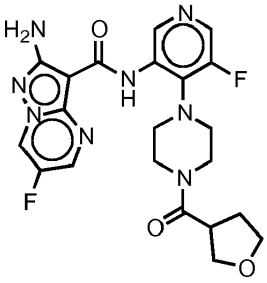


I-N-273



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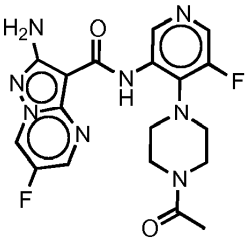

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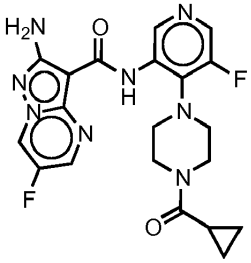
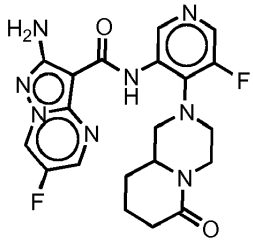


I-N-276



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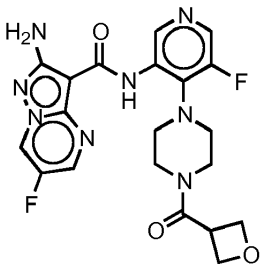

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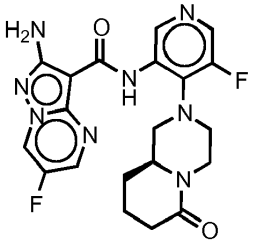
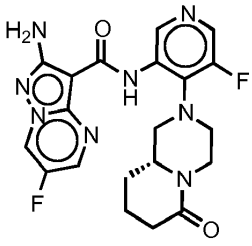
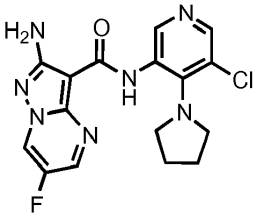


I-N-279



I-N-280



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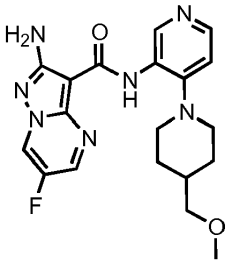

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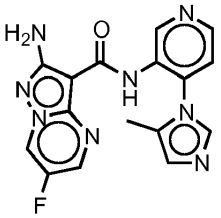

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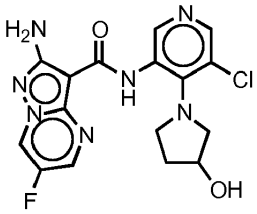
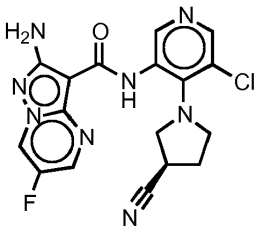


I-N-284



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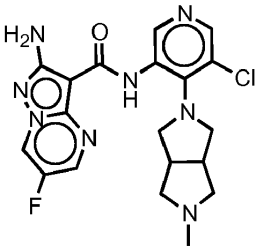

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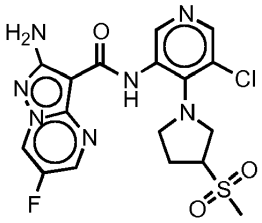
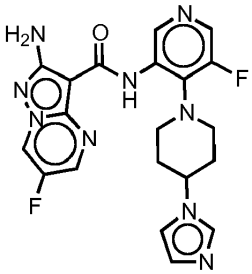


I-N-287



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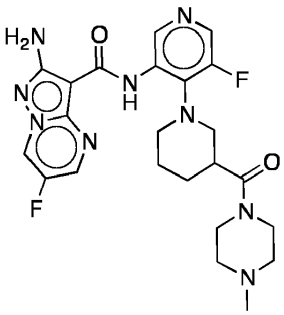

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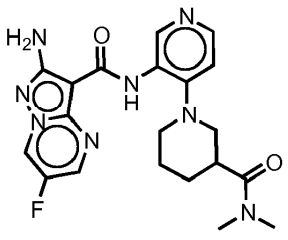
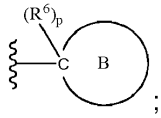


I-N-290.

15. Forbindelsen ifølge krav 9, hvori R^4 er:



;

eventuelt:

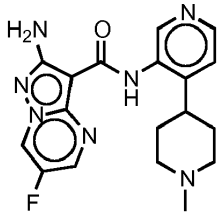
hvori p er 1; eventuelt dertil:

hvori ring B er en 3−7-leddet sykloalifatisk eller heterosyklylring som har 1−2 heteroatomer valgt fra oksygen, nitrogen eller svovel; eventuelt dertil:

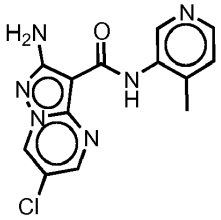
hvori ring B uavhengig velges fra syklopropyl, syklobutyl, syklopentyl, sykloheksyl, sykloheptyl, pyrrolidinyl, piperidinyl, azepanyl, pyrazolidinyl, isoksazolidinyl, oksazolidinyl, tiazolidinyl, imidazolidinyl, piperazinyl, morfolinyl, tiomorfolinyl, 1,3-oksazinanyl, 1,3-tiazinanyl, dihydropyridinyl, dihydroimidazolyl, 1,3-tetrahydropyrimidinyl, dihydropyrimidinyl, 1,4-diazepanyl, 1,4-oksazepanyl, 1,4-tiazepanyl, 1,2,3,6-tetrahydropyridin og azetidinyl; eventuelt dertil:

hvori ring B er piperidinyl

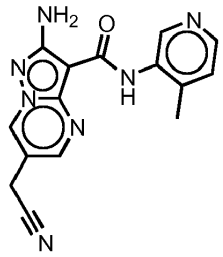
16. Forbindelse ifølge krav 1 uavhengig valgt fra:



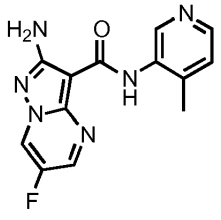
I-C-1



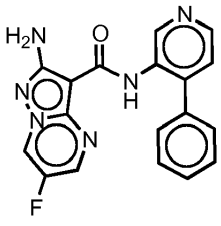
I-C-2



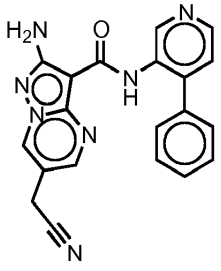
I-C-3



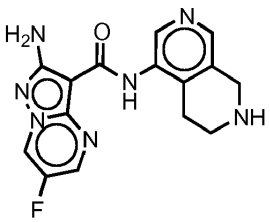
I-C-4



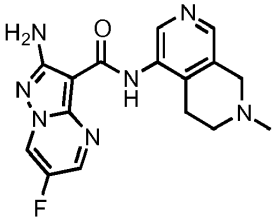
I-C-5



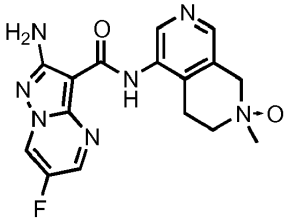
I-C-6



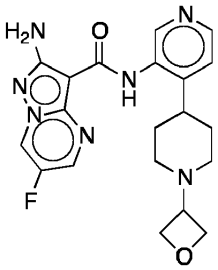
I-C-7



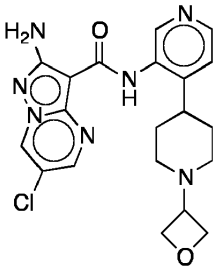
I-C-8



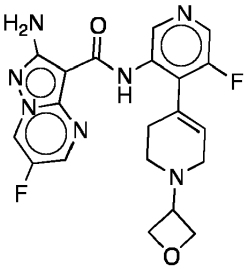
I-C-9 .



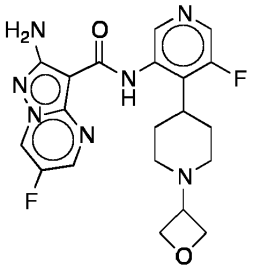
I-C-10



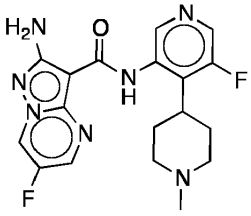
I-C-11



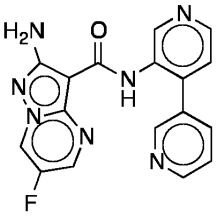
I-C-12



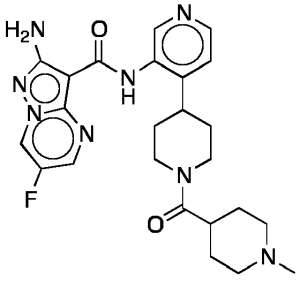
I-C-13



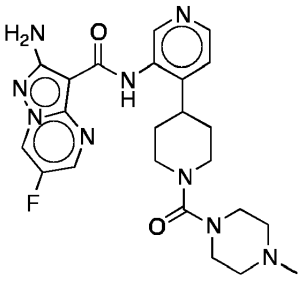
I-C-14



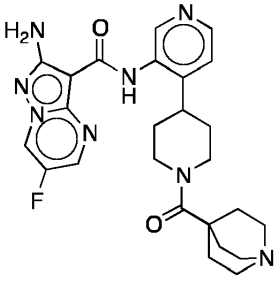
I-C-15



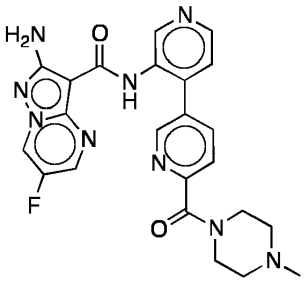
I-C-16



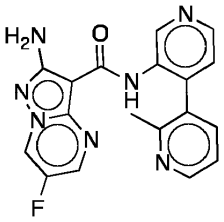
I-C-17



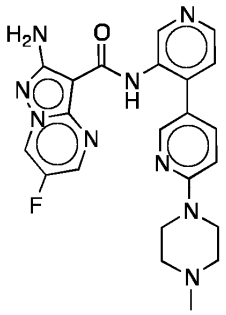
I-C-18



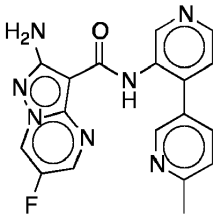
I-C-19



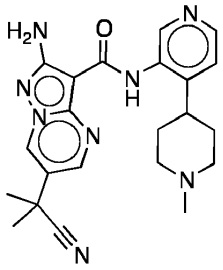
I-C-20



I-C-21



I-C-22



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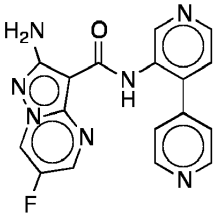

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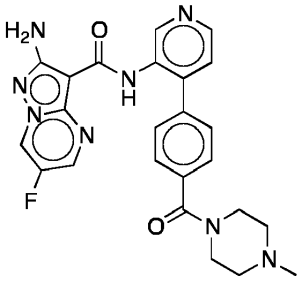
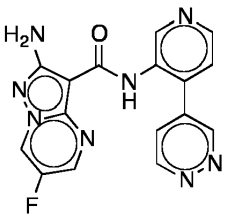


I-C-25



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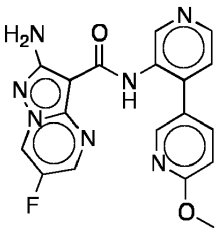

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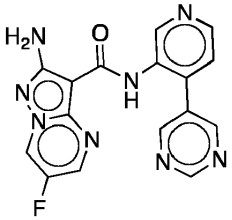

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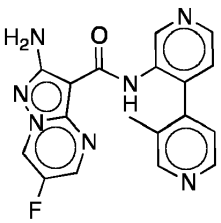

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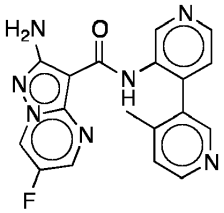

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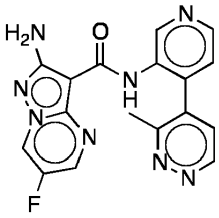
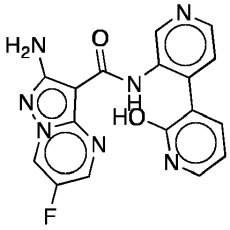


I-C-31



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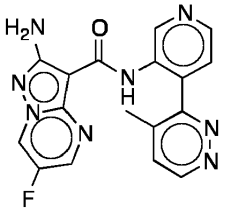

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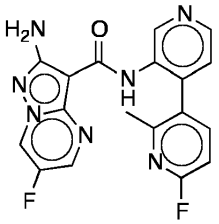

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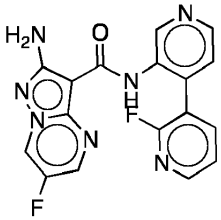

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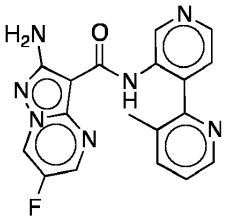

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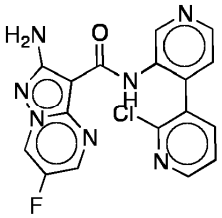

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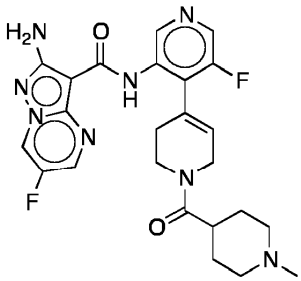

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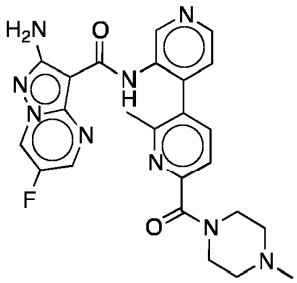

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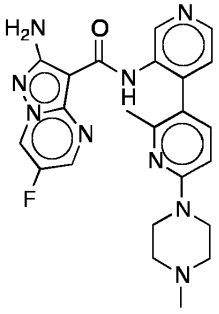

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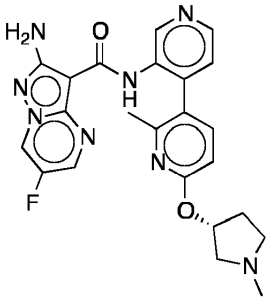

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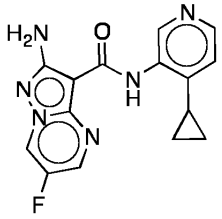

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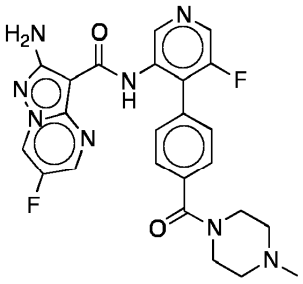

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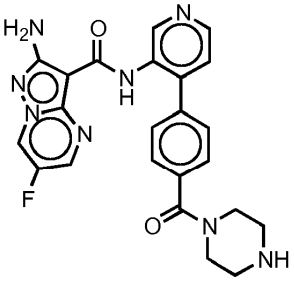

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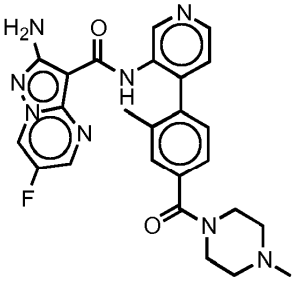

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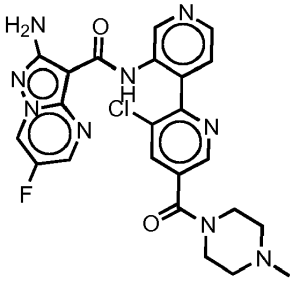

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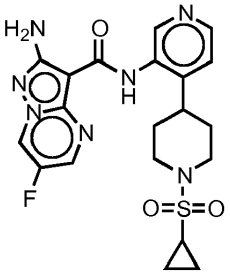

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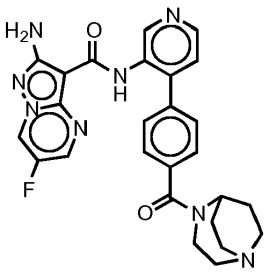

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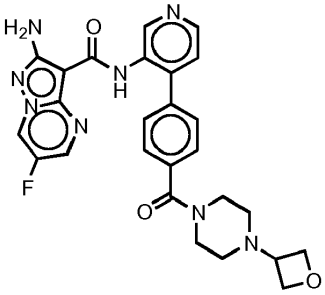
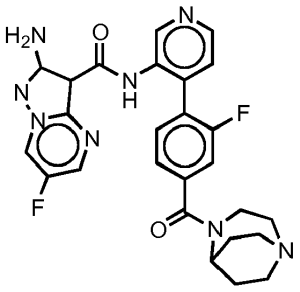


I-C-49



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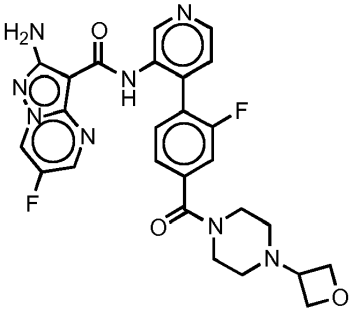

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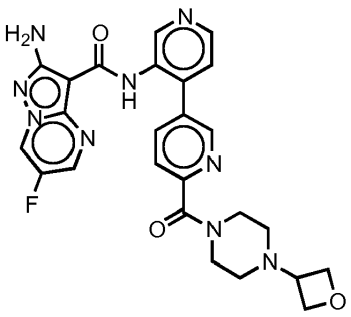

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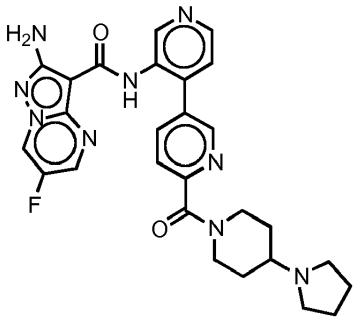

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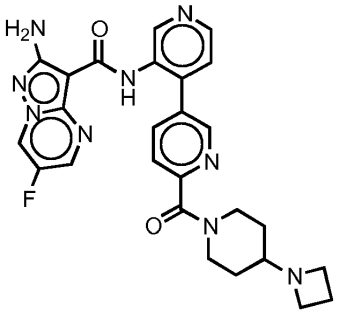

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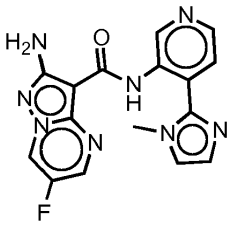

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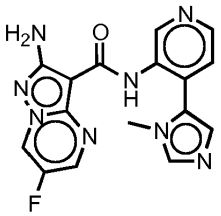
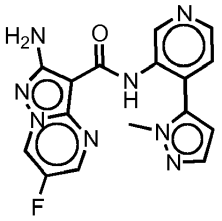


I-C-56



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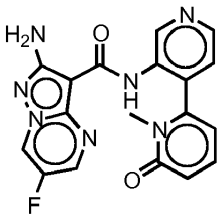
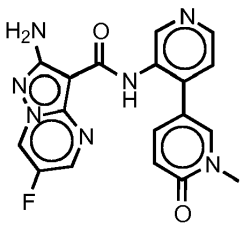


I-C-58



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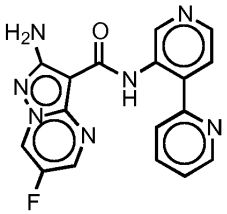

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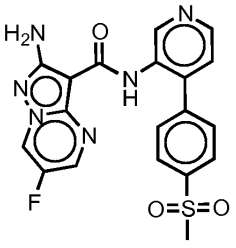
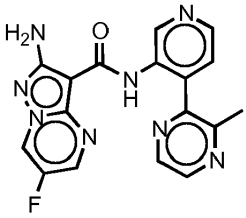
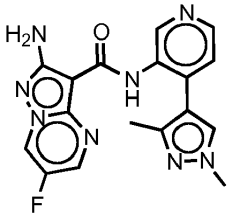


I-C-61



I-C-62



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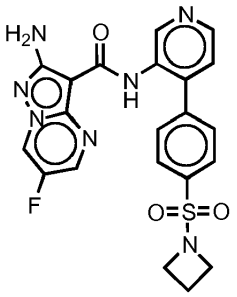

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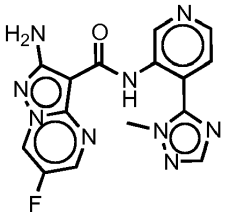

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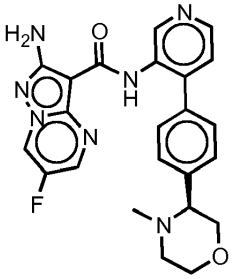
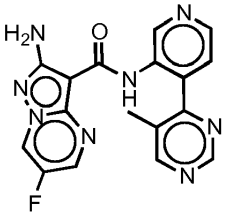
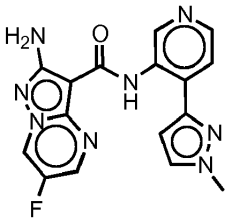


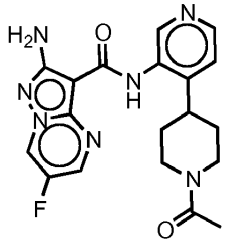
I-C-66



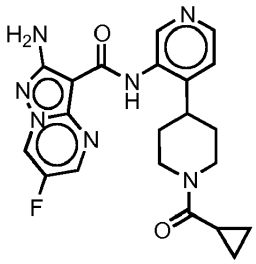
I-C-67



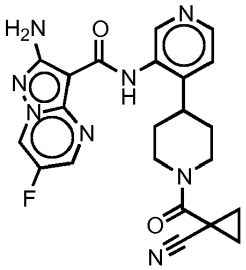
I-C-68



I-C-69



I-C-70



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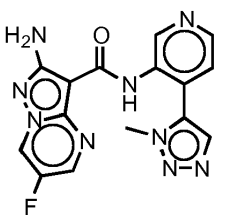
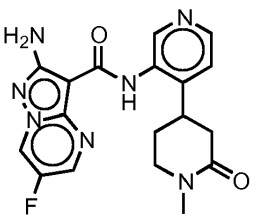
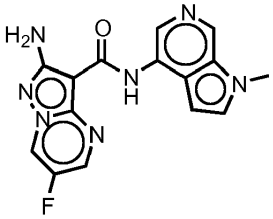


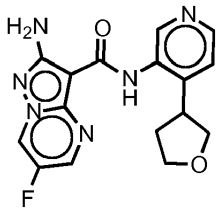
I-C-72



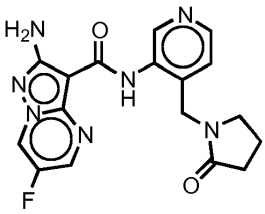
I-C-73



I-C-74



I-C-75



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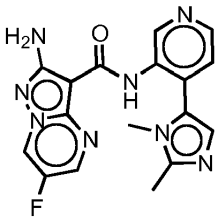

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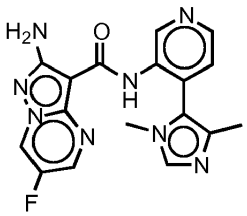
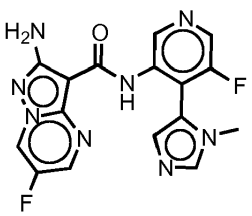
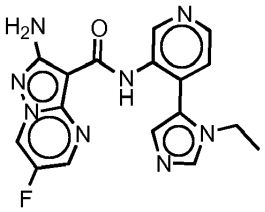


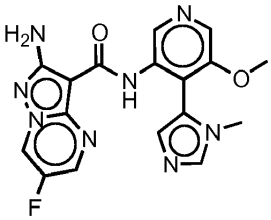
I-C-78



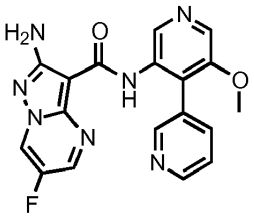
I-C-79



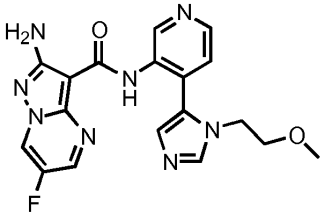
I-C-80



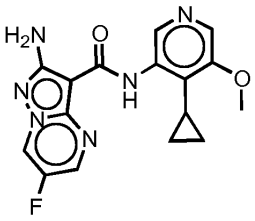
I-C-81



I-C-82



I-C-83



I-C-84

17. Farmasøytisk sammensetning omfattende en forbindelse ifølge et hvilket som helst av kravene 1 til 16 og en farmasøytisk akseptabel bærer.

18. Forbindelse, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16, eller en farmasøytisk sammensetning ifølge krav 17 for anvendelse ved behandlingen av kreft hos en pasient.

19. Forbindelsen, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16, eller en farmasøytisk sammensetning ifølge krav 17 for anvendelse ifølge krav 18, videre omfattende administrering til pasienten av et ytterligere terapeutisk middel uavhengig valgt fra et DNA-skadelig middel; hvori det ytterligere midlet er hensiktsmessig for sykdommen som behandles; og det ytterligere midlet administreres sammen med forbindelsen som en enkelt doseringsform eller separat fra forbindelsen som del av en multippel doseringsform; eventuelt:
hvori (I) det DNA-skadelige midlet er valgt kjemoterapi eller strålebehandling; eventuelt hvori det DNA-skadelige midlet er et alkyleringsmiddel valgt fra temozolomid; eller:
hvori (II) det DNA-skadelige midlet uavhengig velges fra ioniserende stråling, radioetterlignende neokarsinostatin, et platineringsmiddel, en Topo I-inhibitor, en Topo II-inhibitor, en antimetabolitt, et alkyleringsmiddel, et alkylsulfonat eller et antibiotikum; eventuelt
hvori (i) det DNA-skadelige midlet uavhengig velges fra ioniserende stråling, et platineringsmiddel, en Topo I-inhibitor, en Topo II-inhibitor eller et antibiotikum; eller:
hvori (ii) det DNA-skadelige midlet uavhengig velges fra ioniserende stråling, et platineringsmiddel, en Topo I-inhibitor, en Topo II-inhibitor, en antimetabolitt, et alkyleringsmiddel eller et alkylsulfonat; eventuelt:
hvori (a) platineringsmidlet uavhengig velges fra cisplatin, oksaliplatin, karboplatin, nedaplatin, lobaplatin, triplatintetranitrat, pikoplatin, satraplatin, proLindac og aroplatin; Topo I-inhibitoren velges fra kamptotecin, topotekan, irinotekan/SN38, rubitekan og belotekan; Topo II-inhibitoren velges fra etoposid, daunorubicin, doksorubicin, aklarubicin, epirubicin, idarubicin, amrubicin, pirarubicin, valrubicin, zorubicin og teniposid; antimetabolitten velges fra aminopterin, metotreksat, pemetreksed, raltitreksed, pentostatin, kladribin, klofarabin, fludarabin, tioguanin, merkaptopurin, fluoruracil, kapecitabin, tegafur, karmofur, floksuridin, cytarabin, gemcitabin, azacitidin og hydroksyurea; alkyleringsmidlet velges fra mekloretamin, syklofosfamid, ifosfamid, trofosfamid, klorambucil, melfalan, prednimustin, bendamustin, uramustin, estramustin, karmustin, lomustin, semustin, fotemustin, nimustin, ranimustin, streptozocin, busulfan, mannosulfan, treosulfan, carboquon, thioTEPA, triaziquon, trietylenmelamin,

prokarbazin, dakarbazin, temozolomid, altretamin, mitobronitol, aktinomycin, bleomycin, mitomycin og plikamycin; eventuelt:
hvori (aa) platineringsmidlet uavhengig velges fra cisplatin, oksaliplatin, karboplatin, nedaplatin eller satraplatin; Topo I-inhibitoren velges fra kamptotecin, topotekan, irinotekan/SN38, rubitekan; Topo II-inhibitoren velges fra etoposid; antimetabolitten velges fra metotreksat, pemetreksed, tioguanin, fludarabin, kladribin, cytarabin, gemcitabin, 6-merkaptopurin eller 5-fluoruracil; alkyleringsmidlet velges fra nitrogensenneper, nitrosoureaer, triazener, alkylsulfonater, prokarbazin eller aziridiner; og antibiotikumet velges fra familien hydroksyurea, antrasykliner, antracendioner eller streptomycer; eller:
hvori (bb) det DNA-skadelige midlet uavhengig velges fra et platineringsmiddel eller ioniserende stråling; eventuelt hvori det ytterligere midlet er gemcitabin og kreften er kreft i bukspyttkjertelen; eller:
hvori (cc) kjemostrålingen er gemcitabin og stråling; eller:
hvori (b) antimetabolitten er gemcitabin; eller:
hvori (c) det DNA-skadelige midlet er ioniserende stråling; eller:
hvori (d) det DNA-skadelige midlet er et platineringsmiddel uavhengig valgt fra cisplatin eller karboplatin; eller:
hvori (e) det DNA-skadelige midlet er en Topo II-inhibitor valgt fra etoposid; eller:
hvori (f) det DNA-skadelige midlet uavhengig velges fra én eller flere av de følgende: cisplatin, karboplatin, gemcitabin, etoposid, temozolomid eller ioniserende stråling; eventuelt dertil hvori de ytterligere terapeutiske midlene velges fra én eller flere av de følgende: gemcitabin, cisplatin eller karboplatin og etoposid.

20. Forbindelsen, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16, eller en farmasøytisk sammensetning ifølge krav 17 for anvendelse ifølge krav 18 eller krav 19, hvori kreften er en fast tumor valgt fra de følgende kreftformene: Oralt: bukkalt hulrom, leppe, tunge, munn, svelg; Hjerte: sarkom (angiosarkom, fibrosarkom, rhabdomyosarkom, liposarkom), myksom, rhabdomyom, fibrom, lipom og teratom; Lunge: bronkogent karsinom (skvamøs celle eller epidermoid, udifferensiert småcelle, udifferensiert storcelle, adenokarsinom), alveolært (bronkiolært)

karsinom, bronkialt adenom, sarkom, lymfom, kondromatøs hamartom, mesoteliom; Gastrointestinalt: spiserør (skvamøst cellekarsinom, svelg, adenokarsinom, leiomyosarkom, lymfom), mage (karsinom, lymfom, leiomyosarkom), bukspyttkjertel (duktalt adenokarsinom, insulinom, glukagonom, gastrinom, karsinoidtumorer, vipom), tynntarm eller tynntarmer (adenokarsinom, lymfom, karsinoidtumorer, Karposis sarkom, leiomyom, hemangiom, lipom, nevrofibrom, fibrom), tykktarm eller tykktarmer (adenokarsinom, tubulært adenom, villøst adenom, hamartom, leiomyom), tykktarm, tykktarm-endetarm, kolorektalt; endetarm, Urogenitalkanal: nyre (adenokarsinom, Wilms tumor [nefroblastom], lymfom), blære og urinrør (skvamøst cellekarsinom, transisjonelt cellekarsinom, adenokarsinom, prostata (adenokarsinom, sarkom), testikkel (seminom, teratom, embryonalt karsinom, teratokarsinom, koriokarsinom, sarkom, interstitiell cellekarsinom, fibrom, fibroadenom, adenomatoidtumorer, lipom); Lever: hepatom (hepatocellulært karsinom), kolangiokarsinom, hepatoblastom, angiosarkom, hepatocellulært adenom, hemangiom, biliære passasjer; Bein: osteogent sarkom (osteosarkom), fibrosarkom, malignant fibrøst histiocytom, kondrosarkom, Ewings sarkom, malignant lymfom (retikulumcellesarkom), multippelt myelom, malignant storcelletumorkordom, osteokondrom (osteokartilaginære eksostoser), godartet kondrom, kondroblastom, kondromyksofibrom, osteoid osteom og storcelletumorer; Nervesystem: hodeskalle (osteom, hemangiom, granulom, xantom, osteitis deformans), meninges (meningiom, meningiosarkom, gliomatose), hjerne (astrocytom, medulloblastom, gliom, ependymom, germinom [pinealom], glioblastoma multiforme, oligodendrogliom, schwannom, retinoblastom, kongenitale tumorer), nevrofibrom i ryggmargen, meningiom, gliom, sarkom); Gynekologisk/hunnkjønn: livmor (endometriell karsinom), livmorhals (livmorhalskarsinom, pre-tumor cervikal dysplasi), eggstokker (eggstokkarsinom [serøst cystadenokarsinom, mucinøst cystadenokarsinom, uklassifisert karsinom], granulosa-tekalcelletumorer, Sertoli-Leydig-celletumorer, dysgerminom, malignant teratom), vulva (skvamøst cellekarsinom, intraepitelialt karsinom, adenokarsinom, fibrosarkom, melanom), vagina (klarcellet karsinom, skvamøst cellekarsinom, botryoid sarkom (embryonalt rhabdomyosarkom), eggledere (karsinom), bryst; Hud: malignant melanom, basalcellekarsinom, skvamøst cellekarsinom, Karposis sarkom, keratoakantom, føflekk dysplastisk nevi, lipom, angiom, dermatofibrom, keloider,

psoriasis, Skjoldbruskkjertel: papillært thyroideakarsinom, follikulært thyroideakarsinom; medullært thyroideakarsinom, multippel endokrin neoplasi type 2A, multippel endokrin neoplasi type 2B, familiær medullær thyroideakreft, feokromocytom, paragangliom; og Binyrer: nevroblastom: eventuelt: hvori kreften velges fra en kreft i lungen eller bukspyttkjertelen; eventuelt dertil:
hvori kreften er lungekreft; eventuelt dertil:
hvori lungekreften er ikke-småcellet lungekreft eller småcellet lungekreft; eventuelt dertil:
hvori (I) lungekreften er småcellet lungekreft og de ytterligere terapeutiske midlene er cisplatin og etoposid; eller
hvori (II) lungekreften er ikke-småcellet lungekreft og de ytterligere terapeutiske midlene er gemcitabin og cisplatin; eventuelt:
hvori (i) den ikke-småcellede lungekreften er skvamøs ikke-småcellet lungekreft; eller:
hvori (ii) kreftbehandlingen er gemcitabin og stråling.

21. Forbindelsen, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16, eller en farmasøytisk sammensetning ifølge krav 17 for anvendelse ifølge krav 18 eller krav 19,
hvori (I) kreften velges fra lungekreft, hode- og halskreft, kreft i bukspyttkjertelen, magekreft eller hjernekreft; eller:
hvori (II) kreften velges fra ikke-småcellet lungekreft, småcellet lungekreft, kreft i bukspyttkjertelen, kreft i galleveiene, hode- og halskreft, blærekreft, tykktarmskreft, glioblastom, spiserørskreft, brystkreft , hepatocellulært karsinom eller eggstokkreft; eventuelt hvori kreften er brystkreft og det ytterligere terapeutiske midlet er cisplatin; eventuelt dertil hvori kreften er tredobbelt negativ brystkreft.

22. Forbindelse, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16 i kombinasjon med et ytterligere terapeutisk middel valgt fra gemcitabin, strålebehandling, eller både gemcitabin og strålebehandling sammen, for anvendelse i behandlingen av kreft i bukspyttkjertelen.

23. Forbindelse, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16 for anvendelse i en behandling som øker følsomheten av kreftceller i bukspyttkjertelen for en kreftbehandling valgt fra kjemoterapi og stråling; eventuelt:
hvori (I) kjemoterapien er gemcitabin; eller:
hvori (II) kreftbehandlingen er gemcitabin; eller:
hvori (III) kreftbehandlingen er stråling.

24. Forbindelse, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16, eller en farmasøytisk sammensetning ifølge krav 17, i kombinasjon med gemcitabin (100 nM) og/eller stråling (6 Gy) for anvendelse i en behandling som inhiberer fosforylering av Chk1 (Ser 345) i en kreftcelle i bukspyttkjertelen.

25. Forbindelse, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16 for anvendelse i en behandling som sensibiliserer kreftceller i bukspyttkjertelen for kjemisk stråling i kombinasjon med kjemisk stråling.

26. Forbindelse, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16 for anvendelse i en behandling
omfattende (I) radiosensibilisere hypoksiske kreftceller i bukspyttkjertelen i kombinasjon med strålebehandling; eller:
omfattende (II) sensibilisere hypoksiske kreftceller i bukspyttkjertelen i kombinasjon med kjemoterapi.

27. Forbindelsen for anvendelse, eller et farmasøytisk akseptabelt salt derav, ifølge kravene 25 eller 26, hvori kreftcellen er en PSN-1-, MiaPaCa-2- eller PancM-kreftcelle.

28. Forbindelse, eller et farmasøytisk akseptabelt salt derav, ifølge kravene 1 til 16, for anvendelse i en behandling av kreft, behandlingen omfattende forstyrrelse av skadeinduserte cellesykluskontrollpunkter i kombinasjon med strålebehandling og/eller gemcitabin.

29. Forbindelsen, eller et farmasøytisk akseptabelt salt derav, ifølge kravene 1 til 16, for anvendelse i en behandling av kreft i bukspyttkjertelen, behandlingen omfattende inhibering av reparasjon av DNA-skade ved homolog rekombinasjon i en kreftcelle i bukspyttkjertelen i kombinasjon med strålebehandling og/eller gemcitabin.

30. Forbindelsen for anvendelse, eller et farmasøytisk derivat derav, ifølge kravene 26 til 29, hvori forbindelsen administreres til en kreftcelle i bukspyttkjertelen; eventuelt hvori kreftcellene i bukspyttkjertelen avledes fra en bukspyttkjertelcellelinje valgt fra PSN-1, MiaPaCa-2 eller Panc-1.

31. Forbindelse, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16 for anvendelse ved behandling av kreft, behandlingen omfattende
(I) behandling av ikke-småcellet lungekreft i kombinasjon med ett eller flere av de følgende ytterligere terapeutiske midlene: cisplatin eller karboplatin, etoposid og ioniserende stråling; eller:
(II) fremming av celledød i kreftceller; eller:
(III) hindring av cellereparasjon fra DNA-skade; eller
(IV) inhibering av ATR i en biologisk prøve omfattende trinnet å bringe en forbindelse ifølge et hvilket som helst av kravene 1 til 31 i kontakt med den biologiske prøven; eventuelt hvori den biologiske prøven er en celle; eller:
(V) sensibilisering av celler for DNA-skadelige midler.

32. Forbindelsen, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16, eller en farmasøytisk sammensetning ifølge krav 17 for anvendelse ifølge kravene 19 til 31,
hvori (I) cellen er en kreftcelle som har mangler i ATM-signaleringskaskaden; eventuelt:
hvori (i) mangelen er endret ekspresjon eller aktivitet av én eller flere av de følgende: ATM, p53, CHK2, MRE11, RAD50, NBS1, 53BP1, MDC1, H2AX, MCPH1/BRIT1, CTIP eller SMC1; eller:
hvori (ii) mangelen er endret ekspresjon eller aktivitet av én eller flere av de følgende: ATM, p53, CHK2, MRE11, RAD50, NBS1, 53BP1, MDC1 eller H2AX; eller:

hvori (II) cellen er en kreftcelle som uttrykker DNA-skadelige onkogener; eventuelt hvori kreftcellen har endret ekspresjon eller aktivitet av én eller flere av de følgende: K-Ras, N-Ras, H-Ras, Raf, Myc, Mos, E2F, Cdc25A, CDC4, CDK2, Syklin E, Syklin A og Rb; eller: hvori (III) kreften, kreftcellen eller cellen har en mangel i et baseeksisjonsreparasjonsprotein; eventuelt hvori baseeksisjonsreparasjonsproteinet er UNG, SMUG1, MBD4, TDG, OGG1, MYH, NTH1, MPG, NEIL1, NEIL2, NEIL3 (DNA-glykosylaser); APE1, APEX2 (AP-endonukleaser); LIG1, LIG3 (DNA-ligaser I og III); XRCC1 (LIG3-tilbehør); PNK, PNKP (polynukleotidkinase og fosfatase); PARP1, PARP2(Poly(ADP-ribose)-polymeraser); PolB, PolG (polymeraser); FEN1 (endonuklease) eller aprataksin; eventuelt dertil hvori baseeksisjonsreparasjonsproteinet er PARP1, PARP2 eller PolB; eventuelt dertil hvori baseeksisjonsreparasjonsproteinet er PARP1 eller PARP2.

33. Forbindelsen, eller et farmasøytisk akseptabelt salt derav, ifølge et hvilket som helst av kravene 1 til 16, eller en farmasøytisk sammensetning ifølge krav 17 for anvendelse ifølge kravene 19 til 32, videre omfattende administrering til pasienten av et ytterligere terapeutisk middel hvori midlet inhiberer eller modulerer et baseeksisjonsreparasjonsprotein; eventuelt hvori baseeksisjonsreparasjonsproteinet velges fra UNG, SMUG1, MBD4, TDG, OGG1, MYH, NTH1, MPG, NEIL1, NEIL2, NEIL3 (DNA-glykosylaser); APE1, APEX2 (AP-endonukleaser); LIG1, LIG3 (DNA-ligaser I og III); XRCC1 (LIG3-tilbehør); PNK, PNKP (polynukleotidkinase og fosfatase); PARP1, PARP2 (poly(ADP-ribose)-polymeraser); PolB, PolG (polymeraser); FEN1 (endonuklease) eller aprataksin; eventuelt dertil hvori baseeksisjonsreparasjonsproteinet velges fra PARP1, PARP2 eller PolB; eventuelt dertil hvori baseeksisjonsreparasjonsproteinet velges fra PARP1 eller PARP2; eventuelt dertil hvori midlet velges fra Olaparib (også kjent som AZD2281 eller KU-0059436), Iniparib (også kjent som BSI-201 eller SAR240550), Veliparib (også kjent som ABT-888), Rucaparib (også kjent som PF-01367338), CEP-9722, INO-1001, MK-4827, E7016, BMN673 eller AZD2461.